Virginia Commonwealth University
VCU Scholars Compass

Theses and Dissertations | Graduate School

2020

Development of a Screening Assay for Type III Secretion System Inhibitors and High Throughput Screening Campaign of Inhibitors of PRP of Staphylococcus aureus

Heather A. Pendergrass
Virginia Commonwealth University

Follow this and additional works at: https://scholarscompass.vcu.edu/etd

 Part of the Medicinal and Pharmaceutical Chemistry Commons, and the Pathogenic Microbiology Commons

© The Author

Downloaded from
https://scholarscompass.vcu.edu/etd/6506

This Dissertation is brought to you for free and open access by the Graduate School at VCU Scholars Compass. It has been accepted for inclusion in Theses and Dissertations by an authorized administrator of VCU Scholars Compass. For more information, please contact libcompass@vcu.edu.

©Heather Pendergrass, 2020

All rights reserved

DEVELOPMENT OF A SCREENING ASSAY FOR TYPE III SECRETION SYSTEM INHIBITORS AND HIGH THROUGHPUT SCREENING CAMPAIGN OF INHIBITORS OF PRP OF *STAPHYLOCOCCUS AUREUS*

A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Virginia Commonwealth University

by

HEATHER A. P. DAMON

Bachelor of Science (Biochemistry), Virginia Polytechnic Institute and State University, Blacksburg, VA, 2016

Bachelor of Arts (Chemistry), Virginia Polytechnic Institute and State University,

Blacksburg, VA, 2016

Director: DR. AARON E. MAY

Professor of Medicinal Chemistry

Virginia Commonwealth University

Richmond, Virginia

16 NOVEMBER 2020

ACKNOWLEDGMENTS

I would like to acknowledge and thank my committee for the years of guidance and the opportunities this degree will afford me. Drs. Malgorzata Dukat, Shijun Zhang, Gail Christie, and Adam Hawkridge, thank you for your support.

To my husband, Scott Damon: As cliché as it sounds, I could not have done this without you. You have watched this process from start to finish and you have been an indescribably valuable partner to me throughout. Thank you for always encouraging me to keep working when solving a problem seemed impossible and thank you for supporting me through every difficult moment. Your role as an open ear and honest encouragement on the good days and the bad days helped me to remember why I chose to go into research. I could say so much more, but I know you understand already how grateful I am to have you as my partner.

To my parents: Thank you! You raised me with the confidence to take risks by teaching me I can always come home. I was only brave enough to push myself past an undergraduate education into graduate school because I knew that if I failed, I would have you. Mom, you have always been my inspiration to push myself to do things that scare me. You are incredibly strong and the best role model I could have asked for. Growing up and listening to you talk about medications sparked my interest in the field and drove me to learn as much as I can. Dad, I can't tell you how proud I am of you for going back to school and constantly working to make your life better. You're a prime example of how a lot of work and a little grit will pay off in the long run.

"Seesters!" You were my first teachers and I would not be who I am today without you. Sandy, I have always respected the way that you listen to your gut. Regardless of what problems you're facing, you somehow always seem to know what the right solution is and go for it. Natasha, I love the way you take advantage of every moment and never seem tired of trying new things. You will probably live a richer life than anyone else I know, and I hope I can become as adventurous as you one day. Amanda, your commitment to family is amazing. Your boys are so lucky to have you and I wish we lived closer. Gloria, I am amazed with your love of God and your marriage. You have an unwavering faith that I admire, and I hope that I can find myself one day.

Dr. Aaron May, it has been an adventure working as your first graduate student. Thank you for helping me to appreciate to persistence, dedication, and creativity that is required in assay development. I look forward to taking the lessons I have learned in these last few years and applying them.

To the future Dr. Julia Hotinger, thank you for your friendship and company. Working in the lab can be a lonely business, and it was made much easier knowing you were in the other hood, struggling with me. I wish you the best of luck in your final years of struggle and I am always willing to help how I can.

To Adam Johnson, my first lab mate: Thank you for your mentorship. I learned so much in my first year as a graduate student that I continue to carry with me. Thank you for helping me to gain the confidence to work independently in the lab and teaching me how to find the answers I needed.

I want to thank all of the friends that I have made throughout graduate school. Specifically. I would like to thank Dr. Barkha Yadav, Dr. Shravan Morla, Dr. Daniel Afosah, and future Drs. Rosalie Hoyle; Connor O'Hara, M.S.; John Chittum; and Tamim "The Meme" Chiba. You became my work family and this last semester has been difficult. I wish we could have those Friday dinners back and that I could have had another dozen lunches with you in the breakroom.

Finally, I would like to acknowledge the countless people worldwide who have been affected by SARS-CoV-2. I have spent my last eight-and-a-half years researching in infectious disease without fulling grasping the impact a single pathogen can have. All of us in the field of medicinal research and development are fighting to develop new therapies to abate these "bugs" and we are doing it for you.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF SCHEMES

LIST OF ABBREVIATIONS

aa	amino acid
Ab	antibody
ABZ	2-aminobenzoic acid
A/E	attaching/effacing
aEPEC	atypical EPEC
AHL	*N*-acylhomoserine lactones
ATP	adenosine triphosphate
BFP	bundle-forming pili
CBD	chaperone binding domain
Cdk	cyclin-dependent kinase
CFU	colony forming units
Cif	cell cycle inhibiting factor
COPI/II	coat protein complexes I/II
CPG2	carboxypeptidase G2
CR3	complement receptor 3
DAEC	diffusely adherent *E. coli*
DD	death domain
DEPEC	dog EPEC
DHFR	dihydrofolate reductase
DMSO	dimethyl sulfoxide
DNA	deoxyribonucleic acid
DNP	dinitrophenyl

DTT	dithiothreitol
EAEC	enteroaggregative *E. coli*
EAF	EPEC adherence factor
EDTA	ethylenediaminetetraacetic acid
Efa	EHEC factor for adherence
EF-Tu	elongation factor-Tu
EGCG	(-)-epigallocatechin-3-gallate
EHEC	enterohemorrhagic *E. coli*
EibG	*E. coli* immunoglobulin-binding protein
EIEC	enteroinvasive *E. coli*
ELISA	enzyme-linked immunosorbent assay
EPEC	enteropathogenic *E. coli*
ER	endoplasmic reticulum
Esp	*E. coli* secreted protein
ETEC	enterotoxigenic *E. coli*
FADD	Fas receptor-associated death domain protein
FAS	fluorescent actin stain
FcγR	Fc gamma receptor
FITC	fluorescein isothiocyanate
FRET	Förster resonance energy transfer
GAP	GTPase activating proteins
GAPDH	glyceraldehyde-3-phosphate dehydrogenase
GCG	gallocatechin gallate

GDP	guanosine diphosphate
GEF	guanine-nucleotide exchange factor
GFP	green fluorescent protein
Glu-CyFur	glutamate-modified 2-dicyanomethylene-3-cyano-2,5-dihydrofuran
GTP	guanosine triphosphate
HTS	high throughput screening
HUS	hemolytic uremic syndrome
IgM	immunoglobulin M
IκB	inhibitory κB
IKK	inhibitory κB kinase
IL	interleukin
IM	inner membrane
JAM	junctional adhesion molecule
kb	kilobase
kDa	kilo-Dalton
LA	localized adherence
LEE	locus of enterocyte effacement
MA	mersalyl acid
Map	mitochondria-associated protein
MIC	minimal inhibitory concentration
MMP	mitochondrial membrane potential
MRSA	methicillin-resistant *S. aureus*
Nle	non-LEE-encoded

NLRP	nod-like receptor protein
N-WASP	neurological Wiskott-Aldrich syndrome protein
OM	outer membrane
PAK	p21-activated kinase
PCR	polymerase chain reaction
per	plasmid-encoded regulator
Pet	plasmid-encoded toxin
PEPEC	porcine EPEC
Pic	protein involved in intestinal colonization
PTC	peptidyl transferase center
PTMD	putative transmembrane domain
RBC	red blood cell
REPEC	rabbit EPEC
RPS3	ribosomal protein S3
Saa	STEC autoagglutinating adhesin
SAR	structure-activity relationship
Sat	secreted autotransporter toxin
SDS-PAGE	sodium dodecyl sulfate polyacrylamide gel electrophoresis
SepA	Shigella extracellular protein
ShET1/2	Shigella enterotoxins 1/2
SigA	Shigella IgA-like protease
SPATE	serine protease autotransporter of Enterobacteriaceae
ST	heat-stable toxin

STEC	Shiga toxin-producing *E. coli*
STX	Shiga toxin
T3SS	type III secretion system
TAK1	transforming growth factor-β-activated kinase 1
TEER	transepithelial electrical resistance
Tia	toxigenic invasion loci A
Tim17b	translocase of the inner mitochondrial membrane 17b
Tir	translocated intimin receptor
TJ	tight junctions
TLC	thin layer chromatography
TNF	tumor necrosis factor
TNFR	tumor necrosis factor receptor
TRAF	TNF receptor-associated factors
TRADD	TNFR1-associated death domain protein
TRAPP	transport protein particle
VCA	verprolin-homology, cofilin homology, highly acidic
VTEC	Verocytotoxin-producing *E. coli*
WAS	Wiskott-Aldrich syndrome
WASP	WAS protein
WRC	Wave regulatory complex
wt	wild-type
ZO	zonulae occludin

ABSTRACT

DEVELOPMENT OF A SCREENING ASSAY FOR TYPE III SECRETION SYSTEM INHIBITORS AND HIGH THROUGHPUT SCREENING CAMPAIGN OF INHIBITORS OF PRP OF *STAPHYLOCOCCUS AUREUS*

By Heather Pendergrass

A dissertation submitted in partial fulfillment of the requirements for the degree of

Doctor of Philosophy at Virginia Commonwealth University

Virginia Commonwealth University, 2020

Director: Dr. Aaron May

Antibiotics inhibit the growth or survival of bacteria by targeting their essential functions.[1] Due to weaknesses in traditional antibiotics and the increasing prevalence of antibiotic resistance genes, virulence factors are being targeted for therapeutic treatment of bacterial infection.[2] We have developed an assay to quantify and observe type III secretion system (T3SS) activity. The type III secretion system (T3SS) is a virulence factor present in some Gram-negative pathogens including enteropathogenic and enterohemorrhagic *E. coli* (EPEC and EHEC, respectively),[3] and

others.[4–9] The T3SS between EPEC and EHEC are highly conserved and share over 90% sequence identity with the mouse pathogen *Citrobacter rodentium*.[3,10,11] Because of the high similarity between the pathophysiology of these organisms, *C. rodentium* is often used as the mouse model of EPEC and EHEC infection.[12–14] We have developed a construct of *C. rodentium* to produce carboxypeptidase G2 (CPG2), a eukaryotic enzyme that selectively cleaves glutamate residues. We have tagged CPG2 on the N-terminus with an amino acid sequence to target the enzyme for type III secretion.[15] The CPG2 reporter assay was used to screen natural products for their ability to inhibit the T3SS.[16–26]

We also completed a high throughput screening campaign for the identification of inhibitors of phage-related ribosomal protease Prp. This protease is essential for ribosomal assembly in bacteria and previously reported knockdown studies have indicated that bacteria cannot survive without Prp. We have screened over 5000 compounds for their inhibitory activity.

CHAPTER 1

ENTEROPATHOGENIC AND ENTEROHEMORRHAGIC *ESHERICHIA COLI*

1.1 Clinical relevance of *E. coli*

E. coli is a common part of the commensal bacteria residing in the digestive tract of humans and other mammals and birds.[27–29] Typically, *E. coli* is harmless, but some strains cause serious foodborne illnesses that result in an estimated 265,000 infections in the United States every year.[30,31] Many diarrheal infections of *E. coli* go undiagnosed, as many patients do not seek medical treatment.[32] Of the diagnosed gastrointestinal infections, 36% are caused by *E. coli* O157, which typically results in more severe disease outcomes.[30] These include bloody diarrhea, hemolytic uremic syndrome (HUS) and kidney failure.[33,34] The leading cause of HUS is gastrointestinal infection of Shiga toxin-producing *E. coli* (STEC).[35–37] STEC is a designation that can refer to any variant of *E. coli* capable of producing Shiga toxin.[38–40]

Every year, waterborne diarrheal disease kills over 800,000 people, over 25% of whom are children under the age of 5.[41] In addition, pathogenic *E. coli* outbreaks are common in developed nations.[30] In 2011, an outbreak of STEC in Europe resulted in >4000 illnesses, and ~900 cases of HUS.[39,42,43] The cause of the outbreak was contaminated bean sprouts that originated from a vendor in Egypt.[44] A much smaller outbreak occurred in July 2018 in three elementary schools in Gyeongsangbuk-Do Province, South Korea.[45] The illnesses were attributed to water supplies contaminated with non-Shiga toxin-producing *E. coli* that was used in food preparation for the school cafeterias. In another school-related incident in 1996, children in 47 elementary schools across two school districts were hospitalized after consuming uncooked white radish sprouts used in the preparation of their lunches.[46] This outbreak resulted in almost 400 hospitalizations within a ten-day period. The radishes were contaminated with STEC. It was also reported that this

outbreak was one of sixteen total outbreaks (with >10 infected patients) in Japan between May and December of 1996.[46] In total, ~7,900 cases were reported within that time period, 7,470 of which were children infected by school lunches.

1.2 *E. coli* pathotypes

There are six pathotypes, or disease-causing variations of *E. coli*, including enterohemorrhagic *E. coli* (EHEC), also known as Verocytotoxin-producing *E. coli* (VTEC), enteropathogenic *E. coli* (EPEC), enterotoxigenic *E. coli* (ETEC), enteroaggregative *E. coli* (EAEC), enteroinvasive *E. coli* (EIEC) and diffusely adherent *E. coli* (DAEC).[9,47,48] *E. coli* are often referred to by their pathotype followed by a serological classification (for example, EHEC O157:H7). This strain of *E. coli* belongs to the enterohemorrhagic pathotype. The "O" designation refers to the lipopolysaccharide antigen present for this strain,[49] and the "H" designation refers to the flagellar antigen present.[50] If the strain produces Shiga toxins, that may be included in the name as well (for example, EAEC strain STEC O104:H4).[43]

1.3 Epidemiology, symptoms, treatment, and pathogenesis of EPEC and EHEC

1.3.1 Enteropathogenic *E. coli*

The first description of EPEC was published in 1955 after an outbreak of infantile diarrhea in the 1940s and 1950s.[51] EPEC is considered an attaching/effacing (A/E) pathogen due to its characteristic intimate adherence strategy during infection, which results in actin rearrangement and the formation of a pedestal and clearing of intestinal microvilli on epithelial cells.[52,53] EPEC does not produce Shiga toxin, unlike A/E EHEC. Many strains carry an EPEC adherence factor (EAF) plasmid that encodes virulence factors including bundle-forming pili (BFP), but there are

also many strains that do not.[54] Strains that harbor the EAF plasmid are classified as "typical EPEC" and those that do not are classified as "atypical EPEC" (aEPEC). Some aEPEC strains cannot be classified based on traditional O/H-serotyping because they do not carry the plasmid that encodes O-lipopolysaccharides or H-flagellar antigens.[55] Genetic analysis of typical and atypical EPEC indicates that these two classes are vastly different, and aEPEC more closely resembles some EHEC serotypes.[56] Proteomic and genomic analysis indicates that EHEC O157:H7 evolved from an ancestor of aEPEC O55:H7.[57]

Epidemiology. A 2017 report indicated that EPEC is associated with moderate to severe diarrhea in children under 2 years old in some developing nations, and is associated with increased risk of death in patients younger than 11 months.[58] EPEC is typically transmitted through the fecal-oral route from contaminated food and water supply and from infected people. The infectious dose of EPEC is estimated at 2×10^{10} colony forming units (CFU).[59]

Symptoms. Symptoms of an EPEC infection include diarrhea, fever, and vomiting resulting in dehydration.[53] Onset of symptoms typically occurs within a few hours of exposure and lasts for a short time period, but persistence up to two weeks has been observed.[58] Diagnosis can be made based on the presence or absence of virulence genes such as the EAF plasmid or the *eae* gene, which encodes a protein intimin, part of the T3SS.[59,60] In addition, the fluorescent actin staining (FAS) test can be performed.[61] This test involves visualization of fluorescently labeled actin rearrangement because of the A/E histopathology.

Treatment. Treatment of EPEC infection typically involves oral rehydration therapy and antibiotics may be administered if the infection persists; however, clinical isolates have indicated a high degree of antibiotic resistance. Strains have demonstrated resistance against penicillins, cephalosporins, and aminoglycosides. While no vaccine against EPEC infections is available

commercially, there is evidence that some mothers' breast milk contains IgA antibodies against typical antigens, including T3SS-related proteins EspA, EspB, and intimin.[62] The transfer of these antibodies may be responsible for conferring immunity to breastfed infants, and provides evidence that adaptive immunity may provide protection to older patients. This may explain why only extremely young children suffer from severe EPEC infections.[62]

Pathogenesis. A major virulence factor utilized by EPEC is the non-flagellar type III secretion system (T3SS), which is described in detail in section 1.4. The T3SS is also utilized by a diverse assortment of bacteria, including EPEC and EHEC,[63,64] *Citrobacter rodentium*,[65] *Salmonella enterica* serovar Typhimurium,[66,67] *Yersinia pestis*,[68–70] *Pseudomonas* spp.,[7] and *Chlamydia* spp.[71] For EPEC, the T3SS is necessary for the attachment of bacteria to host cell surfaces and propagation of infection.[9] This secretion system is evolutionarily related to flagella, and the bases of flagellar and non-flagellar T3SSs are structurally similar.[66] Whereas flagella secrete proteins necessary for motility, the non-flagellar T3SS has evolved specifically for pathogenic interaction with eukaryotic cells and transports bacterial proteins (effectors) directly into the cytoplasm of intestinal epithelial cells. After secretion, these effectors perform a multitude of tasks within the host cells, including interference with cytoskeletal assembly, allowing for intimate attachment of the pathogen to the host cell or allowing endocytosis of the pathogen, and cell death.[72]

A characteristic symptom of a T3SS-mediated infection is the formation of attaching/effacing (A/E) lesions on the epithelial surface.[73] Other A/E pathogens also rely on the T3SS as a virulence factor, including *C. rodentium* (a well-adopted mouse model for EPEC and EHEC infection),[10] rabbit EPEC (REPEC),[52] porcine EPEC (PEPEC),[74] dog EPEC (DEPEC)[75] and *Escherichia albertii*.[76] The T3SS of A/E pathogens is encoded by a pathogenicity island called the

locus of enterocyte effacement (LEE).[60,77] The LEE is a 35 kb region of chromosomal DNA present in EPEC and EHEC, as well as *C. rodentium*, a murine pathogen with similar symptoms as human *E. coli* infection.[10,60] The sequence homology between the three organisms is >90%, suggesting that *C. rodentium* acquired the T3SS in a horizontal transfer.[10] It is this high homology that allows for *C. rodentium* to act as a mouse model for *E. coli* infection.

The formation of the characteristic A/E lesions of EPEC and EHEC infection are a result of the interactions between intimin and the translocated intimin receptor (Tir).[78] The interaction between intimin and Tir is the most important in EHEC and EPEC intimate attachment to epithelia, and mutational studies confirm that changes to the receptor recognition domain on the C-terminus abolishes attachment capabilities.[59] The relationship between intimin and Tir is unique, in that they are both encoded within the *E. coli* genome and are co-expressed.[78] The genes for these proteins are located within the LEE.[60,79] The T3SS is responsible for translocating Tir to the surface of the target cell, allowing for attachment, while intimin is secreted through the Sec pathway and presented on the surface of the bacterial cell.[80]

Intimin is a 95-kDa protein consisting of three regions.[81] The N-terminus encodes a signal peptide that allows for passage through the Sec pathway. This region is eventually anchored into the peptidoglycan layer. Residues 189 to 550 constitute the β-domain, which floats on the outer membrane, exposing the C-terminus to the surface.[82] The C-terminal region is composed of four sub-domains, D1 through D4.[83] Each of these immunoglobulin-like domains forms a rod responsible for interactions with Tir.[84] Once Tir is translocated into the epithelial cell, it extends both terminal regions toward the cytosol, and forms a β-hairpin with the middle region on the extracellular surface to interact with intimin.

The presence of the intimin-encoding gene *eae* is often used as a characterization and classification tool for pathogenic *E. coli* and is associated with the A/E lesion phenotype. This gene indicates the presence of the T3SS and is therefore associated with more severe clinical outcomes. Studies have indicated that mice dosed with intimin developed a protective immune response to further challenge by *C. rodentium*.[77] More recently, a chimeric vaccine consisting of T3SS protein EspA and intimin decreased intestinal colonization of EHEC O157:H7 in mice.[85] Both studies indicate that a vaccine containing intimin may efficiently protect susceptible patients from infection.

The ~95 kb EAF plasmid, which is characteristic of typical EPEC, encodes 14 genes responsible for BFP formation.[86] BFP is an adhesin that produces a localized adherence (LA) colonization pattern on epithelial cells. LA describes a pattern of growth of discrete clusters of bacteria on cultured mammalian cells. Each individual pilus of BFP is composed of many filaments aggregated together on the outer membrane of the bacterial cell. One pilus is 50 to 500 nm wide and 15 to 20 μM long. Their expression is induced by the presence of eukaryotic cells. When expressed, BFPs form a complex matrix of pili, intertwined with neighboring EPEC cells' BFPs. This results in an interlocking system of *E. coli* and aids in the attachment of bacteria to epithelial cells.

Three of the genes encoded by *pEAF* include the plasmid encoded regulator (*perABC*, also called *bfpTVW*) genes. These proteins are transcriptional regulators of multiple virulence factors, including BFP.[87] The *bfp* operon consists of 14 genes (*bfpABCUDEFPHIJKLM*) that are all required for BFP formation.[88] Before assembly of the major structural pilus, composed of protein BfpA, the monomers of BfpA must be processed by prepilin signal peptidase BfpP. Export of BfpA is dependent upon BfpB, a lipoprotein that also aids in assembly of the pilus. The remaining

functions of the *pEAF*-encoded genes are based on sequence homology with other known type IV pili of other bacterial species. *bfpH* also encodes a lipoprotein, as predicted due to a conserved N-terminal cysteine lipid attachment site. BfpD shares homology with proteins responsible with type IV secretion system biogenesis and contains a nucleotide-binding motif. Sequence homology studies suggest that BfpD and E may be involved with DNA uptake and protein secretion. BfpF, like BfpD, contains a nucleotide-binding domain. BfpF is homologous with *Pseudomonas aeruginosa* protein PilT, which is responsible for pilus-mediated twitching motility, and may provide energy via ATP hydrolysis to power this movement. *bpfI, J,* and *K* encode minor type IV pili structural components that are incorporated within the bundle structure and provide structural integrity and aid in epithelial cell adhesion.[89] Protein BpfL shares no homology with other proteins, but sequence analysis predicts that the protein may form a β-sheet.[88]

EPEC strain UMD880 (*bfpA*$^{+}$ *eae*$^{-}$) rapidly attached to the surface of Caco-2 cells, even though no intimin was expressed.[90] This attachment to the brush border microvilli of the intestinal epithelia did not induce A/E lesion formation, but the extent of adhesion was similar to wild type. When EPEC strain EAV84 (*ΔbfpU*) was cultured with HeLa cells, colony formation was 85% as efficient as wild type.[91] The introduction of a lipid disrupting agent MβCD, however, decreased the % adherence from 85% to 1%, indicating that lipid rafts within epithelial membranes are necessary for attachment in the absence of BFPs.

1.3.2 Enterohemorrhagic *E. coli*

STEC O157:H7 was originally documented as a human pathogen in the 1980s after serotype analysis of samples obtained from patients suffering from an outbreak of hemorrhagic colitis revealed *E. coli* O157:H7 as the causative agent.[92] *E. coli* O157:H7 is the representative

organism for the EHEC pathotype.[93] O157:H7 produces Shiga toxin; therefore it is also considered an STEC. The presence of other virulence mechanisms, however, delegates that O157:H7 have a pathotype separate from other STECs.[38] For that reason, all EHEC strains are also STEC strains, but not all STEC strains can be classified as EHEC.[93]

Epidemiology. This serotype has been implicated as a major cause of bloody diarrhea and HUS.[30] While many patients recover spontaneously from STEC-HUS,[36] some develop end-stage renal damage.[94,95] This pathotype is non-invasive, so the bacterial cells do not cross through the epithelial cell lining; the damage done outside of the gastrointestinal tract can be attributed to release of Shiga toxin.[38] The cohorts most affected by O157:H7 outbreaks are often children under the age of 5 and adults aged 65 and above, with lethality for these groups ranging from 2-7% and 15-23%, respectively.[92] Children who recover from O157:H7 infections have a significant risk of renal failure or residual organ damage that results in chronic and end-stage renal disease, renal hypertension, diabetes mellitus, and some neurological disorders.[92] Transmission of O157:H7 is believed to occur through three major routes: contaminated food and contaminated drinking and swimming water, person-to-person contact, and animal contact. The infectious dose has been estimated as fewer than 50 organisms; reports from a 1996 outbreak of O157:H7 in fermented sausages reported a bacterial load of fewer than one cell per 10 g of contaminated food.[92,96,97]

Diagnostic procedures for O157:H7 include culture analysis of stool samples from infected patients via detection of Shiga toxins and the O157 antigen using enzyme-linked immunosorbent assay (ELISA) kits, and polymerase chain reaction (PCR) analysis of relevant genes.[92,95] Unfortunately, the presence of O157:H7 cells within the colon drops significantly after the first week of infection, while severe HUS symptoms may take 5-13 days to develop, lowering the odds of correct diagnosis to ~70% using stool sample analysis alone.[95] Serological tests for the

identification of immunoglobulin M (IgM) response to the O157 lipopolysaccharide antigen have been developed with better prognostic ability.[98,99] Up to 94% of patients with O157:H7 are correctly diagnosed using serology tests.[95] This higher success rate may be attributable to the long serum life of patients' IgM responses (5 days to 2 months post infection).[95,99] While the serological presence of these antibodies is not sustained long enough to provide protection against future infection,[99] the circulating concentration is sufficient as a diagnostic tool.

Pathogenesis. There are two major contributors to the pathogenesis of EHEC: Shiga toxins and the LEE-encoded T3SS. These two virulence factors contribute to the hallmark symptoms of EHEC infection, including the development of HUS and A/E lesions, respectively.

The Shiga toxin family is composed of Shiga toxin 1 and 2 (STX1 and STX2, respectively).[33,35,100] Shiga toxin consists of one A subunit, which has RNA-glycohydrolase activity, and five B subunits that participate in toxin binding to glycolipid receptor Gb3 on eukaryotic epithelial cell membranes.[100] After docking to the receptor, the toxin may be endocytosed and trafficked to the Golgi apparatus, then to the endoplasmic reticulum, and is ultimately released to the cytoplasm. Here, subunit A acts upon the ribosome as a glycohydrolase and inhibits protein production, killing the epithelial cell. Once the epithelial barrier is damaged, the toxin may pass into the blood stream and bind to platelets expressing Gb3 receptors. This results in the hallmark low-platelet count in STEC patients. The toxin may then be transported to the kidneys, which express high levels of Gb3 receptors, and cause acute renal damage and HUS.[101]

Shiga toxin is encoded as part of a bacteriophage that has been incorporated into the *E. coli* O157:H7 genome.[101,102] Transcription of the bacteriophage is typically repressed due to binding of the repressor cI to one of two operons within the phage.[103] When the SOS response is triggered by damage to DNA, the regulator protein RecA is activated. Activated RecA releases cI from the

phage operon, derepressing transcription. Phage is then produced, as is Shiga toxin, and bacteria are lysed, releasing the toxin.[103] Because of this, strong consideration and care must be taken in choosing treatments for EHEC O157:H7.[101,104–106] Treatment of O157:H7 by certain antibiotics upregulated production of Shiga toxin via activation of the SOS pathway.[102,106–108] The subsequent release of Shiga toxin following bacterial cell lysis causes immense damage.[37,109]

It has been reported that treatment of O157:H7 infection with antibiotics that damage DNA, impair DNA replication, or arrest cell growth can increase a patients' likelihood to develop HUS and other pathologies due to the increase in circulating Shiga toxin.[107,110] For example, fluoroquinolones act by blocking DNA gyrase[111] and trimethoprim interferes with purine and pyrimidine synthesis through inhibition of dihydrofolate reductase.[112] Both induce the SOS response.[107] β-lactam antibiotics induce the SOS response indirectly. The cell wall damage induced by β-lactam treatment stimulates a response from the two-component proteins DpiBA, which impair DNA replication.[113,114] In general, antibiotic treatment of EHEC O157:H7 patients is not recommended.[101] Patients are typically treated for symptom alleviation and renal protection with aggressive intra-venal rehydration. Dialysis has proven helpful in renal recovery from severe cases. Monitoring for neurological symptoms is necessary, and approximately 10% of patients experience stroke, seizures, or coma as a result of toxin exposure.[101] Many toxin-conjugating therapeutics have been designed to neutralize Shiga toxin in vivo, but there are currently no therapeutics targeting Shiga toxin on the market.[115]

1.4 The bacterial type III secretion system

1.4.1 Structure of the T3SS

The T3SS is composed of a base and a hollow, needle-like structure (Figure 1). The T3SS is often referred to as the injectosome, as its function in pathogenesis is injection of effectors into host cells. The anatomy of the T3SS varies slightly across bacterial species, but a common nomenclature exists based on the placement and function of proteins within the injectisome. The proteins for the *E. coli* T3SS are named Esc- proteins, for *E. coli* secretion.

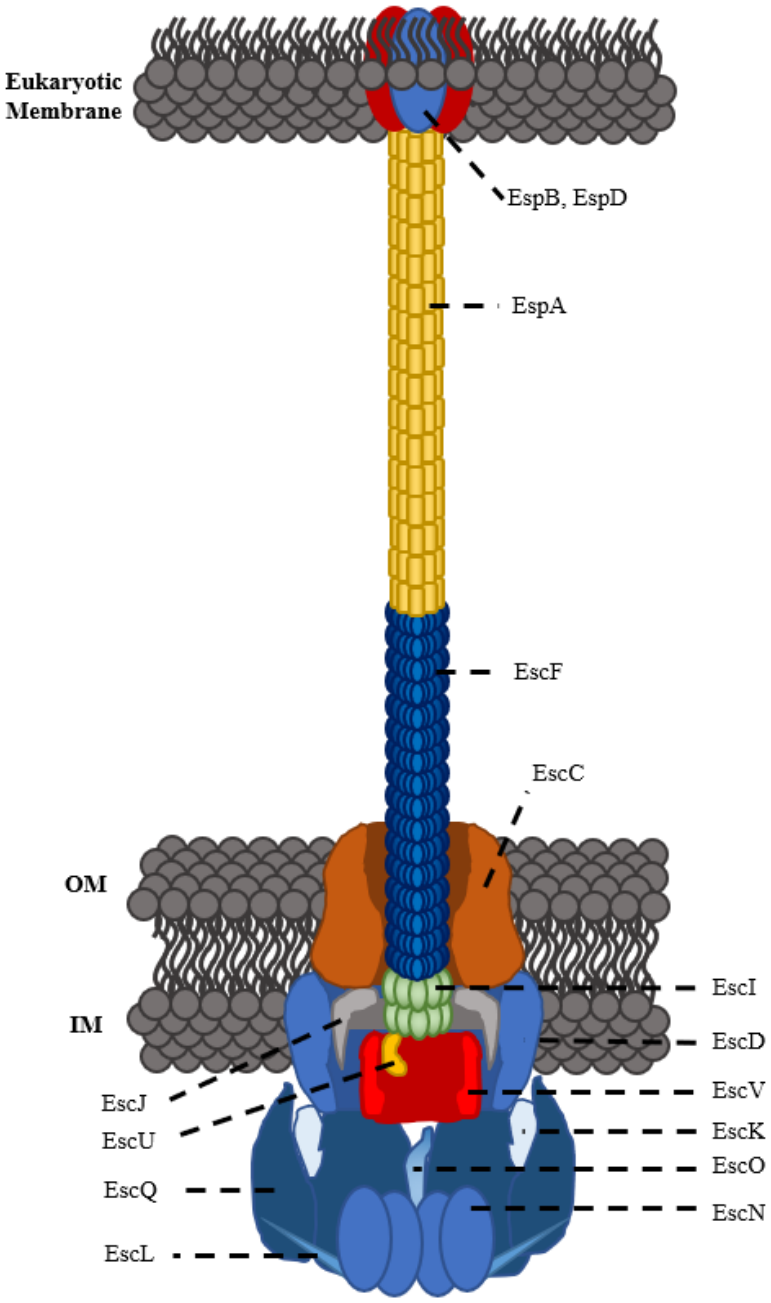


Figure 1. Structure of the T3SS. Outer membrane (OM). Inner membrane (IM). Not drawn to scale.

The T3SS base consists of the ATPase and sorting platform, the cytoplasmic ring, the export apparatus, and the basal body. The sorting platform is composed of the ATPase (EscN), the central stalk protein (EscO), the structural stator protein (EscL), and a final structural protein (EscK). The ATPase (EscN) forms a homo-hexameric ring, which has conserved properties from other known rotary ATPases.[116] The EscO central stalk protein stabilizes the oligomerization of the ATPase and helps prevent ATP-mediated dissociation. EscL mediates interactions between the EscN ATPase and the cytoplasmic ring.[117,118] Pull-down studies indicate that EscL binds to a filamentous component of the translocon, EspA; data also suggest that EscL helps to stabilize EspA in the bacterial cytosol.[119] The final component of the sorting platform, EscK, binds within the inner diameter of the cytoplasmic ring.[118] While the function of EscK is thought to be only structural, functional analysis of an EscK knockout indicates that the presence of EscK is critical for secretion of effectors.[118] The cytoplasmic ring is composed of EscQ, which is held in place by interactions with EscN and EscL, though the arrangement of these proteins is not well understood.

The export apparatus of the T3SS is located within the sorting platform and the inner membrane ring. The export apparatus is composed of a gate protein (EscV), an autoprotease (EscU), and inner membrane components (EscR, S, and T).[120–123] Gate protein EscV is homologous with flagellar protein FlhA, which facilitates transport of sodium ions and protons.[122] EscV is proposed to function as a proton/protein antiporter.[116]

Self-cleavage of the autoprotease EscU is necessary for EPEC-mediated infection of HeLa cells.[124] In addition, an absence of EscU cleavage resulted in decreased accumulation of chaperone CesT on the inner membrane. This suggests that the autoprotease activity of EscU contributes to successful docking of effector/chaperone complexes necessary for type III secretion.[124] The related flagellar autoprotease (FlhB) contributes to substrate switching, an important process that

determines the hierarchal order of protein secretion.[123] It is believed that EscU participates in a similar fashion in substrate switching for non-flagellar type III secretion.[125]

The inner membrane components of the export apparatus are EscR, EscS, and EscT.[121] EscR is the central component of the export apparatus. Evidence suggests that EscR localizes within the bacterial inner membrane, oligomerizes, then initiates the assembly of the rest of the T3SS through interactions with other structural components. EscS is the smallest protein of the T3SS base, with only 81 amino acids and 2 putative transmembrane domains (PTMDs).[120] When either of the PTMDs are replaced with random hydrophobic residues, the T3SS cannot function, suggesting that EscS plays a crucial role in T3SS activity. Studies suggest that the assembly of the base of the T3SS is not dependent on EscS, but that EscS may play a role in adjustments of protein orientation within the base. These adjustments are necessary for the proper arrangement of static and dynamic proteins within the base, which allows for efficient type III secretion. The role of EscT is not well understood, but it has been identified as a T3SS protein based on sequence homology with *Yersinia* T3SS protein YscT.[11]

The basal body of the T3SS consists of inner (IM, EscD, J and I) and outer membrane (OM, EscC) rings, a lytic glycosylase (EtgA), and the needle (EscF). IM protein EscD oligomerizes to form a ring around the export apparatus and spans the inner membrane.[126] The oligomerization domain of EscD is found on the N-terminus. The C-terminal domain binds to OM protein EscC, promoting formation of the OM ring.[126] EscJ belongs to a family of lipoproteins that are known to polymerize to form a 24-mer multi-ring structure in the periplasm.[127] The IM ring components EscD and J are necessary for the assembly of the OM ring, as null mutations in those components results in decreased oligomerization of EscC. Oligomers of protein EscI form an inner rod structure that is essential to type III secretion.[125] EscI interacts with OM secretin EscC and autoprotease

EscU in solution. These interactions, as well as characterization of similar proteins in other T3SSs suggest that EscI is located at the center of the T3SS apparatus and that EscI may be a signaling molecule in the substrate switching process.[128]

The OM ring is composed of EscC, a member of the secretin family of proteins.[129] Secretins transport large proteins through the outer membrane, typically by forming a pore.[130] Members of the secretin family are involved in protein transport through multiple secretion mechanisms not limited to the T3SS.[131] Structural analysis of the *Yersinia enterocolitica* secretin YscC indicated that the OM ring formed by oligomerization consists of 13 subunits that form two stacked rings and a conical domain. While the structure of the rings formed by EscC in *E. coli* are not well understood, studies have shown that proper localization of the OM ring is dependent on EscV and EscN but not dependent on needle EscF formation.[129]

In order for the T3SS machinery to assemble within the peptidoglycan-rich periplasm, the lytic glycosylase EtgA is employed.[132] EtgA and similar lytic glycosylases cleave the β-1,4 glycosidic bond between N-acetylmuramic acid and N-acetylglucosamine within the peptidoglycan layer. This cleavage allows T3SS proteins to arrange within the periplasm and oligomerize to form the base of the structure. Overexpression of EtgA results in cell lysis. Mutation in the catalytic glutamate residue results in attenuation of T3SS-mediated hemolytic activity and a reduction in EspA filamentation.[132]

The final component of the basal body is the needle, which is composed of oligomerized EscF.[63,133] EscF was originally identified as the *E. coli* T3SS needle based on its sequence similarity with T3SS needle proteins MxiH and PrgI from *Shigella* and *Salmonella*, respectively.[133] Analysis of secreted protein concentrations indicated that EscF is required for secretion of translocator proteins EspA, EspB and EspD. EscF is transported to the T3SS by cochaperones

EscE and EscG, which form interactions with the bacterial membrane while in complex with EscF.[134] These cochaperones also prevent premature polymerization of the needle. Null mutants of EscE and EscG do not secrete translocators EspA, EspB or EspD, further implementing EscF as a necessity for type III secretion.

The last structural component of the T3SS is the translocon. The translocon consists of *E. coli* secreted proteins EspA, EspB, and EspD.[135] EspA monomers interact through a coiled-coil domain to form a homo-oligomer filamentous structure, which builds from interactions with the central rod, EscF.[63,136,137] The EspA filament is hollow, with an interior diameter of ~25Å, which is only large enough to allow passage of linear or partially unfolded proteins.[138] Deletion of EspA inhibits bacterial attachment to red blood cells (RBCs).[139] Mutations in pore-forming protein EspD result in a truncated form of EspA that was able to lyse 40% of RBCs when contact between the cells was initiated with centrifugation. EspA spontaneously forms filamentous oligomers in solution, so cytosolic EspA binds to a chaperone protein CesA to prevent premature oligomerization before secretion.[135,140]

Upon interactions of EspA with the host cell membrane, the filament tip serves as a scaffold for pore formation by EspB and EspD.[141] EspB coprecipitates with EspA, and imaging studies suggest that EspB localizes with EspA, indicating that EspB may form important interactions with the T3SS filament.[142] EspB and EspD then form a hetero-oligomeric donut-shaped structure within the cytoplasmic membrane of eukaryotic host cells.[143] The exterior diameter of the structure is between 55 and 65 nm wide. The pore is a funnel shape, with the diameter of the opening becoming smaller towards the cytoplasm of the eukaryotic cell. The minimum diameter of the pore is estimated at 2.5 nm.[144] EspD is critical for lysis of red blood cells (RBCs), while *E. coli* lacking EspB is still capable of a basal level of hemolysis.[139] In addition, analysis of membrane-associated

proteins confirmed membrane-association of EspD consistently after hemolysis. An amphipathic region consisting of residues 66-83 of EspD is responsible for conformational changes to the protein upon exposure to eukaryotic cell membranes.[145] This natively-disordered protein, when inserted into the lipid bilayer of HeLa cells, formed a homodimer thought to increase pore formation. Deletion of residues 66-83 abolished dimerization. The pore formation of EspB and EspD is the final step in the construction of the *E. coli* T3SS.

1.4.2 Mechanisms of action of secreted effectors

Once the T3SS is assembled, effector proteins are transported through the EscF/EspA needle and filament and are delivered into eukaryotic host cells through the EspB/EspD pore. The effectors then perform a collection of actions that promote infection by EPEC or EHEC. Some of these proteins are involved in cytoskeleton remodeling to allow for effacement of the intestinal microvilli and pedestal formation which ultimately leads to intimate attachment of the bacteria to the eukaryotic cell membrane. Some effectors interrupt eukaryotic cell trafficking or phosphorylation pathways, while others interfere with cell survival/death pathways. The process of the sustainment of an intestinal *E. coli* infection by T3SS-harboring EPEC or EHEC relies on the actions of these effectors to maintain an infection.

Cytoskeleton remodeling. Mutations in a particular protein have been implicated in a genetic disorder called Wiskott-Aldrich syndrome (WAS).[146,147] The WAS protein (WASP) is expressed exclusively in hematopoietic cells. WASP has a ubiquitously expressed homolog with ~50% aa identity that is most highly expressed in nerve cells (N-WASP). These proteins are similar in structure and contain many of the same functional domains, including the verprolin-homology, cofilin-homology, highly acidic (VCA) region.[148,149] Together, this VCA binding domain is

essential for activation of the Arp2/3 complex and initiation of actin polymerization. The V region binds actin monomers directly, while the C and A regions bind the Arp2/3 complex.[146,150,151] In the resting state, this process is regulated through autoinhibition of N-WASP.[152] Activators of N-WASP, including the Rho family[153,154] of small GTPases (sGTPases) and the Src family[155,156] of tyrosine kinases, interrupt the autoinhibited structure, exposing the VCA domain for Arp2/3 binding and resulting in actin polymerization.

The Rho family of sGTPases modify a broad range of cellular mechanisms in a GTP-dependent manner.[153] The GDP-bound form is inactive, and the GTP-bound form is active. GTPase activating proteins (GAP) enhance the basal level phosphatase activity of GTPases by aiding in the conversion of GTP to GDP. Guanine-nucleotide exchange factors (GEFs) facilitate the exchange of GDP for GTP, accelerating turnover. The Rho sGTPases involved in N-WASP activation and cytoskeleton remodeling include Rac1 and Cdc42.[157–160]

Pathogenic *E. coli* have evolved an intricate mechanism for hijacking Rho GTPase regulation for the formation of cytoskeleton pedestals (Figure 2).[161] This process involves multiple effector proteins (EspH, EspT, EspM2, EspW and Map). EspH binds to and inhibits Rho GEFs, while EspT, EspM2, and Map mimic specific GEFs. EspT activates Cdc42 and Rac1, EspM2 activates RhoA and induces stress fiber formation. EspW activates Rac1,[162] and Map activates Cdc42. Through these effectors, EPEC and EHEC shut off the eukaryotic cell's mechanism of Rho GTPase modulation and hijack the native system themselves, resulting in N-WASP activation and actin polymerization.

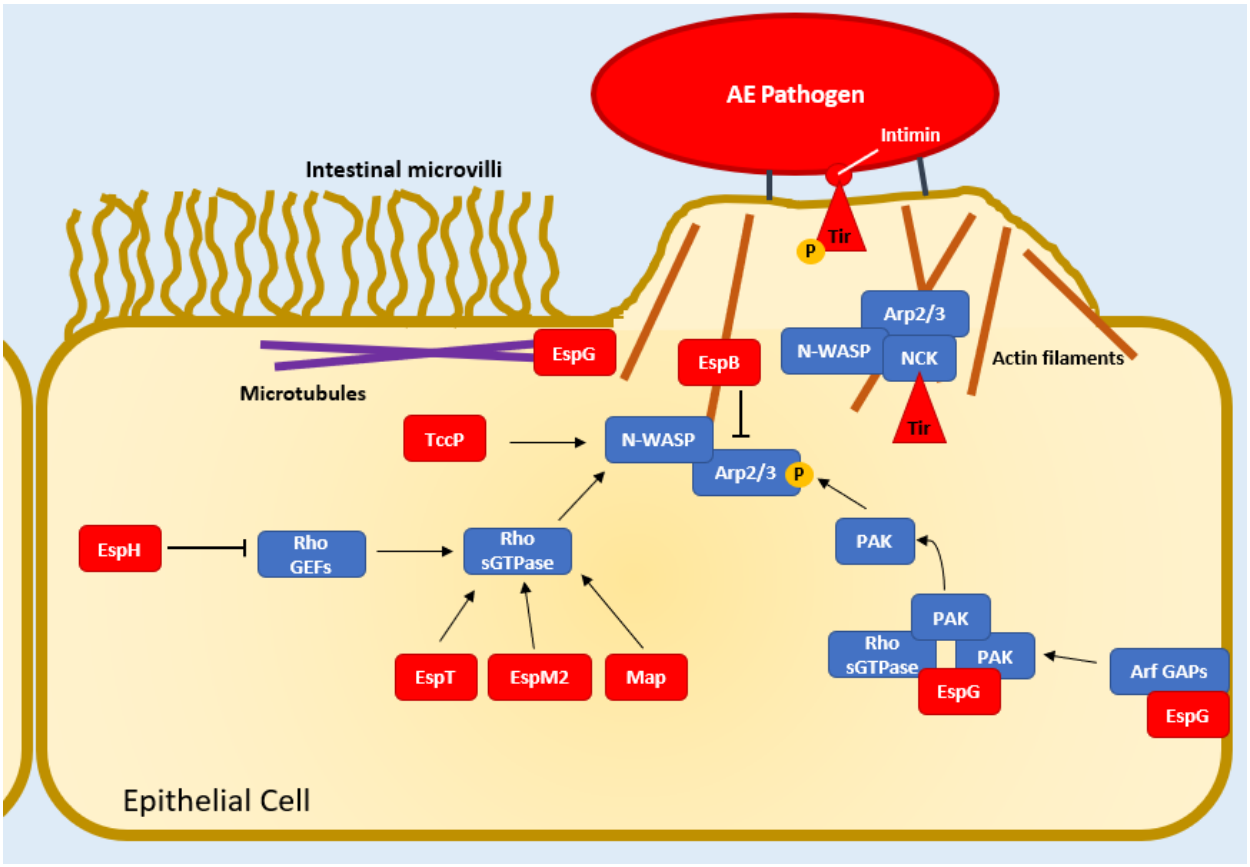


Figure 2. Infection by attaching/effacing (AE) pathogens like *E. coli* and *C. rodentium* results in morphological changes to the surface of the epithelial cell. These changes result in the loss of extracellular microvilli and the formation of a pedestal on which the bacteria are attached. The intracellular mechanisms that result in this dramatic change are brought on by bacterial effector proteins (red) interfering with host actin and microtubule control mechanisms (blue).

Effectors EspG and EspG2 participate in cytoskeleton remodeling during the establishment of infection through multiple pathways.[163–165] These effectors bind directly to tubulin, which causes localized microtubule disruption.[164] Tubulin binding also results in increased actin stress

fiber polymerization. When *C. rodentium* with mutated *espG* was used to infect C57BL/6 mice, the bacteria showed a significantly reduced ability to colonize the gut epithelia compared to *wt* cells.[163] Yeast producing recombinant EspG lost control of microtubule structure and function.

Another mechanism by which EspG interferes with cytoskeleton regulation is through interactions with Arf GAPs and p21-activated kinase (PAK).[165,166] Arf GAPs activate Rac1, a Rho GTPase, to recruit and activate the Wave regulatory complex (WRC), a member of the WASP family.[167] In addition, Arf GAPs consist of multiple membrane-binding domains, which anchors any Arf-containing complex to the plasma membrane. EspG interacts with Arf GAPs, which aids in downstream interactions with PAK.[166] PAK participates in cytoskeleton remodeling through multiple mechanisms, including phosphorylation and activation of the Arp2/3 complex.[168] After injection by the T3SS, EspG localizes in the plasma membrane by binding to Arf GAPs.[165] The inactive PAK homodimer then binds to Rho GTPase, which also localizes PAK to the plasma membrane. PAK-Rho interactions expose the EspG binding site on PAK, allowing for PAK-Rho-EspG complex formation and disassociation of the PAK homodimer, releasing the active PAK monomer. PAK is then free to phosphorylate and activate Arp2/3, stimulating cytoskeleton polymerization.

The characteristic pedestal formation following T3SS-mediated infection is dependent on the translocated intimin receptor Tir.[169,170] Though actin polymerization is activated through multiple mechanisms, Tir serves as a direct connection between the bacterial cell surface and the eukaryotic cytoskeleton.[171,172] Once Tir is translocated into the eukaryotic cell, it may be phosphorylated before localizing within the cell membrane to act as a receptor for intimin expressed on the bacterial outer membrane.[171]

Phosphorylation is necessary for Tir-intimin interaction for EPEC, but it is not necessary for EHEC.[169] After phosphorylation, EPEC Tir recruits N-WASP and Arp2/3 to initiate pedestal formation. The N-terminus of Tir also binds directly to α-actinin, which attaches Tir to the actin filament.[173] Evidence suggests that Tir also interacts with talin and vinculin, other adhesion proteins[172] and cytokeratin 18, an intermediate filament protein.[174] Recruitment of N-WASP is mediated through direct interactions between Tir and Nck, a protein implicated in the attachment of phosphorylated receptors to the cytoskeleton.[175] In EPEC, Tir-Nck interactions are required for subsequent recruitment of N-WASP and Arp2/3. In EHEC, recruitment of cytoskeleton modifiers and the anchoring of Tir to the actin cytoskeleton is mediated through TccP (also known as $EspF_U$).[176] TccP is encoded by EHEC, and the amino acid sequence of TccP consists of a secretion signal necessary for translocation through the T3SS and a 47-amino acid (aa) repeat.[177] A 17-aa motif within the repeat mimics the autoinhibitory fragment of N-WASP. Through competitive interactions with the autoinhibitory binding region on N-WASP, TccP binding exposes the VCA domain and allows N-WASP-Arp2/3 interactions. Since TccP encodes multiple repeats of this domain, multiple N-WASP particles can interact at the same time, resulting in an amplified actin polymerization response.[177]

In addition to its structural pore-forming activity, EspB inhibits Arp2/3-mediated actin polymerization.[178] EspB enhances dimerization of α-catenin.[179] The EspB/α-catenin complex outcompetes Arp2/3 for binding of actin filaments.[178] Interactions between actin and the EspB/α-catenin complex results in a bundling of the filaments. Accumulation of the EspB/α-catenin complex is observed beneath the pedestals formed with the development of A/E lesions, implicating them in attachment of bacteria to host cells during infection.[179]

Avoiding phagocytosis. For *E. coli* to colonize the intestinal epithelia, the bacteria must get past front-line immune response mechanisms by the host. *E. coli* accomplishes this through the secretion of effectors that inhibit uptake of the bacteria into macrophages.[180] Macrophages internalize particulate by depositing opsonins, including C3bi and IgG, onto the cell membranes of their targets.[181,182] Phagocytic receptors expressed on the membrane of the macrophages bind to these opsonins. The receptors for C3bi and IgG are complement receptor 3 (CR3)[181] and Fc gamma receptors (FcγR),[182] respectively. Pathogenic *E. coli* can inhibit the phagocytic uptake of itself (*cis*-inhibition) and other opsonized cells (*trans*-inhibition) through the secretion of effectors EspJ and EspF (Figure 3).[180]

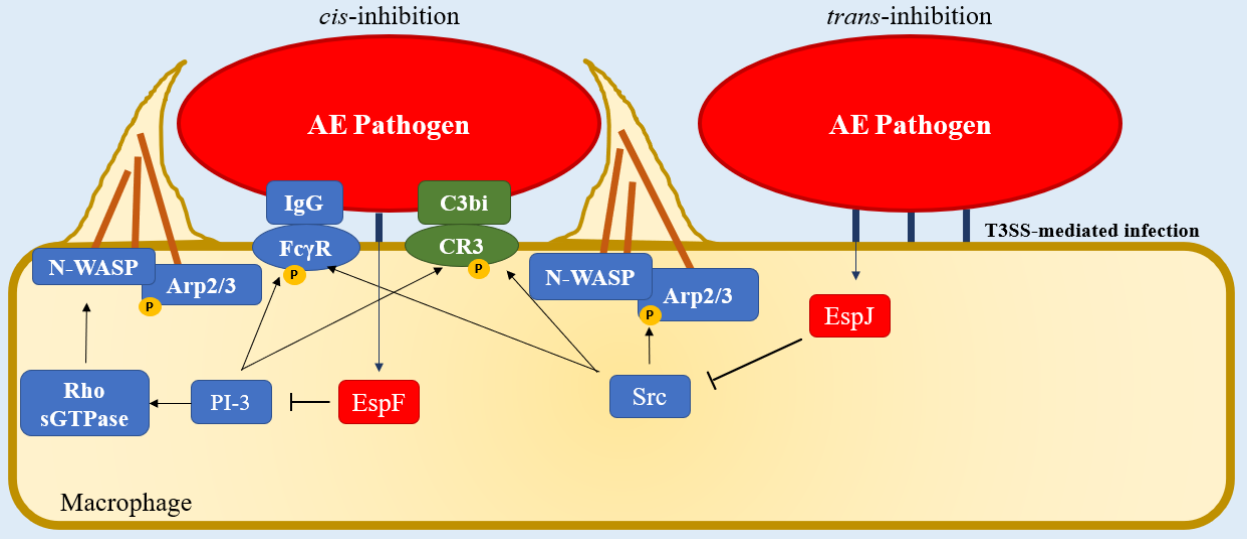


Figure 3. Effectors (red) secreted into host macrophages are able to inhibit the uptake of the cell that secreted them (*cis*-inhibition). Other effectors inhibit the uptake of other bacterial cells (*trans*-inhibition). These effectors were identified by analysis of uptake of opsonized particles into macrophages in the presence of EHEC (*cis*-inhibition) or into macrophages that had been pretreated with EPEC (*trans*-inhibition).

EspJ is capable of *trans*-inhibition of opsono-phagocytosis.[180,183,184] EspJ is an adenosine diphosphate (ADP) ribosyltransferase that inhibits Src kinases.[183] Src kinase is responsible for phosphorylation of Tir and FcγR. Inhibition of Src indirectly results in inhibition of Arp2/3-dependent actin polymerization by inhibiting phosphorylation of Tir. Opsono-phagocytosis is also inhibited by downstream inhibition of FcγR. When J774.A1 macrophages were pre-incubated with EPEC or EHEC, they were incapable of internalizing RBCs that were pre-opsonized with C3bi or IgG.[180] An active T3SS was necessary for inhibition, and mutation in the *espJ* gene abolished the protective phenotype. When Cos-7 cells were co-transfected to express EspJ and FcγR or CR3, EspJ appeared to inhibit uptake of IgG- and C3bi-opsonized RBC into the Cos-7 cells. This result implies that the presence of EspJ in macrophages may be sufficient in protecting bacteria from phagocytosis.

EspF exhibits *cis*-inhibition of phagocytosis of EPEC and EHEC.[180,185] This was demonstrated by incubation of J774.A1 macrophages with EHEC *wt*, *ΔescN*, and *ΔescF*.[180] The *wt* strain was capable of inhibiting uptake, while the T3SS-inhibited *ΔescN* strain and the *escF* mutant showed similar, increased levels of phagocytosis. Mutation in the *espF* gene also resulted in decreased uptake of *E. coli* by M cells.[185] EspF is believed to inhibit phosphatidyl inositol-3 (PI-3) kinase-dependent manner, as inhibition of PI-3 kinase restored the protective phenotype to *espF* mutants.[186] PI-3 kinase is required for FcγR-mediated phagocytosis.[187] PI-3 kinase inhibition results in activation of Cdc42 and Rac1, which implicates EspF in actin reorganization, though this is most likely in reference to inhibition of phagocytosis rather than pedestal formation.

Cell trafficking and secretion. Eukaryotic immune response cells secrete signaling molecules such as cytokines and chemokines in response to infection by pathogens.[188] This process is completed through a secretory pathway that includes intracellular trafficking of enzymes

between the endoplasmic reticulum (ER) and the Golgi apparatus.[189] Major regulators of the essential ER-Golgi membrane trafficking process include Arf1[190] and Rab GTPases[191] and coat protein complexes I (COPI) and II (COPII).[192] Arf1 is involved in membrane transport within the Golgi apparatus as well as Golgi-to-ER trafficking.[190] Rab GTPases are responsible for the fusion of incoming compartments to the Golgi membrane[190,191] as well as correct transport of ER-derived vesicles.[191] COPII coat ER-derived vesicles and form complexes with transport protein particle (TRAPP). These complexes serve as GEFs to activate Rab proteins. COPI coat vesicles that are recycled back to the ER from the Golgi.[193]

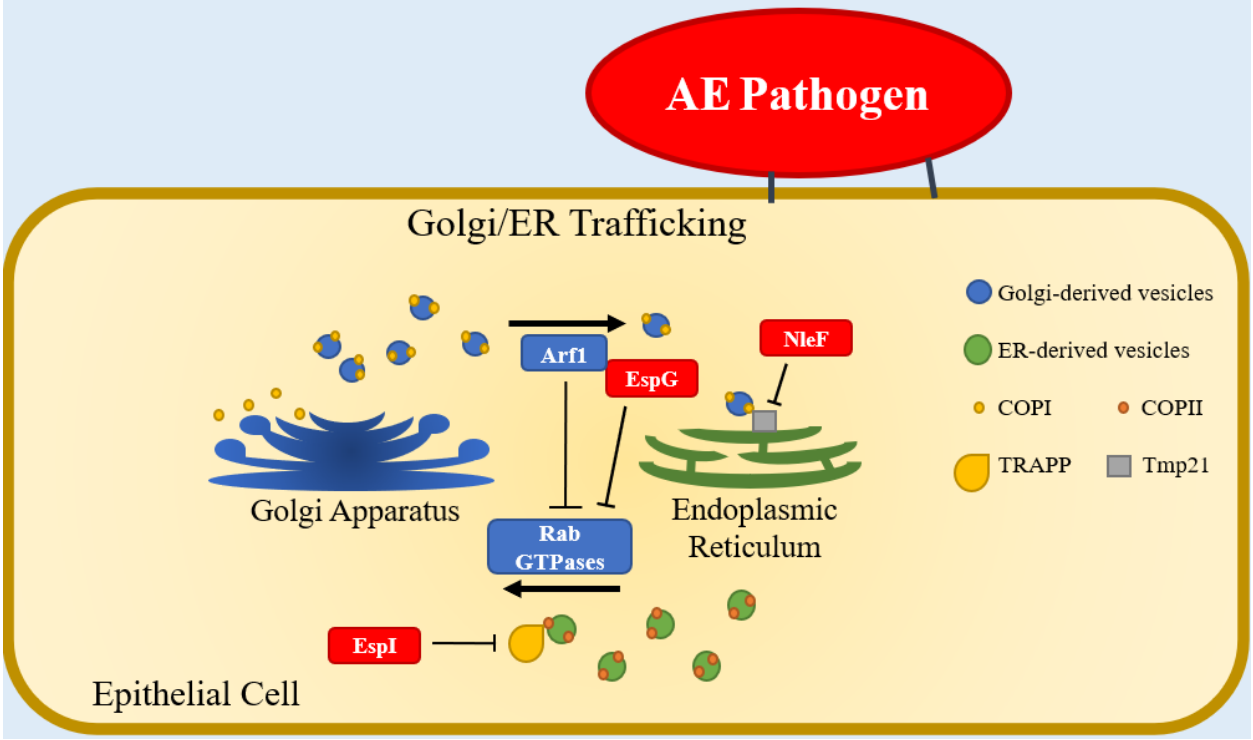


Figure 4. Secreted bacterial effectors (red) interfere with Golgi/ER trafficking by targeting regulatory proteins (blue) or vesicle-associated coating proteins.

EspG forms an Arf1-EspG-Rab1 ternary complex.[194] The formation of this complex results in the redirection of Arf1 activity to inhibit Rab1, significantly decreasing secretion of interleukin-8 (IL-8). EspG stabilizes the active Arf1-GTP complex, inhibiting turnover.[195] This results in the recruitment of Arf1-dependent tethering factors, which ultimately restricts vesicle movement. In addition, EspG acts as a Rab1-specific GAP. Inhibition of Rab1 results in the restriction of vesicle movement. These activities together result in halting of ER-Golgi transport. EspG also binds Arf6 and Rab35, which results in disruption of recycling endosome function and accumulation of recycling cargo in the cytosol.[196]

The non-LEE-encoded (Nle) effector protein NleA, or EspI, destabilizes the COPII complex to inhibit its function.[197] It is theorized that this interference results in inhibition of vesicle uncoating and fusion of the vesicles in ER-Golgi transport. The ability for *C. rodentium* to maintain an infection in mice is dependent on interactions with NleA and the Sec24 subunit of the COPII complex.[197,198] NleF binds to a receptor for the COPI complex, Tmp21.[193] Tmp21 serves to facilitate packing of cargo into COPI-coated vesicles in conjunction with Arf1. The activity of Tmp21 is imperative for the formation of COPI-coated vesicles and retrograde transport from the Golgi to the ER. Interference by NleF results in slowed intracellular trafficking.[193]

NF-κB and MAPK signaling pathway. The NF-κB and MAPK signaling cascades are highly complex pathways that result in global changes in gene transcription and inflammatory signaling in all cell types.[199–202] A highly simplified explanation will be given to describe the influence of T3SS-dependent effectors on these signaling cascades. Transforming growth factor-β-activated kinase 1 (TAK1) can be activated by a multitude of proteins, nod-like receptor proteins (NLRPs), kinases, and ubiquitin ligase tumor necrosis factor (TNF) receptor-associated factors (TRAFs).[199] TAK1 is a complex consisting of the TAK1 kinase and adaptors TAB1, TAB2, and

TAB3.[203] TAB2/3 induce oligomerization and autophosphorylation of TAK1, which is essential for activity. TAK1 then activates inhibitory kappa B kinase (IKK), an activator of the NF-κB pathway. IKK breaks the inhibitory interactions of inhibitory kappa B (IκB) with NF-κB, which is then free to dimerize into functional units, cross into the nucleus, and bind the promoter regions of target genes to activate transcription.[200] These genes produce an immune response through production of interleukin (IL) molecules or other cytokines specific to the pathogen type that initiated the signaling cascade. The mechanisms by which the specificity of the response is accomplished is not well understood. TAK1 may also activate the MAPK p38, JNK and the ERK1/2 pathways.[199] The activated MAPK pathways then induce the downstream expression of inflammatory cytokines.[201,202]

At the initiation of infection, EPEC causes an increase in inflammatory signaling that later diminishes in the later stages of infection (Figure 5).[204] The initial spike in inflammation is due to effector NleF, which is localized to the mitochondria upon secretion into epithelial cells. NleF causes increased translocation of NF-κB to the nucleus and subsequent upregulation of IL-8 expression. Tir, the effector responsible for initiation of attachment and pedestal formation by interacting with the bacterial cell-surface protein intimin, also functions as an inhibitor of NF-κB signaling.[205–207] The C-terminus of Tir mimics an immunoreceptor tyrosine-based inhibitory motif (ITIM) which binds to tyrosine phosphatases SHP-1 and SHP-2.[207] The Tir-SHP1/2 interactions then recruit TAK1 and inhibit its phosphorylation.[206,207] Binding to SHP-2 also leads to deubiquitination and deactivation of TRAF6.[207] These interactions together inhibit NF- κB signaling.

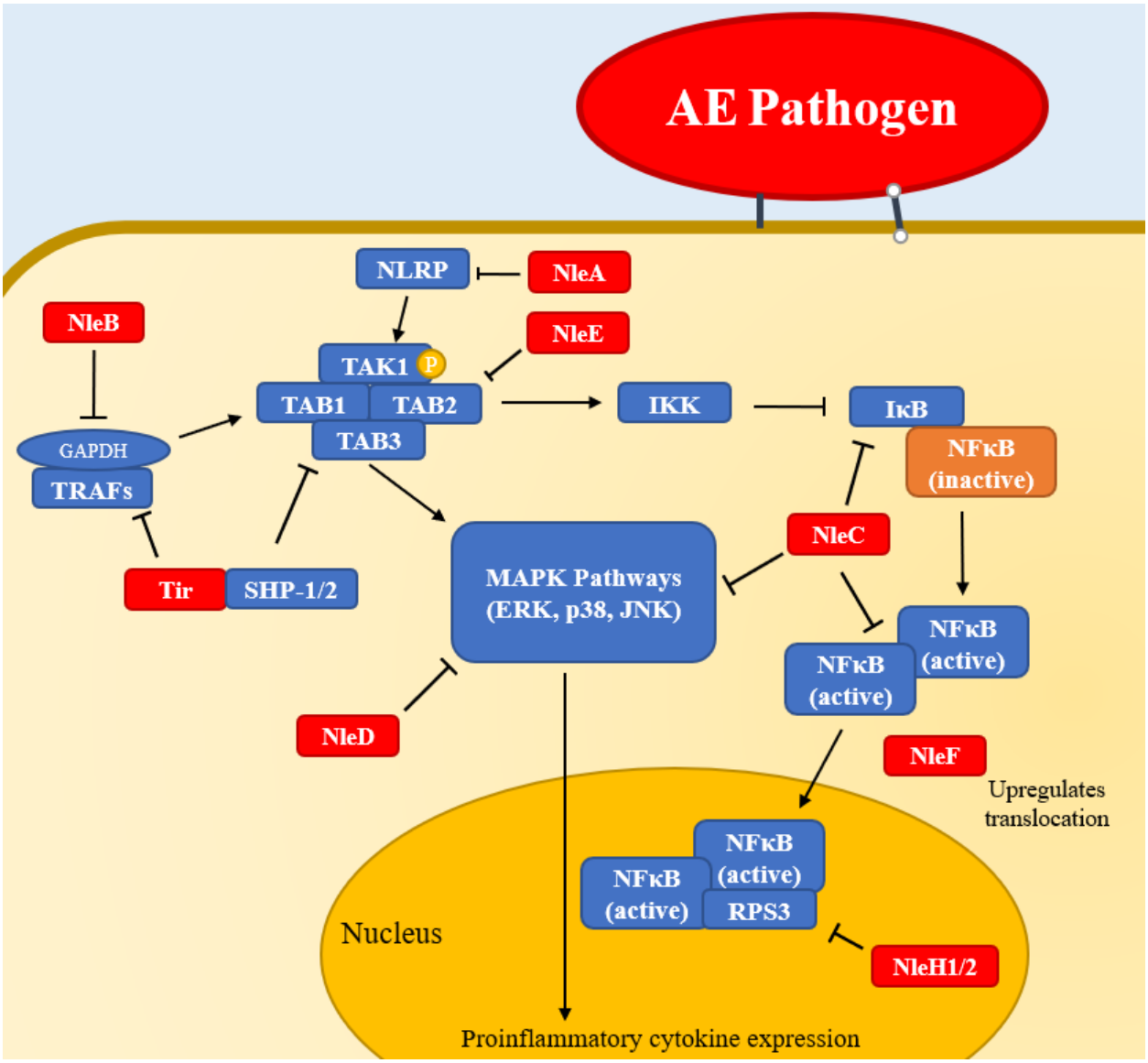


Figure 5. Secreted effectors (red) interfere with NFκB and MAPK signaling pathways (blue) through both activation and inhibition.

NleB, a glycosyltransferase, inhibits NF-κB signaling through modification of glyceraldehyde-3-phosphate dehydrogenase (GAPDH). NleB acetylates GAPDH, which results in decreased polyubiquitination, which is necessary for GAPDH to act as a cofactor for TRAF2. NleB-mediated inhibition of this interaction results in a reduction of NF-κB activation. Mutations

in the *nleB* gene that remove glycosyltransferase activity attenuated infection of mouse intestines *in vivo*. Through a similar mechanism, NleB inhibits ubiquitination of TRAF3, which reduces production of IFN-β.[208]

The NF-κB functional units are Rel proteins, which dimerize to bind to specific nucleotide sequences at the promoter regions of their target genes.[200] NleC is a zinc-dependent metalloprotease known to cleave multiple proteins related to inflammatory regulation,[209] including p300,[210] IκB,[211] and Rel proteins p65 and p50.[212–214] Cleavage of these proteins results in their deactivation and degradation. Mutational studies also suggest that NleC is an inhibitor of the MAPK pathway by inhibition of p38 MAPK phosphorylation.[215] Another zinc-dependent metalloprotease, NleD, cleaves and inactivates MAP kinases JNK and p38, ultimately reducing the expression and secretion of IL-8.[216–218] Cleavage an inactivation of JNK results in decreased cleavage of c-Jun, a subunit of AP-1, a transcriptional regulatory complex responsible for the expression of inflammatory genes.[217]

NleE methylates the active site cysteine on TAB2 and 3, impairing their ability to bind a ubiquitin chain.[203] This directly inactivates the TAK1-TAB complex and results in inhibition of the NF-κB signaling pathway. NleH1 and NleH2 are similar effectors with 84% sequence homology.[219] Both bind to ribosomal protein S3 (RPS3), which inhibits its activity as a guide for NF-κB in the nucleus.[220] NleH1 and NleH2 interact with each other during infection, and NleH1 directly inhibits IKKβ-mediated phosphorylation of RPS3.[221] NleA inhibits IL-1β secretion by interacting with NLRP3, inhibiting inflammasome activation.[222]

EspT acts as a Rac1-specific GEF.[223,224] EspT-mediated Rac1 activation induces the expression of immune response proteins IL-8 and IL-1β in macrophages by activating the JNK

and Erk pathways. Infection of mice with an *espT* mutant strain of *C. rodentium* results in decreased production and secretion of KC, the murine equivalent of IL-8.

Survival pathway/cell death. Programmed cell death, or apoptosis, occurs through two pathways. The intrinsic pathway is mediated by the mitochondria and the extrinsic pathway is mediated by receptors.[225] Both pathways ultimately result in the activation of caspases which leads to cell death. The T3SS of pathogenic *E. coli* secretes effectors that modulate the apoptotic pathways.[225]

There are four major effectors that induce apoptosis during infection: Cif, Map, EspF, and EspH (Figure 6). Cif, or cell cycle inhibiting factor, is not a LEE-encoded effector.[226] The *cif* gene is located on a lambdoid prophage that is present in most strains of EPEC and EHEC. Cif arrests cell cycle progression at the G_2/M phase and causes the accumulation of inactive cyclin-dependent kinase Cdk1, an enzyme required for cell-cycle progression into the mitotic phase.[226] Cif is targeted to the T3SS by a 16-aa N-terminal translocation signal, similar to other type III translocated proteins.[227] Cif shares a catalytic triad with cysteine proteases and acetyltransferases, and mutation of the catalytic residues abolished the cell cycle arrest phenotype.[228] Cif ultimately induces delayed apoptosis 48 hours after infection.[229] When Cif was delivered to eukaryotic cells in the absence of bacteria, Cif induced accumulation of cleaved, activated caspase-3. This result was dependent on the active site cysteine residue, and mutation at that site resulted in decreased levels of caspase-3 accumulation.[229]

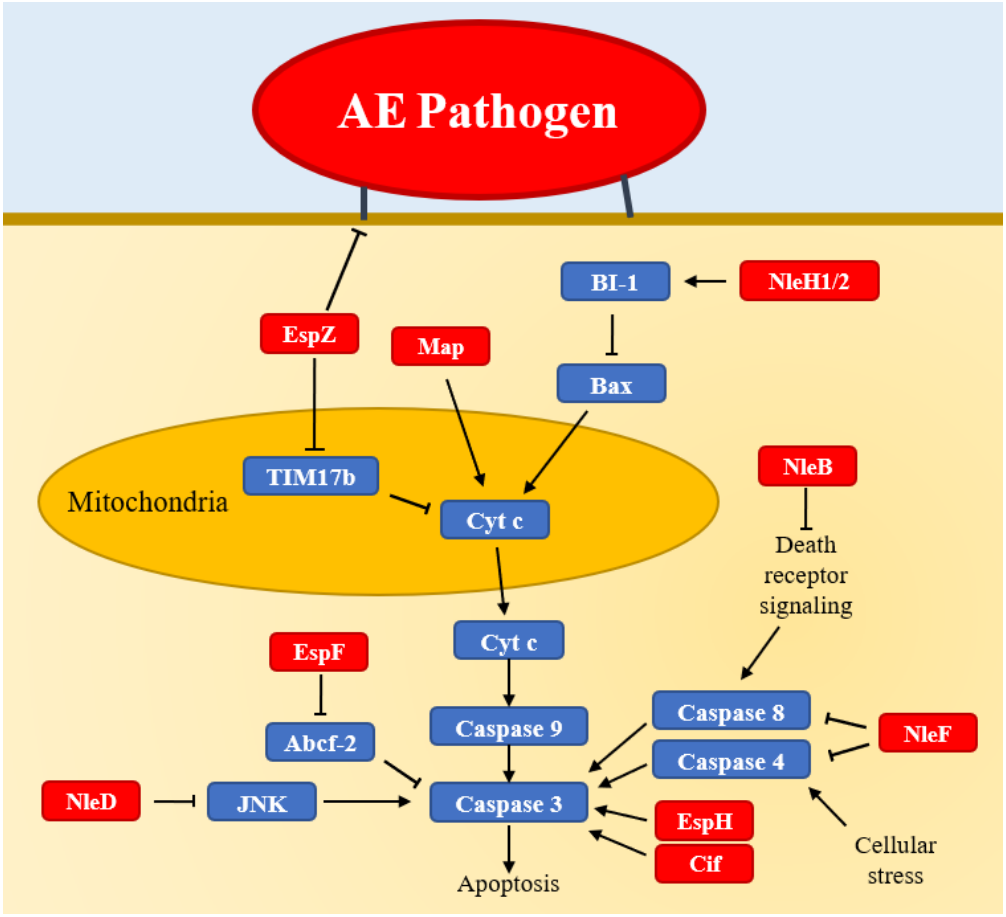


Figure 6. Throughout the infection, bacterial effector molecules (red) modulate intrinsic and extrinsic apoptotic pathways.

The mitochondria-associated protein (Map) is localized to the mitochondria after T3SS-mediated translocation by a mitochondrial-targeting sequence.[230,231] Once there, Map is responsible for morphological changes to the mitochondrial membrane.[231,232] Map then disrupts the mitochondrial membrane potential (MMP), which results in the release of cytochrome c and induction of apoptosis.[230–233] Like Map, EspF is targeted to the mitochondria through an N-terminal sequence,[234] where it destabilizes the MMP and induces cytochrome c release.[234–236] A secondary mechanism of apoptosis induction has also been proposed.[237] Interaction of EspF with ABC transporter family member Abcf1 is thought to result in Abcf1 degradation. Abcf1 activity

potentially results in the inhibition of caspase activation, so degradation of Abcf1 would result in increased accumulation of caspase-3 downstream.[237]

NleH plays a minor role in induction of apoptosis, which is normally counteracted by EspT and EspM2 at biologically relevant concentrations.[161] Overexpression of NleH, the global RhoGEF inhibitor, in epithelial cells resulted in increased caspase-3 activation. This results in downstream activation of intrinsic apoptosis. The ability of effectors EspT and EspM2 to disrupt this activity indicates a built-in mechanism of self-modulation for the T3SS.[161]

NleF is a general inhibitor of apoptosis that acts during a late phase of cell death initiation.[238,239] The C-terminal domain of NleF binds directly to the catalytic domain of caspases-4, -8, and -9, inhibiting their protease activity.[238] Mutations in the C-terminal domain of NleF abolished caspase binding and apoptotic signaling was regained.

The extrinsic induction of apoptosis is inhibited by two effectors, NleD and NleB1. Extrinsic apoptosis is triggered by the recognition of danger signals by cell surface death receptors, which results in the activation of signaling cascades that lead to cell death.[240] Two of the death receptor cascades modulated by T3SS effectors are TNF receptor 1 (TNFR1) and Fas receptor.[240] Association of TNFα with TNFR1 results in the recruitment of TNFR1-associated death domain (DD) protein (TRADD), while association of Fas ligands to the Fas receptor recruits Fas-associated DD protein (FADD).[240] Downstream consequences of activation of these cascades include activation of caspase-8, which further activates executioner caspases, resulting in apoptosis.

NleD inhibits extrinsic apoptosis by cleaving JNK, which is activated downstream of TNFR.[217,218] In addition, when active, JNK phosphorylates and activates the c-Jun subunit of

transcription factor AP-1.[241] AP-1 activation then leads to transcription of apoptosis-related genes. Cleavage of JNK therefore decreases the expression of genes related to cell death.[218,241]

NleB1 is a glycosyltransferase with multiple cellular targets and roles in infection.[242–244] In addition to modulating inflammatory responses, NleB acetylates arginine residues within the DDs of FADD, and TRADD,[244] leading to inhibition of dimerization required for recruitment to death receptors. Downstream effects of this inhibition included reduced activation of caspase-8.[243] The homolog of NleB1, NleB2, was incapable of eliciting the same effects.

Intrinsic apoptosis is directly mediated by the mitochondria.[245,246] This pathway is activated by increased permeabilization of the mitochondrial membrane, which results in the release of cytochrome c into the cytosol.[246] MMP is increased by intracellular protein Bax.[246,247] Cytochrome c accumulation in the cytosol results in the formation of the apoptosome, a caspase-9 activator complex.[248] Caspase-9 then activates executioner complexes including caspases-3 and -7. Effectors that inhibit intrinsic apoptosis include NleH1 and EspZ.[225]

NleH1 reduces disruption in MMP caused by Bax.[219,249] Interactions between NleH1 and Bax inhibitor-1 (BI-1) promotes BI-1-mediated inhibition of Bax.[249] This reduces the permeabilization of the mitochondrial membrane and reduces the accumulation of caspase-3 that is necessary to induce apoptosis.[247] EspZ inhibits apoptosis through multiple mechanisms.[225] EspZ localizes to the mitochondria and stabilizes the MMP by interacting with translocase of the inner mitochondrial membrane 17b (Tim17b).[250] Tim17b is a voltage-gating component of protein transport to the mitochondria. EspZ is also theorized to act as a negative-regulator of T3SS activity.[251] EspZ localizes to the cytosolic region of the plasma membrane and interacts with pore-forming protein EspD. Heterologous overexpression of EspZ in HeLa cells prior to infection with T3SS-harboring EPEC decreased delivery of effector proteins into the HeLa cells.[251]

Disruption of tight junctions. The stability and homeostasis of an epithelial cell membrane relies on the maintenance of tight junctions (TJ).[252] TJs also function in determining the selective paracellular permeability by acting as a gate for ions and proteins to pass through.[253] Disruption of TJ stability results in increased permeability through epithelial membranes and decreased barrier function. The proteins that make up TJs are localized to paracellular regions.[254] These proteins include claudins, occludin, junctional adhesion molecules (JAMs), tricellulin and cytosolic scaffold proteins such as zonulae occludens (ZO) and cingulin (Figure 7).[253–257] Characteristics of a destabilized TJ include increased permeability and delocalization of the TJ proteins.[252] Permeability of cell monolayers can be quantified by measuring the transepithelial electrical resistance (TEER) of the membrane.[258] Decreased TEER indicates increased permeability of the monolayer and a disrupted TJ.

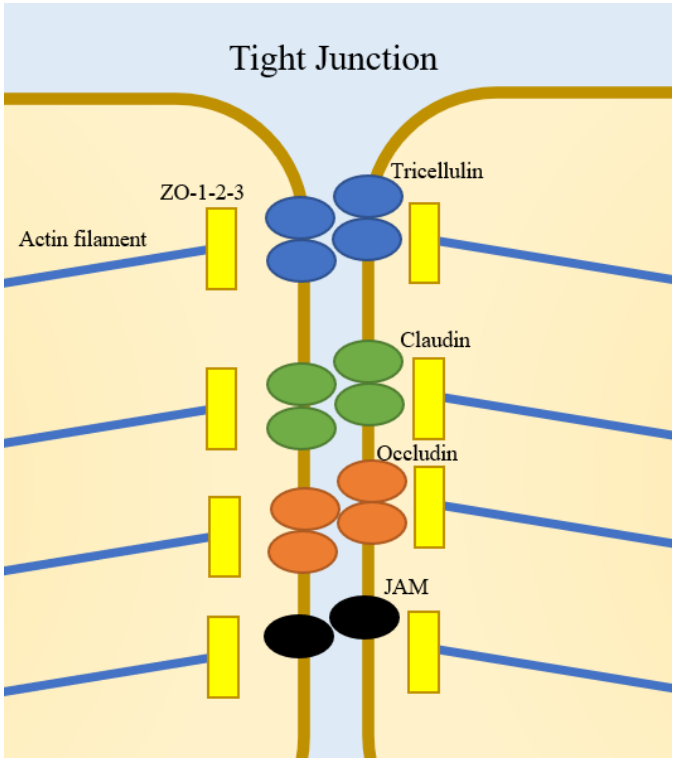


Figure 7. Image of tight junctions.

Pathogenic *E. coli* and *C. rodentium* secrete effectors to disrupt the stability of TJs for the purpose of infection.[252] These effectors (NleA/EspI,[198,259–261] EspF,[262–264] Map,[265] EspG/G2,[252,266,267] and EspM[268]) all serve other functions relating to actin rearrangement, microtubule interactions, interference with ER/Golgi trafficking, induction of inflammatory responses, and modulation of cell survival/death pathways. These primary functions all interfere in some way with TJ performance, and they disassemble TJs as secondary functions.[252] Mutation of any of these effectors results in either decreased TEER measurements on a cell monolayer or delocalization of tagged TJ proteins to other regions of the cell, away from the paracellular space.

1.4.3 Regulation

Chaperones of T3SS effectors. T3SS-specific chaperones are essential for the secretion of their concordant effectors, or substrates. Oftentimes, knockdown or mutations to these chaperones decreases secretory efficiency of their substrates, making chaperones essential for the propagation of T3SS-mediated infection.[269,270] Some chaperones bind to only one substrate[135] while others bind to multiple (Table 1).[271]

Table 1. Type III secretion system chaperones and their substrates.

Chaperone	Substrates
CesT	Tir,[270–273] Map,[270–272] EscJ,[270,271] EscC,[270,271] EspF,[270,271] NleA,[270,271] NleG,[270] NleH1,[270] NleH2,[270] NleF, EspH, EspZ, EspG
CesF	EspF[274]
EscE	EscF[134]
EscG/CesA2	EscF,[134] EspA[135,275]
CesAB	EspA,[140] EspB[140]
CesD	EspB,[276] EspD[276]
CesD2	EspD[277]
TrcA	Intimin[278]

CesL	SepL

Most chaperones function as dimers.[269,279] Associations between a chaperone and its substrate are dependent on a specific aa sequence present on the N-terminus of the substrate called the chaperone binding domain (CBD).[280,281] This region is composed of a secretion signal and a chaperone binding region and is typically 50-100 aa in length, and it binds by wrapping around the dimerized chaperone proteins in a mostly linearized manner that allows for the formation of secondary structures.[279,280] The role of these chaperone-substrate complexes was originally hypothesized to be targeting of the effectors to the T3SS.[282] Evidence in favor of that theory is presented in an ATPase-binding domain specific to EscN that is present on CesT, a promiscuous chaperone that binds Tir and other substrates. CesT can independently bind substrates and the ATPase, and a E142G mutant displayed a decrease in Tir secretion without inhibiting CesT-Tir interactions.[271]

In some cases, the entire effector substrate remains unfolded because of chaperone binding.[135] This is true for EscE and EscG binding to EscF[134] and EspA binding with chaperones CesA[135] or CesAB.[283] In a divergent example, substrates that bind to CesT are only linearized through the CBD.[284] The remainder of their structure is fully formed and enzymatically active. Because the inner diameter of the T3SS needle is only 2-3 nm, these effectors must be unfolded prior to secretion. The ATPase of the *Salmonella* T3SS, InvC, has been implicated as an "unfold-ase" that serves to linearize effectors in an ATP-dependent manner.[285] The conserved structure of the T3SS family of ATPases suggests this may be a universal role for InvC homologs.[66] The ATPase binding domain on CesT supports that claim.[271]

The unfolding activity of the ATPase appears to be substrate-dependent.[269] When dihydrofolate reductase (DHFR) with a stable fold was fused to the secretion signal (but not the

full CBD) of YopE in *Yersinia*, the enzyme could not be secreted.[286] When the entire CBD of YopE was included (residues 1-52), DHFR was successfully secreted, regardless of folding before secretion.[286,287] This indicated that secretion of the enzyme may be dependent on the entire CBD of some effectors.

Chaperones of the T3SS effectors are instrumental in the efficient secretion of their substrates.[271] Mutation or knock-down of chaperones results in decreased concentrations of secreted proteins. Chaperones associate with their substrates in a dimerized form, with the N-terminal CBD wrapped around the dimer.[279] In some cases, chaperones are necessary to keep the effectors linearized before secretion.[135] When the effector is folded before secretion, chaperones work in conjunction with the ATPase located at the base of the T3SS complex to transport linearized peptides through the needle complex, allowing for propagation of infection.[285]

Regulation of expression of the T3SS. In AE pathogens, the T3SS is encoded by the LEE, a highly conserved pathogenicity island (Figure 8).[288] The LEE is a chromosomally encoded 35 kb region[288] that contains 41 genes in seven operons (LEE1-7).[11,289–292] The LEE encodes structural components of the T3SS, regulatory proteins, some secreted effectors and their chaperones, and proteins implicated in attachment. The LEE of EPEC and EHEC have 94% sequence identity and the operons are present in the same order,[293] while the *C. rodentium* LEE shares lower homology.[10,294] In addition, the operon LEE6 in *C. rodentium* is placed differently within the LEE than in EPEC or EHEC.[10,294]

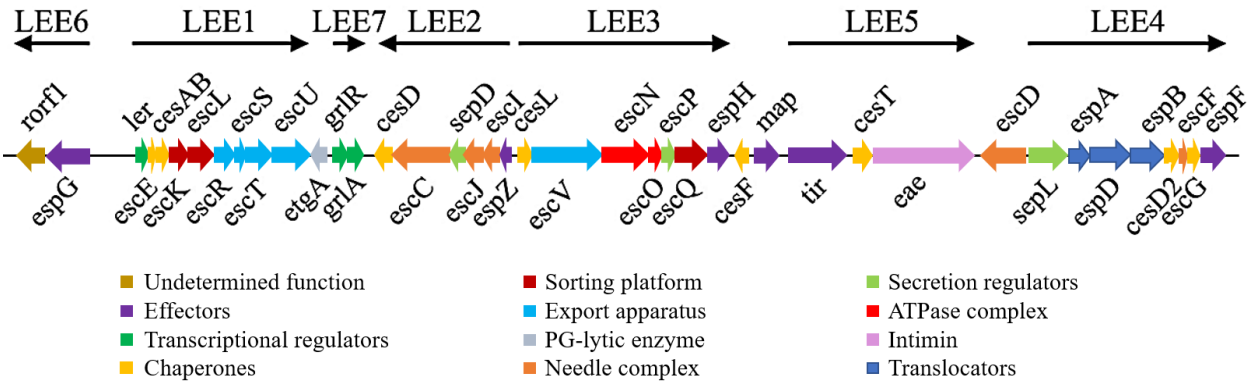


Figure 8. The locus of enterocyte effacement (LEE) of EPEC and EHEC.

Regulation of LEE expression is complex and involves autoregulatory systems, environmental conditions, transcriptional and post-transcriptional regulation, and quorum sensing.[295] The LEE encodes four transcriptional autoregulators: Ler, GrlA, GrlR, and CesL.[289,296] *Ler* is encoded by LEE1 and belongs to the H-NS-like protein family.[289] H-NS, the prototype member of the family, binds and negatively regulates transcription of the LEE.[297–299] Ler displaces H-NS, derepressing LEE expression and acting as a positive feedback loop.[297,300] Ler is essential for expression of the LEE, while simultaneously acting as its own negative regulator through modulating expression of *grlA* and *grlR*.[301,302] GrlA and GrlR are encoded by LEE7.[296,303] GrlA binds directly to the LEE1 promoter region, activating transcription of Ler.[303,304] Ler then activates LEE7 transcription, forming another positive feedback loop.[291] GrlR represses LEE expression through an unknown mechanism.[305,306] It is known, however, that GrlR binds to GrlA, indicating that GrlR may inhibit expression by sequestering available GrlA.[304,306]

There are also several pathotype-specific regulators of the LEE.[3] CesL serves as both a chaperone and a transcriptional regulator of LEE expression in EHEC.[307,308] CesL interacts with Ler, and overexpression leads to sequestration of Ler, resulting in repression of LEE expression.[307]

Typical EPEC encode a positive regulator of expression, PerC, on the EAF plasmid.[87,309] EHEC encodes three PerC homologs, PchA, PchB, and PchC.[310]

Global transcriptional regulators that affect LEE expression include BipA, Cpx, Fis, GadE, Hha, H-NS, H-NST, IHF, RgdR, RpoN, SspA, FusK/R, EutR, LeuO, SdiA, KdpE, QseA, QseC, QseD, QseE, RcsB, RegA, and GlmY/GlmZ.[79,311–313] To add to the complexity, these regulators may not affect transcription in the same way between organisms. For example, global epigenetic modifier Lrp upregulates T3SS activity in EPEC and EHEC while downregulating T3SS expression in *C. rodentium*.[65,314,315]

Hierarchal secretion. The hierarchy of secretion and assembly of T3SS components is important for function of the injectosome. This process is regulated through two molecular switches: EscP/EscU and SepL/SepD.[311,316] These switches regulate the change of proteins secreted from early to middle and late stage substrates. Early stage substrates include structural components such as the inner rod the needle.[317] Middle stage substrates include the translocon proteins EspA, EspB, and EspD. Translocation of the first effector, Tir, marks the initiation of late stage secretion.[80,318]

The first molecular switch is dependent on the interactions between sorting platform protein EscU and ruler protein EscP.[319,320] EscP interacts with the C-terminal region of the autoprotease EscU, which in theory results in a conformational change responsible for a shift in substrate specificity. This shift is substrate specificity allows for middle stage proteins to be secreted.[321] The EscU/EscP interactions are theorized to work in consort with the autoprotease activity of EscU, since a non-cleavable mutant of EscU decreases the secretion of middle and late-stage substrates while decreasing membrane association of multi-effector chaperone CesT.[124,322]

EscP is thought to associate with EscU in an "infrequent ruler model," proposed by Moriya et al. for the flagellar system.[323] In this model, EscP acts as a ruler for the assembly of the needle by oligomerization of EscF. Through direct interaction with EscF monomers, EscP moves through the interior of the needle complex, and secretion of EscF stops after the needle reaches the same length as EscP. EscP is occasionally secreted throughout the process of needle assembly, which temporarily halts the secretion of EscF. The pause in secretion allows for "measurement" of the needle length while subdomains of EscP interact with the inner diameter of the EscF super structure. When the needle length is equal to the length of EscP, these interactions are maximized, allowing time for interactions between EscU at the base of the needle and EscP. This interaction is then proposed to cause the conformational change in the EscU proteins responsible for changing the specificity of effector binding to allow secretion of middle and late stage effectors.[323]

The second molecular switch changes the secretion pattern from translocon-associated proteins to effectors through interactions between SepL and SepD. Null mutations in *sepL* result in abolishment of translocon secretion and increases effector secretion.[296,324,325] This suggests that SepL plays a direct role in enhancing secretion of translocon proteins by inhibiting the secretion of effectors. In EPEC and EHEC, SepL binds to a protein SepD. Deletion of SepD results in the same secretion patterns as the mutant SepL, suggesting that SepL activity is dependent on interactions with SepD.[324–326] These two proteins form a ternary SepD/SepL/CesL/Tir complex.[327] Evidence suggests that gate protein EscV may serve as a docking site for SepL-mediated secretion, though the exact mechanism for that is not well understood.[327] It is hypothesized that SepL may be sequestered by competitive binding of EscD to the Tir binding site, resulting in Tir release and secretion,[325] though much of this process is left to be characterized.

1.4.4 Inhibitors of the *E. coli*/*C. rodentium* T3SS

Caminosides. The first inhibitor of the T3SS discovered was caminoside A (Figure 9).[328] The caminosides are glycolipids isolated from the marine sponge *Caminus sphaeroconia* found in the upper walls of Toucari Caves on the island of Dominica. Marine invertebrates were extracted repetitively with methanol before screening for T3SS inhibitory activity in EPEC. The isolation of caminoside A was a result of a bioassay guided fractionation approach using a protocol designed to screen for T3SS inhibitors using sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and analyzing secretion of effector proteins. Samples having cytotoxic effects against EPEC were dropped from the study.[328]

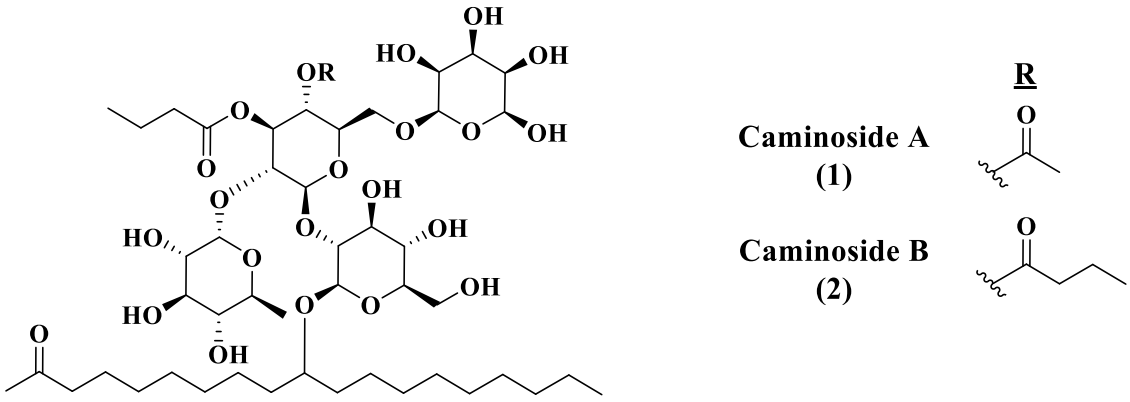
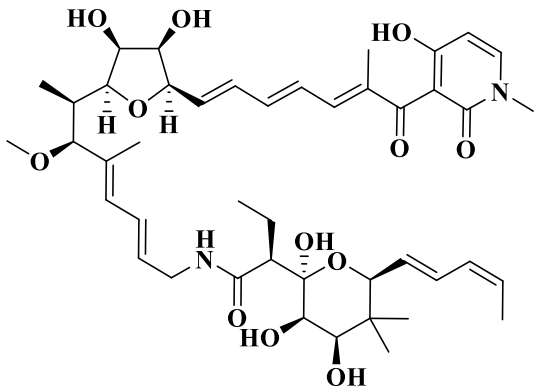


Figure 9. Structures of caminosides A (**1**) and B (**2**).

Caminoside A decreased the secretion of EspB, but not EspC.[328] The structure of caminoside A was elucidated and potency was characterized (IC_{50} = 20 μM), though details on the mechanism of action are still not well understood. Interestingly, though caminoside A has no cytotoxic effect against EPEC, it does have cytotoxic activity against Gram-positive methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant *Enterococcus* (minimal inhibitory concentration, MIC = 12 μg/mL for each). Since the discovery of the caminosides, full

syntheses of caminoside A and B have been published,[329] detailing a synthetic process of 33 and 25 steps, respectively. Despite the promising activity of the caminosides against EPEC, very little has been done since their discovery to further develop these natural products for use as T3SS inhibitors due to difficulties in production or synthesis of the compounds.

Aurodox. Aurodox, a polyketide produced by *Streptomyces goldiniensis*, was originally isolated and characterized as having antibiotic activity against Gram-positive bacteria in 1973 (Figure 10).[330] Aurodox was originally named antibiotic X-5108 when its structure was elucidated and its antibiotic activity was discovered. Later, its molecular target was determined to be elongation factor-Tu (EF-Tu) and structure-activity relationship (SAR) studies were performed to characterize its pharmacophore.[26]



(3)

Figure 10. Structure of aurodox (**3**).

Aurodox was identified as a T3SS inhibitor in 2011 as part of a screen for inhibitors of the T3SS using EPEC-mediated hemolysis.[17,331] The molecular components of the translocon, EspB and EspD, typically form the end of the T3SS needle complex and allow for passage of effectors into the target host cell;[15,73,326] however, they also form pores on the surface of RBCs.[331,332]

Formation of these pores results in leakage of hemoglobin into the extracellular space. The supernatant may then be separated from cellular components and the concentration of hemoglobin may be quantified by measuring the absorbance at 540-590 nm. The higher the hemoglobin concentration, the greater the T3SS activity.

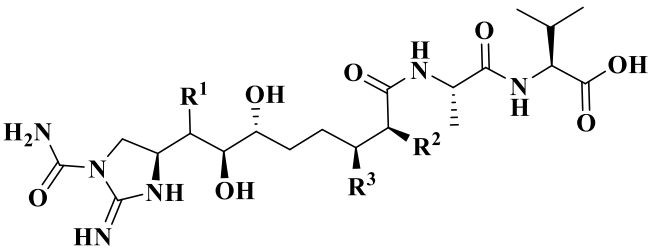
To discover aurodox, a hemolysis screen was performed on 13,300 biological extracts from actinomycetes, fungi, plants, and invertebrates.[17] After extracts from Streptomyces sp. K06-0806 showed potent inhibition of EPEC-mediated hemolysis without significantly affecting bacterial growth, a large culture of Streptomyces sp. K06-0806 was fermented and aurodox was purified. Further testing with purified compound determined the inhibitory potency of aurodox in the hemolysis assay. According to analysis by SDS-PAGE followed by Western blotting, aurodox reduces the amount of secreted proteins EspA, EspB, EspD, EspF and Map without significantly affecting overall protein levels. It was shown that T3SS inhibition (IC_{50} = 1.5 μg/mL) occurs at a concentration much lower than the concentration at which aurodox shows signs of toxicity against Gram-negative bacteria (~10 μg/mL).[17]

Aurodox was later analyzed using an in vivo mouse model using *C. rodentium* to analyze the effectiveness of aurodox on mitigating infection.[10] *C. rodentium* is a commonly used model of EPEC infection in mice, due to a high identity of sequence between the EPEC LEE and the LEE in *C. rodentium*.[10,17] Mice were initially infected with *C. rodentium*, then treated either with 10% dimethyl sulfoxide (DMSO) as a control, a single dose of tetracycline (200 mg/kg), or aurodox (25 mg/kg) every 24 hours for four days. All the mice that were treated with aurodox survived while none of those that were treated with tetracycline survived past day thirteen. These results show the power of T3SS inhibitors to protect against an otherwise lethal dose of pathogen.

A recent study has been published investigating the mechanism of action of aurodox.[25] Aurodox decreased the secretion of effector proteins EspB and Tir via Western blotting. Aurodox was also shown to decrease infectability of epithelial cells by EHEC. Transcriptional analysis on gene expression revealed that aurodox downregulates over 100 genes cell-wide and downregulates 25 of 41 genes related to the T3SS. This suggests that the inhibitory activity of aurodox is a result of a change in gene expression, and not a result of physical manipulation of the T3SS needle complex. One of the genes downregulated by aurodox is *ler*, a major activator of the LEE.[272] In addition, aurodox downregulated the expression of EspG and NleB, which are non-LEE encoded effectors.[25] Importantly, treatment with aurodox does not induce Shiga toxin production in EHEC, suggesting promise for the use of aurodox to treat EHEC infection. If the binding target of aurodox were identified, efforts could be made to strengthen that binding and increase the potency of aurodox further.

Guadinomines. The guadinomines were discovered using EPEC-mediated hemolysis to screen natural product extracts.[333,334] *Streptomyces* sp. K01-0509 was found to produce potent inhibitors of hemolysis.[331,332] Guadinomines A, B, C1, C2, and D were isolated from *Streptomyces* sp. K01-0509, purified and analyzed (Figure 11).[333] Guadinomines A and B are the most potent natural product T3SS inhibitors with IC_{50} = 0.007 and 0.01 μg/mL, respectively. The mechanism of inhibition of the guadinomines are not well understood and yields of guadinomines from culture are low, making further research difficult. The lengthy total syntheses of guadinomine B and C2 have been published, with 33 steps in the longest linear synthetic sequence.[335] In 2012, a study on the biosynthetic pathway of guadinomine A was published.[336] Notably, guadinomine D, having an acylated amine at R^2 is 1000-fold less potent than guadinomine B. This shows the importance of the vicinal diamine to biological activity. The acyl group on guadinomine D may be installed by

enzymes apart from the guadinomine synthetase, since no obvious acylation enzyme is part of the gene cluster. While guadinomines do not appear to produce any antimicrobial activity, Ōmura found that guadinomine B is cytotoxic to Jukat cells at a concentration 100 times higher than the IC_{50} for T3SS inhibition.[333]



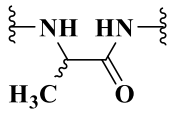
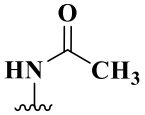
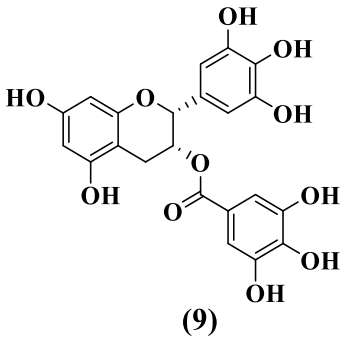
	R^1	R^2	R^3	IC_{50}
Guadinomine A (4)	OH	NH_2	NH_2	38 nM
Guadinomine B (5)	H	NH_2	NH_2	14 nM
Guadinomine C1 (6) and C2 (7) (diasteromers)	H			inactive
Guadinomine D (8)	H		NH_2	1600 nM

Figure 11. Structures of guadinomines A (**4**), B (**5**), C1 (**6**), C2 (**7**), and D (**8**).

Epigallocatechin-3-gallate (EGCG). EGCG is a polyphenolic flavonoid produced by green tea.[337] EGCG is an anti-inflammatory compound that inhibits NF-κB activation and protein kinase C.[338] EGCG is also being explored for its anticancer activity [339] and is a recognized inhibitor of epigenetic modifications such as DNA methylation and histone modification.[340–342] The versatility of EGCG has been explored extensively and it is being reviewed for its potential as a treatment option for many conditions.[343] Previous studies have indicated that at high concentrations, EGCG inhibits the T3SS of multiple organisms including EPEC and EHEC, *S.*

Typhimurium, and *Y. pestis*.[344] This result was explored using ELISA quantification of secreted EspB as well as quantitative analysis of T3SS-mediated hemolytic activity in the presence and absence of 50 μg/mL EGCG. EGCG was also analyzed for its ability to inhibit adherence of EPEC to Hep-2 cells. In this assay, EPEC was cultured with the Hep-2 cells and incubated for 2 hours in the presence and absence of EGCG. The Hep-2 cells were then affixed to a microscope slide and stained with Giemsa. The number of adhered bacteria was then quantified. The presence of EGCG reduced adherence by ~50%. There are currently no works published indicating the potency of EGCG as a T3SS inhibitor for *E. coli*, and all published analysis has been performed at concentrations of 100 μM.



(9)

Figure 12. Structure of epigallocatechin-3-gallate (EGCG, **9**)

Regacin. Regacin reduces the expression of the *C. rodentium* T3SS by inhibiting binding of the transcriptional regulator RegA to its DNA substrates.[16,345] The interaction between RegA and DNA typically enhances type III secretion. Western blot analysis of secreted protein showed that complete inhibition of RegA-DNA interaction resulted in partial, but not complete inhibition of T3SS expression.[16] Regacin is therefore a partial inhibitor of the T3SS.

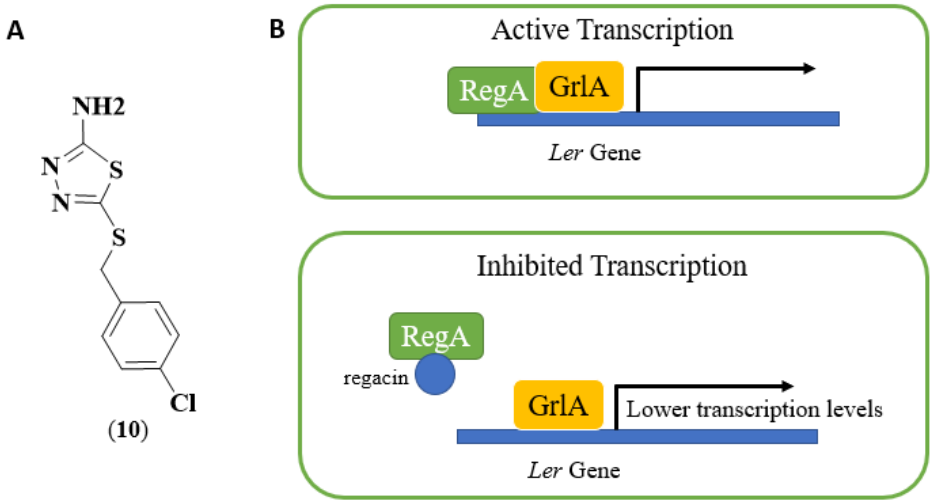
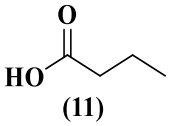


Figure 13. A) Structure of regacin (**10**). **B**) RegA binds to DNA, resulting in expedited activation of the T3SS. When RegA binding to DNA is inhibited by regacin, the T3SS is still partially active because LEE1 transcription and Ler expression are governed by multiple regulators.

Butyric acid. Initial studies relating to the biological effects of butyric acid predate knowledge of the T3SS (Figure 14).[346] In the 1960s, the change in the infectious dose of *S. enteritidis* upon pretreatment of antibiotics was analyzed. The ED_{50} went from 106 to <10 cells when a single dose of streptomycin was administered 24 hours before infection. The authors noted that treatment with antibiotic increased the gut pH and identified that butyric acid and acetic acid were being produced by the gut bacteria. The authors attributed the ability of the mice to tolerate the pathogen to a low gut pH and not a specific inhibitory effect caused by butyric acid. Since these experiments were performed before the discovery of the T3SS, the authors were unaware that they were completing initial studies on the effect T3SS inhibitors have on severity of infection.



(11)

Figure 14. Structure of butyric acid (**11**)

Butyric acid is classified as a short-chain fatty acid (SCFA) and is produced as a fermentation product by commensal *Bacterioidetes* species in mammals.[347] In human intestines butyric acid is typically present at 10-20 mM.[314,347,348] Butyric acid is a major energy source for colonocytes, and the ability of colonic cells to absorb and utilize sodium butyrate is seen as a sign of good health.[348] Administration of butyric acid to the intestines of mice infected with *C. rodentium* results in decreased inflammation and increased mucus production from colonic cells.

Butyric acid interacts with the epigenetic modifier Lrp, a major regulator of gene expression in bacteria.[79,314,315,346–348] Lrp does not control the expression of genes in the same pattern from one organism to another. As a result, butyrate acts as a T3SS inhibitor for some organisms and as a T3SS activator in others.[65,314,315,349] A notable example involves LEE-encoding bacteria EPEC and *C. rodentium*. Activation of Lrp upregulates expression of the LEE in EPEC, while activation of Lrp downregulates expression of the LEE in *C. rodentium*.[65,314,315]

Research into SCFAs as T3SS regulators has focused primarily on the effects of probiotics on infection.[315,347,349] By increasing the concentration of SCFA-producing bacteria in the gut, concentrations of a variety of SCFAs are altered. Depending on the pathogen attempting to infect the gut, differing ratios of SCFAs could have dramatically different results, from improving to worsening infection. Given the prevalence and widespread use of probiotics, this area requires further investigation.

Small molecule inhibitors. There are multiple known small molecule inhibitors of the T3SS of *E. coli* or *C. rodenium*.[350–352] For some of these compounds, the mechanism of action has yet to be elucidated, but with the improved structural characterization technology over the last decade, target-based drug design is becoming possible.[353] A new class of small molecule inhibitor was discovered using a virtual screen for potential compounds to target the EscN ATPase.[350] The screening campaign was conducted using the ATP binding site of EscN (PDB code: 2OMB) and compounds from the ZINC database. The initial 3000 compounds were filtered for predicted cytotoxicity, and the remaining top 70 compounds were purchased for ATP hydrolysis screening using recombinant EscN. Next, compounds were screened for their cytotoxicity toward HeLa cells. Finally, five compounds were screened for their ability to inhibit the T3SS based on the relative secretion of effector EspG1 according to Western blot results. Based on these data, analogs of one compound were designed based on predicted binding pose withing the EscN active site (Figure 15). These compounds were named the WEN compounds. The most efficacious compound was WEN05-03, with a $K_i = 16 \pm 2$ μM.[350]

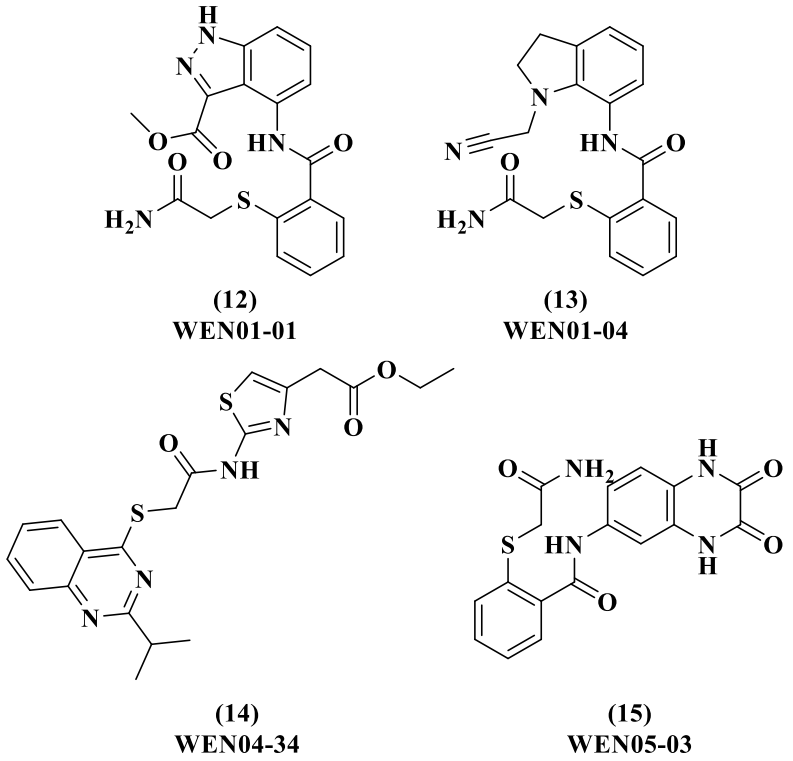


Figure 15. Structures of WEN compounds.

The salicyclidene acylhydrazides (SAs) are a well-characterized structural class of small molecule T3SS inhibitors (Figure 16). They were originally discovered as inhibitors of the T3SS of *Y. pestis*, but have since been indicated as T3SS inhibitors for a collection of pathogens, including *Chlamydia* spp.,[6,12] *S.* Typhimurium,[354] *Shigella* spp.,[355] and EHEC.[352] These compounds induce changes in growth rate of EHEC at 50 μM as a result of their effects on global transcription of genes.[352] Addition of compounds at 20 μM decreased expression of Tir and EspD. The LEE-encoded regulators Ler, GrlA, and GrlR were also downregulated, while regulator genes *pchABC* were downregulated in the presence of one inhibitor, ME0055.

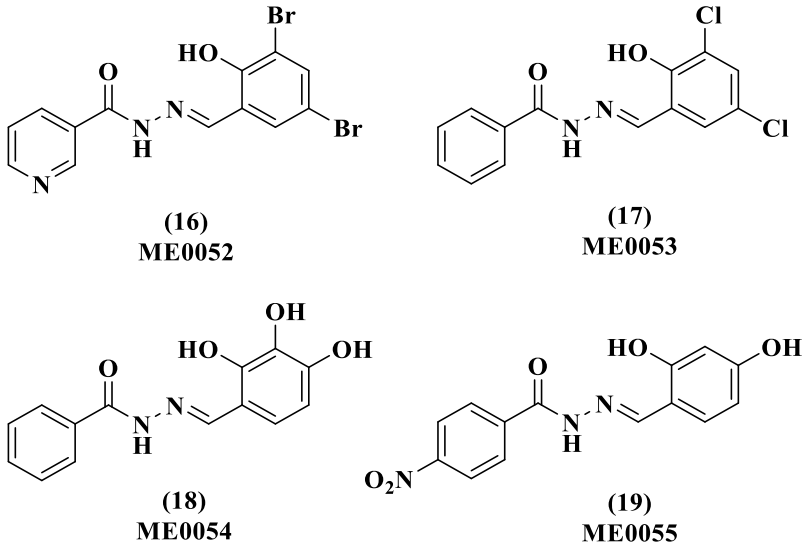


Figure 16. Structures of SA derivatives that inhibit the T3SS in EHEC.

In a recent screen of SA derivatives, the RCZ compounds (Figure 17), two compounds in particular were observed to interact directly with translocon protein EspD.[351] Pull-down assays also indicated binding with EF-Tu and 2-oxoglutarate dehydrogenase. Secretion analysis was then performed on truncated versions of EspD to determine the region of RCZ12 and RCZ20 interactions with the protein. Their results indicated that the coiled-coil domain of EspD is responsible for binding with the compounds. RCZ12 and RCZ20 maintain the ability to affect global gene transcription. To analyze the effect of EspD inhibition on the translation of the LEE, a *ΔespD* mutant was developed. In the absence of compounds, the EspD knockout showed no change in LEE expression. Introduction of RCZ12 and RCZ20 reinstated the downregulation of LEE transcription. This indicated that the regulatory activity of the inhibitors was independent of EspD interactions.[351] Given the similarities between the observed mechanisms of inhibition of the RCZ compounds and aurodox, and given that they all bind to EF-Tu, this may indicate a connection between EF-Tu and expression of the LEE that has not yet been identified.

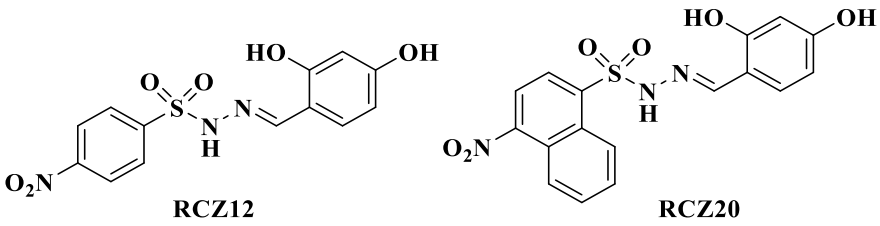


Figure 17. Structures of RCZ12 (**20**) and RCZ20 (**21**).

Coiled-coil peptides It is common for the effectors transported through the T3SS to be composed of a coiled-coil domain, a structure composed of an amphipathic secondary α-helix. The residues within the coiled-coil domains typically consist of a seven-residue repeat. The presence of this domain is hypothesized to play a role in multimeric oligomerization, molecule recognition, and potentially interaction between bacterial and eukaryotic proteins upon translocation. The proteins responsible for forming the filament (EspA) and needle (EscF) have coiled-coil domains, as does the chaperone for EspA (CesA). To analyze potential inhibitory effects of these domains on T3SS function, coiled-coil mimetics were synthesized based on the aa sequences of EspA, EscF, and CesA (Table 2).

Table 2. Sequences of effectors and synthesized coiled-coil peptides. Red residues were changed to increase solubility

Name	Sequence
EspA	KANNLTTTVNNSQLEIQQMSNTLNLLTSARSDMQSLQYRTISGI
Coil A	LTTTVNNSQLEIQQM
Coil B	MSNTLNLLTSARSDM
Coil AB1	KMNNLTTKVNNLQLELQEMRNTLKRLKSAMRRMQ
Coil AB2	KINNLTTKVNNLQLELQEMRNTLKRLKSAMRRMQ
EscF	LSDSVPELLNSTDLVNDPEKMLELQFAVQ
Coil C	LSDSVPELLNSTDLV
Coil D	VNDPEKMLELQFAVQ

CesA	IVSQTRNKELLDKKIRSEIEAIKKIIAEFDVVKESVNELSEKAK
Ces A1	IVSQTRNKELLDKKIRSEIEA
Ces A2	IKKIIAEFDVVKESVNELSEK

The ability of these peptides to inhibit T3SS activity was quantified based on hemolysis of RBCs in the presence of EPEC.[356] T3SS-mediated hemolysis was inhibited by 95% in the presence of Coil A or Coil B at 0.16 mM. Coil AB1 and Coil AB2 showed less potent inhibition of between 10% and 20% at 0.14 mM. Coil B7.1 and Coil B7.2 were only capable of inhibiting the T3SS when they were combined. Coil C and Coil D did not exhibit inhibitory effects to a major extent. Ces A1 did not inhibit hemolysis, but Ces A2 inhibited hemolysis by ~50% at 0.23 mM. With the growing prevalence of peptide drugs approved by the FDA,[357] and given that these coiled peptides target extracellular proteins, these peptides show promise for use as pharmaceutical agents.

Antibodies. Antibodies (Abs) targeting the T3SS have shown promise in inhibition of infection and cell adhesion for many T3SS-harboring pathogens.[358] As the prominent pathogen for infantile diarrhea, Abs targeting the *E. coli* T3SS may have protective benefits as a pharmaceutical agent. Proof of this exists in the practice of mothers breastfeeding their children.[359] Colostrum samples from breastfeeding mothers were obtained and their IgA content was characterized using Western blot analysis. The results indicated that the samples contained IgA that was reactive against intimin, EspA and EspB proteins from *E. coli*. In a similar study, serum from children in Brazil was tested for the presence of IgG protective against EHEC infection.[360] Thirteen of the children had been diagnosed with HUS, while 54 healthy children were analyzed as controls. In both healthy children and children diagnosed with HUS, protective IgG against intimin, EspA, and EspB were present in comparable amounts. This indicates that secondary immunity may be a major contributing factor to the immunization of children against EHEC infection since prior exposure to the bacteria was not necessary for Abs to be present. In another study, rats and chickens were

immunized with recombinant EspA, EscF, or the C-terminal region of intimin.[361] The rat antisera contained IgG Abs that could prevent adherence of EHEC to HeLa cells. Egg powders from the EspA- and intimin-immunized chickens produced IgY Abs that were also protective. While most of the literature on protective Abs target extracellular proteins such as EspA[362,363] and EspB,[363] or membrane-associated proteins such as intimin[364] or Tir,[363,365] vaccination of mice with NleA produces a strong IgG response.[363] Collectively, the research on Ab production against *E. coli* T3SS components implies promise in orally administered Ab as a therapeutic immunization against EHEC infection.

Probiotics. The logic for the protective abilities of probiotics lies in the observation that healthy commensal colonization in the gut reduces the ability of a pathogen to begin an infection.[366,367] Murine models of EPEC and EHEC infection have explored the protective abilities of lactobacillus strains, focusing on the ability of lactobacillus to ameliorate the inflammatory response and leaky tight junctions associated with *E. coli* infection of the colon. Since the mechanism of protective action in these cases are not clear, it is impossible to claim lactobacillus species may inhibit the T3SS. Alternatively, studies on *Saccharomyces boulardii*, a yeast strain that rapidly and ephemerally colonizes the gut of mice, indicate direct inhibition of type III secretion.[368] Mice were treated twice daily with *S. boulardii* beginning two days post-infection with *C. rodentium*. Mice treated with *S. boulardii* regained the weight lost in the first two days post-infection. In addition, transmission electron micrographs of the colonic epithelium of treated mice showed decreased colonization by *C. rodentium* and decreased morphological changes to the microvilli. *C. rodentium* and *S. boulardii* were co-colonized to analyze the effects of the yeast on T3SS effector secretion *in vitro*. Western blot analysis of the secretome and the cell lysates indicated that *S. boulardii* inhibited secretion of EspB and Tir without affecting their expression.

1.5 Conclusion

EPEC and EHEC are major pathogens that infect thousands of children every year in developing nations. These pathogens rely on the T3SS, a bacterial injectosome, to adhere to the colonic epithelium and propagate infection. The T3SS is a syringe-like megastructure encoded by the LEE pathogenicity island that connects the bacterial cytosol to the cytoplasm of the targeted eukaryotic host cell. Once attached, the bacteria secrete effector proteins through the T3SS into the epithelial cells. These effectors then alter host cell machinery and signaling pathways to better suit the bacteria for infection and evade host immune responses. While laboratory research on inhibition of the T3SS in *E. coli* and the mouse model pathogen *C. rodentium* has resulted in the identification of multiple natural product and small molecule inhibitors, there are currently no drugs on the market that target the T3SS directly.

This dissertation will describe the development of a novel assay for the analysis of T3SS activity in *C. rodentium*. This solution-based assay allows for more rapid screening of compounds than what is currently possible without relying on mammalian host cells. Here we will describe the development and optimization of this assay and deliver screening results for compounds specifically chosen to elucidate unknown mechanistic relationships between the T3SS and other bacterial systems.

CHAPTER 2

DEVELOPMENT OF ASSAYS FOR MONITORING T3SS ACTIVITY

2.1 Introduction

The T3SS is an attractive target for antivirulence treatment of bacterial infections. Many known inhibitors of the T3SS are natural products derived from plants, fungi, or other bacteria, originally produced to protect from bacterial invasion. With this understanding, we sought to develop an assay to screen for natural product inhibitors of the T3SS as a starting point for SAR analysis that may lead to a therapeutic. We were also interested in studying the relationships between the T3SS and other mechanisms present within bacterial pathogens.

Since the discovery of the T3SS in the 1990s, multiple assays have been employed for the purpose of analyzing T3SS activity. One strategy involves direct detection of native secreted proteins. Heterologous proteins chosen for the purpose of detection have also been used. Most assays rely on the successful translocation of effectors or attachment of bacteria to eukaryotic host cells.

2.1.1 Western blotting and ELISAs.

The direct detection of secreted effector proteins has been performed using Western blotting or ELISA assays utilizing commercially available antibodies targeting relevant effector proteins. These protocols have been employed to reliably indicate the changes in expression or secretion of effector molecules after the bacteria have been treated with an inhibitor, though these are usually performed to further characterize compounds identified using another method. For example, aurodox was discovered through EPEC-mediated hemolysis of RBCs. When

characterizing aurodox as an inhibitor of the expression of the LEE, the accumulation of certain effectors within the bacteria was visualized by Western blotting.

Immunochemical methods are often employed to indicate changes in the levels of effector secretion. Regacin, an inhibitor of the T3SS of *C. rodentium*, is effective at abrogating infection in *in vivo* mouse models. Regacin competitively targets a regulator of LEE expression. While it was shown that regacin is efficacious enough to inhibit the propagation of infection, Western blotting analysis indicated that expression of the LEE is never entirely inhibited after treatment with this compound. This result was important in that it established that T3SS activity does not need to be entirely abolished for a treatment to be physiologically effective.

2.1.2 Hemolysis of RBCs.

EPEC and EHEC can lyse RBCs as a result of the introduction of pore forming proteins EspB and EspD into the erythrocyte cell membrane. When the pore is formed, the cells are lysed, releasing hemoglobin into solution. The concentration of hemoglobin in solution can then be quantified by absorbance, indicating performance levels of the T3SS. This technique has been used to identify multiple inhibitors of the EPEC T3SS, including aurodox and guadinomines B and D.

While this method has shown to be effective in the discovery of inhibitors, its reliance on translocation of effectors gives no indication to the mechanism of inhibition. This assay also requires fresh red blood cells, since the erythrocyte will lyse much more easily after a few weeks. In addition, further analysis of any identified compounds is necessary. It is possible that iron-chelation would result in a false-positive result, but controls of solubilized hemoglobin are rarely run in tandem with these experiments.

2.1.3 Adhesion assays.

The T3SS is a major contributor to the ability of bacterial cells to adhere to eukaryotic host cells. Some analysis into the ability of compounds to inhibit cellular adhesion have been performed to compliment screens of potential T3SS inhibitors. These assays typically involve fluorescence microscopy to visualize the adherence of the bacteria to the cell surface. Since EPEC, EHEC, and *C. rodentium* are AE pathogens, pedestal formation and changes in eukaryotic morphology may also be noted. These assays are not sufficient for stand-alone screening for T3SS inhibitors because they do not exclude other methods of bacterial adhesion to host cells as targets, so further exploration to determine the mechanism of inhibition is necessary.

2.1.4 Translocation of detection molecules.

CyaA. *Bordetella pertussis,* the causative agent of whooping cough, produces an adenylate cyclase toxin, CyaA.[369] This toxin is dependent on calmodulin, a component of eukaryotic cells, which increases turnover of CyaA by approximately 1000-fold. CyaA has been fused to effector proteins for T3SS-dependent translocation into host cells, where it increases cAMP levels. The concentration of cAMP can then be quantified as a measure of T3SS activity. This reporter system has been used to identify that the pore-forming protein EspB also enters the host cell cytoplasm, rather than remaining membrane-bound.[370] It has also been used to identify the N-terminal secretion signal of Tir.[371]

B-lactamase. A β-lactamase reporter system was developed to identify and to characterize the secretion signals necessary for type III-dependent secretion of Cif, an effector protein necessary for actin-rearrangement in bacterial attachment to host cells.[227] In this method, host cells were incubated with a substrate of β-lactamase, CCF2/AM. CCF2/AM is cell-permeable, non-

fluorescent esterified pro-substrate. Upon cell entry, native esterases cleave CCF2/AM and release the β-lactamase substrate CCF2. CCF2 consists of a cephalosporin linker connecting fluorescein and hydroxycoumarin and is often used in Förster resonance energy transfer (FRET) applications. When hydroxycoumarin is excited at 409 nm, the resulting fluorescent emission excites fluorescein. Fluorescein then emits a fluorescent signal at 520 nm. This result depends on their close proximity. In the bacterial cell, β-lactamase is expressed with an N-terminal secretion tag which allows the enzyme to be translocated into the host cell through the T3SS. β-lactamase then acts upon the CCF2 substrate, cleaving and separating the hydroxycoumarin and the fluorescein, ending their FRET interactions. Therefore, successful translocation of β-lactamase into the host cell can be monitored by decreases in the fluorescent signal at 520 nm.

Green fluorescent protein (GFP). There are two versions of the GFP translocation assay. In one version, the T3SS-harboring bacterial cell is made to express an effector-GFP conjugate. This fused protein is then translocated via the T3SS into a eukaryotic host cell, and accumulation of the effector can be monitored by fluorescence microscopy. This method has been used to determine localization points for specific effectors in regions of the eukaryotic cell.

The second version of the GFP translocation method involves split-GFP. The bacteria are made to express a fused protein consisting of an effector and GFP1-10, a non-fluorescent subunit of GFP. This conjugate is then translocated via the T3SS into a eukaryotic host cell that expresses GFP11. Upon interactions between GFP1-10 and GFP11, the molecule becomes fluorescent. T3SS activity can therefore be quantified as a function of fluorescence. This method has typically been used to indicate localization patterns of effectors within host cells. Given that this method does not rely on host cell enzymes for signal production, our initial efforts in assay development began with a split-GFP system.

Nature has been producing inhibitors of T3SS activity to protect itself from infection by bacterial pathogens, giving precedence for the effectiveness of T3SS inhibitors for abrogation of infection. Further development of T3SS inhibitors as therapeutics is ongoing, but results have so far indicated that this is a promising strategy. This dissertation describes the development of an assay for the identification and in vitro characterization of inhibitors of the T3SS in *C. rodentium* through the following aims:

Aim 1. Develop a screening assay that quantifies T3SS activity as a function of secreted protein or enzyme. This assay will not require eukaryotic cells to lend simplicity to the method and allow for easier replication of results.

Aim 2. Screen for inhibitors of the T3SS and identify natural products that are capable of inhibiting the T3SS. These compounds will be rationally chosen based on their known bioactivity as inhibitors of the T3SS of other organisms, inhibitors of quorum sensing, or as antibiotics.

2.2 Experimental

2.2.1 Materials

Media was purchased from Difco™ (LB broth), Amresco (SOB broth) and Gibco™ (DMEM without glucose). The antibiotic chloramphenicol was purchased from Fisher. Aurodox, piericidin A and fusaric acid were purchased from Santa Cruz Biotechnology, Inc. (Dallas, TX). Carvacrol, thymol and *trans*-cinnamaldehyde were purchased from Tokyo Chemical Industry Co, Ltd. (Portland, OR). (-)-Epigallocatechin-3-gallate, oligomycin A and nosiheptide were purchased from Cayman Chemical Company (Ann Arbor, MI). Gallocatechin gallate, berberine chloride and *trans*-4-nitrocinnamaldehyde were purchased from Alfa Aesar (Haverhill, MA). *trans*-4-Methoxycinnamaldehyde, ellagic acid and patulin were purchased from Acros Organics B.V.B.A.

(Fair Lawn, NJ). *trans*-4-Dimethylaminocinnamaldehyde was purchased from Chem-Impex Int'l, Inc. (Wood Dale, IL). Tannic acid, N-(β-ketocaproyl)-L-homoserine lactone, N-(*p*-coumaroyl)-L-homoserine lactone, phloretin, 3-oxo-N-(2-oxocyclohexyl)-dodecanamide, N-(3-oxooctanoyl)-L-homoserine lactone, and penicillic acid were purchased from Sigma-Aldrich (St. Louis, MO). 2-Heptyl-3-hydroxy-4(1H)-quinolone was purchased from Chemodex (St. Gallen, Switzerland). Bergamottin was purchased from Honeywell Fluka™ (Morris Plains, NJ). Naringenin was purchased from Combi-Blocks, Inc. (San Diego, CA). Rotenone was purchased from Enzo Life Sciences, Inc. (Farmingdale, NY). Sanguinarine chloride was purchased from J&K Scientific (Beijing, China). Curvularin and harzianopyridone was purchased from AdipoGen Life Sciences (San Diego, CA).

2.2.2 Cell lines

The *cpg2* gene was amplified using polymerase chain reaction (PCR) with primers ALJ82 (5'-cgctgcttctacactagggcggcagcttgtaggtatcgcaGCTCTGGCTCAGAAACGTGA-3') and ALJ84 (5'-TTACTTACCTGCACCCAGATCCA-3'), that were purchased from Life Technologies. The pBAD vector, purchased from Thermo Fisher Scientific, was amplified using PCR with primers ALJ89 (5'-ATCTGGGTGCAGGTAAGTAAGTTGCTCAGGTTTCACTTGTTTTCA-3') and ALJ88 (5'- gccctagtgtagaagcagcgTTACTAATTCCATTAAGCATGGTTAATTCCTC-CTGTTAGCCCAAA-3') purchased from Invitrogen (Carlsbad, CA). The lowercase sequences indicate the EspF secretion signal that was incorporated via PCR. Amplification was performed using HS-Taq DNA polymerase (New England BioLabs®, Inc.). Amplified fragments were gel purified and the recombinant plasmid was assembled using the isothermal Gibson method on a T100 Thermal Cycler (Bio-Rad, Hercules, CA). *C. rodentium* DBS100 (ATCC 51459) cells were

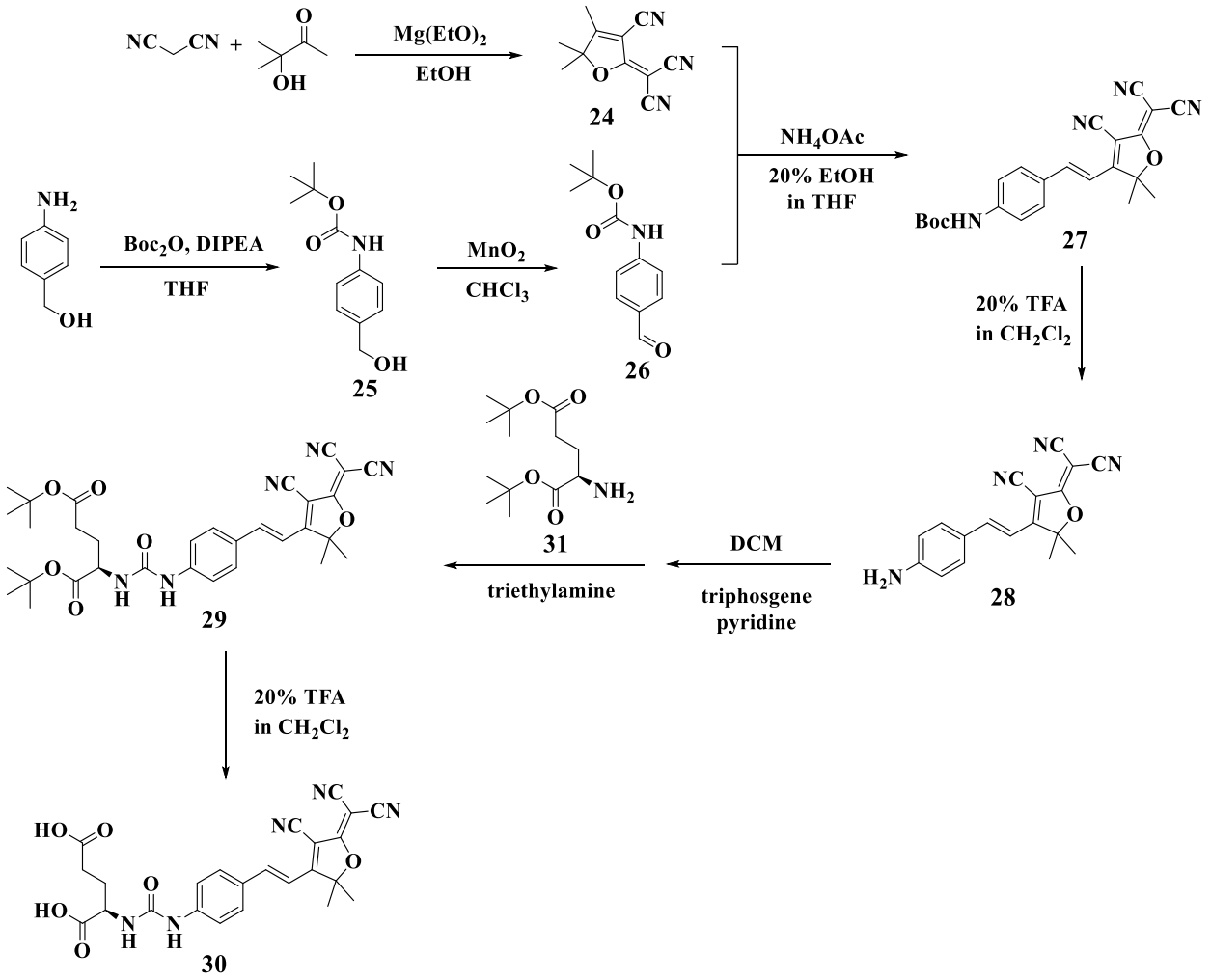
made competent by washing 2x with ice cold 10% glycerol. 70 μL-aliquots of competent *C. rodentium* cells were transformed with the pBAD-EspF-CPG2 plasmid by electroporation using a BIORAD Micropulser™ on the E1 setting. Cells were immediately resuspended in preheated SOB media and incubated at 37 °C for one hour. 5 μL, 100 μL, and concentrated pellet samples of cells were spread on LB agar plates containing 30 μg/mL chloramphenicol and incubated overnight at 37 °C. Transformants were confirmed by DNA sequencing using pBAD forward and reverse primers.

2.2.3 Enzyme expression and lysate production

1 mL of overnight culture of *C. rodentium*-EspF-CPG2 was added to 1 L LB media containing 30 μg/mL chloramphenicol and 1% arabinose (purchased from Alfa Aesar at 99% purity, resuspended in DI water and sterile filtered with a Gelman Laboratory Acrodisc® syringe filter, 0.2 μm) and grown overnight at 37 °C with shaking. Cells were pelleted by centrifugation at 4000 rpm for 20 minutes at 4 °C. Pellets were resuspended with 25 mL CPG2 buffer. Cells were lysed by sonication with a Fisherbrand™ Model 120 Sonic Dismembrator with the 1/8-inch probe. Lysate was centrifuged again to remove cellular debris before aspirating off the liquid layer.

2.2.4 Synthesis of Glu-CyFur

The Glu-CyFur substrate was synthesized as previously described.[372] The synthesis follows Scheme 1. This seven-step synthesis produced ~3 grams of material that were used for the completion of this project.



Scheme 1. Synthesis of Glu-CyFur.

The synthesis of Glu-CyFur followed the previously published synthetic scheme.[372] The synthesis involved the production of 4-(Boc-amino)benzaldehyde (**26**) and 3-cyano-2-dicyanomethylene-4,5,5-trimethyl-2,5-dihydrofuran (**24**).[373,374] **24** and **26** were then coupled via condensation in the presence of ammonium acetate to give (E)-*tert*-butyl-4-(2-(4-cyano-5-(dicyanomethylene)-2,2-dimethyl-2,5-dihydrofuran-3-yl)vinyl)phenylcarbamate (**27**).[375] Following acid-dissociation of the Boc protecting group, the aniline was activated for alkylation

with triphosgene, then alkylated with Boc-protected glutamate to give **29**.[372] Deprotection of **29** gave Glu-CyFur (**30**). Products were confirmed by NMR or tracked by TLC.

3-Cyano-2-dicyanomethylene-4,5,5-trimethyl-2,5-dihydrofuran (24). 3-Hydroxy-3-methyl-2-butanone (1.03 mL) and malononitrile (1.63 mL) were mixed with 32 mL EtOH. Magnesium ethoxide (1.26 g) was added to the solution before heating at reflux overnight. The solution turned from light red to dark brown overnight. The solution was cooled to room temperature and concentrated by rotary evaporation, affording a dark brown sludge. The residue was suspended in dichloromethane and filtered to remove a dark solid. The filtrate was then concentrated again by rotary evaporation, yielding a dark red residue. This residue was washed with deionized water. The remaining residue was dissolved in heated ethanol and recrystallized to form a fluffy light solid (0.358 g, 20.5%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.63 (6H, s), 2.36 (3H, s).

4-(Boc-amino)benzyl alcohol (25). *p*-Aminobenzyl alcohol (543 mg) was dissolved in anhydrous dioxanes. DIPEA (0.8 mL) and di-tert-butyl dicarbonate (1 mL) were added to the solution, which was heated at reflux overnight. The solution was then cooled to room temperature and evaporated under vacuum. The residue was dissolved in ethyl acetate and washed with HCl (0.1 N) solution to remove unreacted starting material. The organic layer was then dried with magnesium sulfate and evaporated under vacuum to give 1.2 g. The crude product was carried forward without purification. ^{1}H NMR: δ 1.55 (9H, s), 1.71 (1H, s), 4.66 (2H, s), 7.29 (1H, s), 7.32 (2H, d, J = 8.6), 7.38 (2H, d, J = 8.4).

4-(Boc-amino)benzaldehyde (26). The crude product (**25,** 1 g) was dissolved in dry dichloromethane in a 20-dram vial. Manganese dioxide was added in excess (~4 equivalents). The reaction vessel was immersed in a sonicator (Bransonic B200 Ultrasonic Cleaner) which ran continuously. The sonication added kinetic energy and heat to the reaction. Reaction progress was monitored by thin layer chromatography (TLC) stained with vanillin. Once the starting material was fully converted to the aldehyde product, the mixture was filtered through celite and concentrated in vacuo. The residue was dissolved in ethyl acetate and the components were separated by silica gel chromatography (EtOAC:hexanes, 1:1, Rf = 0.5) before being evaporated in vacuo (0.98 g, 98%).

(E)-*tert*-Butyl-4-(2-(4-cyano-5-(dicyanomethylene)-2,2-dimethyl-2,5-dihydrofuran-3-yl)vinyl)phenylcarbamate (27). 24 (297.1 mg) and **26** (555 mg) were dissolved in 10 mL of a 20% ethanol solution in dioxane. Once dissolved, ammonium acetate (250.9 mg) was added to the solution, which was set to stir overnight at room temperature. After 12 hours, the solution was diluted with deionized water (1:1) and the product was extracted 3 times with 15 mL EtOAc. The EtOAc was then washed with brine and dried over sodium sulfate and filtered. The filtrate was concentrated in vacuo and the product was purified by silica gel chromatography (EtOAc:hexanes, 1:2, Rf = 0.25). The reddish yellow product were pooled and concentrated in vacuo (599.2 mg, quantitative yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.52 (6H, s), 1.53 (9H, s), 7.45 (1H, d, J = 8.6 Hz), 7.53 (2H, d, J = 8.6 Hz), 7.71 (1H, d, J = 8.6 Hz), 7.82 (2H, d, J = 8.6).

(E)-2-(4-(4-Aminostyryl)-3-cyano-5,5-dimethylfuran-2(5H)-ylidene)malononitrile (28). 27 (599.2 mg) was dissolved in 40 mL of 20% TFA in dichloromethane. The solution was stirred for

2 hours at room temperature before concentrating to the powder product (448.7 mg, quantitative yield).

(R,E)-Di-tert-butyl-2-(3-(4-(2-(4-cyano-5-(dicyanomethylene)-2,2-dimethyl-2,5-dihydrofuran-3-yl)vinyl)phenyl)ureido)pentanedioate (29). 28 (171 mg) and pyridine (0.24 mL) were added to dichloromethane (2.2 mL) and stirred on ice until cold. Triphosgene (1.32 mL) was added dropwise and the solution was stirred on ice for 1 hour. The solution was then concentrated in vacuo and the residue was diluted with triethylamine (0.92 mL). **31** (676.25 mg) was added to the solution and dissolved. The reaction stirred at room temperature for 1 hour before being diluted in deionized water. The product was extracted 3 times with dichloromethane (1 mL). The organic layer was then washed with 1% HCl followed by a brine wash. The solution was dried over sodium sulfate and filtered before the volume was reduced in vacuo. The product was then separated on a silica gel column (EtOAc:hexanes, 1:1, Rf = 0.4). Collected 50 fractions. NMR confirmed the product in fraction 36. Fractions 31 to 45 were pooled and concentrated by rotary evaporation, yielding a bright red solid (139.6 mg, 42%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (2H, m), 1.46 (9H, s), 1.50 (9H, s), 1.81 (6H, d, J = 8.2 Hz), 1.99 (1H, m), 2.12 (1H, m), 2.39 (2H, m), 4.41 (1H, m), 7.01 (1H, d, J = 16.2 Hz), 7.46 (1H, d, J = 8 Hz), 7.55 (4H, q, J = 8.6, J = 11.9), 7.70 (1H, d, J = 8.5).

Glu-CyFur (30). 29 (139.6 mg) was dissolved in 20% TFA in dichloromethane (2 mL) and set to stir at room temperature for 1 hour. The product was concentrated by rotary evaporation to give the final Glu-CyFur product (108.3 mg, quantitative yield).

2.2.5 Qualitative Glu-CyFur concentration analysis

Cell lysate containing CPG2 was diluted 1:1 with CPG2 stability buffer (CPG2 buffer: 50 mM Tris pH 7.4, 0.1 mM ZnSO4, 0.04% Tween 20). Glu-CyFur was added to the listed concentrations and DMSO concentration was normalized. As a control, Glu-CyFur was added directly to the CPG2 stability buffer to the listed concentration. After incubating at room temperature for 30 minutes, the photo was taken to document the degree of color change.

2.2.6 Temperature stability testing

Cell lysate containing CPG2 was aliquoted into PCR tubes (0.1 mL each). The tubes were incubated at the listed temperatures in a T100 Thermal Cycler (Bio-Rad Laboratories, Hercules, CA) for 25 minutes before the temperatures were unified at 37 ˚C. Glu-CyFur was added to 50 μM and the solutions incubated at room temperature for 20 minutes. The absorbance at 570 nm was then recorded.

2.2.7 Compound screening

An overnight culture of *C. rodentium*-EspF-CPG2 (grown in LB containing 30 μg/mL chloramphenicol) was diluted 1:100 in LB containing 30 μg/mL chloramphenicol and the test compound. After three hours, the cells were pelleted by centrifugation and resuspended to an absorbance measurement at 600 nm (OD_{600}) of 0.75 in Dulbecco's modified Eagle's medium (DMEM) with 1% arabinose to initiate T3SS expression and CPG2 production. The DMEM also contained the compound or a vehicle control. After 6 hours incubation at 37 °C, cells were pelleted and supernatant was diluted 1:1 in buffer designed to aid in CPG2 activity (CPG2 buffer: 50 mM Tris pH 7.4, 0.1 mM ZnSO4, 0.04% Tween 20) in a Greiner Bio-one polypropylene black, F-

shape, 384-well plate. Controls with vehicle or lacking arabinose were used. The substrate Glu-CyFur (Figure 2B) was added to each well to a final concentration of 10 µM, and fluorescence was measured with a BMG Labtech CLARIOstar© Plus plate reader, where λ_{ex} = 563 nm and λ_{em} = 610 nm. As glutamate is cleaved by CPG2, fluorescence increases.

2.2.8 Cytotoxicity screening

An overnight culture of *C. rodentium* was grown in LB media at 37 °C with shaking. The culture was diluted 1:100 in LB before compounds were added at the concentrations listed and vehicle was used as a control. 0.5-mL culture replicates of 5 were left to incubate for 6 hours in CytoOne 96-well flat bottom plates with the lid at 37 °C, with shaking in the BioTek Synergy HTX plate reader and incubator. Cell density was measured as OD_{600} once every hour with the BioTek Synergy HTX plate reader and incubator, beginning at the time of dilution.

2.2.9 CPG2 direct inhibition analysis

These studies were conducted to ensure the compounds were not interfering with the ability of CPG2 to cleave Glu-CyFur. 1 mL of overnight culture of *C. rodentium*-EspF-CPG2 was added to 1-L LB media containing chloramphenicol and 1% arabinose and grown overnight at 37 °C with shaking. Cells were pelleted by centrifugation at 4000 rpm for 20 minutes at 4 °C. Pellets were resuspended with 25 mL CPG2 buffer. Cells were lysed by sonication with a Fisherbrand™ Model 120 Sonic Dismembrator with the 1/8-inch probe. 50 µL of cell lysate containing CPG2 was transferred to a Greiner Bio-one Polypropylene black, F-shape, 384-well plate. Compound was added to the concentration listed, and vehicle was used as a control. Glu-CyFur was added to 10

μM with a Labcyte Echo550 acoustic liquid handler, and fluorescence was observed on a BMG Labtech CLARIOstar© Plus plate reader (λ_{ex} = 563 nm and λ_{em} = 610 nm).

2.2.10 Data analysis

The % inhibition was calculated from the rate of change in fluorescence compared to an uninhibited control using the following equation:

$$\%\ Inhibition = 100 * \left(1 - \frac{m_C}{m_V}\right)$$

Where *m* = slope, *C* = compound, and *V* = vehicle

2.3 Split-GFP assay

2.3.1 Rationale and assay design

In understanding the standards of the field of T3SS research, we sought to develop a screening assay for utilization in our lab. We initially drove to develop a solution-based screen involving bacterial cells that would secrete a detector molecule into the extracellular space for analysis. Ideally, we would be able to perform this assay in a plate format which would allow for the testing of multiple compounds at once. To begin our design, we chose to modify one of the simpler assays known in the field, the split-GFP reporter system. Our first modification would be maintaining the gene for GFP1-10 on a plasmid with a secretion tag. We chose the secretion tag from EspF, as that was reported as one of the most efficient tags for heterologous secretion in *E. coli*. We also chose to keep the gene on a plasmid so that we could have independent control of GFP1-10 production, separate from T3SS activation. This independent control of production allows us to separate expression of the LEE from expression of our reporter enzyme. since many

inhibitors function by decreasing LEE expression, we did not want to depend on LEE expression for production of GFP1-10.

The next major modification made involved developing an assay that was not reliant on eukaryotic host cells. Most of the assays developed for monitoring T3SS activity involve host functions to work. For example, CyaA changes levels of eukaryotic proteins as a quantifiable measure. The β-lactamase assay depends on eukaryotic esterases to uncage CCF2 before functioning properly. Interferences in these systems would result in a false positive reading and would be difficult to discern or troubleshoot. We therefore decided to develop a simple assay with hits that were easy to confirm by removing the dependence on eukaryotic cells.

We were also interested in developing an assay that provided both quantitative and qualitative results. Many of the inhibitors of the T3SS have unknown mechanisms of action, and the discovery of their molecular targets is more difficult than it is for traditional antibiotics. Following treatment of a cytotoxic compound, random mutations that result in antibiotic resistance allow for selective growth of resistant strains. The only bacteria that will grow are those cells that are resistant to the antibiotic. Inhibition of the T3SS does not result in the death of the bacteria, so we wanted a qualitative signal that would signify an active—or inhibited—T3SS. This would allow for the screening of random mutants for strains resistant to a T3SS inhibitor. While we are still making progress toward that project, this motivated us to use the split-GFP reporter method.

2.3.2 Results and Discussion

The plasmid design and production were successfully completed by the laboratory technician Adam Johnson, MS. The *gfp1-10* gene was amplified using primers designed with hanging complementary overlaps with plasmid pBAD. The primers also incorporated an N-

terminal His6 tag. After PCR amplification of the plasmid and the gene of interest, the final plasmid was assembled using the Gibson method. The plasmid was introduced to *C. rodentium* DBS100 by electroporation and successful transformants were confirmed by nucleotide sequencing. Expression of GFP1-10 was confirmed by SDS-PAGE analysis and Western blotting using an anti-His antibody (Figure 18).

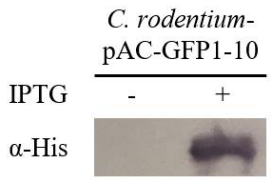


Figure 18. GFP1-10 was produced and secreted by *C. rodentium.* Bacterial cells were incubated for 6 hours in DMEM with or without IPTG to induce GFP1-10 expression from the pBAD plasmid. After incubation, cells were pelleted, and 1 mL of the supernatant was concentrated by TCA precipitation. 2 μL of supernatant was loaded into each lane. After transferring to a nitrocellulose membrane, the protein was visualized with anti-His6 primary antibody.

To perform this assay, *C. rodentium*-EspF-His-GFP1-10 was incubated in DMEM in the presence of screening compounds. DMEM activates the T3SS of *C. rodentium*. During this incubation, EspF-His-GFP1-10 production was initiated with IPTG. The cells were incubated until they reach the end of the log growth phase, typically after 6 hours. At that point, the cells were pelleted by centrifugation and the supernatant was aspirated off. GFP11 was added to the supernatant, and the fluorescent signal obtained correlated to the concentration of GFP1-10, which is dependent on T3SS activity.

The assay was never successful, though we could confirm by Western blot that the supernatant contained GFP1-10 (Figure 18). We hypothesized that not enough GFP1-10 was being secreted into the dilute supernatant to produce a signal above the lower limit of quantification. One of the limits of this design is that protein is secreted and diluted into the extracellular space. The GFP1-10 system works well in situations where GFP concentrates at a particular location within a cell, but our design appeared to produce insufficient signal. We therefore decided to move into a different design involving a secreted enzyme. The enzyme would be capable of substrate turnover so that every secreted molecule would produce an amplified signal.

2.4 CPG2 reporter assay

2.4.1 Rational and design

Results from the split-GFP design were not promising for a solution-based screen. Previous work with split-GFP has been conducted within compartmentalized systems, such as translocation to and localization within a eukaryotic cell observed through fluorescence microscopy. We concluded that diffusion of the GFP subunits within solution gave too weak of a signal for quantification in our system. Since the two subunits had to interact to form the fluorescent GFP, a large quantity of GFP 1-10 must be secreted into the supernatant for the signal produced to reach the lower limit of quantification. We therefore concluded that altering our design to secrete an enzyme would be beneficial. We could then rely on the catalytic turnover of the secreted enzyme to produce an amplified signal. By measuring the relative rate of change of fluorescence over time, we could perform a comparative analysis based on the concentration of enzyme in the extracellular space. Since the concentration of enzyme is dependent on type III secretion, higher concentrations

of enzyme in the supernatant would indicate an active T3SS, while lower concentrations of enzyme would indicate inhibition of the T3SS.

Yount et al. reported the secretion of a zinc-dependent protease, carboxypeptidase G2 (CPG2), from *S. enterica*.[372] CPG2 was fused to the C-terminus of *Salmonella* effector SopE2 and expressed with an HA tag for visualization. The SopE2-CPG2-HA construct was expressed on a pWSK29 plasmid under the control of the native SopE2 promoter. The enzyme was successfully secreted and refolded in the supernatant, as indicated by enzymatic activity. This system has been used to screen for inhibitors of the *Salmonella* T3SS in a 96-well plate. We chose to adapt this method for the screening of *E. coli* and *C. rodentium* T3SS inhibitors.

CPG2 is a metalloprotease that specifically cleaves glutamate residues. The assay described by Yount et al. utilizes a CPG2-specific substrate, glutamate-modified 2-dicyanomethylene-3-cyano-2,5-dihydrofuran (Glu-CyFur), which is fluorescent when cleaved by CPG2. Glu-CyFur has been characterized as an efficient CPG2 substrate ($k_{cat} = 0.25 \pm 0.03$ s^{-1}, $K_M = 1.87 \pm 0.53$ μM). When the glutamate residue on Glu-CyFur was replaced with aspartate, CPG2 would not cleave the substrate. The synthesis of Glu-CyFur has been described previously (Scheme 1).

We have altered the design of the CPG2 reporter system for compatibility with the LEE-encoded T3SS. We expressed CPG2 with the EspF N-terminal secretion tag, as reported previously. The EspF-CPG2 construct was expressed on a pBAD plasmid under the control of an arabinose-induced promoter rather than the LEE-encoded promoters (Figure 19). This independent control of expression allows observation of many mechanisms of T3SS inhibition. By having a consistently-expressed reporter enzyme, it is possible to observe any potential T3SS-mediated secretion. In contrast, studies have indicated that some promoter regions are not essential for all

T3SS-mediated expression and downregulation may decrease T3SS activity without inhibiting it entirely. If an inhibitor targeted the promoter region controlling CPG2 expression in our system, it may only inhibit CPG2 transcription rather than T3SS activity. By controlling CPG2 expression with a well-characterized promoter that is not related to the LEE, we can more definitively characterize any observed inhibition.

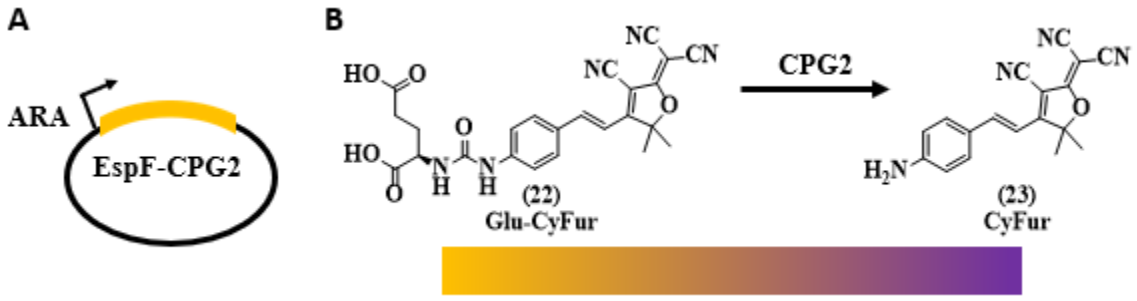


Figure 19. A plasmid was constructed to produce CPG2 for the purpose of enzymatic cleavage of the Glu-CyFur substrate. **A**) The gene for CPG2 was tagged on the N-terminus with the secretion signal from effector EspF. Expression of EspF-CPG2 is under the control of an arabinose promoter. **B**) CPG2 cleaves the non-fluorescent, yellow substrate Glu-CyFur (**22**), releasing fluorescent, purple compound, CyFur (**23**).

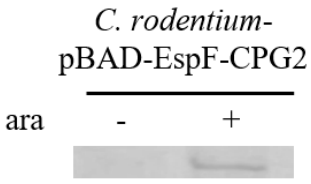


Figure 20. *C. rodentium* was made to produce CPG2 with the N-terminal secretion tag from EspF. Protein production was induced with arabinose (ara) and the cells were

incubated for 6 hours before cells were pelleted and 1 mL of the supernatant was concentrated using TCA precipitation. 5 μL was loaded into each lane.

The initial design of the CPG2 reporter assay was typical of an EPEC screening assay in that it involved an incubation period with compounds, an incubation period to allow for optimal T3SS-mediated accumulation of enzyme in the supernatant, and a quantification step. In this scheme, the *C. rodentium* cells are incubated in DMEM with arabinose to initiate T3SS activity and CPG2 production. Any compounds being screened for inhibitory activity are also present at this stage to inhibit initiation of type III secretion. After six hours of incubation, the previously-determined time for maximal effector accumulation, the bacteria are pelleted by centrifugation, and the supernatant is removed. The supernatant is then diluted 1:1 in a buffer specifically designed to aid in CPG2 folding and enzymatic activity. Glu-CyFur is added to the supernatant to a final concentration of 10 mM immediately before fluorescence measurement. Fluorescence is measured for approximately 10 minutes and the initial slope is quantified as a measure of T3SS activity.

2.4.2 Assay optimization

Analysis of enzyme stability. CPG2-mediated cleavage of Glu-CyFur is visible to the naked eye (Figure 20). Uncleaved substrate is yellowish orange in appearance, and cleavage results in a purple color. The ease of observation allowed for qualitative analysis of enzymatic activity under different environmental conditions. For these initial studies, EspF-CPG2 was overexpressed in *C. rodentium*. The cells were washed and lysed by saponification in CPG2 buffer. This lysate was then used to confirm enzymatic activity of the tagged enzyme, test for pH stability, and analyze

a range of concentrations of Glu-CyFur for optimization of visual results. The tagged enzyme was found to be active with no changes in performance at pH between 7 and 1.5.

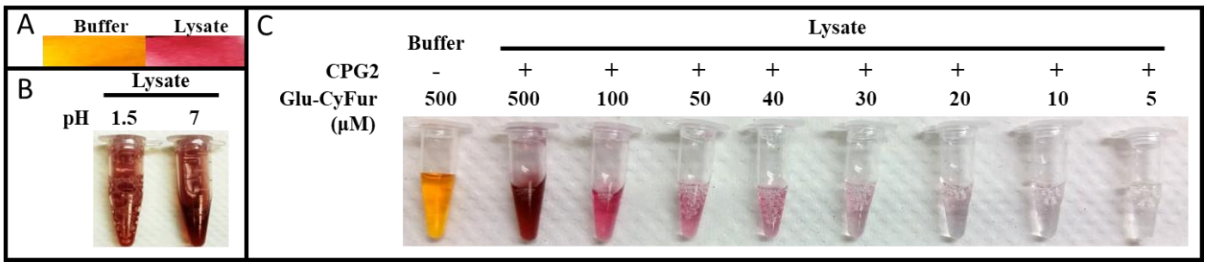


Figure 21. Initial qualitative studies on enzyme production by *C. rodentium*. **A**) 500 μM Glu-CyFur in buffer or whole-cell lysate containing CPG2. **B**) Acid stability screening; whole-cell lysate containing CPG2 adjusted to pH = 1.5 before adding 500 μM Glu-CyFur. There is no observable change to CPG2 activity with pH. **C**) Visible color change for differing concentrations of Glu-CyFur.

Multiple concentrations of Glu-CyFur were analyzed for their appearance after cleavage by CPG2. Analysis of inhibition may be analyzed visually as well as quantified with fluorescence. In the initial stages of compound analysis, controls were analyzed visually in addition to quantifying the fluorescent signal to confirm the success of the attempt. These initial qualitative analyses aided in observational conclusions drawn from screening. We also analyzed the effect of temperature on the stability of CPG2. Cell lysate containing CPG2 was incubated at temperatures ranging from 37 ˚C to 55 ˚C before analyzing the resulting activity. The Glu-CyFur substrate may be analyzed by absorbance (at 570 nm) as well as fluorescence. We measured the absorbance at 570 nm for the solutions after incubation at the listed temperatures (Table 3) and determined that,

while the resulting values differ greatly depending on temperature, the difference between the lysate of induced cells and uninduced cells was consistent.

Table 3. CPG2 activity is affected by temperature. Cells were incubated with or without 1% arabinose to induce CPG2 production. The cells were then lysed by sonication, resulting in a solution containing the active enzyme. The lysate was aliquoted (100 µL) into PCR tubes and incubated at the listed temperatures for 25 minutes before the temperature was unified to 37 ˚C. Glu-CyFur was added to 50 µM and the absorbance at 570 nm was observed.

Temperature (˚C)		37	38.2	40.3	43.9	48.1	51.2	53.5	55
Arabinose	+	0.535	0.633	0.581	0.765	0.948	0.869	0.84	1.302
	-	0.147	0.164	0.178	0.18	0.27	0.38	0.52	0.72

Quantification of signal. Since a version of this assay was previously published, much of the method was already established. Optimization studies for the CPG2 buffer contents and concentrations, Glu-CyFur concentrations, compound concentrations, and incubation times were all reported previously. The analyses we performed included the media for incubation and arabinose concentrations.

We observed changes in the performance of the assay when the incubations were performed in LB vs DMEM (Figure 22). We initially hoped to perform the CPG2 expression and compound incubation during the logarithmic growth phase, as was done for the *Salmonella* CPG2 reporter assay. Unfortunately, the signal we were able to obtain was much lower than expected. We then attempted the assay in DMEM. The results indicated that we were secreting more CPG2 after DMEM incubation than after LB incubation. The *C. rodentium* T3SS is not activated in LB,

while switching to DMEM is well understood to be a T3SS activating strategy. In addition, glucose acts as an inhibitor of arabinose-induced expression.

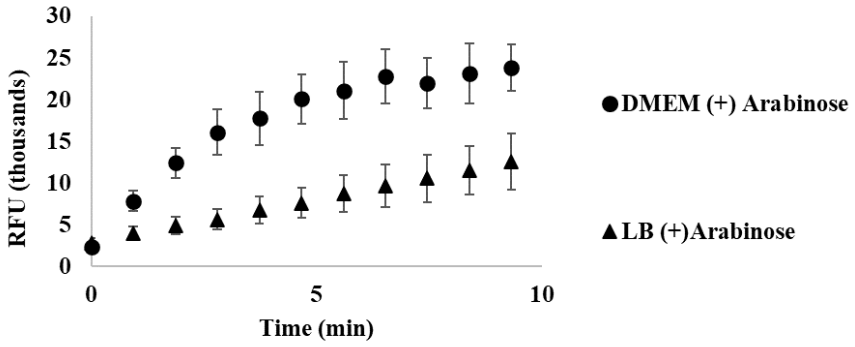


Figure 22. The media the cells are incubated in during CPG2 induction affects the amount of CPG2 secreted. DMEM incubation results in much higher CPG2 activity in the supernatant.

We analyzed the effects of the addition of glucose to the DMEM. Glucose (4.5 g/L) appeared to inhibit CPG2 expression entirely, while incubating the cells in DMEM that did not contain glucose with 1% arabinose increased the resultant signal (Figure 23). We chose to analyze 4.5 g/L of glucose because that is glucose content of the LB media used. The expression of CPG2 may not have been entirely inhibited in the initial LB study due to the growth of the bacteria in LB and the consumption of the glucose by the bacteria. Since the *C. rodentium* do not grow during the DMEM incubation, glucose consumption is lessened, and expression is inhibited to a greater extent.

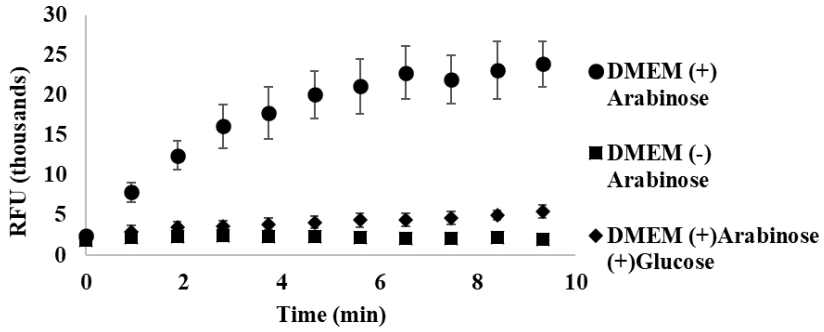


Figure 23. Glucose inhibits arabinose induction of CPG2. Adding 4.5 g/L glucose to the DMEM results in inhibited CPG2 secretion similar to the uninduced cells.

We analyzed the arabinose content and the effect it had on signal generation. The concentrations of arabinose tested were 1%, 5%, and 10% (wt/vol %) in DMEM with chloramphenicol. After a 6-hour incubation of *C. rodentium* harboring the EspF-CPG2 construct, the activity of secreted CPG2 was analyzed. The results indicated that the 5% arabinose concentration performed as well as the 10% samples. The uninhibited slope was slightly higher for the 5% arabinose samples. Our goal was to produce CPG2 at a slow rate to reduce the accumulation of folded enzyme in the cytosol before secretion, so we analyzed different conditions to improve the 1% arabinose signal.

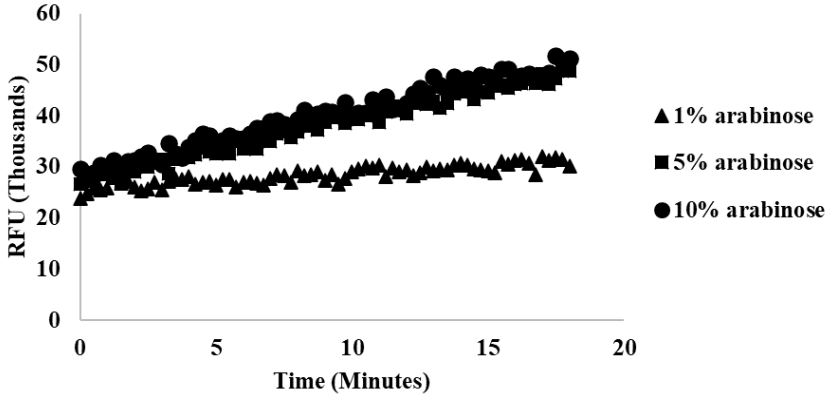


Figure 24. During the incubation period, arabinose is present to induce CPG2 production. At 1% arabinose, the signal produced is much lower than when arabinose is present at 5% or 10%.

The next condition we chose to optimize was the ratio of supernatant to CPG2 buffer. In the original publication of this method, the supernatant is diluted into a buffer specifically designed to aid in CPG2 performance. Since the enzyme must be linearized to pass through the T3SS and then refolded in the extracellular space, the presence of a buffer to aid in the refolding and enzymatic activity of the metalloprotease is justified. The reported buffer:supernatant ratio was 90:10. We were interested in how changing the concentration of supernatant would affect signal, and if signal would be negatively impacted by increased concentrations of poorly-folded CPG2. We analyzed the change in signal produced when the buffer:supernatant ratio is adjusted to 50:50 (Figure 24). With a larger proportion of the solution being supernatant, we found that we could get similar performance between 1% arabinose incubation and 5% arabinose incubation. With this improvement in signal, we moved forward with studies utilizing 1% arabinose during incubation and a 50:50 ratio of buffer:supernatant before introduction of the supernatant.

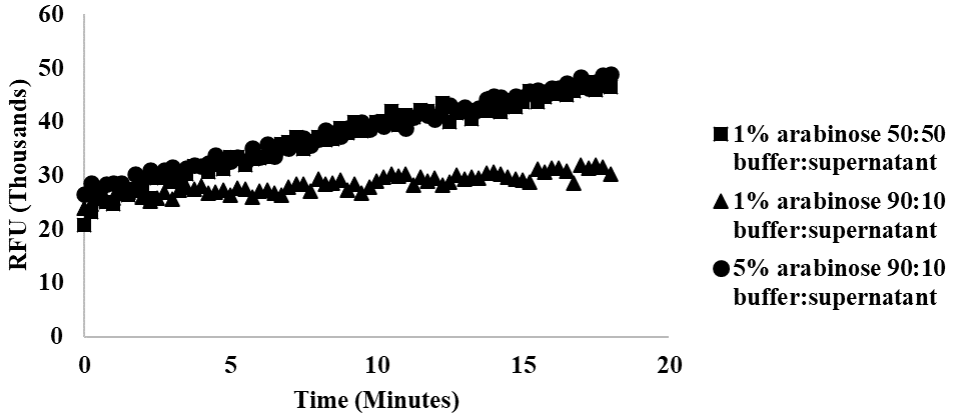


Figure 25. The buffer:supernatant ratio used in analysis has a large effect on performance. When the ratio of buffer:supernatant is 90:10, the signal obtained in the presence of 1% arabinose is significantly lower than when 5% is present. That activity is regained if the buffer:supernatant ratio is changed to 50:50.

Once the reagents and conditions for the assay were optimized, we decided to test the sensitivity of our assay. Regacin is a known inhibitor of the *C. rodentium* T3SS.[16] Regacin was originally discovered as a competitive inhibitor of transcriptional regulator RegA. Regacin interferes with the ability of RegA to bind to DNA by interacting with a conserved DNA-binding motif on RegA. SDS-PAGE analysis of the secreted protein profiles of a RegA knockout compared to *wt* ± regacin indicated that altering RegA activity downregulated T3SS expression without showing cytotoxicity or inhibiting bacterial cell growth. Compared to the *wt* control, effectors EspA, EspB, EspD and Tir show decreased concentrations in the supernatant in the presence of regacin. Importantly, however, they are still visibly secreted and make up a majority of the secretome. This decrease in T3SS-mediated secretion still proved capable of abrogating colonization of mouse colons though the T3SS was not entirely inactive.

We were interested in using regacin as an example of a partial inhibitor of the T3SS to analyze the sensitivity of our assay. By growing *C. rodentium*-EspF-CPG2 in the presence of 400 μM regacin (10-fold higher than the IC_{50} against RegA) and then incubating the bacteria in DMEM + 1% arabinose and 400 μM regacin, we observed partial inhibition of CPG2 secretion (Figure 26). At this concentration, RegA is fully inhibited, so transcription of T3SS-related genes is downregulated. We observed this downregulation clearly in our assay while still seeing the secretion indicated by PAGE analysis performed previously.[16]

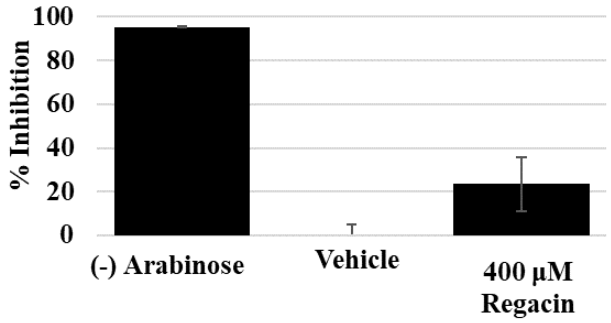


Figure 26. The CPG2 reporter assay can differentiate between partial and total inhibition. At 10X the IC_{50} concentration, regacin shows partial inhibition of the T3SS. Since regacin is only a partial inhibitor of type III secretion, these results indicate that our assay is sensitive enough to delineate partial and total inhibition.

After completing optimization studies and initial screening of inactive or partially inhibited T3SS, we began screening compounds. The compounds screened were chosen to analyze the relationship between T3SS activity and other cellular mechanisms, including epigenetic modification and quorum sensing. We also analyzed the known inhibitor EGCG and its analog gallocatechin gallate (GCG), which has not been analyzed previously. Some compounds, such as the SAs, inhibit the T3SSs of multiple organisms. For this reason, we screened known inhibitors of other T3SSs for their ability to inhibit in *C. rodentium*.

2.5 Results and discussion

2.5.1 Known *E. coli* T3SS inhibitors

Some compounds are known for their ability to inhibit the T3SS of *E. coli*, including aurodox, carvacrol, thymol, and EGCG. Aurodox was originally discovered as an antibiotic of

Gram-positive bacteria.[330] Recently, it has been characterized as a T3SS inhibitor in *C. rodentium* capable of attenuating infection in mice.[17] Studies on gene expression indicate that aurodox downregulates T3SS-related genes by an unknown mechanism.[25] Those same studies indicate that aurodox decreases the expression of *ler*, a major activator of the T3SS by 25% compared to untreated cells. In total, 25 of the 41 LEE-encoded genes were downregulated by treatment with aurodox.

The consequence of this downregulation on the secretion of effectors is not known. The authors analyzed the secretion of effectors Tir and EspB/D, which are all downregulated in the presence of aurodox.[25] They also analyzed the translocation of labeled effectors into mammalian cells, which requires the pore-forming activity of EspB/D. Because our assay does not depend on translocation into a host cell and does not measure the secretion of any particular effector, we are able to distinguish between the complete abolishment of secretion and downregulation of some effectors.

Our screen with aurodox indicate that, while the compound does decrease the amount of CPG2 secreted into the supernatant, some secretion still occurs at concentrations higher than the IC_{50} (Figure 27). We found that at 50 μM, secretion is inhibited to ~50%. The concentration-dependent data corroborates the published results in that *ler* downregulation decreases T3SS activity to some extent.[25] Importantly, the published data also showed that the structural proteins involved in the formation of the base of the T3SS are not downregulated. Our results indicate that secretion of effectors may be possible if the base is assembled.

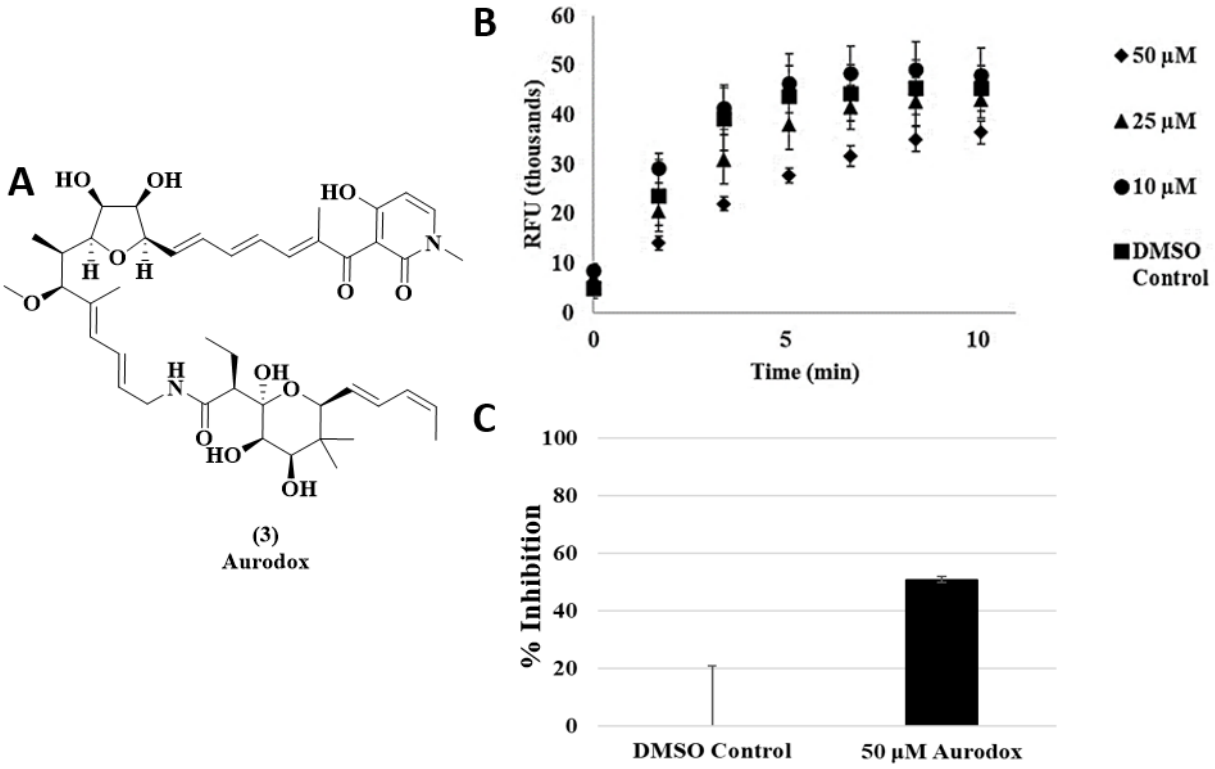


Figure 27. Aurodox (**3**) partially inhibits type III secretion. **A**) Increasing concentrations of **3** results in decreases in secretion of CPG2. **B**) High concentrations of **3** (50 µM, 10x the IC_{50} as determined by hemolysis assays) results in ~50% inhibition of secretion. **3** downregulates the expression of the major activator *ler*, without inhibiting secretion entirely.

Thymol and carvacrol are the principal compounds in thyme essential oil.[376] Thyme has a long history of being used for medicinal and culinary purposes in the Mediterranean and surrounding regions.[377] Their effects on EHEC virulence properties have also been explored.[378] In that study, the ability of thymol and carvacrol to alter the expression of virulence-related genes was observed. Thymol and carvacrol both downregulated genes related to chemotaxis, motility, and the T3SS through an unknown mechanism. The expression levels of *sepD* and *escC* were

described to have changed between "-1 and -5-fold" indicating mild downregulation of these genes. In our studies with thymol and carvacrol, we could not find evidence of observable inhibition of secretion (Figure 28).

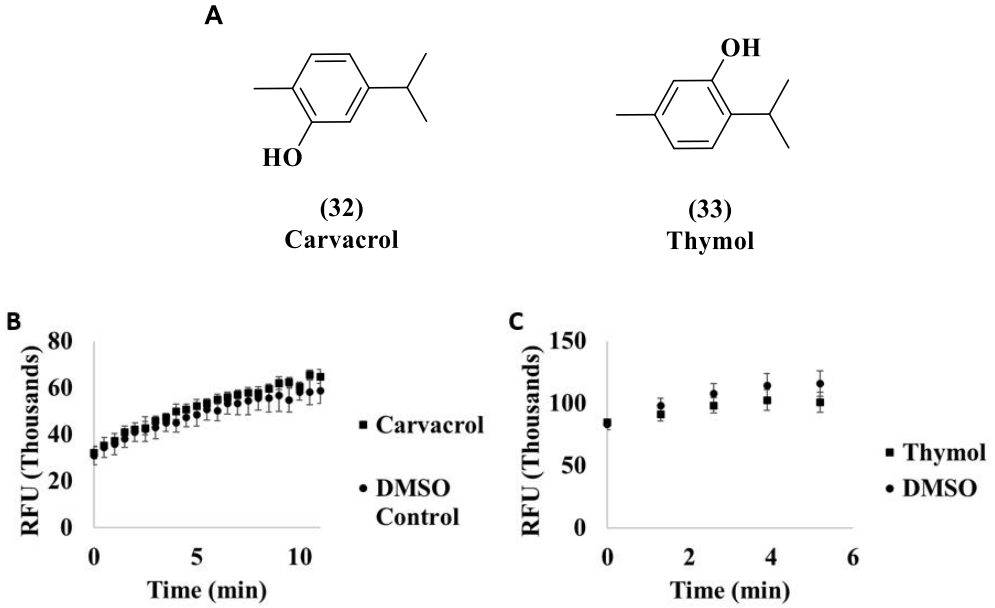


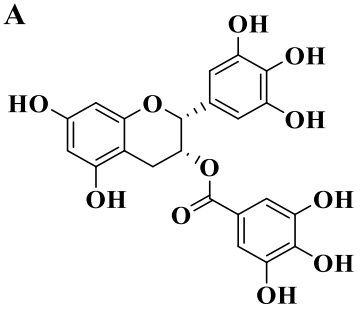
Figure 28. Carvacrol (**32**) and thymol (**33**) do not inhibit secretion of CPG2. **A**) Structures of **32** and **33**. **B**) **32** did not appear to inhibit the secretion of CPG2 compared to the DMSO vehicle control at 50 μM. **C**) **33** did not inhibit the secretion of CPG2 at 50 μM.

EGCG is a major polyphenolic compound in green tea.[337] It has been explored for potential therapeutic uses against a collection of diseases due to its anti-inflammatory activity and its reported histone deacetylase inhibitory properties.[23,338–341,343] One study implicated EGCG as an inhibitor of the T3SS in multiple organisms, including *E. coli*, *S.* Typhimurium, and *Y. pseudotuberculosis*.[18] In this study, inhibition by EGCG was characterized according to model assays for these organisms. EGCG was found to inhibit secretion of EspB in a concentration-

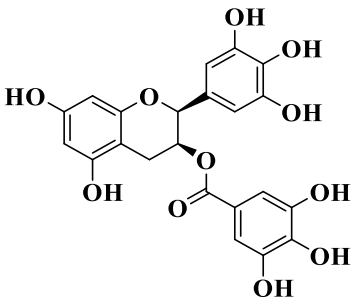
dependent manner by ELISA. The hemolytic activity of *E. coli* was inhibited 80% by 50 μg/mL (109 μM) EGCG. Adherence to Hep-2 cells was inhibited by 65% at the same concentration.

We were interested in characterizing EGCG-dependent inhibition of the T3SS at lower concentrations (Figure 29). We also tested the EGCG epimer, gallocatechin gallate (GCG), for its ability to inhibit the T3SS in our assay. The compounds were initially screened at 100 μM and 25 μM. EGCG and GCG inhibited secretion to approximately the same extent. Further analysis of EGCG displayed concentration-dependent inhibition of type III secretion with an IC_{50} of approximately 2.5 μM. No cytotoxicity was observed upon EGCG treatment up to 50 μM. EGCG was tested for inhibition of CPG2 directly, as inhibiting the enzyme would give similar results as inhibiting secretion. EGCG did not inhibit the CPG2-dependent of the substrate at 100 μM.

A



(9)
(-)-Epigallocatechin-3-gallate



(35)
Gallocatechin-3-gallate

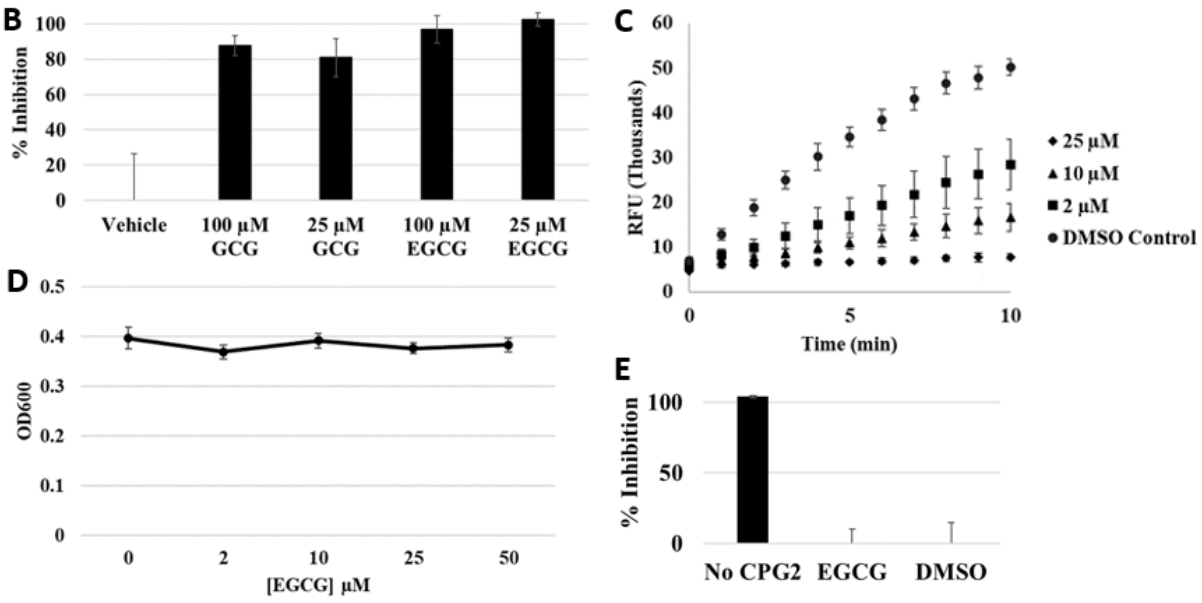


Figure 29. Inhibition of the T3SS by (-)-epigallocatechin-3-gallate (EGCG, **9**) and gallocatechin gallate (GCG, **35**). **A**) Structures of **9** and **35. B**) **9** and **35** were screened at the listed concentrations in the CPG2-reporter assay. DMSO was used as the vehicle control. **9** and **35** display ≥ 80% inhibition at 25 µM. **C**) **9** was screened at 2 µM, 10 µM, and 25 µM and displayed concentration-dependent inhibition of T3SS-mediated CPG2 activity. **D**) **9** was screened for cytotoxicity against *C. rodentium*. **9** is not cytotoxic. **E**) **9** does not inhibit CPG2 directly. **9** was added to cell lysate containing CPG2 to a final concentration of 50 µM, and CPG2 activity was comparable to the DMSO control.

Since the activity of the T3SS is usually measured by assays that rely on successful translocation of effectors into a host cell, every part of the T3SS must be functioning properly in order for activity to be observed. While this may be physiologically relevant, the ability to determine the mechanism of inhibition is entirely lost. We were able to show that partial downregulation of the expression of the LEE does not abolish secretion. Aurodox, thymol, and

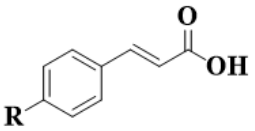
carvacrol all have shown that they negatively regulate the expression of T3SS-related genes, but our assay indicates that they are not capable of inhibiting secretion entirely.

2.5.2 Quorum sensing regulators

Some of the first work done to characterize the T3SS involved analyzing regulatory mechanisms of expression of the LEE.[60,289,379] Expression of the T3SS-related genes has since been linked to major global regulators of *E. coli* as well as other adaptive virulence mechanisms, such as quorum sensing.[379] Quorum sensing is a mechanism of regulation of gene expression in response to environmental chemical signals. These signaling molecules are indicative of cell density and increases in their concentrations result in alterations in expression patterns in genes related to antibiotic resistance, horizontal gene transfer, biofilm formation, and secretion systems. Quorum sensing is imperative for successful propagation of infection and evasion of antibiotic treatment. The links between quorum sensing and the T3SS, while understood, have not been explored in terms of identification of potential therapeutic targets. We chose several modulators of quorum sensing to analyze their effects on T3SS activity. These include analogs of *trans*-cinnamaldehyde (**36-39**), ellagic acid (**40**), tannic acid (**41**), secreted quorum sensing signaling molecules L-homoserine lactone analogs (**42-46**), bergamottin (**47**), naringenin (**48**), penicillic acid (**49**), and patulin (**50**).

Tannic acid (**41**) is a well-known inhibitor of quorum sensing and it has been used as a positive control in screens for quorum sensing inhibitiors.[380] Tannic acid and *trans*-cinnamaldehyde (**36**) were identified as inhibitors of the AHL synthase production in 2014.[23] In one study, we analyzed *para*-substituted analogs of *trans*-cinnamaldehyde. We were initially interested in examining the inhibitory activity of **36** in our CPG2 reporter assay. Our initial results

indicated that **36** does not inhibit CPG2 secretion. We screened analogs of **36** and found that para substitution with a dimethylamino group (**39**) results in 76.5% inhibition of type III secretion. Since these analogs have not been analyzed, it is unclear if there is a parallel pattern of inhibition in quorum sensing.



Compound	R	% Inhibition ± SD
trans-Cinnamaldehyde (**36**)	H	**4.2 ± 5.2**
trans-4-Methoxycinnamaldehyde (**37**)	MeO	**0.4 ± 1.0**
4-Nitrocinnamaldehyde (**38**)	NO_2	**15 ± 9.8**
4-(Dimethylamino)cinnamaldehyde (**39**)	$N(CH_3)_2$	**76 ± 5**

Figure 30. Of the *trans*-cinnamaldehyde analogs studied, only 4-(dimethylamino)cinnamaldehyde (**39**) shows inhibition in the CPG2 reporter assay. Compounds were screened at 50 μM.

We next analyzed ellagic acid (**40**) and tannic acid (**41**), which have the same mechanism of quorum sensing inhibition as **36**, to see if we would observe comparable results. One previously published study compared the AHL-inhibitory abilities of tannic acid, EGCG, and ellagic acid, all polyphenolic compounds containing a gallic acid moiety.[24] All three compounds indicated an ability to inhibit AHL signaling. We were interested in comparing their T3SS inhibitory activity. We initially screened **40** and **41** at 50 μM in our CPG2 reporter assay (Figure 31). We found that **41** is a more potent inhibitor than **40** and decided to characterize this inhibition further. **41** shows concentration-dependent inhibition of T3SS-mediated CPG2 translocation with an IC_{50} of <1 μM.

Our results indicate that these polyphenolic compounds may inhibit the T3SS in a mechanism separate from their quorum sensing targets, since *trans*-cinnamaldehyde does not appear to inhibit the T3SS.

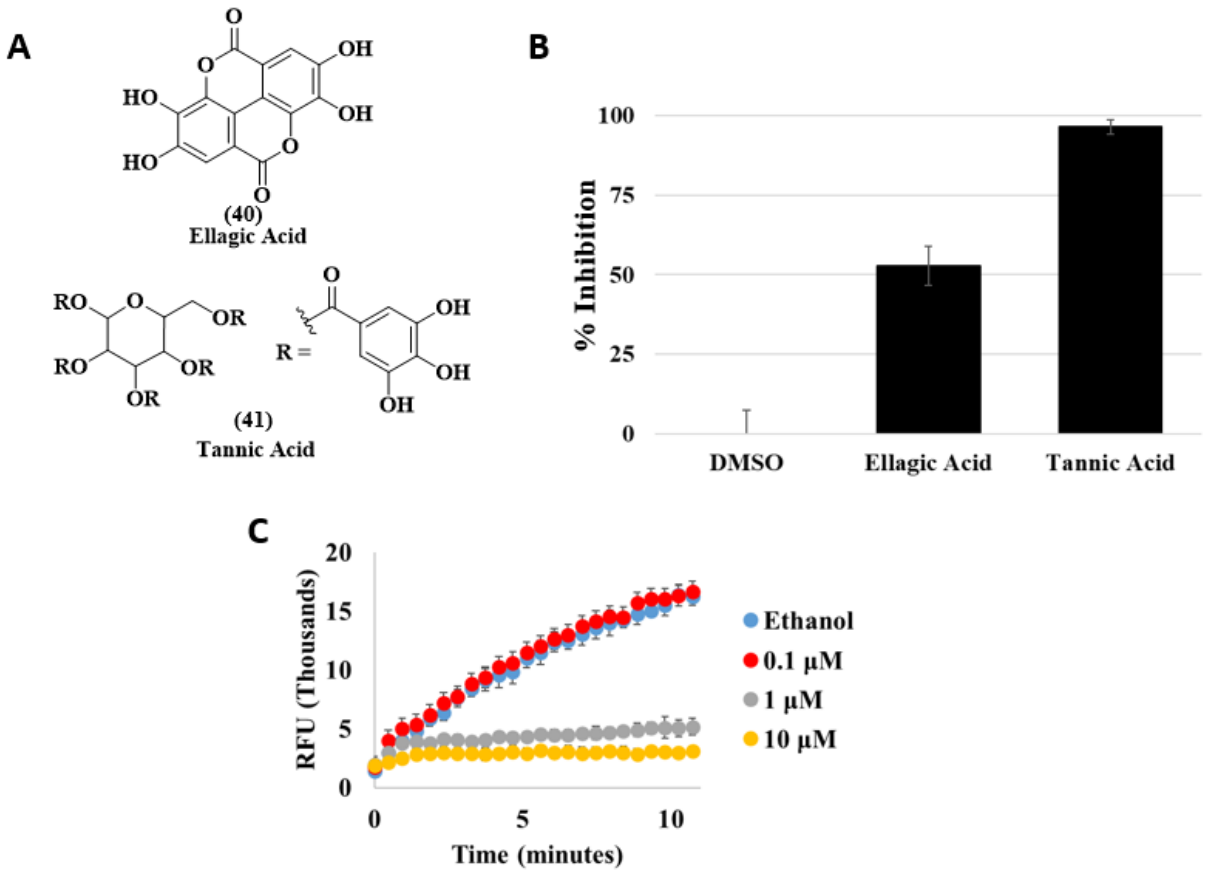
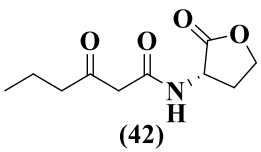


Figure 31. A) Ellagic acid (**40**) and tannic acid (**41**) are polyphenols containing gallate. **B**) **40** has an IC_{50} of approximately 50 µM. **41** inhibits T3SS activity almost entirely at that concentration. **C**) **41** inhibits the secretion of CPG2 in a concentration-dependent manner.

The best-characterized quorum sensing pathway involves the N-acylhomoserine lactones (AHL) autoinducers.[381] AHLs are synthesized by AHL synthases, and consist of a homoserine lactone ring that is N-acylated. These molecules induce the expression of the biosynthetic mechanisms that result in their production, making them autoinducers. We analyzed a collection

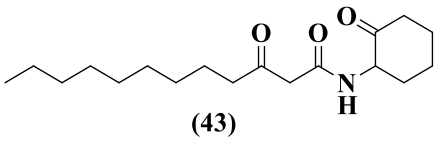
of *N*-acylhomoserine lactones for their ability to overcome tannic acid inhibition of the T3SS (Figure 32). An initial screen was run to identify the effects of the AHLs independently (20 μM, Figure 32B). The compounds were then rescreened in the presence of tannic acid (Figure 32C). The *C. rodentium* cells harboring the pBAD-EspF-CPG2 plasmid were incubated in the presence of 1 μM tannic acid in addition to the listed AHL at 20 μM. DMSO was normalized and used as the vehicle control.

A



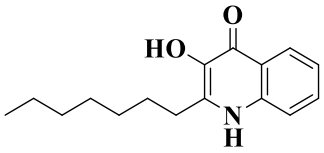
(42)

N-(β-ketocaproyl)-L-homoserine lactone



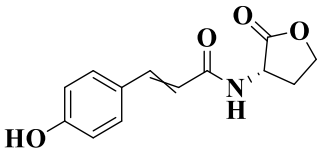
(43)

3-oxo-*N*-(2-oxocyclohexyl)-dodecanamide



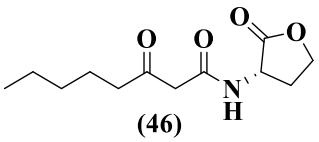
(44)

2-heptyl-3-hydroxy-4(1H)-quinolone



(45)

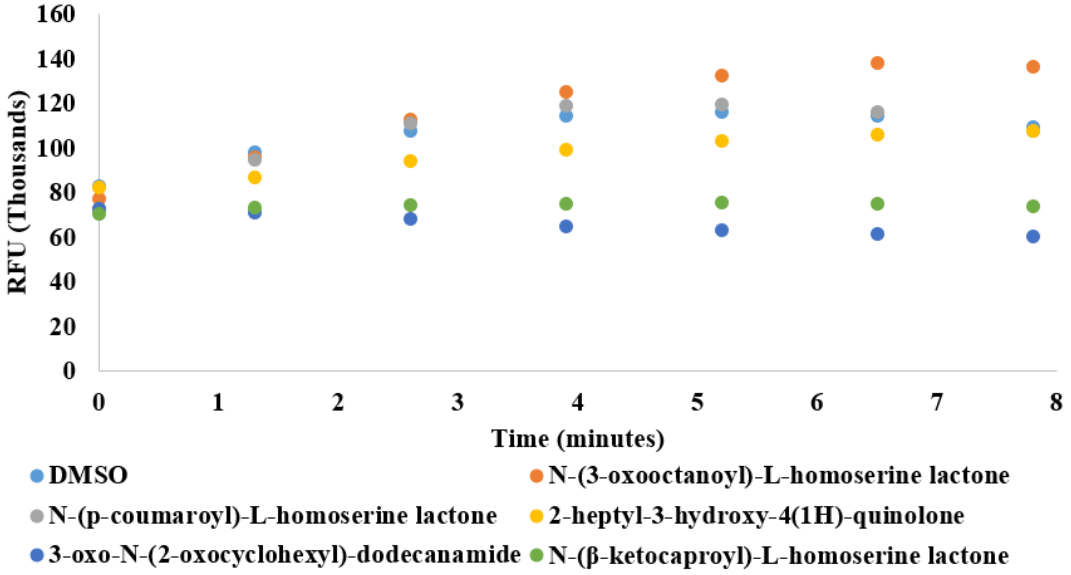
N-(p-coumaroyl)-L-homoserine lactone



(46)

N-(3-oxooctanoyl)-L-homoserine lactone

B



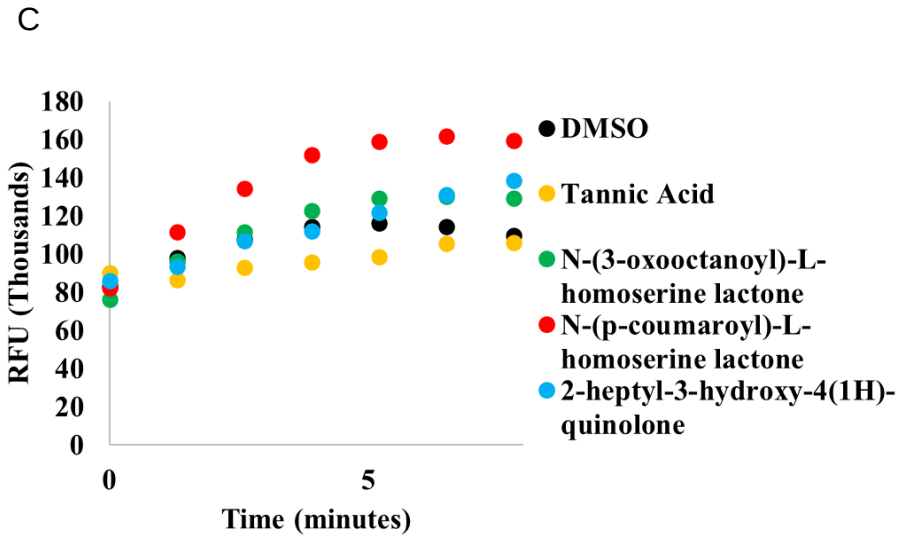


Figure 32. *N*-acylhomoserine lactones (AHLs) and their ability to overcome tannic acid inhibition. **A**) Structures of the AHLs analyzed. **B**) AHLs were studied in the CPG2 reporter assay for their effect on the T3SS. **42** and **43** appear to inhibit T3SS activity, so they were not carried forward to test their ability to overcome **41** inhibition. **C**) AHLs were analyzed in the CPG2 reporter assay in the presence of 1 μM **41**. While **44** and **46** appear to overcome tannic acid inhibition to the extent of regaining control activity, **45** appears to enhance T3SS activity.

From the initial screen, it appeared that 42 and 43 inhibited T3SS activity. We then rescreened **44-46** for their effect on tannic acid's inhibitory activity. We observed that **44** and **46** were able to overcome the inhibition to the same level as the DMSO control, while **45** appeared to increase T3SS activity significantly. These results indicate that tannic acid's inhibition of the T3SS may be related to AHL signaling mechanisms in *C. rodentium*. The ability to overcome tannic acid inhibition indicates a competitive relationship between AHLs and the T3SS target of tannic acid that should be further analyzed.

Bergamottin (**47**) and naringenin (**48**) are cytochrome p450 inhibitors derived from grapefruit juice (Figure 33). **47** has been indicated as an inhibitor of biofilm formation in EHEC O157:H7.[382] **48** is a flavonoid compound shown to inhibit the production of AHLs and decrease the expression of some quorum sensing-related genes in *P. aeruginosa*. Our screening of these compounds indicated that neither bergamottin nor naringenin act as inhibitors of the *C. rodentium* T3SS (Figure 33).

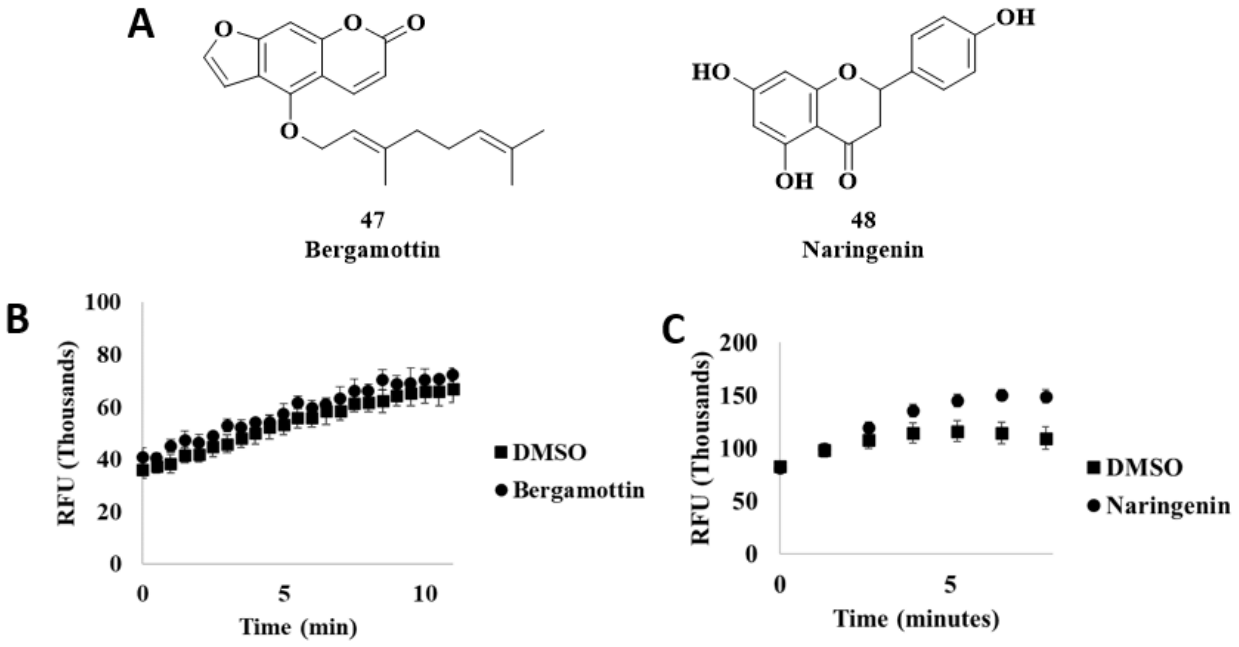


Figure 33. Bergamottin and naringenin do not inhibit the T3SS at 50 μM. **A**) Structures of bergamottin (**47**) and naringenin (**48**). **B**) When **47** was analyzed in the CPG2 reporter assay at 50 μM, no inhibition was observed. **C**) 50 μM **48** did not inhibit T3SS-mediated secretion of CPG2.

Penicillic acid (**49**) and patulin (**50**) are secondary metabolites produced by *Penicillium* spp. of fungi. Both compounds were found to downregulate the expression of QS-related genes in *P. aeruginosa*.[383] Our results indicate that **49** and **50** are not inhibitors of the T3SS at 50 μM.

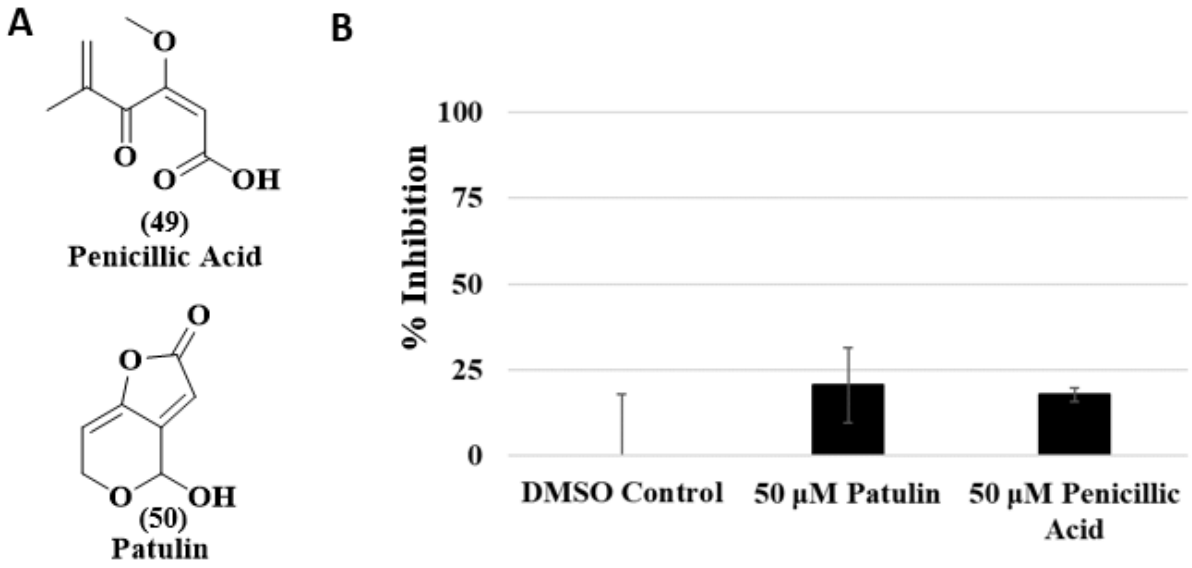


Figure 34. Penicillic acid and patulin do not inhibit the T3SS at 50 μM. **A**) Structures of penicillic acid (**49**) and patulin (**50**). **B**) Compared to the DMSO vehicle control, 50 μM of **49** or **50** does not inhibit T3SS-mediated secretion of CPG2.

Our screen of quorum sensing modulators revealed a correlation between polyphenolic compounds with gallic acid moieties as a structural class of T3SS inhibitors. Tannic acid (**41**) has a known mechanism of quorum sensing inhibition that it shares with *trans*-cinnamaldehyde (**36**). **41** most likely has a separate mechanism of action as a T3SS inhibitor, since **36** does not share the same efficacy. It is possible that **41**, EGCG (**9**), and ellagic acid (**40**) act through related

mechanisms given their structural similarities, but much more investigation is required to corroborate those claims.

2.5.4 Inhibitors of the T3SS in other organisms

Inhibition of the T3SS can be performed through a multitude of pathways. Some inhibitors that have been characterized appear to foster the ability to inhibit the T3SS across different organisms. The mechanisms by which this is possible are not well understood, but a few known cases involve gene expression. These include the previously mentioned inhibitors SAs and EGCG. We used this knowledge, and the success of EGCG in our assay, as inspiration to analyze a collection of inhibitors of the T3SS of other organisms. These include piericidin A (**51**), rotenone (**52**), fusaric acid (**53**), sanguinarine chloride (**54**), and phloretin (**55**).

51 was originally discovered as an insecticide by bioactivity-guided fractionation of *Streptomyces* sp. 16-22 extract.[384] In this study, it was noted that **51** did not appear toxic to Gram-negative bacteria such as *E. coli* and *Xanthomonas oryzae,*[384] though **51** was later characterized as an antibiotic against Gram-positive bacteria.[385] **51** targets NADH dehydrogenase within complex I (100% inhibition at 0.03 nmol compound per mg protein), a complex important in mitochondrial electron transport. A high throughput screen to discover new inhibitors of the *Y. pseudotuberculosis* T3SS revealed **51** as an inhibitor.[5] SDS-PAGE analysis indicated that secretion of effector YopE was decreased by 65% at 71 μM compound. **51** was also shown to potently inhibit translocation of effector YopM (75% decrease at 71 μM) into Chinese hamster ovary (CHO) cells. The mechanism of inhibition by **51** is not entirely understood, though **51** decreases the assembly of needle structures while having no effect on expression of T3SS-related genes.[386] Analysis of another Complex I inhibitor, **52**, indicated that a separate T3SS target may be present.[21] We

analyzed both **51** and **52** in the CPG2 reporter assay (Figure 35). Neither appear to act as inhibitors of the T3SS in *C. rodentium*.

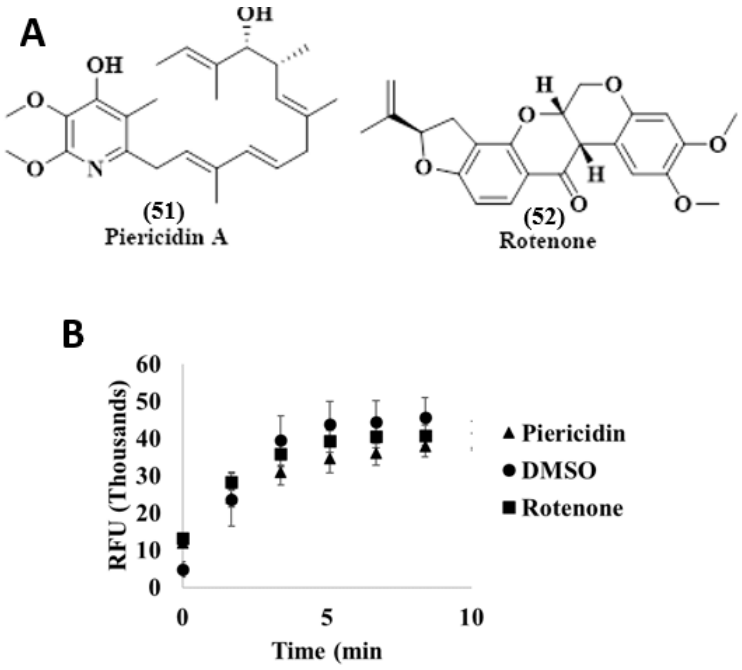


Figure 35. Piericidin A and rotenone do not inhibit the *C. rodentium* T3SS. **A**) Structures of piericidin A (**51**) and rotenone (**52**). **B**) Neither compound appears to inhibit the T3SS-mediated secretion of CPG2.

53 is an inhibitor of the T3SS in *S. enterica.*[387] The inhibitory effect of **53** cannot be overcome by overexpression of T3SS activator HilA. **53** also appears to have no effect on the transcription of T3SS-related genes or transcriptional pathways, so its mechanism of action is unknown. Our studies with **53** indicate that it does not inhibit the T3SS of *C. rodentium* (Figure 36).

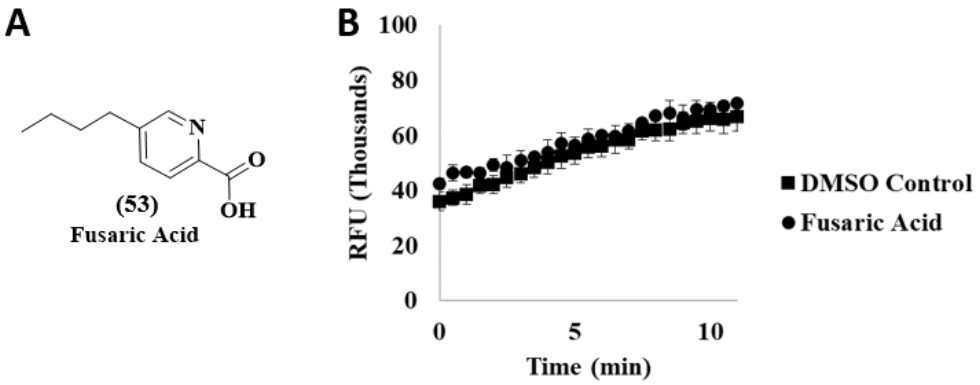


Figure 36. Fusaric acid does not inhibit the T3SS of *C. rodentium*. **A**) Structure of fusaric acid (**53**). **B**) At 50 μM, **53** does not inhibit T3SS-mediated secretion of CPG2.

54 is a T3SS inhibitor against *S*. Typhimurium.[388] Overexpression of T3SS activator HilA overcomes the inhibitory effects of **54**, indicating a possible mechanism of action. When we analyzed **54** for its inhibitory properties in *C. rodentium*, we found no evidence of inhibition (Figure 37).

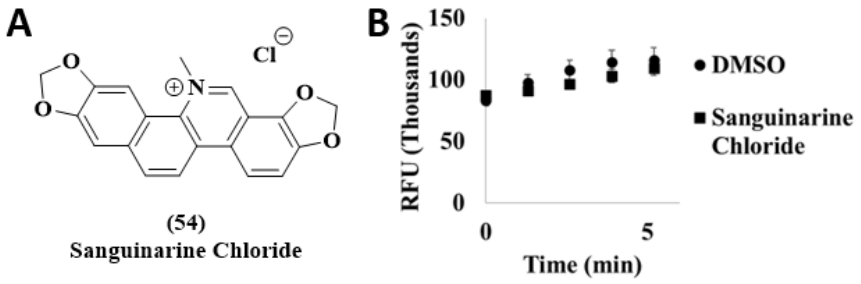


Figure 37. Sanguinarine chloride does not inhibit the T3SS of *C. rodentium*. **A**) Structure of sanguinarine chloride (**54**). **B**) At 50 μM, (**54**) does not inhibit the T3SS-mediated secretion of CPG2.

55 is an apple-derived flavonoid. It has been implicated as an inhibitor of the expression of T3SS-related genes in the plant pathogen *P. syringae*.[389] Research also implicates a mechanism of resistance to **55**, and data suggest that phloretin induces the expression of a multidrug resistance efflux pump that rapidly transports it out of *P. syringae*. In addition, **55** has been characterized as an inhibitor of biofilm formation in EHEC.[22] The mechanism in EHEC also appears to be a consequence of altered gene expression. This evidence notwithstanding, the ability of **55** to alter the expression of T3SS-related genes in *E. coli* or *C. rodentium* has not yet been explored. We sought to identify if the T3SS was inhibited by **55** in the CPG2 reporter assay. Our results indicate that the expression of the T3SS is not downregulated enough to see a decrease in secretion of CPG2 (Figure 38).

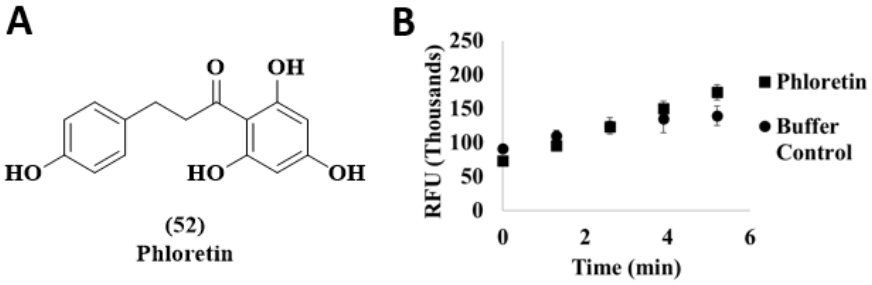


Figure 38. Phloretin does not inhibit the T3SS. **A**) Structure of phloretin (**55**). **B**) At 50 μM, **55** does not inhibit the T3SS-mediated secretion of CPG2.

Our assay was unable to recognize any inhibitory effects from compounds known to inhibit other T3SSs. This result is unsurprising, given the accumulation of genetic and structural differences between the injectosomes of unrelated organisms. Many of the inhibitors from this category that we tested have unknown mechanisms of T3SS inhibition, so the relatability from their target organism to *C. rodentium* is consequently undefined.

2.5.5 Natural product antibiotics

There are several examples of sublethal concentrations of antibiotics resulting in inhibition of the T3SS, including aurodox,[17] piericidin,[21] thymol,[378] and carvacrol.[378] These compounds were originally recognized for their antibiotic effects and were later characterized as inhibitors of the T3SS. Guided by this precedent, we screened natural product antibiotics for their potential to inhibit T3SS-mediated secretion of CPG2. These compounds include oligomycin A (**56**), nosiheptide (**57**), harzianopyridone (**58**), berberine chloride (**59**), and curvularin (**60**).

56 is an antifungal agent with activity against *Aspergillus* spp. and *Penicillium* spp.[390] It was isolated from several species of *Streptomyces*, a bacterial component of soil.[19,391,392] **56** is an inhibitor of ATP synthase, attributing to its toxicity for multiple cell types.[393] **56** is one of nine compounds in the oligomycin family, all of which are substituted macrolide rings consisting of ketones.[394] Unfortunately, **56** is almost insoluble in water and presents toxicity in mice, so its potential for use as a therapeutic is limited.[395] Our study of **56** initially showed some evidence of inhibition of T3SS activity (Figure 39). At 50 μM, **56** appeared to inhibit T3SS-dependent secretion of CPG2. We also analyzed **56** for its cytotoxicity against *C. rodentium* at that concentration and found that **56** enhances cell growth. This is a characteristic of T3SS inhibitors previously attributed to inhibitors of the T3SS of *Y. pestis*.[70] **56** also does not inhibit CPG2 directly.

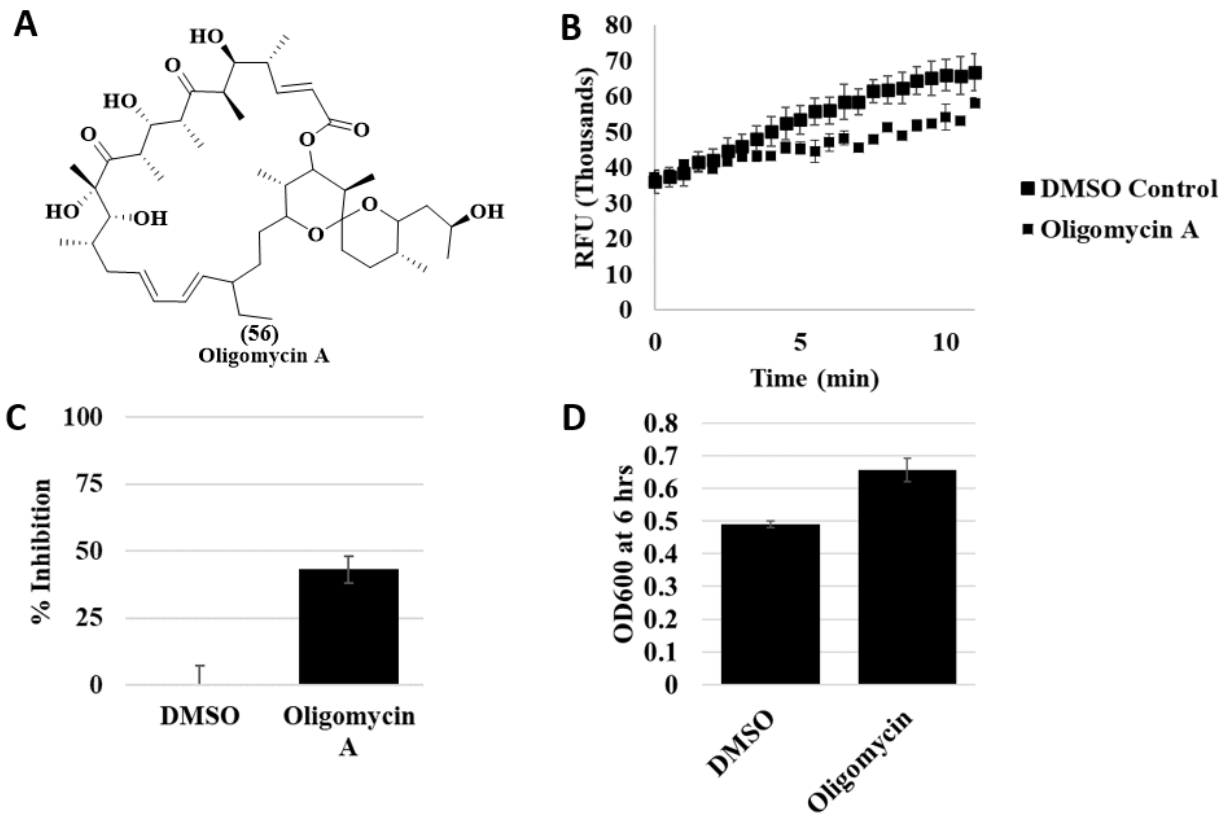


Figure 39. Oligomycin A inhibits the T3SS of *C. rodentium*. **A**) Structure of oligomycin A (**56**). **B**) At 50 μM, **56** inhibits the T3SS. **C**) At 50 μM, the T3SS-mediated secretion of CPG2 is inhibited by 43 ± 5%. **D**) **56** is not cytotoxic to *C. rodentium* at 50 μM.

57 is a thiopeptide antibiotic with cytotoxicity toward Gram-positive bacteria including *S. aureus* and *Clostridium difficile*.[396] Much of the study surrounding **57** for the last few decades has been focused on synthesizing it or optimizing a biosynthetic procedure for its production.[397–401] **57** is an inhibitor of Ef-Tu, which is the same antibiotic target as **3**.[20] Interestingly, at 50 μM, **57** appeared to inhibit T3SS-dependent secretion of CPG2 to a greater extent than **3** did. Studies on the cytotoxicity of **57** toward *C. rodentium* indicated that at 50 μM, the bacteria were viable. When the T3SS is active, bacterial growth rate naturally slows due to the consumption of resources resulting from production of the macromolecular needle structure. Inhibitors of the T3SS may

restore the growth rate in bacteria by redistributing resources.[70] **57** therefore represents the second case of an Ef-Tu inhibitor for Gram-positive bacteria showing an ability to inhibit the T3SS in Gram-negative bacteria.

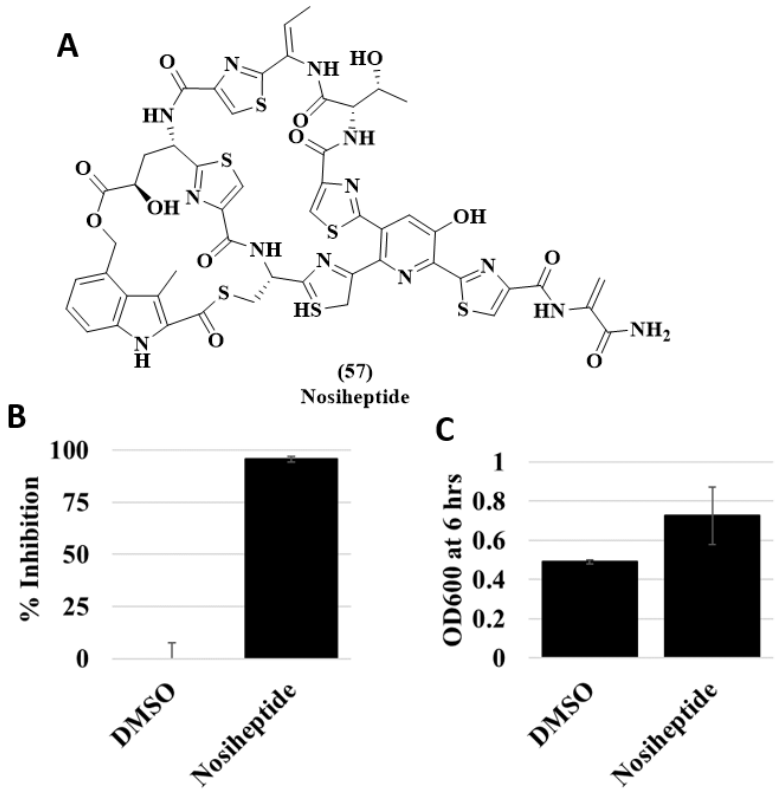


Figure 40. 57 is an inhibitor of Ef-Tu and the T3SS. A) The structure of nosiheptide (**57**). **B**) At 50 μM, **57** inhibits T3SS-mediated secretion of CPG2 by 96 ± 1%. **C**) **57** increases the growth rate of *C. rodentium*.

58 is a secondary metabolite of the fungus *Trichoderma*.[402] This compound has antifungal and antiviral activity.[403,404] **58** belongs to a structural group of compounds called atpenins, which inhibit mitochondrial complex II, or succinate-ubiquinone oxidoreductase.[405] **59** is an isolate from the plant *Berberis vulgaris*. It has proven effective for multiple conditions, including for the

treatment of Leishmaniasis,[406] glioblastoma,[407] cardiac dysfunction,[408] and insulin resistance,[409] along with possessing anti-inflammatory activity. Further *in vivo* analysis also indicates that **59** is cytotoxic to some of the most prevalent strains of MRSA[410] and oral *Streptococci* spp.[411] **60** is a lactone derived from *Penicillium gilmanii* fungus.[412] **60** is an inhibitor of TGF-β signaling related to angiogenesis.[413] **60** is also an antifungal agent, and the analog αβ-dehydrocurvularin possesses antibiotic activity towards *S. aureus*.[414] **58-60** were all screened in the CPG2 reporter assay. While none of them signified inhibition of the T3SS at 50 μM, **59** appears to activate the T3SS to some extent (Figure 41).

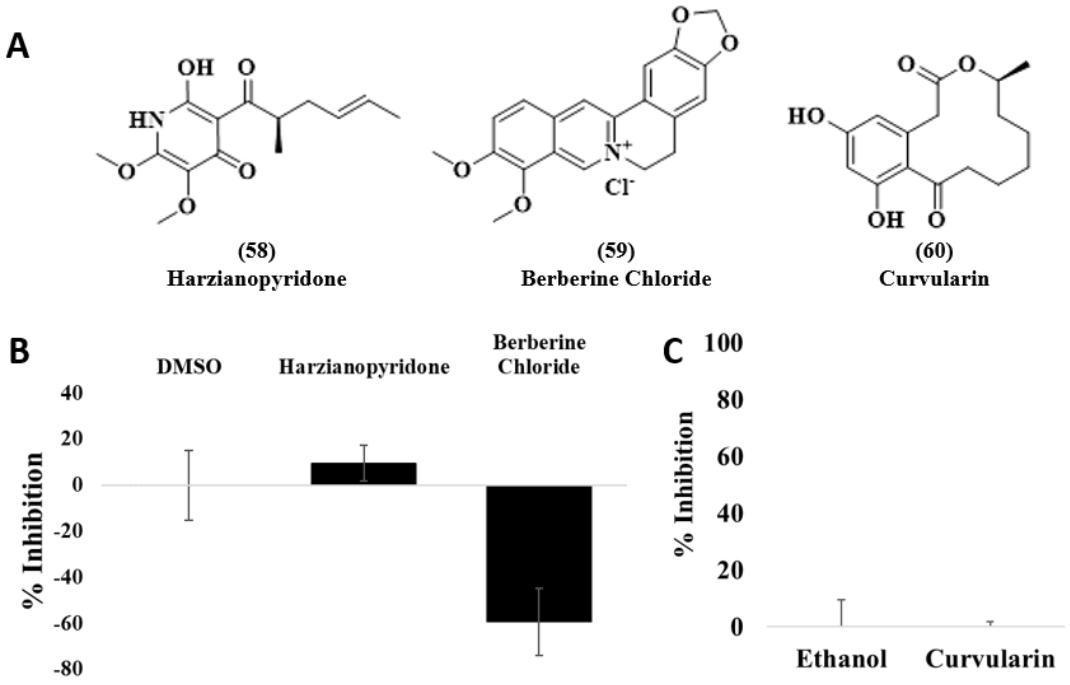


Figure 41. **58-60** are cytotoxic to various organisms. **A**) Structures of harzianopyridone (**58**), berberine chloride (**59**), curvularin (**60**). **B**) **58** (50 μM) does not inhibit the T3SS. **59** (50 μM) appears to enhance T3SS activity. **C**) **60** (50 μM) does not inhibit relative to a vehicle control (ethanol).

The initial success of the antibiotic compounds oligomycin A and nosiheptide requires further investigation for analysis. The toxicity of oligomycin A in mice limits its ability to be studied in *in vitro* models of *C. rodentium* infection, though biochemical analysis of its role as an ATP synthase inhibitor may be helpful in determining its mechanism of T3SS antagonism. Nosiheptide shares an antibacterial target with aurodox in Ef-Tu. The correlation between Ef-Tu inhibition and T3SS moderation has not been identified, though this is the third known case of Ef-Tu interactions coinciding with T3SS inhibition.[17,20,351] Projects elucidating this relationship are currently under discussion for the future of our group.

2.6 Conclusions and limitations

We have successfully developed a solution-based assay for the screening of T3SS inhibitors. Our *C. rodentium* construct secretes CPG2 into the supernatant to concentrations sufficient to produce a quantifiable signal. We have successfully screened a collection of compounds in the original large-volume format at 1 mL. Aurodox and regacin, partial inhibitors of LEE expression, presented as partial inhibitors, indicating that this assay is sensitive enough to decipher between varying degrees of activity. This assay was used to characterize the efficacy of inhibitor EGCG and its IC_{50} value was determined for the first time. In addition, the epimer GCG was determined as an inhibitor of T3SS activity as well. We identified structurally similar polyphenolic-gallate compounds tannic acid and ellagic acid as T3SS inhibitors for the first time as well.

Aurodox and nosiheptide are both recognized as antibiotics targeting EF-Tu, a moderator of protein production. Our CPG2-reporter assay recognizes both compounds as inhibitors of the

T3SS. The mechanism of inhibition of aurodox is related to downregulation of expression of the LEE. We have not identified the mechanism of action of nosiheptide. A small molecule SA analog was also identified as a potential binder of EF-Tu in pull-down analysis,[351] and they recognized a downregulation of LEE expression with treatment of the compound. The authors did not acknowledge the potential connection between EF-Tu inhibition and downregulation of the LEE.

The future research for the May group involves elucidating the relationship between EF-Tu interaction and T3SS activity. The EF-Tu mutations necessary for an aurodox-resistance phenotype are known. The May group intends to construct aurodox-resistant *C. rodentium* mutant strains through site-directed mutagenesis. These mutants will then be analyzed for changes in their T3SS activity in the presence of aurodox. If the mutants are resistant to the T3SS inhibitory functions of aurodox, the connection between EF-Tu inhibition and T3SS activity will be elucidated. If the mutants are not resistant, it will be confirmed that EF-Tu is not the molecular target for T3SS inhibition.

Another future project for the May group involves optimizing the plated format of the assay to allow for more rapid screening. While I have performed a screen of the epigenetics library in a 96-well plate, the gain in fluorescence was very low for controls. The signal never exceeded 150 RFU for any of the control wells, while a test-tube screen allows for gains by the thousands. Changes in incubation times and conditions may be necessary to produce better results.

Julia Hotinger, a PhD candidate in the May group, is developing an *in vivo* monitoring assay to study the potential protective effects of compounds against *C. rodentium* infection. This assay directly monitors damage to the colonic epithelium as a function of leakage into the bloodstream. Compounds that have been identified in the CPG2 reporter assay are currently being screened in this mouse model, which will provide invaluable evidence of *in vivo* efficacy.

CHAPTER 3

SCREENING CAMPAIGN FOR THE IDENTIFICTION OF INHIBITORS OF NOVEL BACTERIAL RIBOSOMAL PROCESSING PROTEASE PRP

3.1 Introduction

In 2019, over 2.8 million cases of antibiotic-resistant infections occurred in the United States, resulting in ~35,000 deaths.[415] Approximately 10,600 of these deaths are attributable to methicillin-resistant *Staphylococcus aureus* (MRSA), a Gram-positive bacterial pathogen responsible for skin infections, pneumonia, and sepsis. Since 2006, contractions of MRSA have been monitored by the National and State Healthcare-Associated Infections Report through the Centers for Disease Control and Prevention (CDC).[416] Over the first decade of monitoring, the rate of hospital-acquired MRSA infections decreased due to vigilant implementation of protocols designed to improve patients' protection from infection. These efforts notwithstanding, the overall rate MRSA infection remains high, with >323,000 cases reported in 2017.[415]

Many *S. aureus* strains have been identified as harboring antibiotic resistance genes. Clinical isolates have indicated strains that are resistant to the PhLOPSA antibiotics (Phenicols, Lincosamides, Oxazolidines, Pleuromutilins, and Streptogramin A),[417] chlorohexidine,[418] and vancomycin[419] in addition to methicillin.[420] Vancomycin-resistant *S. aureus* (VRSA) is growing in clinical importance as the therapeutic options for VRSA are limited.[419] One strain of VRSA that was isolated was resistant to methicillin, teicoplanin, erythromycin, clindamycin, ciprofloxacin, gentamycin, and trimethoprim-sulfamethoxazole treatment.[421] As this pathogen continues to acquire genes for antibiotic resistance, new antibiotics need to be developed as therapeutics to fight *S. aureus* infection.

The bacterial ribosome is the target of many antibiotics currently on the market. These include macrolides, lincosamides, oxazolidinones, and tetracyclines.[422] These compounds each block amino acid polymerization to proteins by interfering with ribosomal processing of aminoacyl-tRNA. The bacterial ribosome consists of a combination of ribosomal proteins and rRNA that form two subunits. These subunits are characterized by their sedimentation rate. The larger subunit is referred to as the 50S ribosomal subunit while the smaller is 30S. The complete ribosome is 70S. The 50S and 30S subunits come together to form the APE sites necessary for mRNA translation, with each subunit forming part of the sites. The 50S subunit contains the catalytic site of the ribosome, the peptidyl transferase center (PTC). The PTC is stabilized by the amino terminus of the ribosomal protein L27.[423]

It was recently discovered that an N-terminal extension on L27 is conserved in Firmicutes, including *Staphylococcus, Bacillus*, *Listeria*, *Clostridium*, and *Streptococcus*.[424] This extension must be cleaved for proper assembly and function of the ribosome in these organisms, as an extension of L27 would result in steric hindrance capable of halting protein production. Phage-related ribosomal protease (Prp) is responsible for cleavage of the N-terminal extension from the ribosomal protein L27.[424] *S. aureus* L27 knockouts are nonviable in the presence of "pre-cleaved" L27 that lacked the N-terminal peptide extension or in the presence of "uncleavable" L27 mutants.[425] This indicates that the cleavage process performed by Prp is necessary for cell survival. The interaction between Prp and L27 is critical in ribosomal assembly and cleavage of the N-terminal sequence of L27 by Prp is a requirement for a functional ribosome in bacteria that contain the L27 N-terminal extension.[424] These studies implicate Prp as a promising new target for antimicrobial therapy.

Due to its recent discovery, Prp has never been targeted for inhibition. This means that resistance to Prp inhibitors is unlikely to have already occurred in nature. Deadly drug-resistant *S. aureus*, *Streptococcus pneumoniae*, and *Clostridium difficile* should be susceptible to Prp inhibition, similar to non-resistant strains. Any Prp inhibitor should be selective for a small subset of pathogenic bacteria because most bacteria do not encode Prp.[424] In addition, those Firmicutes that do express the N-terminal L27 extension have varying sequences within the cleavage domain, so an inhibitor of Prp may be designed to selectively inhibit in one organism. This would result in less selective pressure is being exerted across all bacteria as a whole, which should slow the rate of formation of resistance, and cause fewer side effects from killing commensal bacteria.

Mutational studies exploring the importance of specific amino acids of the N-terminal L27 extension have indicated that Prp presents substrate specificity. Mutations F8A and F9A resulted in an uncleavable protein. Unpublished work by Dr. Gail Christie and Dr. Darrell Peterson indicates that Q7A and Q7E are also uncleavable, while A10G and A10S can be cleaved by Prp. Since the cleavage site of Prp is between F9 and A10, these results indicate that the interactions between Prp and L27 that are important for cleavage exist primarily on the amino-terminal side of the cut site. This information may be implemented in design of specific L27 peptidomimetic inhibitors of Prp.

In this dissertation, we describe a high throughput screening campaign using a modified and miniaturized form of the fluorogenic assay previously developed. We also discuss the optimization of a new fluorogenic substrate and the subsequent screening of broad-spectrum protease inhibitors and organomercurial compounds.

3.2 Experimental

3.2.1 Materials

Prp was produced and isolated as described previously.[424] Peptide substrate, consisting of fluorophore FITC or ABZ conjugated to the Prp-specific cleavage sequence of L27 and DNP quencher (FITC/ABZ-KLNLQFFASKK-DNP), was purchased from United Biosystems (Herndon, VA). The ApexScreen compound library was purchased from TimTec, Inc. (New Castle County, DE). Phenyl mercuric borate was sourced from Aldrich Chemical Company, Inc (St. Louis, MO). Methyl mercuric chloride was from Pfaltz & Bauer, Inc (Waterbury, CT). Mersalyl acid was sourced from Bios Laboratories, Inc (New Haven, CT). Ethylmercurylthiosalicylic acid was sourced from Fisher Scientific Company (Waltham, MA). Phenyl mercuric acetate, *o*-chloromercuryl phenol, *p*-chloromercuribenzoic acid and phenylmercuric salicylate were sourced from K&K Laboratories, Inc (Plainview, NY). *p*-Acetoxymercurianiline was sourced from Polysciences, Inc (Warrington, PA). Dimercurial acetate was sourced from Anatrace Products, LLC (Maumee, OH). Thiomersal was sourced from Sigma Chemical Company (St. Louis, MO). Merbromin was sourced from ICN Pharmaceuticals, Inc. (Costa Mesa, CA).

3.2.2 Screening assay

The peptide substrate was reconstituted in dimethyl sulfoxide (DMSO) to 1 mM, and its concentration was determined by measuring absorbance at 325 nm at 0.1 cm pathlength with a BioTek Synergy HTX plate reader. 20 µL aliquots were stored at -20 °C until use. The assay was performed with purified Prp, produced as previously described at 20 nM and peptide at a final concentration of 500 nM (FITC). Assays were performed in sodium phosphate buffer (50 mM, pH 7) with 1.5 mM dithiothreitol (DTT) and 2.35 mM ethylenediaminetetraacetic acid (EDTA) and 0.01% Tween 20.

Assay buffer was dispensed into 1536-well plates (Fisherbrand 1536-well black flat-bottom) with the Multidrop™ Combi nL Reagent Dispenser (to 5 µL) before the addition of Prp to 21.4 nM using a Labcyte Echo550 acoustic liquid handler. Compounds being screened were then added to the desired concentration with a Labcyte Echo550 acoustic liquid handler before incubating at room temperature for 30 minutes. Peptide substrate was added to 0.5 µM immediately before monitoring fluorescence with a BMG Labtech CLARIOstar© Plus plate reader. When Prp cleaved the peptide, the quencher and FITC were released. The concentration of free fluorescent FITC was directly related to the intensity of the fluorescent signal ($\lambda_{ex}/\lambda_{em}$ = 488-15/530-15 nm). Fluorescence was monitored for 45 minutes.

3.2.3 Data analysis

The Z factor is a statistical parameter used for validation and evaluation of the quality of a high throughput screening (HTS) assay.[426] To calculate the Z factor for this screening assay, the inhibitor mersalyl acid (MA) was screened at 0.1 mM using the procedure above. The % inhibition by MA was calculated from the rate of change in fluorescence compared to an uninhibited control using the following equation:

$$\%\ Inhibition = 100 * \left(1 - \frac{m_{MA}}{m_V}\right)$$

Where *m* = slope, *MA* = mersalyl acid, and *V* = vehicle

The % inhibition by MA and the vehicle control was then used to calculate the Z factor using the equation below.

$$Z\ Factor = 1 - \left[\frac{3(\sigma_{MA} + \sigma_V)}{|\mu_{MA} - \mu_V|}\right]$$

Where σ = standard deviation, μ = mean, *MA* = mersalyl acid, and *V* = vehicle

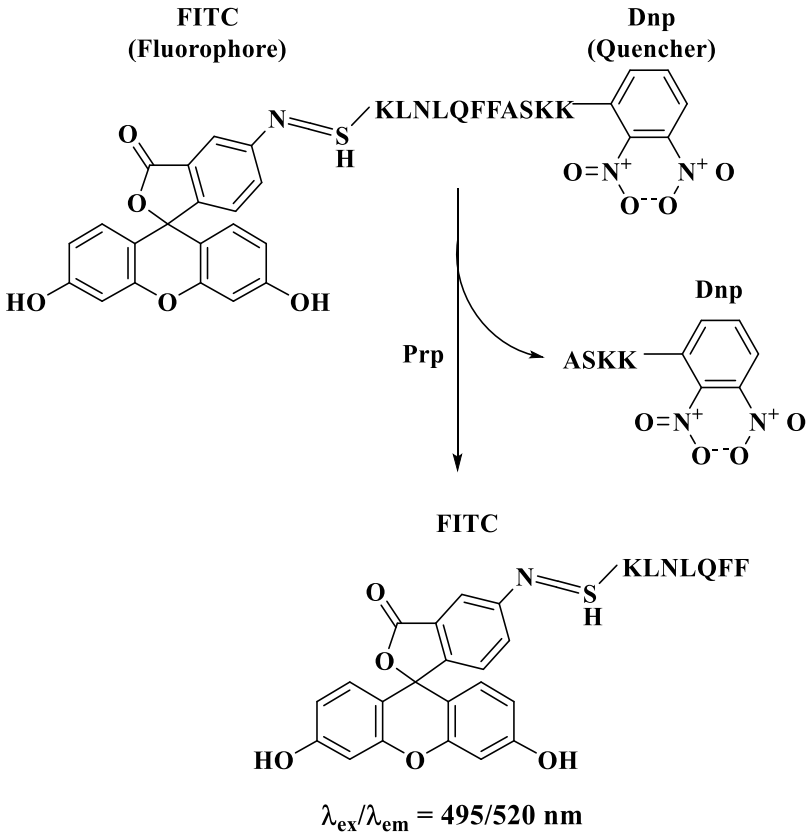
3.2.4 Fluorescent interference assay

This experiment is performed to identify any non-specific interactions between the screening compounds and the substrate after cleavage. Assay buffer was dispensed into 1536-well plates (Fisherbrand 1536-well black flat-bottom) with the Multidrop™ Combi nL Reagent Dispenser (to 5 µL) before the addition of compounds to the screening concentration with a Labcyte Echo550 acoustic liquid handler. A "pre-cleaved" version of the substrate (ABZ-KLNLQFF) was then dispensed using a Labcyte Echo550 acoustic liquid handler to 1 µM. This compound is fluorescent, so any interference with the fluorescence of the substrate will be apparent by a decrease in the signal obtained in the presence of the compound. The fluorescence of the solution is measured for approximately 40 minutes with a BMG Labtech CLARIOstar© Plus plate reader (λex/λem = 320-15 nm/420-15 nm).

3.3 Preliminary Studies

Assay miniaturization. The assay previously described involves a fluorophore/quencher system linked by the amino acid sequence for the L27 cleavage domain. The fluorophore was 2-aminobenzoic acid (ABZ) and the quencher was dinitrophenyl (DNP). When these two domains are held in close proximity by the intact linker, the fluorogenic signal of ABZ is quenched by DNP. When the linker is cleaved by Prp, DNP and ABZ are separated and ABZ becomes fluorescent, and the signal observed increases over time as more substrate is processed.

A



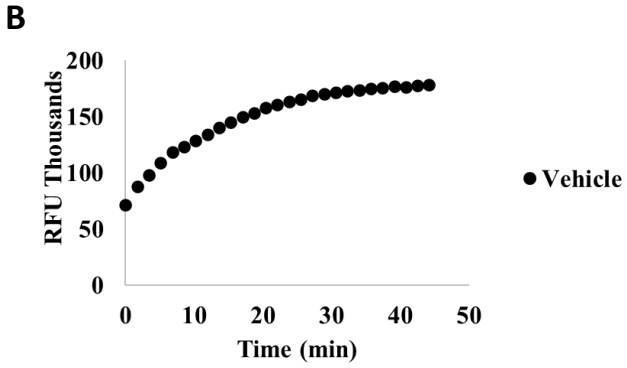


Figure 42. A) Scheme of the fluorogenic assay. Prp cleaves the pre-fluorescent substrate and releases the fluorophore (FITC). **B**) Fluorescence increases over time as the substrate is being processed. The compound mersalyl acid was used as a positive control and inhibits Prp activity completely at 100 μM.

At the onset off this study, the assay as developed previously was performed in a volume of 60 μL. To conserve material and perform more rapid screening, lab member Adam Johnson miniaturized the assay to 5 μL. Upon initial screening in this smaller volume, the signal observed decreased significantly and could not be quantified accurately. He hypothesized that this issue may have come from protein adhesion to the walls of the wells. As volume decreases, the surface-to-volume ratio increases. In any screening environment, some proteins adhere to the walls and the bottom of the wells. This adherence allows for the successful implementation of ELISA protocols and other solid phase assays that depend upon protein adherence. In this case, this solution-based assay requires that the enzyme and substrate be soluble and available in solution. To approach this problem, a small amount of a detergent was added to the assay buffer (0.01% Tween 20). This limited the adherence of the enzyme and substrate to the walls of the well and the signal was restored. I adopted this assay to screen a library of over 5000 compounds for their ability to inhibit Prp.

Optimization using FITC fluorophore. Once the high throughput screening campaign was underway, it became apparent that many of the compounds we screened were fluorescent at the same wavelength as ABZ. A few of the compounds we screened resulted in signals that were above the upper limit of quantification, so no meaningful data could be collected. We replaced the ABZ moiety in the assay substrate with a new fluorophore, fluorescein isothiocyanate (FITC). This fluorophore has higher excitation/emission wavelengths than ABZ (495 nm/519 nm rather than 320 nm/420 nm). By screening the fluorescent compounds with this new fluorophore, we were able to collect meaningful data for all the compounds in the library.

The concentration of the ABZ-conjugated substrate was 1 μM for screening. This concentration gave ample signal while being low enough not to outcompete the compounds being

screened (~35 μM). When the new fluorophore was introduced, the signal obtained from the cleavage of 1 μM was above the upper limit of quantification (Figure 43). A lower concentration of the FITC-conjugated substrate was therefore used for screening (0.5 μM). This was the only significant change made to the screening protocol.

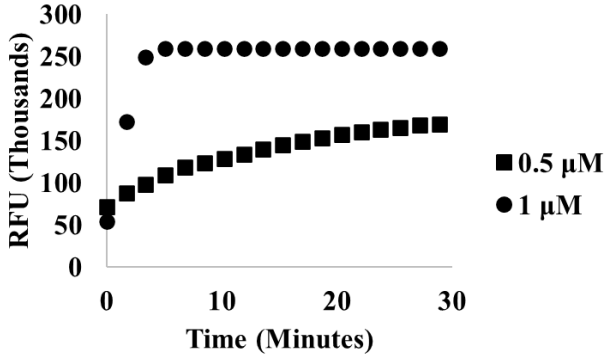


Figure 43. The FITC-conjugated substrate gives a signal above the upper limit of quantification if screened at 1 μM. The signal is optimal at 0.5 μM since the signal does not exceed the quantitative limits of the instrument.

3.4 Results and discussion

3.4.1 Calculating the Z-factor

Mersalyl acid was screened at 100 μM using the FITC-conjugated substrate. Figure 44 shows a representation of positive and negative control conditions for the fluorogenic cleavage assay. As Prp cleaved the 11-mer peptide, the quencher was released from the fluorophore and fluorescence increased. When an inhibitor was present, in this case mersalyl acid, Prp was incapable of cleaving the peptide and fluorescence did not increase. Using this data, the Z factor was calculated based on percent inhibition (Equations 1, 2). The Z factor is 0.67.

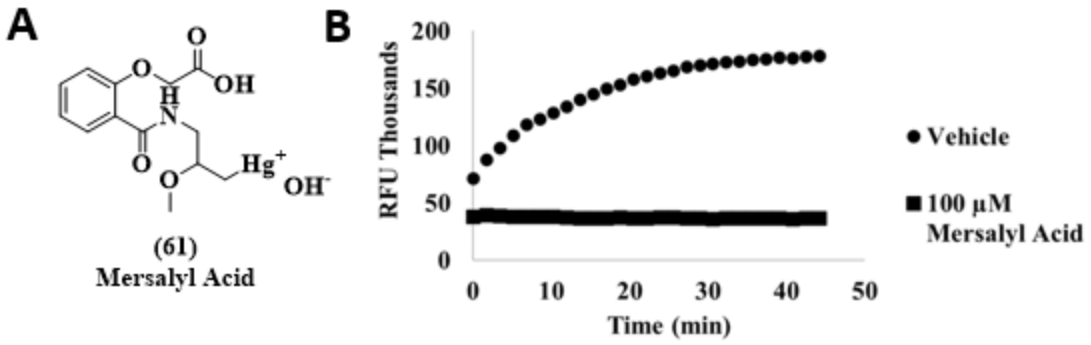


Figure 44. A) Structure of mersalyl acid (**61**). **B**) **61** inhibits Prp at 100 µM and was used as a positive control to calculate the Z factor (Z-factor = 0.67).

3.4.2 ApexScreen 5040 library

The ApexScreen library consists of 5040 diverse structures. These compounds were initially screened in singlet using the ABZ-conjugated substrate (Appendix I). Any compounds fluorescent at the screening wavelength were rescreened using the FITC-conjugated substrate. None of the fluorescent compounds were ultimately inhibitors of Prp. Compounds that appeared to inhibit Prp after the initial screen were then screened in triplicate at lower concentrations to identify concentration-dependent inhibition. These compounds were also screened for fluorescent interference with ABZ-KLNLQFF fluorescent substrate. At this stage, most compounds were eliminated for either non-repeatable inhibition or for interference with the fluorescence of the substrate post-cleavage. One compound appeared to inhibit Prp (Figure 45). This compound is (*E*)-4-(4-bromostyryl)pyridine. A post-doctoral fellow, John Saathoff, synthesized this compound as well as one analog (Figure 45) for further screening.

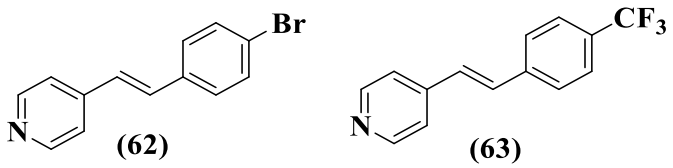


Figure 45. Analogs of the screening hit synthesized by John Saathoff.

We were unable to recreate the inhibition seen in the plate screening. The bromo-substituted compound **62** had no activity against Prp. The trifluoromethyl-substituted compound **63** was a very weak inhibitor, but we were able to observe concentration-dependent inhibition (Figure 46). Because of the weak activity, the compound was abandoned. Ultimately, this library did not present any hits to pursue further.

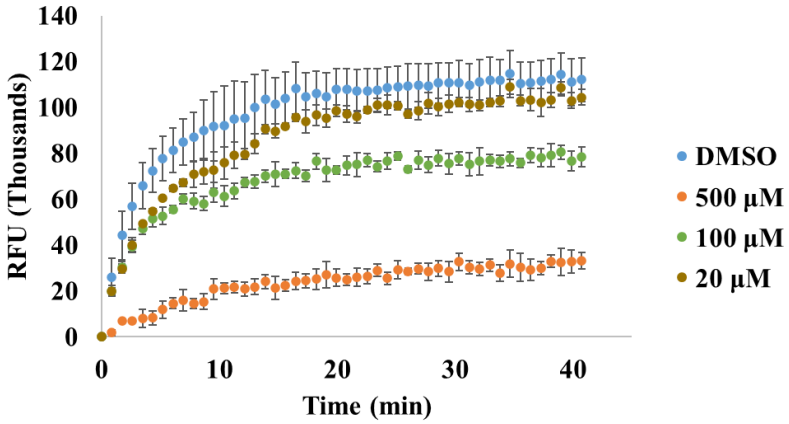


Figure 46. 63 exhibited concentration-dependent inhibition of Prp.

3.4.3 Protease inhibitors

We screened a collection of broad-spectrum protease inhibitors (Figure 47) and other small-spectrum inhibitors. We were interested in exploring whether the active site of Prp would

be able to interact with these compounds. Ultimately, we found that none of these protease inhibitors included in the library were able to inhibit Prp.

The broad-spectrum inhibitors in this collection included peptides containing epoxides or aldehydes, where enzymatic activity would result in covalent linkage of the inhibitor to the protease. The compounds tested in this screen include CA-074Me (**64**), leupeptin (**65**), loxistatin acid (**66**), mg101 (**67**), E-64 (**68**), and aloxistatin (**69**, Figure 47).

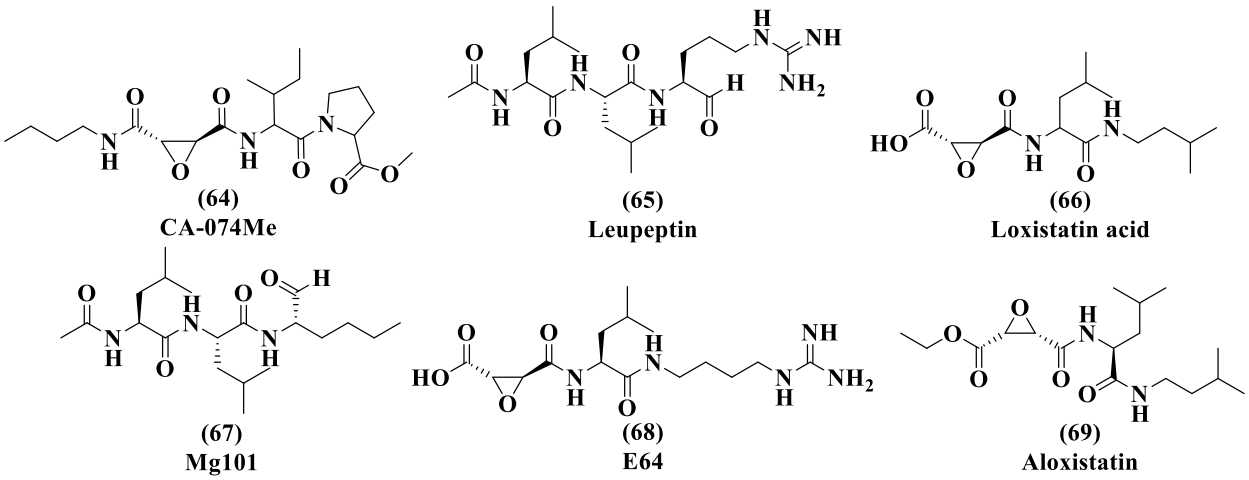


Figure 47. Structures of compounds analyzed for Prp inhibitory activity: CA-074ME (**64**), leupeptin (**65**), loxistatin acid (**66**), mg101 (**67**), E64 (**68**), and aloxistatin (**69**).

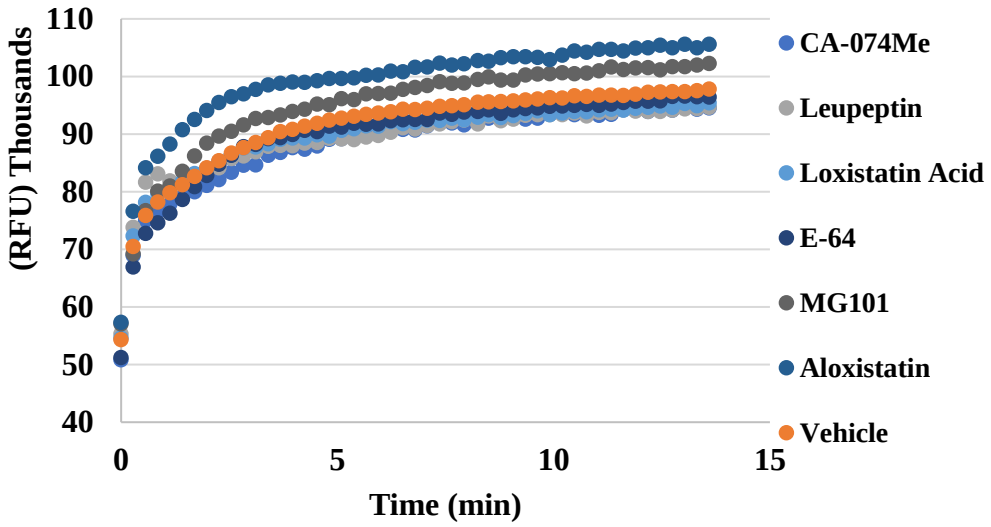


Figure 48. Fluorogenic cleavage data curves for the suicide inhibitors **64-69**.

CA-074Me is a cell-membrane permeable analogue of CA-074 and acts as an irreversible cathepsin B inhibitor.[427] Leupeptin, an isolate from *Actinomycetes*, was first implicated as an inhibitor of plasmin, trypsin, papain, and thrombokinase in 1969.[428] Leupeptin was then discovered as an inhibitor of *Leishmania donovani* cysteine protease.[429] E64 is an irreversible cysteine protease inhibitor.[430] Loxistatin acid is a synthetic and cell permeable derivative of E-64, and irreversibly inhibits cysteine proteases cathepsins B, H, and L.[430] Mg101 is a broad-spectrum, potent inhibitor of cysteine proteases including lysosomal cathepsins and calpains.[431] Aloxistatin is also a broad-spectrum cysteine protease inhibitor that has blood platelet aggregation inhibitory properties.[432] The collection of these compounds was selected for their range of specificity for protease targets. Our results indicate that none of these broad-spectrum antibiotics are capable of inhibiting Prp at 100 μM (Figure 48), which suggests that Prp has a high level of substrate specificity. Rational design of an L27 mimetic with a warhead capable of covalent modification of the active site of Prp may be a promising direction in which to design a specific Prp inhibitor.

3.4.4 Mercurial compounds

We also screened a collection of organomercurial compounds (Figure 49). These compounds were analyzed in response to the discovery of the inhibitory ability of mersalyl acid. The compounds selected for screening were phenyl mercuric borate (**70**), methyl mercuric chloride (**71**), mersalyl acid (**72**), ethylmercurylthiosalicylic acid (**73**), phenyl mercuric acetate (**74**), *p*-acetoxymercurianiline (**75**), *o*-chloromercuryl phenol (**76**), phenylmercuric salicylate (**77**), thiomersal (**78**), merbromin (**79**), and *p*-chloromercuribenzoic acid (**80**). Compounds were initially analyzed at 100 μM concentration in duplicate (Table 4) and those indicating high levels of inhibition (**70-77**, 80% inhibition or higher) were rescreened at 1 μM in triplicate. The percent inhibition at 1 μM is given in Table 5.

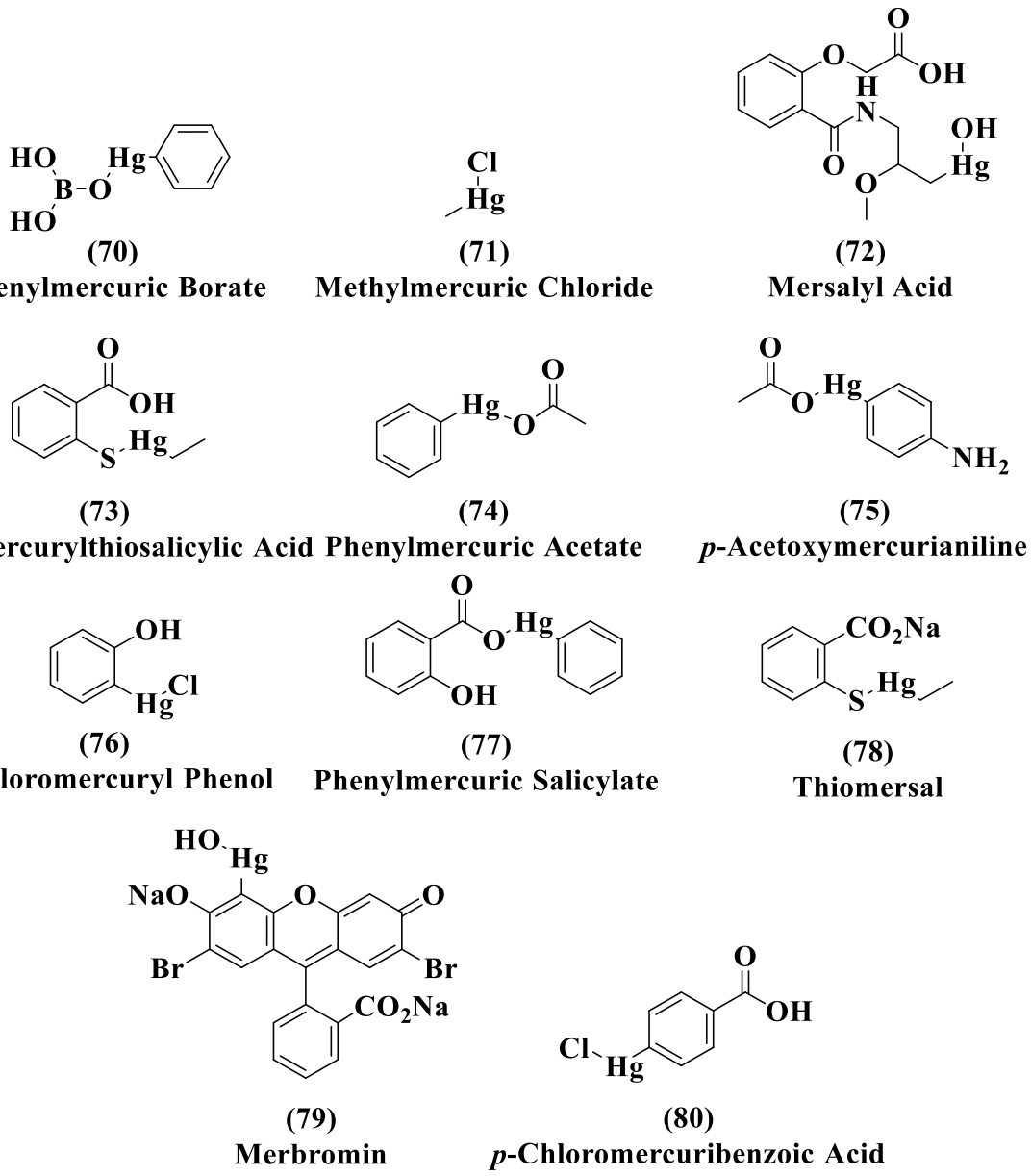


Figure 49. Structures of organomercurials analyzed for Prp inhibitory activity: phenylmercuric borate (**70**), methylmercuric chloride (**71**), mersalyl acid (**72**), ethylmercurylthiosalicylic acid (**73**), phenylmercuric acetate (**74**), *p*-acetoxymercurianiline (**75**), *o*-chloromercuryl phenol (**76**), phenylmercuric salicylate (**77**), thiomersal (**78**), merbromin (**79**), *p*-chloromercuribenzoic acid (**80**).

Table 4. Calculated inhibitory levels of **70-80**. Compounds were screened in triplicate, so standard deviation cannot be calculated. **70-77** were rescreened at 1 μM but **78-80** were abandoned due to lack of inhibition at 100 μM.

Compound (100 μM)	Slope	% Inhib.
70 Trial 1	-52	101
70 Trial 2	-33	100
71 Trial 1	-101	101
71 Trial 2	-60	101
72 Trial 1	-69	101
72 Trial 2	-46	101
73 Trial 1	-56	101
73 Trial 2	-19	100
74 Trial 1	89	99
74 Trial 2	170	98
75 Trial 1	210	96
75 Trial 2	172	97
76 Trial 1	158	98
76 Trial 2	36	100
77 Trial 1	1397	81
77 Trial 2	1523	79
78 Trial 1	7452	-1
78 Trial 2	7212	3
79 Trial 1	7014	6
79 Trial 2	6905	7
80 Trial 1	7062	5
80 Trial 2	7459	-1

Table 5. Inhibition data for compounds **70-77**, which appear to inhibit Prp. Compounds were screened at 1 μM and DMSO concentration was normalized.

Compound	% Inhibition at 1 μM
70	71 ± 17
71	64 ±7

72	59 ± 5
73	36 ± 1
74	29 ± 6
75	28 ± 2
76	16 ± 2
77	8 ± 3

Given the unusual inhibitory profile of Prp to traditional broad-spectrum protease inhibitors, we pursued other compounds capable of inhibition. Mercury is thiophilic,[433] and we suspected that the active-site cysteine of Prp could be inhibited by certain commercially available organomercurials. Mersalyl is an organomercurial that has been used therapeutically as a diuretic[434,435] and served as a positive control in the development of our HTS assay. Phenylmercuric borate (Merfen orange),[436,437] mersalyl,[434,435] phenylmercuric acetate,[438,439] thiomersal,[440,441] and merbromin (Mercurochrome)[437,442] have been used for their antiseptic properties in topical ointments. Phenylmercuric acetate is used as an antimicrobial in eyedrops and is used to combat ocular fungal pathogens in addition to its herbicidal functionality.[439] Thiomersal (also known as thimerosal) was a preservative in vaccines meant to prevent fungal growth within the vials.[440,441] The resulting controversy caused by thiomersal's mercury content has become a popular topic for groups interested in adverse effects caused by vaccination. In recent redeeming research, the toxicity of thiomersal is being investigated for its potential as a cancer treatment.[434,443–445] Thiomersal is capable of inducing apoptosis in multiple cancer cell types, including prostate,[443] gastric,[444] and oral cancers.[445] This indicates the opportunity for further research into mercury-containing compounds as a strategy to target harmful cell types using their innate toxicity. Our research contributes to this trend by revealing the potential for organomercurial compounds as antibiotics and inhibitors of Prp.

3.5 Conclusions

As a novel, never-drugged, essential enzyme for Firmicutes, Prp has high potential as an antibiotic target. Research into inhibiting Prp indicates that the active site cannot be targeted by known broad-spectrum protease inhibitors. This specificity notwithstanding, we have demonstrated that Prp can be inhibited by small-molecule organomercurial compounds. Because of the toxicity related to organomercurials, though, these compounds may not behave well as therapeutics, so other options must be explored. Given the specificity of the binding site of Prp, a rationally designed suicide inhibitor based on the L27 extension may be a promising project for the future.

REFERENCES

(1) Kola, M.; Urba, K. Antibiotic selective pressure and development of bacterial resistance. *Int. J. Antimicrob. Agents* **2001**, *17*, 357–363.

(2) Keyser, P.; Elofsson, M.; Rosell, S.; Wolf-Watz, H. Virulence blockers as alternatives to antibiotics: type III secretion inhibitors against Gram-negative bacteria. *J. Intern. Med.* **2008**, *264*, 17–29.

(3) Gaytan, M. O.; Martinez-Santos, V. I.; Soto, E.; Gonzalez-Pedrajo, B. Type three secretion system in attaching and effacing pathogens. *Front. Cell. Infect. Microbiol.* **2016**, *6*, 129.

(4) Tsai, C. L.; Burkinshaw, B. J.; Strynadka, N. C. J.; Tainer, J. A. The *Salmonella* type III secretion system virulence effector forms a new hexameric chaperone assembly for export of effector/chaperone complexes. *J. Bacteriol.* **2015**, *197*, 672–675.

(5) Duncan, M. C.; Wong, R.; Dupzyk, A. J.; Bray, W. M.; Linington, R. G. Inhibitors of the *Yersinia pseudotuberculosis* type III secretion system. *Antimicrob. Agents Chemother.* **2014**, *58*, 1118–1126.

(6) Bailey, L.; Gylfe, Å.; Sundin, C.; Muschiol, S.; Elofsson, M.; Nordström, P.; Henriques-Normark, B.; Lugert, R.; Waldenström, A.; Wolf-Watz, H.; et al. Small molecule inhibitors of type III secretion in *Yersinia* block the *Chlamydia pneumoniae* infection cycle. *FEBS Lett.* **2007**, *581*, 587–595.

(7) Collmer, A.; Badel, J. L.; Charkowski, A. O.; Deng, W. L.; Fouts, D. E.; Ramos, A. R.; Rehm, A. H.; Anderson, D. M.; Schneewind, O.; van Dijk, K.; et al. *Pseudomonas syringae* Hrp type III secretion system and effector proteins. *Proc. Natl. Acad. Sci. U. S. A.* **2000**, *97*, 8770–8777.

(8) Cornelis, G. R. The type III secretion injectisome. *Nat. Rev. Microbiol.* **2006**, *4*, 811–825.

(9) Clements, A.; Young, J. C.; Constantinou, N.; Frankel, G. Infection strategies of enteric pathogenic *Escherichia coli. Gut Microbes* **2012**, *3*, 71–87.

(10) Deng, W.; Li, Y.; Vallance, B. A.; Finlay, B. B. Locus of enterocyte effacement from *Citrobacter rodentium*: sequence analysis and evidence for horizontal transfer among attaching and effacing pathogens. *Am. Soc. Microbiol*. **2001**, *69*, 6323–6335.

(11) Elliott, S. J.; Wainwright, L. A.; McDaniel, T. K.; Jarvis, K. G.; Deng, Y. K.; Lai, L. C.; McNamara, B. P.; Donnenberg, M. S.; Kaper, J. B. The complete sequence of the locus of enterocyte effacement (LEE) from enteropathogenic *Escherichia coli* E2348/69. *Mol. Microbiol.* **1998**, *28*, 1–4.

(12) Muschiol, S.; Bailey, L.; Gylfe, Å.; Sundin, C.; Hultenby, K.; Bergström, S.; Elofsson, M.; Wolf-Watz, H.; Normark, S.; Henriques-Normark, B. A small-molecule inhibitor of type III secretion inhibits different stages of the infectious cycle of *Chlamydia trachomatis. Proc. Natl. Acad. Sci. U. S. A.* **2006**, *103*, 14566–14571.

(13) Kühne, S. A.; Hawes, W. S.; La Ragione, R. M.; Woodward, M. J.; Whitelam, G. C.; Gough, K. C. Isolation of recombinant antibodies against EspA and intimin of *Escherichia coli* O157:H7. *J. Clin. Microbiol*. **2004**, *42*, 2966–2976.

(14) Cardenal-Muñoz, E.; Ramos-Morales, F. Analysis of the expression, secretion and translocation of the *Salmonella enterica* type III secretion system effector SteA. *PLoS One* **2011**, *6*, e26930.

(15) Munera, D.; Crepin, V. F.; Marches, O.; Frankel, G. N-terminal type III secretion signal of enteropathogenic *Escherichia coli* translocator proteins. *J. Bacteriol*. **2010**, *192*, 3534–3539.

(16) Yang, J.; Hocking, D. M.; Cheng, C.; Dogovski, C.; Perugini, M. A.; Holien, J. K.; Parker, M. W.; Hartland, E. L.; Tauschek, M.; Robins-Browne, R. M. Disarming bacterial virulence

through chemical inhibition of the DNA binding domain of an AraC-like transcriptional activator protein. *J. Biol. Chem*. **2013**, *288*, 31115–31126.

(17) Kimura, K.; Iwatsuki, M.; Nagai, T.; Matsumoto, A.; Takahashi, Y.; Shiomi, K.; Omura, S.; Abe, A. A small-molecule inhibitor of the bacterial type III secretion system protects against *in vivo* infection with *Citrobacter rodentium. J. Antibiot. (Tokyo).* **2011**, *64*, 197–203.

(18) Khebizi, N.; Boudjella, H.; Bijani, C.; Bouras, N.; Klenk, H. P.; Pont, F.; Mathieu, F.; Sabaou, N. Oligomycins A and E, major bioactive secondary metabolites produced by *Streptomyces* sp. strain HG29 isolated from a Saharan soil. *Journal de Mycologie Medicale*. **2018**, 150–160.

(19) Cundliffe, E.; Thompson, J. The mode of action of nosiheptide (Multhiomycin) and the mechanism of resistance in the producing organism. *J. Gen. Microbiol*. **1981**, *126*, 185–192.

(20) Morgan, J. M.; Duncan, M. C.; Johnson, K. S.; Diepold, A.; Lam, H.; Dupzyk, A. J.; Martin, L. R.; Wong, R.; Armitage, J. P.; Linington, R. G. Piericidin A1 bocks *Yersinia* Ysc type III secretion system needle assembly. *Am. Soc. Microbiol*. **2017**, *2*, e00030-17.

(21) Lee, J. H.; Regmi, S. C.; Kim, J. A.; Cho, M. H.; Yun, H.; Lee, C. S.; Lee, J. Apple flavonoid phloretin inhibits *Escherichia coli* O157:H7 biofilm formation and ameliorates colon inflammation in rats. *Infect. Immun*. **2011**, *79*, 4819–4827.

(22) Chang, C. Y.; Krishnan, T.; Wang, H.; Chen, Y.; Yin, W. F.; Chong, Y. M.; Tan, L. Y.; Chong, T. M.; Chan, K. G. Non-antibiotic quorum sensing inhibitors acting against N-acyl homoserine lactone synthase as druggable target. *Sci. Rep*. **2014**, *4*, 7245.

(23) Huber, B.; Eberl, L.; Feucht, W.; Polster, J. Influence of polyphenols on bacterial biofilm formation and quorum-sensing. *Zeitschrift fur Naturforsch*. **2003**, *58*, 879–884.

(24) McHugh, R. E.; O'Boyle, N.; Connoly, J. P. R.; Hoskisson, P. A.; Roe, A. J. Characterization of the mode of action of aurodox, a type III secretion system inhibitor from *Streptomyces goldiniensis*. *Infect. Immun*. **2019**, *87*, e00595-18.

(25) Chinali, G. Synthetic analogs of aurodox and kirromycin active on elongation factor Tu from *Escherichia coli*. *J. Antibiot. (Tokyo).* **1981**, *34*, 1039–1045.

(26) Nakasone, N.; Higa, N.; Toma, C.; Ogura, Y.; Suzuki, T.; Yamashiro, T. Epigallocatechin gallate inhibits the type III secretion system of Gram-negative enteropathogenic bacteria under model conditions. *Fed. Eur. Microbiol. Soc. Lett.* **2017**, *364*, fnx111.

(27) Bélanger, L.; Garenaux, A.; Harel, J.; Boulianne, M.; Nadeau, E.; Dozois, C.M. *Escherichia coli* from animal reservoirs as a potential source of human extraintestinal pathogenic *E. coli*. *FEMS Immunol. Med. Microbiol*. **2011**, *62*, 1–10.

(28) Katouli, M. Population structure of gut *Escherichia coli* and its role in development of extra-intestinal infections. *Iran. J. Microbiol*. **2010**, *2*, 59–72.

(29) Tenaillon, O.; Skurnik, D.; Picard, B.; Denamur, E. The population genetics of commensal *Escherichia coli*. *Nat. Rev. Microbiol*. **2010**, *8*, 207–217.

(30) Center for Disease Control and Prevention (CDC). National Enteric Disease Surveillance: STEC Surveillance Overview; **2012**.

(31) Centers for Disease Control and Prevention (CDC). Surveillance for Foodborne Disease Outbreaks United States, 2017, Annual Report.; **2019**.

(32) Arendt, S.; Rajagopal, L.; Strohbehn, C.; Stokes, N.; Meyer, J.; Mandernach, S. Reporting of foodborne illness by U.S. consumers and healthcare professionals. *Int. J. Environ. Res. Public Health* **2013**, *10*, 3684–3714.

(33) Proulx, F.; Seidman, E. G.; Karpman, D. Pathogenesis of Shiga toxin-associated hemolytic uremic syndrome. *Pediatr. Res*. **2001**, *50*, 163–171.

(34) Law, D. Virulence factors of *Escherichia coli* O157 and Other Shiga toxin-producing *E. coli*. *J. Appl. Microbiol*. **2000**, *88*, 729–745.

(35) Obrig, T. G.; Karpman, D. Shiga toxin pathogenesis: kidney complications and renal failure. *Curr. Top. Microbiol. Immunol*. **2012**, *357*, 105–136.

(36) Kaplan, B. S.; Meyers, K. E.; Schulman, S. L. The pathogenesis and treatment of hemolytic uremic syndrome. *J. Am. Soc. Nephrol*. **1998**, *9*, 1126–1133.

(37) Ylinen, E.; Salmenlinna, S.; Halkilahti, J.; Jahnukainen, T.; Korhonen, L.; Virkkala, T.; Rimhanen-Finne, R.; Nuutinen, M.; Kataja, J.; Arikoski, P.; et al. Hemolytic uremic syndrome caused by Shiga toxin–producing *Escherichia coli* in children: incidence, risk factors, and clinical outcome. *Pediatr. Nephrol*. **2020**, *35*, 1749–1759.

(38) Etcheverría, A. I.; Padola, N. L. Shiga toxin-producing *Escherichia coli*: factors involved in virulence and cattle colonization. *Virulence* **2013**, *4*, 366–372.

(39) Navarro-Garcia, F. *Escherichia coli* O104:H4 pathogenesis: an enteroaggregative *E. coli*/Shiga toxin-producing *E. coli* explosive cocktail of high virulence. *Microbiol. Spectr*. **2014**, *2*, EHEC-0008-2013.

(40) Vila, J.; Vargas, M.; Henderson, I.R.; Gascón, J.; Nataro, J.P. Enteroaggregative *Escherichia coli* virulence factors in traveler's diarrhea strains. *J. Infect. Dis.* **2000**, *182*, 1780–1783.

(41) Organization, W. H. Water-related diseases https://www.who.int/water_sanitation _health/diseases-risks/diseases/diarrhoea/en/ (accessed Aug 14, 2020).

(42) Soon, J. M.; Seaman, P.; Baines, R. N. *Escherichia coli* O104:H4 outbreak from sprouted seeds. *Int. J. Hyg. Environ. Health* **2013**, *216*, 346–354.

(43) Wu, C.-J.; Hsueh, P.-R.; Ko, W.-C. A new health threat in Europe: Shiga toxin-producing *Escherichia coli* O104:H4 infections. *J. Microbiol. Immunol. Infect.* **2011**, *44*, 390–393.

(44) Robert Koch-Institute (RKI). Report: Final presentation and evaluation of epidemiological findings in the EHEC O104:H4 outbreak, Germany 2011; 2011.

(45) Lim, M.-A.; Kim, J.-Y.; Acharya, D.; Bajgain, B. B.; Park, J.-H.; Yoo, S.-J.; Lee, K. A diarrhoeagenic enteropathogenic *Escherichia coli* (EPEC) infection outbreak that occurred among elementary school children in Gyeongsangbuk-Do Province of South Korea was associated with consumption of water-contaminated food items. *Int. J. Environ. Res. Public Health* **2020**, *17*, 3149.

(46) Michino, H.; Araki, K.; Minami, S.; Takaya, S.; Sakai, N.; Miyazaki, M.; Ono, A.; Yanagawa, H. Massive outbreak of *Escherichia coli* O157:H7 infection in schoolchildren in Sakai Citi, Japan, associated with consumption of white radish sprouts. *Am. J. Epidemiol.* **1999**, *150*, 265–290.

(47) Croxen, M. A.; Law, R. J.; Scholz, R.; Keeney, K. M.; Wlodarska, M.; Finlay, B. B. Recent advances in understanding enteric pathogenic *Escherichia coli. Clin. Microbiol. Rev*. **2013**, *26*, 822–880.

(48) Peña-Gonzalez, A.; Soto-Girón, M. J.; Smith, S.; Sistrunk, J.; Montero, L.; Páez, M.; Ortega, E.; Hatt, J. K.; Cevallos, W.; Trueba, G.; et al. Metagenomic signatures of gut infections caused by different *Escherichia coli* pathotypes. *Appl. Environ. Microbiol*. **2019**, *85*, e01820-19.

(49) DebRoy, C.; Fratamico, P. M.; Yan, X.; Baranzoni, G.; Liu, Y.; Needleman, D. S.; Tebbs, R.; O'Connell, C. D.; Allred, A.; Swimley, M.; et al. Comparison of O-antigen gene clusters of all O-serogroups of *Escherichia coli* and proposal for adopting a new nomenclature for O-typing. *PLoS One* **2016**, *11*, e0147434.

(50) Prager, R.; Strutz, U.; Fruth, A.; Tschäpe, H. Subtyping of pathogenic *Escherichia coli* strains using flagellar (H)-antigens: serotyping versus *fliC* polymorphisms. *Int. J. Med. Microbiol*. **2003**, *292*, 477–486.

(51) Neter, E.; Westphal, O.; Lüderitz, O.; Gino, R.M.; Gorzynski, E.A. Demonstration of antibodies against enteropathogenic *Escherichia coli* in sera of children of various ages. *Pediatrics* **1955**, *16*, 801–808.

(52) Moon, H. W.; Whipp, S. C.; Argenzio, R. A.; Levine, M. M.; Giannella, R. A. Attaching and effacing activities of rabbit and human enteropathogenic *Escherichia coli* in pig and rabbit intestines. *Infect. Immun*. **1983**, *41*, 1340–1351.

(53) Ulshen, M. M.; Rollo, J. L. Pathogenesis of *Escherichia coli* gastroenteritis in man—another mechanism. *N. Engl. J. Med.* **1980**, *302*, 99–101.

(54) Scaletsky, I. C.; Souza, T. B.; Aranda, K. R.; Okeke, I. N. Genetic elements associated with antimicrobial resistance in enteropathogenic *Escherichia coli* (EPEC) from Brazil. *BMC Microbiol.* **2010**, *10*, 25.

(55) Hernandes, R. T.; Elias, W. P.; Vieira, M. A. M.; Gomes, T. A. T. An overview of atypical enteropathogenic *Escherichia coli*. *FEMS Microbiol. Lett*. **2009**, *297*, 137–149.

(56) Whittam, T. S.; Wolfe, M. L.; Wachsmuth, I. K.; Ørskov, F.; Ørskov, I.; Wilson, R. A. Clonal relationships among *Escherichia coli* strains that cause hemorrhagic colitis and infantile diarrhea. *Infect. Immun*. **1993**, *61*, 1619–1629.

(57) Zhou, Z.; Li, X.; Liu, B.; Beutin, L.; Xu, J.; Ren, Y.; Feng, L.; Lan, R.; Reeves, P. R.; Wang, L. Derivation of *Escherichia coli* O157:H7 from its O55:H7 precursor. *PLoS One* **2010**, *5*, e8700.

(58) Troeger, C.; Forouzanfar, M.; Rao, P. C.; Khalil, I.; Brown, A.; Reiner, R. C.; Fullman, N.; Thompson, R. L.; Abajobir, A.; Ahmed, M.; et al. Estimates of global, regional, and national morbidity, mortality, and aetiologies of diarrhoeal diseases: a systematic analysis for the global burden of disease study 2015. *Lancet Infect. Dis.* **2017**, *17*, 909–948.

(59) Donnenberg, M. S.; Tacket, C. O.; James, S. P.; Losonsky, G.; Nataro, J. P.; Wasserman, S. S.; Kaper, J. B.; Levine, M. M. Role of the *eaeA* gene in experimental enteropathogenic *Escherichia coli* infection. *J. Clin. Invest.* **1993**, *92*, 1412–1417.

(60) McDaniel, T. K.; Jarvis, K. G.; Donnenberg, M. S.; Kaper, J.B. A genetic locus of enterocyte effacement conserved among diverse enterobacterial pathogens. *Proc. Natl. Acad. Sci.* **1995**, *92*, 1664–1668.

(61) Vieira, M. A.; Dias, R. C. B.; dos Santos, L. F.; Rall, V. L. M.; Gomes, T. A. T.; Hernandes, R. T. Diversity of strategies used by atypical enteropathogenic *Escherichia coli* to induce attaching and effacing lesion in epithelial cells. *J. Med. Microbiol.* **2019**, *68*, 940–951.

(62) Noguera-Obenza, M.; Ochoa, T. J.; Gomez, H. F.; Guerrero, M. L.; Herrera-Insua, I.; Morrow, A. L.; Ruiz-Palacios, G.; Pickering, L. K.; Guzman, C. A.; Cleary, T. G. Human milk secretory antibodies against attaching and effacing *Escherichia coli* antigens. *Emerg. Infect. Dis.* **2003**, *9*, 545–551.

(63) Sekiya, K.; Ohishi, M.; Ogino, T.; Tamano, K.; Sasakawa, C.; Abe, A. Supermolecular structure of the enteropathogenic *Escherichia coli* type III secretion system and its direct interaction with the EspA-sheath-like structure. *Proc. Natl. Acad. Sci.* **2001**, *98*, 11638–11643.

(64) Vikram, A.; Jayaprakasha, G. K.; Jesudhasan, P. R.; Pillai, S. D.; Patil, B. S. Suppression of bacterial cell-cell signalling, [*sic*] biofilm formation and type III secretion system by citrus flavonoids. *J. Appl. Microbiol*. **2010**, *109*, 515–527.

(65) Cordone, A.; Lucchini, S.; Felice, M. De; Ricca, E. Direct and indirect control of Lrp on LEE pathogenicity genes of *Citrobacter rodentium*. *FEMS Microbiol. Lett*. **2011**, *325*, 64–70.

(66) Paul, K.; Erhardt, M.; Hirano, T.; Blair, D. F.; Hughes, K. T. Energy source of flagellar type III secretion. *Nature* **2008**, *451*, 489–492.

(67) Rüssmann, H.; Shams, H.; Poblete, F.; Fu, Y.; Galán, J. E.; Donis, R. O. Delivery of epitopes by the *Salmonella* type III secretion system for vaccine development. *Science* **1998**, *281*, 565–568.

(68) Bartra, S. S.; Lorica, C.; Qian, L.; Gong, X.; Bahnan, W.; Barreras, H.; Hernandes, R.; Li, Z.; Plano, G. V.; Schesser, K. Chromosomally-encoded *Yersinia pestis* type III secretion effector proteins promote infection in cells and in mice. *Front. Cell. Infect. Microbiol.* **2019**, *9*, 23.

(69) Marketon, M. M.; DePaolo, R. W.; DeBord, K. L.; Jabri, B.; Scheewind, O. Plague bacteria target immune cells during infection. *Science* **2005**, *309*, 1739–1742.

(70) Pan, N. J.; Brady, M. J.; Leong, J. M.; Goguen, J. D. Targeting type III secretion in *Yersinia pestis. Antimicrob. Agents Chemother*. **2009**, *53*, 385–392.

(71) Dai, W.; Li, Z. Conserved type III secretion system exerts important roles in *Chlamydia trachomatis*. *Int. J. Exp. Pathol*. **2014**, *7*, 5404–5414.

(72) Pinaud, L.; Sansonetti, P. J.; Phalipon, A. Host Cell Targeting by Enteropathogenic Bacteria T3SS Effectors. Trends Microbiol. 2018, 26 (4), 266–283. https://doi.org/10.1016/j.tim.2018.01.010.

(73) Shaw, R. K.; Cleary, J.; Murphy, M. S.; Frankel, G.; Knutton, S. Interaction of enteropathogenic *Escherichia coli* with human intestinal mucosa: role of effector proteins in brush border remodeling and formation of attaching and effacing lesions. *Infect. Immun*. **2005**, *73*, 1243–1251.

(74) Vidotto, M. C.; Florian, E. C. T.; Ono, M. A. Prevalence of the *Paa* gene (porcine Attaching and effacing associated) in porcine enteropathogenic *Escherichia coli* (PEPEC) associated with postweaning diarrhea in South Brazil. *Brazilian J. Microbiol*. **2013**, *44*, 515–517.

(75) An, H.; Fairbrother, J. M.; Dubreuil, J. D.; Harel, J. Cloning and characterization of the *eae* gene from a dog attaching and effacing *Escherichia coli* strain 4221. *FEMS Microbiol. Lett*. **1997**, *148*, 239–245.

(76) Ooka, T.; Tokuoka, E.; Furukawa, M.; Nagamura, T.; Ogura, Y.; Arisawa, K.; Harada, S.; Hayashi, T. Human gastroenteritis outbreak associated with *Escherichia albertii*, Japan. *Emerg. Infect. Dis.* **2013**, *19*, 144–146.

(77) Ghaem-Maghami, M.; Simmons, C. P.; Daniell, S.; Pizza, M.; Lewis, D.; Frankel, G.; Dougan, G. Intimin-specific immune responses prevent bacterial colonization by the attaching-effacing pathogen *Citrobacter rodentium*. *Infect. Immun*. **2001**, *69*, 5597–5605.

(78) McWilliams, B. D.; Torres, A. G. Enterohemorrhagic *Escherichia coli* adhesins. *Contrib. Microbiol.* **2013**, *8*, EHEC-0003-2013.

(79) Franzin, F. M.; Sircili, M. P. Locus of enterocyte effacement: a pathogenicity island involved in the virulence of enteropathogenic and enterohemorragic *Escherichia coli* subjected to a complex network of gene regulation. *Biomed Res. Int*. **2015**, *2015*, 534738.

(80) Mills, E.; Baruch, K.; Charpentier, X.; Kobi, S.; Rosenshine, I. Real-time analysis of effector translocation by the type III secretion system of enteropathogenic *Escherichia coli*. *Cell Host Microbe* **2008**, *3*, 104–113.

(81) Yi, Y.; Ma, Y.; Gao, F.; Mao, X.; Peng, H.; Feng, Y.; Fan, Z.; Wang, G.; Guo, G.; Yan, J.; et al. Crystal structure of EHEC intimin: insights into the complementarity between EPEC and EHEC. *PLoS One* **2010**, *5*, e15285.

(82) Touzé, T.; Hayward, R. D.; Eswaran, J.; Leong, J. M.; Koronakis, V. Self-association of EPEC intimin mediated by the β-barrel-containing anchor domain: a role in clustering of the Tir receptor. *Mol. Microbiol*. **2004**, *51*, 73–87.

(83) Kelly, G.; Prasannan, S.; Daniell, S.; Fleming, K.; Frankel, G.; Dougan, G.; Connerton, L.; Matthews, S. Structure of the cell-adhesion fragment of intimin from enteropathogenic *Escherichia coli*. *Nat. Struct. Biol*. **1999**, *6*, 313–318.

(84) Batchelor, M.; Prasannan, S.; Daniell, S.; Reece, S.; Connerton, I.; Bloomberg, G.; Dougan, G.; Frankel, G.; Matthews, S. Structural basis for recognition of the translocated intimin receptor (Tir) by intimin from enteropathogenic *Escherichia coli*. *EMBO J*. **2000**, *19*, 2452–2464.

(85) Rad, H. S.; Mousavi, S. L.; Rasooli, I.; Amani, J.; Jalali-Nadooshan, M. R. EspA-intimin chimeric protein, a candidate vaccine against *Escherichia coli* O157:H7. *Iran. J. Microbiol*. **2013**, *5*, 244–251.

(86) Girón, J. A.; Ho, A. S. Y.; Schoolnik, G. K. An inducible bundle-forming pilus of enteropathogenic *Escherichia coli*. *Science* **1991**, *254*, 710–713.

(87) Tobe, T.; Schoolnik, G. K.; Sohel, I.; Bustamante, V. H.; Puente, J. L. Cloning and characterization of *bfpTVW*, genes required for the transcriptional activation of *bfpA* in enteropathogenic *Escherichia coli*. *Mol. Microbiol*. **1996**, *21*, 963–975.

(88) Sohel, I.; Puente, J. L.; Ramer, S. W.; Bieber, D.; Wu, C.-Y.; Schoolnik, G. K. Enteropathogenic *Escherichia coli*: identification of a gene cluster coding for bundle-forming pilus morphogenesis. *J. Bacteriol*. **1996**, *178*, 2613–2628.

(89) de la Peña, C. F. M.; Masi, L. D.; Nisa, S.; Mulvey, G.; Tong, J.; Donnenberg, M. S.; Armstrong, G. D. BfpI, BfpJ, and BfpK minor pilins are important for the function and biogenesis of bundle-forming pili expressed by enteropathogenic *Escherichia coli. J. Bacteriol*. **2016**, *198*, 846–856.

(90) Cleary, J.; Lai, L.-C.; Shaw, R. K.; Straatman-Iwanowska, A.; Donnenberg, M. S.; Frankel, G.; Knutton, S. Enteropathogenic *Escherichia coli* (EPEC) adhesion to intestinal epithelial cells: role of bundle-forming pili (BFP), EspA filaments and intimin. *Microbiology* **2004**, *150*, 527–538.

(91) Allen-Vercoe, E.; Waddell, B.; Livingstone, S.; Deans, J.; DeVinney, R. Enteropathogenic *Escherichia coli* Tir translocation and pedestal formation requires membrane cholesterol in the absence of bundle-forming pili. *Cell. Microbiol*. **2006**, *8*, 613–624.

(92) Karch, H.; Bielaszewska, M.; Bitzan, M.; Schmidt, H. Epidemiology and diagnosis of Shiga toxin-producing *Escherichia coli* infections. *Diagn. Microbiol. Infect. Dis*. **1999**, *34*, 229–243.

(93) Griffin, P. M.; Tauxe, R. V. The epidemiology of infections caused by *Escherichia coli* O157:H7, other enterohemorrhagic *E. coli*, and the associated hemolytic uremic syndrome. *Epidemiol. Rev*. **1991**, *13*, 60–98.

(94) Bitzan, M.; Lapeyraque, A.-L. Postinfectious hemolytic uremic syndrome. *Pediatr. Kidney Dis.* **2016**, *17*, 653–731.

(95) Wijnsma, K. L.; van Bommel, S. A. M.; van der Velden, T.; Volokhina, E.; Schreuder, M. F.; van den Heuvel, L. P.; van de Kar, N. C. A. J. Fecal diagnostics in combination with serology: best test to establish STEC-HUS. *Pediatr. Nephrol*. **2016**, *31*, 2163–2170.

(96) Sartz, L.; De Jong, B.; Hjertqvist, M.; Plym-Forshell, L.; Alsterlund, R.; Löfdahl, S.; Osterman, B.; Ståhl, A.; Eriksson, E.; Hansson, H.-B.; et al. An outbreak of *Escherichia coli* O157:H7 infection in southern Sweden associated with consumption of fermented sausage; aspects of sausage production that increase the risk of contamination. *Epidemiol. Infect*. **2008**, *136*, 370–380.

(97) Tilden, J.; Young, W.; McNamara, A.-M.; Custer, C.; Boesel, B.; Lambert-Fair, M. A.; Majkowski, J.; Vugia, D.; Werner, S. B.; Hollingsworth, J.; et al. A new route of transmission for *Escherichia coli*: infection from dry fermented salami. *Am. J. Public Health* **1996**, *86*, 1142–1145.

(98) Pulz, M.; Matussek, A.; Monazahian, M.; Tittel, A.; Nikolic, E.; Hartmann, M.; Bellin, T.; Buer, J.; Gunzer, F. Comparison of a Shiga toxin enzyme-linked immunosorbent assay and two types of PCR for detection of Shiga toxin-producing *Escherichia coli* in human stool specimens. *J. Clin. Microbiol*. **2003**, *41*, 4671–4675.

(99) Ludwig, K.; Bitzan, M.; Bobrowski, C.; Müller-Wiefel, D. E. *Escherichia coli* O157 fails to induce a long-lasting lipopolysaccharide-specific, measurable humoral immune response in children with hemolytic-uremic Syndrome. *J. Infect. Dis*. **2002**, *186*, 566–569.

(100) Melton-Celsa, A. R. Shiga toxin (Stx) classification, structure, and function. *Microbiol. Spectr*. **2014**, *2*, EHEC-0024-2013.

(101) Serna, A.; Boedeker, E. C. Pathogenesis and treatment of Shiga toxin-producing *Escherichia coli* infections. *Curr. Opin. Gastroenterol*. **2008**, *24*, 38–47.

(102) Kimmitt, P. T.; Harwood, C. R.; Barer, M. R. Toxin gene expression by Shiga toxin-producing *Escherichia coli*: the role of antibiotics and the bacterial SOS response. *Emerg. Infect. Dis.* **2000**, *6*, 458–465.

(103) Pacheco, A. R.; Sperandio, V. Shiga toxin in enterohemorrhagic *E. coli*: regulation and novel anti-virulence strategies. *Front. Cell. Infect. Microbiol*. **2012**, *2*, 81.

(104) Bitzan, M. Treatment options for HUS secondary to *Escherichia coli* O157:H7. *Kidney Int.* **2009**, *75*, S62–S66.

(105) Panos, G. Z.; Betsi, G. I.; Falagas, M. E. Systematic review: are antibiotics detrimental or beneficial for the treatment of patients with *Escherichia coli* O157:H7 infection? *Aliment. Pharmacol. Ther.* **2006**, *24*, 731–742.

(106) Nassar, F. J.; Rahal, E. A.; Sabra, A.; Matar, G. M. Effects of subinhibitory concentrations of antimicrobial agents on *Escherichia coli* O157:H7 Shiga toxin release and role of the SOS response. *Foodborne Pathog. Dis*. **2013**, *10*, 805–812.

(107) Baharoglu, Z.; Mazel, D. SOS, the formidable strategy of bacteria against aggressions. *FEMS Microbiol. Rev*. **2014**, *38*, 1126–1145.

(108) Fadlallah, S. M.; Rahal, E. A.; Sabra, A.; Kissoyan, K. A. B.; Matar, G. M. Effect of rifampicin and gentamicin on Shiga toxin 2 expression level and the SOS response in *Escherichia coli* O104:H4. *Foodborne Pathog. Dis.* **2015**, *12*, 47–55.

(109) Ochoa, T. J.; Chen, J.; Walker, C. M.; Gonzales, E.; Cleary, T. G. Rifaximin does not induce toxin production or phage-mediated lysis of Shiga toxin-producing *Escherichia coli*. *Antimicrob. Agents Chemother*. **2007**, *51*, 2837–2841.

(110) Wong, C. S.; Jelacic, S.; Habeeb, R. L.; Watkins, S. L.; Tarr, P. I. The risk of the hemolytic-uremic syndrome after antibiotic treatment of *Escherichia coli* O157:H7 infections. *N. Engl. J. Med.* **2000**, *342*, 1930–1936.

(111) Hooper, D. C. Mechanisms of action of antimicrobials: focus on fluoroquinolones. *Clin. Infect. Dis.* **2001**, *32*, 9–15.

(112) Hitchings, G. H. Mechanism of action of trimethoprim-sulfamethoxazole. *J. Infect. Dis*. **1973**, *128*, S433–S436.

(113) Miller, C.; Ingmer, H.; Thomsen, L. E.; Skarstad, K.; Cohen, S. N. DpiA binding to the replication origin of *Escherichia coli* plasmids and chromosomes destabilizes plasmid inheritance and induces the bacterial SOS response. *J. Bacteriol*. **2003**, *185*, 6025–6031.

(114) Miller, C.; Thomsen, L. E.; Gaggero, C.; Mosseri, R.; Ingmer, H.; Cohen, S. N. SOS response induction by β-lactams and bacterial defense against antibiotic lethality. *Science* **2004**, *305*, 1629–1631.

(115) Hall, G.; Kurosawa, S.; Stearns-Kurosawa, D. J. Shiga toxin therapeutics: beyond neutralization. *Toxins* **2017**, *9*, 291.

(116) Majewski, D. D.; Worrall, L. J.; Hong, C.; Atkinson, C. E.; Vuckovic, M.; Watanabe, N.; Yu, Z.; Strynadka, N. C. J. Cryo-EM structure of the homohexameric T3SS ATPase-central stalk complex reveals rotary ATPase-like asymmetry. *Nat. Commun*. **2019**, *10*, 626.

(117) Biemans-Oldehinkel, E.; Sal-Man, N.; Deng, W.; Foster, L. J.; Finlay, B. B. Quantitative proteomic analysis reveals formation of an EscL-EscQ-EscN type III complex in enteropathogenic *Escherichia coli*. *J. Bacteriol*. **2011**, *193*, 5514–5519.

(118) Soto, E.; Espinosa, N.; Díaz-Guerrero, M.; Gaytán, M. O.; Puente, J. L.; González-Pedrajo, B. Functional characterization of EscK (Orf4), a sorting platform component of the enteropathogenic *Escherichia coli* injectisome. *J. Bacteriol*. **2017**, *199*, e00538.

(119) Ku, C.-P.; Lio, J. C.-W.; Wang, S.-H.; Lin, C.-N.; Syu, W.-J. Identification of a third EspA-binding protein that forms part of the type III secretion system of enterohemorrhagic *Escherichia coli*. *J. Biol. Chem.* **2009**, *284*, 1686–1693.

(120) Tseytin, I.; Mitrovic, B.; David, N.; Langenfeld, K.; Zarivach, R.; Diepold, A.; Sal-Man, N. The role of the small export apparatus protein, SctS, in the activity of the type III secretion system. *Front. Microbiol*. *2019*, *10*, 2551.

(121) Tseytin, I.; Madar, A.; Mitrovic, B.; Deng, W.; Finlay, B. B.; Sal-Man, N. The third transmembrane domain of EscR is critical for function of the enteropathogenic *Escherichia coli* type III secretion system. *mSphere* **2018**, *3*, e00162-18.

(122) Minamino, T.; Morimoto, Y. V.; Hara, N.; Aldridge, P. D.; Namba, K. The bacterial flagellar type III export gate complex is a dual fuel engine that can use both H^+ and Na^+ for flagellar protein export. *PLoS Pathog*. **2016**, *12*, e1005495.

(123) Ferris, H. U.; Furukawa, Y.; Minamino, T.; Kroetz, M. B.; Kihara, M.; Namba, K.; Macnab, R. M. FlhB regulates ordered export of flagellar components via autocleavage mechanism. *J. Biol. Chem*. **2005**, *280*, 41236–41242.

(124) Thomassin, J.-L.; He, X.; Thomas, N. A. Role of EscU auto-cleavage in promoting type III effector translocation into host cells by enteropathogenic *Escherichia coli*. *BMC Microbiol*. **2011**, *11*, 205.

(125) Sal-Man, N.; Deng, W.; Finlay, B. B. EscI: a crucial component of the type III secretion system forms the inner rod structure in enteropathogenic *Escherichia coli*. *Biochem. J.* **2012**, *442*, 119–125.

(126) Tseytin, I.; Dagan, A.; Oren, S.; Sal-Man, N. The role of EscD in supporting EscC polymerization in the type III secretion system of enteropathogenic *Escherichia coli*. *Biochim. Biophys. Acta - Biomembr.* **2018**, *1860*, 384–395.

(127) Spreter, T.; Yip, C. K.; Sanowar, S.; André, I.; Kimbrough, T. G.; Vuckovic, M.; Pfuetzner, R. A.; Deng, W.; Yu, A. C.; Finlay, B. B.; et al. A conserved structural motif mediates formation of the periplasmic rings in the type III secretion system. *Nat. Struct. Mol. Biol.* **2009**, *16*, 468–476.

(128) Burghout, P.; van Boxtel, R.; van Gelder, P.; Ringler, P.; Müller, S. A.; Tommassen, J.; Koster, M. Structure and electrophysiological properties of the YscC secretin from the type III secretion system of *Yersinia enterocolitica*. *J. Bacteriol.* **2004**, *186*, 4645–4654.

(129) Gauthier, A.; Puente, J. L.; Finlay, B. B. Secretin of the enteropathogenic *Escherichia coli* type III secretion system requires components of the type III apparatus for assembly and location. *Infect. Immun.* **2003**, *71*, 3310–3319.

(130) Reddy, B. L.; Saier, M. H. Properties and phylogeny of 76 families of bacterial and eukaryotic organellar outer membrane pore-forming proteins. *PLoS One* **2016**, *11*, e0152733.

(131) Howard, S. P.; Estrozi, L. F.; Bertrand, Q.; Contreras-Martel, C.; Strozen, T.; Job, V.; Martins, A.; Fenel, D.; Schoehn, G.; Dessen, A. Structure and assembly of pilotin-dependent and -independent secretins of the type II secretion system. *PLoS Pathog.* **2019**, *15*, e1007731.

(132) García-Gómez, E.; Espinosa, N.; de la Mora, J.; Dreyfus, G.; González-Pedrajo, B. The muramidase EtgA from enteropathogenic *Escherichia coli* is required for efficient type III secretion. *Microbiology* **2011**, *157*, 1145–1160.

(133) Wilson, R. K.; Shaw, R. K.; Daniell, S.; Knutton, S.; Frankel, G. Role of EscF, a putative needle complex protein, in the type III protein translocation system of enteropathogenic *Escherichia coli*. *Cell. Microbiol*. **2001**, *3*, 753–762.

(134) Sal-man, N.; Setiaputra, D.; Scholz, R.; Deng, W.; Yu, A. C. Y.; Strynadka, N. C. J.; Finlay, B. B. EscE and EscG are cochaperones for the type III needle protein EscF of enteropathogenic *Escherichia coli*. *J. Bacteriol*. **2013**, *195*, 2481–2489.

(135) Yip, C. K.; Finlay, B. B.; Strynadka, N. C. J. Structural characterization of a type III secretion system filament protein in complex with its chaperone. *Nat. Struct. Mol. Biol*. **2005**, *12*, 75–81.

(136) Delahay, R. M.; Knutton, S.; Shaw, R. K.; Hartland, E. L.; Pallen, M. J.; Frankel, G. The coiled-coil domain of EspA is essential for the assembly of the type III secretion translocon on the surface of enteropathogenic *Escherichia coli*. *J. Biol. Chem*. **1999**, *274*, 35969–35974.

(137) Knutton, S.; Rosenshine, I.; Pallen, M. J.; Nisan, I.; Neves, B. C.; Bain, C.; Wolff, C.; Dougan, G.; Frankel, G. A novel EspA-associated surface organelle of enteropathogenic *Escherichia coli* involved in protein translocation into epithelial cells. *EMBO J.* **1998**, *17*, 2166–2176.

(138) Daniell, S. J.; Kocsis, E.; Morris, E.; Knutton, S.; Booy, F. P.; Frankel, G. 3D structure of EspA filaments from enteropathogenic *Escherichia coli*. *Molec. Microbiol*. **2003**, *49*, 301–308.

(139) Shaw, R. K.; Daniell, S.; Ebel, F.; Frankel, G.; Knutton, S. EspA filament-mediated protein translocation into red blood cells. *Cell. Microbiol*. **2001**, *3*, 213–222.

(140) Creasey, E. A.; Friedberg, D.; Shaw, R. K.; Umanski, T.; Knutton, S.; Rosenshine, I.; Frankel, G. CesAB is an enteropathogenic *Escherichia coli* chaperone for the type-III translocator proteins EspA and EspB. *Microbiology* **2003**, *149*, 3639–3647.

(141) Luo, W.; Donnenberg, M. S. Interactions and predicted host membrane topology of the enteropathogenic *Escherichia coli* translocator protein EspB. *J. Bacteriol*. **2011**, *193*, 2972–2980.

(142) Hartland, E. L.; Daniell, S. J.; Delahay, R. M.; Neves, B. C.; Wallis, T.; Shaw, R. K.; Hale, C.; Knutton, S.; Frankel, G. The type III protein translocation system of enteropathogenic *Escherichia coli* involves EspA-EspB protein interactions. *Mol. Microbiol*. **2000**, *35*, 1483–1492.

(143) Ide, T.; Laarmann, S.; Greune, L.; Schillers, H.; Oberleithner, H.; Schmidt, M. A. Characterization of translocation pores inserted into plasma membranes by type III-secreted Esp proteins of enteropathogenic *Escherichia coli*. *Cell. Microbiol*. **2001**, *3*, 669-679.

(144) Chatterjee, A.; Caballero-Franco, C.; Bakker, D.; Totten, S.; Jardim, A. Pore-forming activity of the *Escherichia coli* type III secretion system protein EspD. *J. Biol. Chem*. **2015**, *290*, 25579–25594.

(145) Dasanayake, D.; Richaud, M.; Cyr, N.; Caballero-Franco, C.; Pittroff, S.; Finn, R. M.; Ausió, J.; Luo, W.; Donnenberg, M. S.; Jardim, A. The N-terminal amphipathic region of the *Escherichia coli* type III secretion system protein EspD is required for membrane insertion and function. *Mol. Microbiol*. **2011**, *81*, 734–750.

(146) Miki, H.; Takenawa, T. Regulation of actin dynamics by WASP family proteins. *J. Biochem*. **2003**, *134*, 309–313.

(147) Stewart, D. M.; Tian, L.; Nelson, D. L. Mutations that cause the Wiskott-Aldrich Syndrome impair the interaction of Wiskott-Aldrich syndrome protein (WASP) with WASP interacting protein. *J. Immunol*. **1999**, *162*, 5019–5024.

(148) Miki, H.; Miura, K.; Takenawa, T. N-WASP, a novel actin-depolymerizing protein, regulates the cortical cytoskeletal rearrangement in a PIP2-dependent manner downstream of tyrosine kinases. *EMBO J.* **1996**, *15*, 5326–5335.

(149) Machesky, L. M.; Insall, R. H. Scar1 and the related Wiskott-Aldrich Syndrome Protein, WASP, regulate the actin cytoskeleton through the Arp2/3 complex. *Curr. Biol*. **1998**, *8*, 1347–1356.

(150) Miki, H.; Takenawa, T. Direct binding of the verprolin-homology domain in N-WASP to actin is essential for cytoskeletal reorganization. *Biochem. Biophys. Res. Commun.* **1998**, *243*, 73–78.

(151) Rohatgi R.; Ma L.; Miki H.; Lopez M.; Kirchhausen T.; Takenawa T.; Kirschner M.W. The interaction between N-WASP and the Arp2/3 complex links Cdc42-dependent signals to actin assembly. *Cell* **1999**, *97*, 221–231.

(152) Miki, H.; Sasaki, T.; Takai, Y.; Takenawa, T. Induction of filopodium formation by a WASP-related actin-depolymerizing protein N-WASP. *Nature* **1998**, *391*, 93–96.

(153) Spiering, D.; Hodgson, L. Dynamics of the Rho-family small GTPases in actin regulation and motility. *Cell Adhes. Migr*. **2011**, *5*, 170–180.

(154) Ridley, A. J. Rho GTPases and actin dynamics in membrane protrusions and vesicle trafficking. *Trends Cell Biol*. **2006**, *16*, 522–529.

(155) Suetsugu, S.; Hattori, M.; Miki, H.; Tezuka, T.; Yamamoto, T.; Mikoshiba, K.; Takenawa, T. Sustained activation of N-WASP through phosphorylation is essential for neurite extension. *Dev. Cell* **2002**, *3*, 645–658.

(156) Banin, S.; Truong, O.; Katz, D. R.; Waterfield, M. D.; Brickell, P. M.; Gout, I. Wiskott-Aldrich syndrome protein (WASP) is a binding partner for c-Src family protein-tyrosine kinases. *Curr. Biol*. **1996**, *6*, 981–988.

(157) Miki, H.; Suetsugu, S.; Takenawa, T. WAVE, a novel WASP-family protein involved in actin reorganization induced by Rac. *EMBO J.* **1998**, *17*, 6932–6941.

(158) Symons, M.; Derry, J. M. J.; Karlak, B.; Jiang, S.; Lemahieu, V.; McCormick, F.; Francke, U.; Abo, A. Wiskott-Aldrich syndrome protein, a novel effector for the GTPase CDC42Hs, is implicated in actin polymerization. *Cell* **1996**, *84*, 723–734.

(159) Kempiak, S. J.; Yamaguchi, H.; Sarmiento, C.; Sidani, M.; Ghosh, M.; Eddy, R. J.; DesMarais, V.; Way, M.; Condeelis, J.; Segall, J. E. A neural Wiskott-Aldrich syndrome protein-mediated pathway for localized activation of actin polymerization that is regulated by cortactin. *J. Biol. Chem.* **2005**, *280*, 5836–5842.

(160) Nakagawa, H.; Miki, H.; Ito, M.; Ohashi, K.; Takenawa, T.; Miyamoto, S. N-WASP, WAVE and Mena play different roles in the organization of actin cytoskeleton in lamellipodia. *J. Cell Sci.* **2001**, *114*, 1555–1565.

(161) Wong, A. R. C.; Clements, A.; Raymond, B.; Crepin, V. F.; Frankel, G. The interplay between the *Escherichia coli* Rho guanine nucleotide exchange factor effectors and the mammalian RhoGEF inhibitor EspH. *mBio* **2012**, *3*, e00250-11.

(162) Sandu, P.; Crepin, V. F.; Drechsler, H.; McAinsh, A. D.; Frankel, G.; Berger, C. N. The enterohemorrhagic *Escherichia coli* effector EspW triggers actin remodeling in a Rac1-depedent manner. *Infect. Immun.* **2017**, *85*, e00244-17.

(163) Hardwidge, P. R.; Deng, W.; Vallance, B. A.; Rodriguez-Escudero, I.; Cid, V. J.; Molina, M.; Finlay, B. B. Modulation of host cytoskeleton function by the enteropathogenic *Escherichia coli* and *Citrobacter rodentium* effector protein EspG. *Infect. Immun.* **2005**, *73*, 2586–2594.

(164) Shaw, R. K.; Smollett, K.; Cleary, J.; Garmendia, J.; Straatman-Iwanowska, A.; Frankel, G.; Knutton, S. Enteropathogenic *Escherichia coli* type III effectors EspG and EspG2 disrupt the microtubule network of intestinal epithelial cells. *Infect. Immun.* **2005**, *73*, 6283–6289.

(165) Singh, V.; Davidson, A.; Hume, P. J.; Koronakis, V. Pathogenic *Escherichia coli* hijacks GTPase-activated p21-activated kinase for actin pedestal formation. *mBio* **2019**, *10*, e01876-19.

(166) Germane, K. L.; Spiller, B. W. Structural and functional studies indicate that the EPEC effector, EspG, directly binds p21-activated kinase. *Biochemistry* **2011**, *50*, 917–919.

(167) Singh, V.; Davidson, A. C.; Hume, P. J.; Humphreys, D.; Koronakis, V. Arf GTPase interplay with Rho GTPases in regulation of the actin cytoskeleton. *Small GTPases* **2019**, *10*, 411–418.

(168) LeClaire, L. L.; Baumgartner, M.; Iwasa, J. H.; Mullins, R. D.; Barber, D. L. Phosphorylation of the Arp2/3 complex is necessary to nucleate actin filaments. *J. Cell Biol*. **2008**, *182*, 647–654.

(169) DeVinney, R.; Stein, M.; Reinscheid, D.; Abe, A.; Ruschkowski, S.; Finlay, B. B. Enterohemorrhagic *Escherichia coli* O157:H7 produces Tir, which is translocated to the host cell membrane but is not tyrosine phosphorylated. *Infect. Immun*. **1999**, *67*, 2389–2398.

(170) Kenny, B. Phosphorylation of tyrosine 474 of the enteropathogenic *Escherichia coli* (EPEC) Tir receptor molecule is essential for actin nucleating activity and is preceded by additional host modifications. *Mol. Microbiol*. **1999**, *31*, 1229–1241.

(171) de Grado, M.; Abe, A.; Gauthier, A.; Steele-Mortimer, O.; DeVinney, R.; Finlay, B. B. Identification of the intimin-binding domain of Tir of enteropathogenic *Escherichia coli. Cell. Microbiol*. **1999**, *1*, 7–17.

(172) Freeman, N. L.; Zurawski, D. V.; Chowrashi, P.; Ayoob, J. C.; Huang, L.; Mittal, B.; Sanger, J. M.; Sanger, J. W. Interaction of the enteropathogenic *Escherichia coli* protein, translocated intimin receptor (Tir), with focal adhesion proteins. *Cell Motil. Cytoskeleton* **2000**, *47*, 307–318.

(173) Goosney, D. L.; DeVinney, R.; Pfuetzner, R. A.; Frey, E. A.; Strynadka, N. C.; Finlay, B. B. Enteropathogenic *E. coli* translocated intimin receptor, Tir, interacts directly with α-actinin. *Curr. Biol*. **2000**, *10*, 735–738.

(174) Batchelor, M.; Guignot, J.; Patel, A.; Cummings, N.; Cleary, J.; Knutton, S.; Holden, D. W.; Connerton, I.; Frankel, G. Involvement of the intermediate filament protein cytokeratin-18 in actin pedestal formation during EPEC infection. *EMBO Rep*. **2004**, *5*, 104–110.

(175) Gruenheid, S.; DeVinney, R.; Bladt, F.; Goosney, D.; Gelkop, S.; Gish, G. D.; Pawson, T.; Finlay, B. B. Enteropathogenic *E. coli* Tir binds Nck to initiate actin pedestal formation in host cells. *Nat. Cell Biol*. **2001**, *3*, 856–859.

(176) Garmendia, J.; Phillips, A. D.; Carlier, M. F.; Chong, Y.; Schüller, S.; Marches, O.; Dahan, S.; Oswald, E.; Shaw, R. K.; Knutton, S.; et al. TccP is an enterohaemorrhagic *Escherichia coli* O157:H7 type III effector protein that couples Tir to the actin-cytoskeleton. *Cell. Microbiol*. **2004**, *6*, 1167–1183.

(177) Sallee, N. A.; Rivera, G. M.; Dueber, J. E.; Vasilescu, D.; Mullins, R. D.; Mayer, B. J.; Lim, W. A. The pathogen protein EspFU hijacks actin polymerization using mimicry and multivalency. *Nature* **2008**, *454*, 1005–1008.

(178) Hamaguchi, M.; Hamada, D.; Suzuki, K. N.; Sakata, I.; Yanagihara, I. Molecular basis of actin reorganization promoted by binding of enterohaemorrhagic *Escherichia coli* EspB to α-catenin. *FEBS J.* **2008**, *275*, 6260–6267.

(179) Kodama, T.; Akeda, Y.; Kono, G.; Takahashi, A.; Imura, K.; Iida, T.; Honda, T. The EspB protein of enterohaemorrhagic *Escherichia coli* interacts directly with α-catenin. *Cell. Microbiol*. **2002**, *4*, 213–222.

(180) Marchès, O.; Covarelli, V.; Dahan, S.; Cougoule, C.; Bhatta, P.; Frankel, G.; Caron, E. EspJ of enteropathogenic and enterohaemorrhagic *Escherichia coli* inhibits opsono-phagocytosis. *Cell. Microbiol*. **2008**, *10*, 1104–1115.

(181) Wright, S. D.; Reddy, P. A.; Jong, M. T. C.; Erickson, B. W. C3bi receptor (complement receptor type 3) recognizes a region of complement protein C3 containing the sequence Arg-Gly-Asp. *Proc. Natl. Acad. Sci. USA* **1987**, *84*, 1965–1968.

(182) Lund, J.; Takahashi, N.; Pound, J. D.; Goodall, M.; Jefferis, R. Multiple interactions of IgG with its core oligosaccharide can modulate recognition by complement and human Fc gamma receptor I and influence the synthesis of its oligosaccharide chains. *J. Immunol*. **2007**, *157*, 4963–4969.

(183) Young, J. C.; Clements, A.; Lang, A. E.; Garnett, J. A.; Munera, D.; Arbeloa, A.; Pearson, J.; Hartland, E. L.; Matthews, S. J.; Mousnier, A.; et al. The *Escherichia coli* effector EspJ blocks Src kinase activity via amidation and ADP ribosylation. *Nat. Commun*. **2014**, *5*, 5887.

(184) Pollard, D. J.; Berger, C. N.; So, E. C.; Yu, L.; Hadavizadeh, K.; Jennings, P.; Tate, E. W.; Choudhary, J. S.; Frankel, G. Broad-spectrum regulation of nonreceptor tyrosine kinases by the bacterial ADP-ribosyltransferase EspJ. *mBio* **2018**, 9, e00170-18.

(185) Martinez-Argudo, I.; Sands, C.; Jepson, M. A. Translocation of enteropathogenic *Escherichia coli* across an in vitro M cell model is regulated by its type III secretion system. *Cell. Microbiol.* **2007**, *9*, 1538–1546.

(186) Quitard, S.; Dean, P.; Maresca, M.; Kenny, B. The enteropathogenic *Escherichia coli* EspF effector molecule inhibits PI-3 kinase-mediated uptake independently of mitochondrial targeting. *Cell. Microbiol.* **2006**, *8*, 972–981.

(187) Beemiller, P.; Zhang, Y.; Mohan, S.; Levinsohn, E.; Gaeta, I.; Hoppe, A. D.; Swanson, J. A. A Cdc42 activation cycle coordinated by PI 3-kinase during Fc receptor-mediated phagocytosis. *Mol. Biol. Cell* **2010**, *21*, 470–480.

(188) Turner, M. D.; Nedjai, B.; Hurst, T.; Pennington, D. J. Cytokines and chemokines: at the crossroads of cell signalling [*sic*] and inflammatory disease. *Biochim. Biophys. Acta - Mol. Cell Res*. **2014**, *1843*, 2563–2582.

(189) Szul, T.; Grabski, R.; Lyons, S.; Morohashi, Y.; Shestopal, S.; Lowe, M.; Sztul, E. Dissecting the role of the ARF guanine nucleotide exchange factor GBF1 in Golgi biogenesis and protein trafficking. *J. Cell Sci*. **2007**, *120*, 3929–3940.

(190) Suda, Y.; Kurokawa, K.; Nakano, A. Regulation of ER-Golgi transport dynamics by GTPases in budding yeast. *Front. Cell Dev. Biol*. **2018**, *5*, 122.

(191) Sandoval, C. O.; Simmen, T. Rab proteins of the endoplasmic reticulum: functions and interactors. *Biochem. Soc. Trans*. **2012**, *40*, 1426–1432.

(192) Brandizzi, F.; Barlowe, C. Organization of the ER-Golgi interface for membrane traffic control. *Natl. Rev. Mol. Cell Biol*. **2013**, *14*, 382–392.

(193) Olsen, R. L.; Echtenkamp, F.; Cheranova, D.; Deng, W.; Finlay, B. B.; Hardwidge, P. R. The enterohemorrhagic *Escherichia coli* effector protein NleF binds mammalian Tmp21. *Vet. Microbiol*. **2013**, *164*, 164–170.

(194) Dong, N.; Zhu, Y.; Lu, Q.; Hu, L.; Zheng, Y.; Shao, F. Structurally distinct bacterial TBC-like GAPs Link Arf GTPase to Rab1 inactivation to counteract host defenses. *Cell* **2012**, *150*, 1029–1041.

(195) Selyunin, A. S.; Reddick, L. E.; Weigele, B. A.; Alto, N. M. Selective protection of an Arf1-GTP signaling axis by a bacterial scaffold induces bidirectional trafficking arrest. *Cell Rep.* **2011**, *6*, 878–891.

(196) Furniss, R. C. D.; Slater, S.; Frankel, G.; Clements, A. Enterohaemorrhagic *E. coli* modulates an ARF6:Rab35 signaling axis to prevent recycling endosome maturation during infection. *J. Mol. Biol*. **2016**, *428*, 3399–3407.

(197) Kim, J.; Thanabalasuriar, A.; Chaworth-Musters, T.; Fromme, J. C.; Frey, E. A.; Lario, P. I. I.; Metalnikov, P.; Rizg, K.; Thomas, N. A.; Lee, S. F.; et al. The bacterial virulence factor NleA inhibits cellular protein secretion by disrupting mammalian COPII function. *Cell Host Microbe* **2007**, *2*, 160–171.

(198) Thanabalasuriar, A.; Bergeron, J.; Gillingham, A.; Mimee, M.; Thomassin, J.-L.; Strynadka, N.; Kim, J.; Gruenheid, S. Sec24 interaction is essential for localization and virulence-associated function of the bacterial effector protein NleA. Cell. Microbiol. **2012**, *14*, 1206–1218.

(199) Mihaly, S. R.; Ninomiya-Tsuji, J.; Morioka, S. TAK1 control of cell death. *Cell Death Differ.* **2014**, *21*, 1667–1676.

(200) Dorrington, M. G.; Fraser, I. D. C. NF-κB signaling in macrophages: dynamics, crosstalk, and signal integration. *Front. Immunol*. **2019**, *10*, 705.

(201) Zeke, A.; Misheva, M.; Reményi, A.; Bogoyevitch, M. A. JNK signaling: regulation and functions based on complex protein-protein partnerships. *Microbiol. Mol. Biol. Rev*. **2016**, *80*, 793–835.

(202) Morrison, D. K. MAP Kinase Pathways. *Cold Spring Harb. Perspect. Biol.* **2012**, *4*, 892–908.

(203) Zhang, L.; Ding, X.; Cui, J.; Xu, H.; Chen, J.; Gong, Y. N.; Hu, L.; Zhou, Y.; Ge, J.; Lu, Q.; et al. Cysteine methylation disrupts ubiquitin-chain sensing in NF-κB activation. *Nature* **2012**, *481*, 204–210.

(204) Pallett, M. A.; Berger, C. N.; Pearson, J. S.; Hartland, E. L.; Frankel, G. The type III secretion effector NleF of enteropathogenic *Escherichia coli* activates NF-κB early during infection. *Infect. Immun*. **2014**, *82*, 4878–4888.

(205) Ruchaud-Sparagano, M. H.; Mühlen, S.; Dean, P.; Kenny, B. The enteropathogenic *E. coli* (EPEC) Tir effector inhibits NF-κB activity by targeting TNFα receptor-associated factors. *PLoS Pathog*. **2011**, *7*, e1002414.

(206) Zhou, R.; Chen, Z.; Hao, D.; Wang, Y.; Zhang, Y.; Yi, X.; Lyu, L. D.; Liu, H.; Zou, Q.; Chu, Y.; et al. Enterohemorrhagic *Escherichia coli* Tir inhibits TAK1 activation and mediates immune evasion. *Emerg. Microbes Infect*. **2019**, *8*, 734–748.

(207) Yan, D.; Quan, H.; Wang, L.; Liu, F.; Liu, H.; Chen, J.; Cao, X.; Ge, B. Enteropathogenic *Escherichia coli* Tir recruits cellular SHP-2 through ITIM motifs to suppress host immune response. *Cell. Signal*. **2013**, *25*, 1887–1894.

(208) Gao, X.; Pham, T. H.; Feuerbacher, L. A.; Chen, K.; Hays, M. P.; Singh, G.; Rueter, C.; Hurtado-Guerrero, R.; Hardwidge, P. R. *Citrobacter rodentium* NleB protein inhibits tumor necrosis factor (TNF) receptor-associated factor 3 (TRAF3) ubiquitination to reduce host type I interferon production. *J. Biol. Chem*. **2016**, *291*, 18232–18238.

(209) Hodgson, A.; Wier, E. M.; Fu, K.; Sun, X.; Yu, H.; Zheng, W.; Sham, H. P.; Johnson, K.; Bailey, S.; Vallance, B. A.; et al. Metalloprotease NleC suppresses host NF-κB/inflammatory responses by cleaving p65 and interfering with the p65/RPS3 interaction. *PLoS Pathog*. **2015**, *11*, e1004705.

(210) Shames, S. R.; Bhavsar, A. P.; Croxen, M. A.; Law, R. J.; Mak, S. H. C.; Deng, W.; Li, Y.; Bidshari, R.; de Hoog, C. L.; Foster, L. J.; et al. The pathogenic *Escherichia coli* type III secreted protease NleC degrades the host acetyltransferase p300. *Cell. Microbiol*. **2011**, *13*, 1542–1557.

(211) Mühlen, S.; Ruchaud-Sparagano, M. H.; Kenny, B. Proteasome-independent degradation of canonical NFκB complex components by the NleC protein of pathogenic *Escherichia coli*. *J. Biol. Chem*. **2011**, *286*, 5100–5107.

(212) Shames, S. R.; Finlay, B. B. Proteolytic cleavage of NF-κB p65: a novel mechanism for subversion of innate immune signaling by pathogenic *E. coli*. *Front. Microbiol*. **2011**, *2*, 38.

(213) Pearson, J. S.; Riedmaier, P.; Marchès, O.; Frankel, G.; Hartland, E. L. A Type III effector protease NleC from enteropathogenic *Escherichia coli* targets NF-κB for degradation. *Mol. Microbiol.* **2011**, *80*, 219–230.

(214) Yen, H.; Ooka, T.; Iguchi, A.; Hayashi, T.; Sugimoto, N.; Tobe, T. NleC, a type III secretion protease, compromises NF-κB activation by targeting p65/RelA. *PLoS Pathog*. **2010**, 6, e1001231.

(215) Sham, H. P.; Shames, S. R.; Croxen, M. A.; Ma, C.; Chan, J. M.; Khan, M. A.; Wickham, M. E.; Deng, W.; Finlay, B. B.; Vallance, B. A. Attaching and effacing bacterial effector NleC suppresses epithelial inflammatory responses by inhibiting NF-κB and p38 mitogen-activated protein kinase activation. *Infect. Immun.* **2011**, *79*, 3552–3562.

(216) Creuzburg, K.; Giogha, C.; Lung, T. W. F.; Scott, N. E.; Mühlen, S.; Hartland, E. L.; Pearson, S. The type III effector NleD from enteropathogenic Escherichia coli differentiates between host substrates p38 and JNK. *Infect. Immun*. **2016**, *85*, e00620-16.

(217) Marchés, O.; Wiles, S.; Dziva, F.; Ragione, R. M. La; Schüller, S.; Best, A.; Phillips, A. D.; Hartland, E. L.; Woodward, M. J.; Stevens, M. P.; et al. Characterization of two non-locus of

enterocyte effacement-encoded type III-translocated effectors, NleC and NleD, in attaching and effacing pathogens. *Infect. Immun*. **2005**, *73*, 8411–8417.

(218) Baruch, K.; Gur-Arie, L.; Nadler, C.; Koby, S.; Yerushalmi, G.; Ben-Neriah, Y.; Yogev, O.; Shaulian, E.; Guttman, C.; Zarivach, R.; et al. Metalloprotease type III effectors that specifically cleave JNK and NF-κB. *EMBO J.* **2011**, *30*, 221–231.

(219) Pham, T. H.; Gao, X.; Tsai, K.; Olsen, R.; Wan, F.; Hardwidge, P. R. Functional differences and interactions between the *Escherichia coli* type III secretion system effectors NleH1 and NleH2. *Infect. Immun*. **2012**, *80*, 2133–2140.

(220) Gao, X.; Wan, F.; Mateo, K.; Callegari, E.; Wang, D.; Deng, W.; Li, F.; Chaussee, M. S.; Finlay, B. B.; Lenardo, M. J.; et al. Bacterial effector binding to ribosomal protein S3 subverts NF-κB function. *PLoS Pathog*. **2009**, 5, e1000708.

(221) Wan, F.; Weaver, A.; Gao, X.; Bern, M.; Hardwidge, P. R.; Lenardo, M. J. IKKβ phosphorylation regulates RPS3 nuclear translocation and NF-κB function during infection with *Escherichia coli* strain O157:H7. *Nat. Immunol*. **2011**, 12, 335-343.

(222) Yen, H.; Sugimoto, N.; Tobe, T. Enteropathogenic *Escherichia coli* uses NleA to inhibit NLRP3 inflammasome activation. *PLoS Pathog*. **2015**, *11*, e1005121.

(223) Raymond, B.; Crepin, V. F.; Collins, J. W.; Frankel, G. The WxxxE effector EspT triggers expression of immune mediators in an Erk/JNK and NF-κB-dependent manner. *Cell. Microbiol*. **2011**, *13*, 1881–1893.

(224) Bulgin, R.; Arbeloa, A.; Goulding, D.; Dougan, G.; Crepin, V. F.; Raymond, B.; Frankel, G. The T3SS effector EspT defines a new category of invasive enteropathogenic *E. coli* (EPEC) which form intracellular actin pedestals. PLoS Pathog. 2009, 5, e1000683.

(225) Santos, A. S.; Finlay, B. B. Bringing down the host: enteropathogenic and enterohaemorrhagic Escherichia coli effector-mediated subversion of host innate immune pathways. *Cell. Microbiol*. **2015**, *17*, 318–332.

(226) Marchès, O.; Ledger, T. N.; Boury, M.; Ohara, M.; Tu, X.; Goffaux, F.; Mainil, J.; Rosenshine, I.; Sugai, M.; Rycke, J. De; et al. Enteropathogenic and enterohaemorrhagic *Escherichia coli* deliver a novel effector called Cif, which blocks cell cycle G_2/M transition. *Mol. Microbiol.* **2003**, *50*, 1553–1567.

(227) Charpentier, X.; Oswald, E. Identification of the secretion and translocation domain of the enteropathogenic and enterohemorrhagic *Escherichia coli* effector Cif, using TEM-1 β-lactamase as a new fluorescence-based reporter. *J. Bacteriol*. **2004**, *186*, 5486–5495.

(228) Hsu, Y.; Jubelin, G.; Taieb, F.; Nougayrède, J.-P.; Oswald, E.; Stebbins, C. E. Structure of the cyclomodulin Cif from pathogenic *Escherichia coli*. *J. Mol. Biol*. **2009**, *384*, 465–477.

(229) Samba-Louaka, A.; Nougayrède, J.; Watrin, C.; Oswald, E.; F. Taieb. The enteropathogenic Escherichia coli effector Cif induces delayed apoptosis in epithelial cells. *Infect. Immun*. **2009**, *77*, 5471–5477.

(230) Kenny, B.; Jepson, M. Targeting of an enteropathogenic *Escherichia coli* (EPEC) effector protein to host mitochondria. *Cell. Microbiol*. **2000**, *2*, 579-590.

(231) Ma, C.; Wickham, M. E.; Guttman, J. A.; Deng, W.; Walker, J.; Madsen, K. L.; Jacobson, K.; Vogl, W. A.; Finlay, B. B.; Vallance, B. A. *Citrobacter rodentium* infection causes both mitochondrial dysfunction and intestinal epithelial barrier disruption *in vivo*: role of mitochondrial associated protein (Map). *Cell. Microbiol*. **2006**, *8*, 1669–1686.

(232) Papatheodorou, P.; Domańska, G.; Öxle, M.; Mathieu, J.; Selchow, O.; Kenny, B.; Rassow, J. The enteropathogenic *Escherichia coli* (EPEC) Map effector is imported into the mitochondrial

matrix by the TOM/Hsp70 system and alters organelle morphology. *Cell. Microbiol*. **2006**, *8*, 677–689.

(233) Kenny, B.; Ellis, S.; Leard, A. D.; Warawa, J.; Mellor, H.; Jepson, M. A. Co-ordinate regulation of distinct host cell signalling [*sic*] pathways by multifunctional enteropathogenic *Escherichia coli* effector molecules. *Cell. Microbiol*. **2002**, *44*, 1095–1107.

(234) Nougayrède, J.; Donnenberg, M. S. Enteropathogenic *Escherichia coli* EspF is targeted to mitochondria and is required to initiate the mitochondrial death pathway. *Cell. Microbiol*. **2004**, *6*, 1097–1111.

(235) Crane, J. K.; McNamara, B. P.; Donnenberg, M. S. Role of EspF in host cell death induced by enteropathogenic *Escherichia coli*. *Cell. Microbiol*. **2001**, *3*, 197-211.

(236) Nagai, T.; Abe, A.; Sasakawa, C. Targeting of enteropathogenic *Escherichia coli* EspF to host mitochondria is essential for bacterial pathogenesis. *J. Biol. Chem*. **2005**, *280*, 2998–3011.

(237) Nougayrède, J.; Foster, G. H.; Donnenberg, M. S. Enteropathogenic *Escherichia coli* effector EspF interacts with host protein Abcf2. *Cell. Microbiol*. **2007**, *9*, 680–693.

(238) Blasche, S.; Mörtl, M.; Steuber, H.; Siszler, G.; Nisa, S.; Schwarz, F.; Blasche, S.; Mo, M.; Lavrik, I.; Gronewold, T. M. A.; Maskos, K.; Donnenberg, M. S.; et al. The *E. coli* effector protein NleF is a caspase inhibitor. *PLoS One* **2013**, *8*,e58937.

(239) Song, T.; Li, K.; Zhou, W.; Zhou, J.; Jin, Y.; Dai, H.; Xu, T.; Hu, M.; Ren, H.; Yue, J.; et al. A type III effector NleF from EHEC inhibits epithelial inflammatory cell death by targeting caspase-4. *Biomed Res. Int*. **2017**, *2017*, 4101745.

(240) Ashkenazi, A.; Dixit, V. M. Death receptors: signaling and modulation. *Apoptosis* **1998**, *281*, 1305–1308.

(241) Shaulian, E.; Karin, M. AP-1 in cell proliferation and survival. *Oncogene* **2001**, *20*, 2390–2400.

(242) Gao, X.; Wang, X.; Pham, T. H.; Feuerbacher, L. A.; Lubos, M. L.; Huang, M.; Olsen, R.; Mushegian, A.; Slawson, C.; Hardwidge, P. R. NleB, a bacterial effector with glycosyltransferase activity, targets GADPH function to inhibit NF-κB activation. *Cell Host Microbe* **2013**, *13*, 87–99.

(243) Pearson, J. S.; Giogha, C.; Ong, S. Y.; Kennedy, C. L.; Kelly, M.; Robinson, K. S.; Lung, T. W. F.; Mansell, A.; Riedmaier, P.; Oates, C. V. L.; Zaid, A.; Mühlen, S.; Crepin, V. F.; Wong, T.; Lung, F.; Mansell, A.; et al. A type III effector antagonizes death receptor signalling [*sic*] during bacterial gut infection. *Nature* **2013**, *501*, 247–251.

(244) Li, S.; Zhang, L.; Yao, Q.; Li, L.; Dong, N.; Rong, J.; Gao, W.; Ding, X.; Sun, L.; Chen, X.; et al. Pathogen blocks host death receptor signalling [*sic*] by arginine GlcNAcylation of death domains. *Nature* **2013**, *501*, 242-245.

(245) Wang, C.; Youle, R. J. The role of the mitochondria in apoptosis. *Annu. Rev. Genet*. **2009**, *43*, 95–118.

(246) Tsujimoto, Y.; Nakagawa, T.; Shimizu, S. Mitochondrial membrane permeability transition and cell death. *Biochim. Biophys. Acta* **2006**, *1757*, 1297–1300.

(247) Chipuk, J. E.; Kuwana, T.; Bouchier-Hayes, L.; Droin, N. M.; Newmeyer, D. D.; Schuler, M.; Green, D. R. Direct activation of Bax by p53 mediates mitochondrial membrane permeabilization and apoptosis. *Science* **2004**, *303*, 1010–1015.

(248) Kim, H.; Du, F.; Fang, M.; Wang, X. Formation of apoptosome is initiated by cytochrome *c*-induced DATP hydrolysis and subsequent nucleotide exchange on Apaf-1. *Proc. Natl. Acad. Sci*. **2005**, *102*, 17545–17550.

(249) Hemrajani, C.; Berger, C. N.; Robinson, K. S.; Marchès, O.; Mousnier, A.; Frankel, G. NleH effectors interact with Bax inhibitor-1 to block apoptosis during enteropathogenic *Escherichia coli* infection. *Proc. Natl. Acad. Sci.* **2010**, *107*, 3129–3134.

(250) Shames, S. R.; Croxen, M. A.; Deng, W.; Finlay, B. B. The type III system-secreted effector EspZ localizes to host mitochondria and interacts with the translocase of inner mitochondrial membrane 17b. *Infect. Immun.* **2011**, *79*, 4784–4790.

(251) Berger, C. N.; Crepin, V. F.; Baruch, K.; Mousnier, A.; Rosenshine, I.; Frankel, G. EspZ of enteropathogenic and enterohemorrhagic Escherichia coli regulates type III secretion system protein translocation. *mBio* **2012**, *3*, e00317-12.

(252) Ugalde-Silva, P.; Gonzalez-Lugo, O.; Navarro-Garcia, F. Tight junction disruption induced by type 3 secretion system effectors injected by enteropathogenic and enterohemorrhagic *Escherichia coli*. *Front. Cell. Infect. Microbiol*. **2016**, *6*, 87.

(253) Van Itallie, C. M.; Anderson, J. M. Claudins and epithelial paracellular transport. *Annu. Rev. Physiol*. **2006**, *68*, 403–429.

(254) González-Mariscal, L.; Betanzos, A.; Nava, P.; Jaramillo, B. E.; Tight junction proteins. *Prog. Biophys. Mol. Biol*. **2003**, *81*, 1–44.

(255) Furuse, M.; Fujita, K.; Hiiragi, T.; Fujimoto, K.; Tsukita, S. Claudin-1 and -2: novel integral membrane proteins localizing at tight junctions with no sequence similarity to occludin. *J. Cell Biol.* **1998**, *141*, 1539–1550.

(256) Furuse, M.; Hirase, T.; Itoh, M.; Nagafuchi, A.; Yonemura, S.; Tsukita, S.; Tsukita, S. Occludin: a novel integral membrane protein localizing at tight junctions. *J. Cell Biol*. **1993**, *123*, 1777–1788.

(257) Martìn-Padura, I.; Lostaglio, S.; Schneemann, M.; Williams, L.; Romano, M.; Fruscella, P.; Panzeri, C.; Stoppacciaro, A.; Ruco, L.; Villa, A.; et al. Junctional adhesion molecule, a novel member of the immunoglobulin superfamily that distributes at intercellular junctions and modulates monocyte transmigration. *J. Cell Biol*. **1998**, *142*, 117–127.

(258) Srinivasan, B.; Kolli, A. R.; Esch, M. B.; Abaci, H. E.; Shuler, M. L.; Hickman, J. J. TEER measurement techniques for *in vitro* barrier model systems. *J. Lab Autom*. **2015**, *20*, 107–126.

(259) Thanabalasuriar, A.; Koutsouris, A.; Hecht, G.; Gruenheid, S. The bacterial virulence factor NleA's involvement in intestinal tight junction disruption during enteropathogenic *E. coli* infection is independent of its putative PDZ binding domain. *Gut Microbes* **2010**, *1*, 114–118.

(260) Thanabalasuriar, A.; Koutsouris, A.; Weflen, A.; Mimee, M.; Hecht, G.; Gruenheid, S. The bacterial virulence factor NleA is required for the disruption of intestinal tight junctions by enteropathogenic *Escherichia coli*. *Cell. Microbiol*. **2010**, *12*, 31–41.

(261) Thanabalasuriar, A.; Kim, J.; Gruenheid, S. The inhibition of COPII trafficking is important for intestinal epithelial tight junction disruption during enteropathogenic *Escherichia coli* and *Citrobacter rodentium* infection. *Microbes Infect.* **2013**, *15*, 738–744.

(262) McNamara, B. P.; Koutsouris, A.; O'Connell, C. B.; Nougayréde, J.; Donnenberg, M. S.; Hecht, G. Translocated EspF protein from enteropathogenic *Escherichia coli* disrupts host intestinal barrier function. *J. Clin. Invest*. **2001**, *107*, 621–629.

(263) Viswanathan, V. K.; Koutsouris, A.; Lukic, S.; Pilkinton, M.; Simonovic, I.; Simonovic, M.; Hecht, G. Comparative analysis of EspF from enteropathogenic and enterohemorrhagic *Escherichia coli* in alteration of epithelial barrier function. *Infect. Immun*. **2004**, *72*, 3218–3227.

(264) Peralta-Ramírez, J.; Hernandez, M.; Manning-Cela, R.; Luna-Muñoz, J.; Garcia-Tovar, C.; Nougayréde, J. P.; Oswald, E.; Navarro-Garcia, F. EspF interacts with nucleation-promoting

factors to recruit junctional proteins into pedestals for pedestal maturation and disruption of paracellular permeability. *Infect. Immun*. **2008**, *76*, 3854–3868.

(265) Dean, P.; Kenny, B. Intestinal barrier dysfunction by enteropathogenic *Escherichia coli* is mediated by two effector molecules and a bacterial surface protein. *Mol. Microbiol*. **2004**, *54*, 665–675.

(266) Tomson, F. L.; Viswanathan, V. K.; Kanack, K. J.; Kanteti, R. P.; Straub, K. V.; Menet, M.; Kaper, J. B.; Hecht, G. Enteropathogenic *Escherichia coli* EspG disrupts microtubules and in conjunction with Orf3 enhances perturbation of the tight junction barrier. *Mol. Microbiol*. **2005**, *56*, 447–464.

(267) Glotfelty, L. G.; Zahs, A.; Hodges, K.; Shan, K.; Alto, N. M.; Hecht, G. A. Enteropathogenic *E. coli* effectors EspG1/G2 disrupt microtubules, contribute to tight junction perturbation and inhibit restoration. *Cell Microbiol*. **2014**, *16*, 1767–1783.

(268) Simovitch, M.; Sason, H.; Cohen, S.; Zahavi, E. E.; Melamed-Book, N.; Weiss, A.; Aroeti, B.; Rosenshine, I. EspM inhibits pedestal formation by enterohaemorrhagic *Escherichia coli* and enteropathogenic *E. coli* and disrupts the architecture of a polarized epithelial monolayer. *Cell. Microbiol.* **2010**, *12*, 489–505.

(269) Wilharm, G.; Dittmann, S.; Schmid, A.; Heesemann, J. On the role of specific chaperones, the specific ATPase, and the proton motive force in type III secretion. *Int. J. Med. Microbiol*. **2007**, *297*, 27–36.

(270) Runte, C. S.; Jain, U.; Getz, L. J.; Secord, S.; Kuwae, A.; Abe, A.; LeBlanc, J. J.; Stadnyk, A. W.; Kaper, J. B.; Hansen, A.-M.; et al. Tandem tyrosine phosphosites in the enteropathogenic *Escherichia coli* chaperone CesT are required for differential type III effector translocation and virulence. *Mol. Microbiol*. **2018**, *108*, 536–550.

(271) Thomas, N. A.; Deng, W.; Puente, J. L.; Frey, E. A.; Yip, C. K.; Strynadka, N. C. J.; Finlay, B. B. CesT is a multi-effector chaperone and recruitment factor required for the efficient type III secretion of both LEE- and non-LEE-encoded effectors of enteropathogenic *Escherichia coli*. *Mol. Microbiol*. **2005**, *57*, 1762–1779.

(272) Creasey, E. A.; Delahay, R. M.; Bishop, A. A.; Shaw, R. K.; Kenny, B.; Knutton, S.; Frankel, G. CesT is a bivalent enteropathogenic *Escherichia coli* chaperone required for translocation of both Tir and Map. *Mol. Microbiol.* **2003**, *47*, 209–221.

(273) Abe, A.; de Grado, M.; Pfuetzner, R. A.; Sánchez-SanMartín, C.; DeVinney, R.; Puente, J. L.; Strynadka, N. C. J.; Finlay, B. B. Enteropathogenic *Escherichia coli* translocated intimin receptor, Tir, requires a specific chaperone for stable secretion. *Mol. Microbiol*. **1999**, *33*, 1162–1175.

(274) Elliott, S. J.; O'Connell, C. B.; Koutsouris, A.; Brinkley, C.; Donnenberg, M. S.; Hecht, G.; Kaper, J. B. A gene from the locus of enterocyte effacement that is required for enteropathogenic *Escherichia coli* to increase tight-junction permeability encodes a chaperone for EspF. *Infect. Immun.* **2002**, *70*, 2271–2277.

(275) Su, M. S.-W.; Kao, H- C.; Lin, C.-N.; Syu, W.-J. Gene L0017 encodes a second chaperone for EspA of enterohaemorrhagic *Escherichia coli* O157:H7. *Microbiology* **2008**, *154*, 1094–1103.

(276) Wainwright, L. A.; Kaper, J. B. EspB and EspD require a specific chaperone for proper secretion from enteropathogenic *Escherichia coli*. *Mol. Microbiol*. **1998**, *27*, 1247–1260.

(277) Neves, B. C.; Mundy, R.; Petrovska, L.; Dougan, G.; Knutton, S.; Frankel, G. CesD2 of enteropathogenic *Escherichia coli* is a second chaperone for the type III secretion translocator protein EspD. *Infect. Immun*. **2003**, *71*, 2130–2141.

(278) Tobe, T.; Tatsuno, I.; Katayama, E.; Wu, C.-Y.; Schoolnik, G. K.; Sasakawa, C. A novel chromosomal locus of enteropathogenic *Escherichia coli* (EPEC), which encodes a *bfpT*-regulated chaperone-like protein, TrcA, involved in microcolony formation by EPEC. *Mol. Microbiol*. **1999**, *33*, 741–752.

(279) Stebbins, C. E.; Galán, J. E. Maintenance of an unfolded polypeptide by a cognate chaperone in bacterial type III secretion. *Nature* **2001**, *414*, 77–81.

(280) Lloyd, S. A.; Sjöström, M.; Andersson, S.; Wolf-Watz, H. Molecular characterization of type III secretion signals via analysis of synthetic N-terminal amino acid sequences. *Mol. Microbiol.* **2002**, *43*, 51–59.

(281) Woestyn, S.; Sory, M.; Boland, A.; Lequenne, O.; Cornelis, G. R. The cytosolic SycE and SycH chaperones of *Yersinia* protect the region of YopE and YopH involved in translocation across eukaryotic cell membranes. *Mol. Microbiol*. **1996**, *20*, 1261–1271.

(282) Gauthier, A.; Finlay, B. B. Translocated intimin receptor and its chaperone interact with ATPase of the type III secretion apparatus of enteropathogenic *Escherichia coli*. **2003**, *185*, 6747–6755.

(283) Chen, L.; Ai, X.; Portaliou, A. G.; Minetti, C. A. S. A.; Remeta, D. P.; Economou, A. Substrate-activated conformational switch on chaperones encodes a targeting signal in type III secretion. *Cell Rep.* **2013**, *3*, 709–715.

(284) Luo, Y.; Bertero, M. G.; Frey, E. A.; Pfuetzner, R. A.; Wenk, M. R.; Creagh, L.; Marcus, S. L.; Lim, D.; Sicheri, F.; Kay, C.; et al. Structural and biochemical characterization of the type III secretion chaperones CesT and SigE. *Nature* **2001**, *8*, 1031–1036.

(285) Akeda, Y.; Galán, J. E. Chaperone release and unfolding of substrates in type III secretion. *Nature* **2005**, *437*, 911–915.

(286) Feldman, M. F.; Müller, S.; Wüest, E.; Cornelis, G. R. SycE allows secretion of YopE – DHFR hybrids by the *Yersinia enterocolitica* type III Ysc system. *Mol. Microbiol.* **2002**, *46*, 1183–1197.

(287) Wilharm, G.; Lehmann, V.; Neumayer, W.; Tr, J.; Trček, J.; Heesemann, J. *Yersinia enterocolitica* type III secretion: evidence for the ability to transport proteins that are folded prior to secretion. *BMC Microbiol*. **2004**, 9, 27.

(288) Jarvis, K. G.; Girón, J. A.; Jerse, A. N. N. E.; McDaniel, T. K.; Donnenberg, M. S.; Kaper, J. B. Enteropathogenic *Escherichia coli* contains a putative type III secretion system necessary for the export of proteins involved in attaching and effacing lesion formation. *Proc. Natl. Acad. Sci*. **1995**, *92*, 7996–8000.

(289) Mellies, J. L.; Elliott, S. J.; Sperandio, V.; Donnenberg, M. S.; Kaper, J. B. The Per regulon of enteropathogenic *Escherichia coli*: identification of a regulatory cascade and a novel transcriptional activator , the locus of enterocyte effacement (LEE)-encoded regulator (Ler). *Mol. Microbiol*. **1999**, *33*, 296–306.

(290) Sanchez-SanMartín, C.; Bustamante, V. H.; Calva, E.; Puente, J. L. Transcriptional regulation of the *orf19* gene and the *tir-cesT-eae* operon of enteropathogenic *Escherichia coli*. *J. Bacteriol.* **2001**, *183*, 2823–2833.

(291) Barba, J.; Bustamante, H.; Flores-Valdez, M. A.; Deng, W.; Finlay, B. B. Puente, J. L. A positive regulatory loop controls expression of the locus of enterocyte effacement-encoded regulators Ler and GrlA. *J. Bacteriol.* **2005**, *187*, 7918–7930.

(292) Yerushalmi, G.; Litvak, Y.; Gur-Arie, L.; Rosenshine, I. Dynamics of expression and maturation of the type III secretion system of enteropathogenic *Escherichia coli*. *J. Bacteriol*. **2014**, *196*, 2798–2806.

(293) Perna, N. T.; Mayhew, G.; Pósfai, G.; Elliott, S.; Donnenberg, M. S.; Kaper, J. B.; Blattner, F. R. Molecular evolution of a pathogenicity island from enterohemorrhagic *Escherichia coli* O157:H7. *Infect. Immun*. **1998**, *66*, 3810–3817.

(294) Petty, N. K.; Bulgin, R.; Crepin, V. F.; Cerdeño-Tárraga, A. M.; Schroeder, G. N.; Quail, M. A.; Lennard, N.; Corton, C.; Barron, A.; Clark, L.; et al. The *Citrobacter rodentium* genome sequence reveals convergent evolution with human pathogenic *Escherichia coli*. *J. Bacteriol*. **2010**, *192*, 525–538.

(295) Connolly, J. P. R.; Finlay, B. B.; Roe, A. J. From ingestion to colonization: the influence of the host environment on tegulation of the LEE encoded type III secretion system in enterohaemorrhagic *Escherichia coli*. *Front. Microbiol.* **2015**, *6*, 568.

(296) Deng, W.; Puente, J., L.; Gruenheid, S.; Li, Y.; Vallance, B. A.; Vázques, A.; Barba, J.; Ibarra, J. A.; O'Donnell, P.; Metalnikov, P.; et al. Dissecting virulence: systematic and functional analyses of a pathogenicity island. *Proc. Natl. Acad. Sci*. **2004**, *101*, 3597–3602.

(297) Bustamante, V. H.; Santana, E. C.; Calva, E.; Puente, J. L.; Transcriptional regulation of type III secretion genes in enteropathogenic *Escherichia coli*: Ler antagonizes H-NS-dependent repression. *Mol. Microbiol*. **2001**, *39*, 664–678.

(298) Umanski, T.; Rosenshine, I.; Friedberg, D. Thermoregulated expression of virulence Genes in enteropathogenic *Escherichia coli*. *Microbiology* **2002**, *148*, 2735–2744.

(299) Dorman, C. J. H-NS : A universal regulator for a dynamic genome. *Nat. Rev*. **2004**, *2*, 391-400.

(300) Winardhi, R. S.; Gulvady, R.; Mellies, J. L.; Yan, J. Locus of enterocyte effacement-encoded regulator (Ler) of pathogenic *Escherichia coli* competes off histone-like nucleoid-

structuring protein (H-NS) through noncooperative DNA binding. *J. Biol. Chem*. **2014**, *289*, 13739–13750.

(301) Berdichevsky, T.; Friedberg, D.; Nadler, C.; Rokney, A.; Oppenheim, A.; Rosenshine, I. Ler is a negative autoregulator of the LEE1 operon in enteropathogenic *Escherichia coli*. *J. Bacteriol*. **2005**, *187*, 349–357.

(302) Bhat, A.; Shin, M.; Jeong, J.; Kim, H.; Lim, H.; Rhee, J.H.; Paik, S.-T.; Takeyasu, K.; Tobe, T.; Ye, H.; DNA looping-dependent autorepression of *LEE1* P1 promoters by Ler in enteropathogenic *Escherichia coli* (EPEC). *Proc. Natl. Acad. Sci*. **2014**, *111*, E2586–E2595.

(303) Islam, M. S.; Bingle, L. E. H.; Pallen, M. J.; Busby, S. J. W. Organization of the *LEE1* operon regulatory region of enterohaemorrhagic *Escherichia coli* O157:H7 and activation by GrlA. *Mol. Microbiol.* **2011**, *79*, 468–483.

(304) Jiménez, R.; Cruz-Migoni, S. B.; Huerta-Saquero, A.; Bustamante, V. H.; Puente, L. Molecular characterization of GrlA, a specific positive regulator of Ler expression in enteropathogenic *Escherichia coli*. *J. Bacteriol.* **2010**, *192*, 4627–4642.

(305) Creasey, E. A.; Delahay, R. M.; Daniell, S. J.; Frankel, G. Yeast two-hybrid system survey of interactions between LEE-encoded proteins of enteropathogenic *Escherichia coli*. *Microbiology* **2003**, *149*, 2093–2106.

(306) Padavannil, A.; Jobichen, C.; Mills, E.; Velazquez-Campoy, A.; Li, M.; Leung, K. Y.; Mok, Y. K.; Rosenshine, I.; Sivaraman, J. Structure of GrlR-GrlA complex that prevents GrlA activation of virulence genes. *Nat. Commun*. **2013**, *4*, 2546.

(307) Tsai, N.; Wu, Y.; Chen, J.; Wu, C.; Tzeng, C.; Syu, W. Multiple functions of *l0036* in the regulation of the pathogenicity island of enterohaemorrhagic *Escherichia coli* O157:H7. *Biochem. J.* **2006**, *599*, 591–599.

(308) Younis, R.; Bingle, L. E. H.; Rollauer, S.; Munera, D.; Busby, S. J.; Johnson, S.; Deane, J. E.; Lea, S. M.; Frankel, G.; Pallen, M. J. SepL resembles an aberrant effector in binding to a class 1 type III secretion chaperone and carrying an N-terminal secretion signal. *J. Bacteriol*. **2010**, *192*, 6093–6098.

(309) Gómez-Duarte, O. G.; Kaper, J. B. A Plasmid-encoded regulatory region activates chromosomal *eaeA* expression in enteropathogenic *Escherichia coli*. *Infect. Immun*. **1995**, *63*, 1767–1776.

(310) Iyoda, S.; Watanabe, H. Positive effects of multiple *pch* genes on expression of the locus of enterocyte effacement genes and adherence of enterohaemorrhagic *Escherichia coli* O157:H7 to HEp-2 cells. *Microbiology* **2004**, *150*, 2357–2371.

(311) Deane, J. E.; Abrusci, P.; Johnson, S.; Lea, S. M. Timing is everything: the regulation of type III secretion. *Cell. Mol. Life Sci.* **2010**, *67*, 1065–1075.

(312) Yang, J.; Tauschek, M.; Hart, E.; Hartland, E. L.; Robins-Browne, R. M. Virulence regulation in *Citrobacter rodentium*: the art of timing. *Microb. Biotechnol*. **2010**, *3*, 259–268.

(313) Levine, J. A.; Hansen, A.; Michalski, J. M.; Hazen, T. H.; Rasko, D. A.; Kaper, J. B. H-NST induces LEE expression and the formation of attaching and effacing lesions in enterohemorrhagic *Escherichia coli*. *PLoS One* **2014**, *9*, e86618.

(314) Nakanishi, N.; Tashiro, K.; Kuhara, S.; Hayashi, T.; Sugimoto, N.; Tobe, T. Regulation of virulence by butyrate sensing in enterohaemorrhagic *Escherichia coli*. *Microbiology* **2009**, *155*, 521–530.

(315) Takao, M.; Yen, H.; Tobe, T. LeuO enhances butyrate-induced virulence expression through a positive regulatory loop in enterohaemorrhagic *Escherichia coli*. *Mol. Microbiol*. **2014**, *93*, 1302–1313.

(316) Tree, J. J.; Wolfson, E. B.; Wang, D.; Roe, A. J.; Gally, D. L. Controlling injection: regulation of type III secretion in enterohaemorrhagic *Escherichia coli. Cell Press* **2009**, *17*, 361–370.

(317) Wagner, S.; Königsmaier, L.; Lara-Tejero, M.; Lefebre, M.; Marlovits, T. C.; Galán, J. E. Organization and coordinated assembly of the type III secretion export apparatus. *Proc. Natl. Acad. Sci*. **2010**, *107*, 17745–17750.

(318) Thomas, N. A.; Deng, W.; Baker, N.; Puente, J.; Finlay, B. B. Hierarchical delivery of an essential host colonization factor in enteropathogenic *Escherichia coli. J. Biol. Chem*. **2007**, *282*, 29634–29645.

(319) Minamino, T.; Macnab, R. M. Domain structure of *Salmonella* FlhB, a flagellar export component responsible for substrate specificity switching. *J. Bacteriol*. **2000**, *182*, 4906–4914.

(320) Feria, J. V. M.; Lefebre, M. D.; Stierhof, Y.-D.; Galán, J. E.; Wagner, S.; Role of autocleavage in the function of a type III secretion specificity switch protein in *Salmonella enterica* serovar Typhimurium. *mBio* **2015**, *6*, e01459-15.

(321) Feria, J. M.; García-Gómez, E.; Espinosa, N.; Minamino, T.; Namba, K.; González-Pedrajo, B. Role of EscP (Orf16) in injectisome biogenesis and regulation of type III protein secretion in enteropathogenic *Escherichia coli. J. Bacteriol*. **2012**, *194*, 6029–6045.

(322) Zarivach, R.; Deng, W.; Vuckovic, M.; Felise, H. B.; Nguyen, H. V; Miller, S. I.; Finlay, B. B.; Strynadka, N. C. J. Structural analysis of the essential self-cleaving type III secretion proteins EscU and SpaS. *Nature* **2008**, *453*, 124–127.

(323) Moriya, N.; Minamino, T.; Hughes, K. T.; Macnab, R. M.; Namba, K. The type III flagellar export specificity switch is dependent on FliK ruler and a molecular clock. *J. Mol. Biol*. **2006**, *359*, 466–477.

(324) O'Connell, C. B.; Creasey, E. A.; Knutton, S.; Elliott, S.; Crowther, L. J.; Luo, W.; Albert, M. J.; Kaper, J. B.; Frankel, G.; Donnenberg, M. S. SepL, a protein required for enteropathogenic *Escherichia coli* type III translocation, interacts with secretion component SepD. *Mol. Microbiol.* **2004**, *52*, 1613–1625.

(325) Wang, D.; Roe, A. J.; McAteer, S.; Shipston, M. J.; Gally, D. L. Hierarchal type III secretion of translocators and effectors from *Escherichia coli* O157:H7 requires the carboxy terminus of SepL that binds to Tir. *Mol. Microbiol*. **2008**, *69*, 1499–1512.

(326) Deng, W.; Yu, H. B.; Li, Y.; Finlay, B. B. SepD/SepL-dependent secretion signals of the type III secretion system translocator proteins in enteropathogenic *Escherichia coli*. *J. Bacteriol*. **2015**, *197*, 1263–1275.

(327) Gaytán, M. O.; Monjarás Feria, J.; Soto, E.; Espinosa, N.; Benítez, J. M.; Georgellis, D.; González-Pedrajo, B. Novel insights into the mechanism of SepL-mediated control of effector secretion in enteropathogenic *Escherichia coli. MicrobiologyOpen* **2018**, 7, e571.

(328) Linington, R. G.; Robertson, M.; Gauthier, A.; Finlay, B. B.; van Soest, R.; Andersen, R. J. Caminoside A, an antimicrobial glycolipid isolated from the marine sponge *Caminus sphaeroconi*a. *Org. Lett*. **2002**, *4*, 4089–4092.

(329) Zhang, Z.; Zong, C.; Song, G.; Lv, G.; Chun, Y.; Wang, P.; Ding, N.; Li, Y. Total synthesis of caminoside b, a novel antimicrobial glycolipid isolated from the marine sponge *Caminus sphaeroconia*. *Carbohydr. Res*. **2010**, *345*, 750–760.

(330) Berger, J.; Lehr, H. H.; Teitel, S.; Maehr, H.; Grunberg, E. A new antibiotic X-5108 of *Streptomyces* origin I. production, isolation and properties. *J. Antibiot. (Tokyo)*. **1972**, *26*, 15–22.

(331) Warawa, J.; Finlay, B. B.; Kenny, B. Type III secretion-dependent hemolytic activity of enteropathogenic *Escherichia coli. Infect. Immun*. **1999**, *67*, 5538–5540.

(332) Swimm, A. I.; Kalman, D. Cytosolic extract induces Tir translocation and pedestals in EPEC-infected red blood cells. *PLoS Pathog*. **2008**, *4*, 38–54.

(333) Iwatsuki, M.; Uchida, R.; Yoshijima, H.; Ui, H.; Shiomi, K.; Matsumoto, A.; Takahashi, Y.; Abe, A.; Tomoda, H.; Satoshi, O. Guadinomines, type III secretion system inhibitors, produced by *Streptomyces* sp. K01-0509 I. Taxonomy, fermentation, isolation and biological properties. *J. Antibiot. (Tokyo).* **2008**, *61*, 222–229.

(334) Iwatsuki, M.; Uchida, R.; Yoshijima, H.; Ui, H.; Shiomi, K.; Kim, Y.; Hirose, T.; Sunazuka, T.; Abe, A.; Tomoda, H. Guadinomines, type III secretion system inhibitors, produced by *Streptomyces* sp. K01-0509. *J. Antibiot. (Tokyo).* **2008**, *61*, 230–236.

(335) Hirose, T.; Sunazuka, T.; Tsuchiya, S.; Tanaka, T.; Kojima, Y.; Mori, R.; Iwatsuki, M. Total synthesis and determination of the absolute configuration of guadinomines B and C2. *Chem. a Eur. J.* **2008**, *14*, 8220–8238.

(336) Holmes, T. C.; May, A. E.; Zaleta-Rivera, K.; Ruby, J. G.; Skewes-Cox, P.; Fischbach, M. A.; DeRisi, J. L.; Iwatsuki, M.; Ōmura, S.; Khosla, C. Molecular insights into the biosynthesis of guadinomine: a type III secretion system inhibitor. *J. Am. Chem. Soc*. **2012**, *134*, 17797–17806.

(337) Afzal, M.; Safer, A. M.; Menon, M. Green tea polyphenols and their potential role in health and disease. *Inflammopharmacology* **2015**, *23*, 151–161.

(338) Yang, J.; Han, Y.; Chen, C.; Sun, H.; He, D.; Guo, J.; Jiang, B.; Zhou, L.; Zeng, C. EGCG attenuates high glucose-induced endothelial cell inflammation by suppression of PKC and NF-κB signaling in human umbilical vein endothelial cells. *Life Sci.* **2013**, *92*, 589–597.

(339) Shankar, S.; Marsh, L.; Srivastava, R. K. EGCG inhibits growth of human pancreatic tumors orthotopically implanted in Balb C nude mice through modulation of FKHRL1/FOXO3a and neuropilin. *Mol. Cell. Biochem*. **2013**, *372*, 83–94.

(340) Nandakumar, V.; Vaid, M.; Katiyar, S. K. (-)-Epigallocatechin-3-gallate reactivates silenced tumor suppressor genes, *Cip1/p21* and p*16*^{INK4a}, by reducing DNA methylation and increasing histones acetylation in human skin cancer cells. *Carcinogenesis* **2011**, *32*, 537–544.

(341) Rajendran, P.; Ho, E.; Williams, D. E.; Dashwood, R. H. Dietary phytochemicals, HDAC inhibition, and DNA damage/repair defects in cancer cells. *Clin. Epigenetics* **2011**, *3*, 4.

(342) Khan, M. A.; Hussain, A.; Sundaram, M. K.; Alalami, U.; Gunasekera, D.; Ramesh, L.; Hamza, A.; Quraishi, U. (-)-Epigallocatechin-3-gallate reverses the expression of various tumor-suppressor genes by inhibiting DNA methyltransferases and histone deacetylases in human cervical cancer cells. *Oncol. Rep*. **2015**, *33*, 1976–1984.

(343) Chu, C.; Deng, J.; Man, Y.; Qu, Y. Green tea extracts epigallocatechin-3-gallate for different treatments. *Biomed Res. Int*. **2017**, *2017*, 5615647.

(344) Nakasone, N.; Higa, N.; Toma, C.; Ogura, Y.; Suzuki, T.; Yamashiro, T. Epigallocatechin gallate inhibits the type III secretion system of Gram-negative enteropathogenic bacteria under model conditions. *FEMS Microbiol. Lett*. **2017**, *364*, fnx111.

(345) Marshall, N. C.; Finlay, B. B. Targeting the type III secretion system to treat bacterial infections. *Expert Opin. Ther. Targets* **2014**, *18*, 137–152.

(346) Bohnhoff, B. Y. M.; Miller, C. P.; Martin, W. R. Resistance of the mouse's intestinal tract to experimental *Salmonella* infection. *J. Exp. Med*. **1964**, *120*, 805–816.

(347) Sun, Y.; O'Riordan, M. X. D. Regulation of bacterial pathogenesis by intestinal short-chain fatty acids. *Adv. Appl. Microbiol*. **2013**, *85*, 93–118.

(348) Pomare, E. W.; Branch, H. W. J.; Naylor, C. P. E.; Macfarlane, T. Short chain fatty acids in human large intestine, portal, hepatic and venous blood. *Gut* **1987**, *28*, 1221–1227.

(349) Baek, C.; Wang, S.; Roland, K. L.; Curtis, R. Leucine-responsive regulatory protein (Lrp) acts as a virulence repressor in *Salmonella enterica* serovar Typhimurium. *J. Bacteriol*. **2009**, *191*, 1278–1292.

(350) Bzdzion, L.; Krezel, H.; Wrzeszcz, K.; Grzegorek, I.; Nowinska, K.; Chodaczek, G.; Swietnicki, W. Design of small molecule inhibitors of type III secretion system ATPase EscN from enteropathogenic *Escherichia coli*. *ABP Biochim. Pol*. **2017**, *64*, 49-63.

(351) Zambelloni, R.; Connolly, J. P. R.; Uribe, A. H.; Burgess, K.; Marquez, R.; Roe, A. J. Novel compounds targeting the enterohemorrhagic *Escherichia coli* type three secretion system reveal insights into mechanisms of secretion inhibition. *Molec. Microbiol*. **2017**, *105*, 606–619.

(352) Tree, J. J.; Wang, D.; McInally, C.; Mahajan, A.; Layton, A.; Houghton, I.; Elofsson, M.; Stevens, M. P.; Gally, D. L.; Roe, A. J. Characterization of the effects of salicylidene acylhydrazide compounds on type III secretion in *Escherichia coli* O157:H7. *Infect. Immun*. **2009**, *77*, 4209–4220.

(353) Lyons, B. J.; Strynadka, N. C. J. On the road to structure-based development of anti-virulence therapeutics targeting the type III secretion system injectisome. *Med. Chem. Commun*. **2019**, *10*, 1273–1289.

(354) Hudson, D. L.; Layton, A. N.; Field, T. R.; Bowen, A. J.; Wolf-Watz, H.; Elofsson, M.; Stevens, M. P.; Galyov, E. E. Inhibition of type III secretion in *Salmonella enterica* serovar Typhimurium by small-molecule inhibitors. *Antimicrob. Agents Chemother*. **2007**, *51*, 2631–2635.

(355) Veenendaal, A. K. J.; Sundin, C.; Blocker, A. J. Small-molecule type III secretion system inhibitors block assembly of the *Shigella* type III secreton. *J. Bacteriol*. **2009**, *191*, 563–570.

(356) Larzábal, M.; Baldoni, H. A.; Suvire, F. D.; Curto, L. M.; Gomez, G. E.; Da Silva, W. M.; Giudicessi, S. L.; Camperi, S. A.; Delfino, J. M.; et al. An inhibitory mechanism of action of

coiled-coil peptides against type three secretion system from enteropathogenic *Escherichia coli*. *J. Pept. Sci*. **2019**, 25, e3149.

(357) Kaspar, A. A.; Reichert, J. M. Future directions for peptide therapeutics development. *Drug Discov. Today* **2013**, *18*, 807–817.

(358) Hotinger, J. A.; May, A. E. Antibodies inhibiting the type III secretion system of Gram-negative pathogenic bacteria. *Antibodies* **2020**, *9*, 35.

(359) Loureiro, I.; Frankel, G.; Adu-Bobie, J.; Dougan, G.; Trabulsi, L. R.; Carneiro-Sampaio, M. M. Human colostrum contains IgA antibodies reactive to enteropathogenic *Escherichia coli* virulence-associated proteins: intimin, BfpA, EspA, and EspB. *J. Pediatr. Gastroenterol. Nutr*. **1998**, *27*, 166-171.

(360) Guirro, M.; de Souza, R. L.; Piazza, R. M. F.; Guth, B. E. C. Antibodies to intimin and *Escherichia coli*-secreted proteins EspA and EspB in sera of Brazilian children with hemolytic uremic syndrome and healthy controls. *Vet. Immunol. Immunopathol*. **2013**, *152*, 121–125.

(361) Cook, S. R.; Maiti, P. K.; DeVinney, R.; Allen-Vercoe, E.; Bach, S. J.; McAllister, T. A. Avian- and mammalian-derived antibodies against adherence-associated proteins inhibit host cell colonization by *Escherichia coli* O157:H7. *J. Appl. Microbiol*. **2007**, *103*, 1206–1219.

(362) Yu, S.; Gu, J.; Wang, H.; Wang, Q.; Luo, P.; Wu, C.; Zhang, W.; Guo, G.; Tong, W.; Zou, Q.; et al. Identification of a novel linear epitope on EspA from enterohemorrhagic *E. coli* using a neutralizing and protective monoclonal antibody. *Clin. Immunol*. **2011**, *138*, 77–84.

(363) Desin, T. S.; Townsend, H. G.; Potter, A. A. Antibodies directed against Shiga-toxin producing *Escherichia coli* serotype O103 type III secreted proteins block adherence of heterologous STEC serotypes to HEp-2 cells. *PLoS One* **2015**, *10*, e0139803.

(364) Saberianfar, R.; Chin-Fatt, A.; Scott, A.; Henry, K. A.; Topp, E.; Menassa, R. Plant-produced chimeric V_HH-sIgA against enterohemorrhagic *E. coli* intimin shows cross-serotype inhibition of bacterial adhesion to epithelial cells. *Front. Plant Sci*. **2019**, *10*, 270.

(365) Ruano-Gallego, D.; Yara, D. A.; Di Ianni, L.; Frankel, G.; Schüller, S.; Fernández, L. Á. A nanobody targeting the translocated intimin receptor inhibits the attachment of enterohemorrhagic *E. coli* to human colonic mucosa. *PLoS Pathog*. **2019**, *15*, e1008031.

(366) Ubeda, C.; Djukovic, A.; Isaac, S. Roles of the intestinal microbiota in pathogen protection. *Clin. Transl. Immunol*. **2017**, *6*, e128.

(367) Liu, Y.; Tran, D. Q.; Rhoads, M. Probiotics in disease prevention and treatment. *Physiol. Behav*. **2018**, *58*, S164–S179.

(368) Wu, X.; Vallance, B. A.; Boyer, L.; Bergstrom, K. S. B.; Walker, J.; Madsen, K.; O'Kusky, J. R.; Buchan, A. M.; Jacobson, K. *Saccharomyces boulardii* ameliorates *Citrobacter rodentium*-induced colitis through actions on bacterial virulence factors. A*m. J. Physiol. – Gastrointest. Liver Physiol*. **2007**, *294*, 295–306.

(369) Sory, M. P.; Cornelis, G. R. Translocation of a hybrid YopE-adenylate cyclase from *Yersinia enterocolitica* into HeLa cells. *J. Mol. Microbiol*. **1994**, *14*, 583–594.

(370) Wolff, C.; Nisan, I.; Hanski, E.; Frankel, G.; Rosenshine, I. Protein translocation into host epithelial cells by infecting enteropathogenic *Escherichia coli*. *Mol. Microbiol*. **1998**, *28*, 143–155.

(371) Crawford, J. A.; Kaper, J. B. The N-terminus of enteropathogenic *Escherichia coli* (EPEC) Tir mediates transport across bacterial and eukaryotic cell membranes. *Mol. Microbiol*. **2002**, *46*, 855–868.

(372) Yount, J. S.; Tsou, L. K.; Dossa, P. D.; Kullas, A. L.; van der Velden, A. W. M.; Hang, H. C. Visible fluorescence detection of type III protein secretion from bacterial pathogens. *J. Am. Chem. Soc*. **2010**, *132*, 8244–8245.

(373) Zhang, T.; Guo, K. P.; Qiu, L.; Shen, Y. Magnesium ethoxide as an effective catalyst in the synthesis of dicayanomethylendihydrofurans [*sic*]. *Synth. Commun*. **2006**, *36*, 1367–1372.

(374) Byun, J. H.; Kim, H. Y.; Kim, Y. S.; Mook-Jung, I.; Kim, D. J.; Lee, W. K.; Yoo, K. H. Aminostyrylbenzofuran derivatives as potent inhibitors for Aβ fibril formation. *Bioorganic Med. Chem. Lett.* **2008**, *18*, 5591–5593.

(375) Tsou, L. K.; Zhang, M. M.; Hang, H. C. Clickable fluorescent dyes for multimodal bioorthogonal imaging. *Org. Biomol. Chem*. **2009**, *7*, 5055–5058.

(376) Salehi, B.; Mishra, A. P.; Shukla, I.; Sharifi-Rad, M.; Contreras, M. del M.; Segura-Carretero, A.; Fathi, H.; Nasrabadi, N. N.; Kobarfard, F.; Sharifi-Rad, J. Thymol, thyme, and other plant sources: health and potential uses. *Phytother. Res*. **2018**, *32*, 1688–1706.

(377) Fachini-Queiroz, F. C.; Kummer, R.; Estevão-Silva, C. F.; Carvalho, M. D. D. B.; Cunha, J. M.; Grespan, R.; Bersani-Amado, C. A.; Cuman, R. K. N. Effects of thymol and carvacrol, constituents of *Thymus vulgaris* L. essential oil, on the inflammatory response. *Evidence-based Complement. Altern. Med*. **2012**, *2012*. 657026.

(378) Yuan, W.; Yuk, H.-G. Effects of sublethal thymol, carvacrol, and *trans*-cinnamaldehyde adaptation on virulence properties of *Escherichia coli* O157:H7. *Appl. Environ. Microbiol*. **2019**, *85*, e00281-19.

(379) Sperandio, V.; Mellies, J. L.; Nguyen, W.; Shin, S.; Kaper, J. B. Quorum sensing controls expression of the type III secretion gene transcription and protein secretion in enterohemorrhagic and enteropathogenic *Escherichia coli*. *Proc. Natl. Acad. Sci.* **1999**, *96*, 26.

(380) Thakur, P.; Chawla, R.; Tanwar, A.; Chakotiya, A. S.; Narula, A.; Goel, R.; Arora, R.; Sharma, R. K. Attenuation of adhesion, quorum sensing and biofilm mediated virulence of carbapenem resistant *Escherichia coli* by selected natural plant products. *Microb. Pathog*. **2016**, *92*, 76–85.

(381) Galloway, W. R. J. D.; Hodgkinson, J. T.; Bowden, S. D.; Welch, M.; Spring, D. R. Quorum sensing in Gram-negative bacteria: small-molecule modulation of AHL and AI-2 quorum sensing pathways. *Chem. Rev*. **2011**, *111*, 28–67.

(382) Reen, F. J.; Gutiérrez-Barranquero, J. A.; Parages, M. L.; O'Gara, F. Coumarin: a novel player in microbial quorum sensing and biofilm formation inhibition. *Appl. Microbiol*. *Biotechnol*. **2018**, *102*, 2063–2073.

(383) Rasmussen, T. B.; Skindersoe, M. E.; Bjarnsholt, T.; Phipps, R. K.; Christensen, K. B.; Jensen, P. O.; Andersen, J. B.; Koch, B.; Larsen, T. O.; Hentzer, M.; et al. Identity and effects of quorum-sensing inhibitors produced by *Penicillium* species. *Microbiology* **2005**, *151*, 1325–1340.

(384) Tamura, S.; Takahashi, N.; Miyamoto, S.; Mori, R.; Suzuki, S.; Nagatsu, J. Isolation and physiological activities of piericidin A, a natural insecticide produced by *Streptomyces*. *Agric. Biol. Chem*. **1963**, *27*, 576–582.

(385) Hall, C.; Wu, M.; Crane, F. L. Piericidin A: a new inhibitor of mitochondrial electron transport. *Biochem. Biophys. Res. Commun*. **1966**, *25*, 373–377.

(386) Auerbuch, V.; Golenbock, D. T.; Isberg, R. R. Innate immune recognition of *Yersinia pseudotuberculosis* type III secretion. *PLoS Pathog.* **2009**, 5, e1000686.

(387) Li, J.; Sun, W.; Guo, Z.; Lu, C.; Shen, Y. Fusaric acid modulates type three secretion system of *Salmonella enterica* serovar Typhimurium. *Biochem. Biophys. Res. Commun*. **2014**, *449*, 455–459.

(388) Zhang, Y.; Liu, Y.; Wang, T.; Deng, X.; Chu, X. Natural compound sanguinarine chloride targets the type III secretion system of *Salmonella enterica* serovar Typhimurium. *Biochem. Biophys. Reports* **2018**, *14*, 149–154.

(389) Vargas, P.; Farias, G. A.; Nogales, J.; Prada, H.; Carvajal, V.; Barón, M.; Rivilla, R.; Martín, M.; Olmedilla, A.; Gallegos, M. T. Plant flavonoids target *Pseudomonas syringae* pv. tomato DC3000 flagella and type III secretion system. *Environ. Microbiol. Rep*. **2013**, *5*, 841–850.

(390) Smith, R. M.; Peterson, W. H.; Mccoy, E. Oligomycin, a new antifungal antibiotic. *Antibiot. Chemother*. **1954**, *4*, 962–970.

(391) Kim, H. S.; Han, S. B.; Kim, H. M.; Kim, Y. H. O.; Lee, J. J. Demethylhomooligomycin B, a new immunosuppresant [*sic*] antibiotic from *Streptomyces ostreogriseus*. *J. Antibiot. (Tokyo).* **1996**, *49*, 1275–1277.

(392) Yamazaki, M.; Yamashita, T.; Harada, T.; Nishikiori, T.; Saito, S.; Shimada, N.; Fujii, A. Homooligomycins A and B, new antitumor antibiotics from *Streptomyces bottropensis*: producing organism, fermentation, isolation, structure elucidation and biological properties. *J. Antibiot. (Tokyo).* **1992**, *45*, 171–179.

(393) Palmer, R. A.; Potter, B. S. X-ray structures and absolute configurations of the antibiotics oligomycins A, B and C: inhibitors of ATP synthase. *J. Chem. Crystallogr*. **2008**, *38*, 243–253.

(394) Sato, S.; Iwata, F.; Yamada, S.; Katayama, M. Neomaclafungins A-I: oligomycin-class macrolides from a marine-derived actinomycete. *J. Nat. Prod*. **2012**, *75*, 1974–1982.

(395) Chui, R.; Derakhchan, K.; Vargas, H. M. Oligomycin A induced toxicity and profound hemodynamic effects in intact Sprague-Dawley rats. *Fed. Am. Soc. Exp. Biol*. **2011**, *25*, lb363–lb363.

(396) Haste, N. M.; Thienphrapa, W.; Tran, D. N.; Loesgen, S.; Sun, P.; Nam, S. J.; Jensen, P. R.; Fenical, W.; Sakoulas, G.; Nizet, V.; et al. Activity of the thiopeptide antibiotic nosiheptide against contemporary strains of methicillin-resistant *Staphylococcus aureus. J. Antibiot. (Tokyo).* **2012**, *65*, 593–598.

(397) Yu, Y.; Duan, L.; Zhang, Q.; Liao, R.; Ding, Y.; Pan, H.; Wendt-Pienkowski, E.; Tang, G.; Shen, B.; Liu, W. Nosiheptide biosynthesis featuring a unique indole side ring formation on the characteristic thiopeptide framework. *ACS Chem. Biol*. **2009**, *4*, 855–864.

(398) Badding, E. D.; Grove, T. L.; Gadsby, L. K.; LaMattina, J. W.; Boal, A. K.; Booker, S. J. Rerouting the pathway for the biosynthesis of the side ring system of nosiheptide: the roles of NosI, NosJ, and NosK. *J. Am. Chem. Soc.* **2017**, *139*, 5896–5905.

(399) Wojtas, K. P.; Riedrich, M.; Lu, J. Y.; Winter, P.; Winkler, T.; Walter, S.; Arndt, H. D. Total synthesis of nosiheptide. *Angew. Chemie - Int. Ed*. **2016**, *55*, 9772–9776.

(400) Mocek, U.; Knaggs, A. R.; Tsuchiya, R.; Nguyen, T.; Beale, J. M.; Floss, H. G. Biosynthesis of the modified peptide antibiotic nosiheptide in *Streptomyces actuosus. J. Am. Chem. Soc.* **1993**, *115*, 7557–7568.

(401) Prange, T.; Ducruix, A.; Pascard, C. Structure of nosiheptide, a plythiazole-containing antibiotic. *Nature* **1977**, *265*, 189–190.

(402) Vinale, F.; Sivasithamparam, K.; Ghisalberti, E. L.; Marra, R.; Barbetti, M. J.; Li, H.; Woo, S. L.; Lorito, M. A novel role for *Trichoderma* secondary metabolites in the interactions with plants. *Physiol. Mol. Plant Pathol*. **2008**, *72*, 80–86.

(403) Ióca, L. P.; Romminger, S.; Santos, M. F. C.; Bandeira, K. F.; Rodrigues, F. T.; Kossuga, M. H.; Nicacio, K. J.; Ferreira, E. L. F.; Morais-Urano, R. P.; Passos, M. S.; et al. A strategy for

the rapid identification of fungal metabolites and the discovery of the antiviral activity of pyrenocine a and harzianopyridone. *Quim. Nova* **2016**, *39*, 720–731.

(404) Bat-Erdene, U.; Kanayama, D.; Tan, D.; Turner, W. C.; Houk, K. N.; Ohashi, M.; Tang, Y. Iterative catalysis in the biosynthesis of mitochondrial complex II inhibitors harzianopyridone and atpenin B. *J. Am. Chem. Soc.* **2020**, *142*, 8550–8554.

(405) Miyadera, H.; Shiomi, K.; Ui, H.; Yamaguchi, Y.; Masuma, R.; Tomoda, H.; Miyoshi, H.; Osanai, A.; Kita, K.; Ōmura, S. Atpenins, potent and specific inhibitors of mitochondrial complex II (succinate-ubiquinone oxidoreductase). *Proc. Natl. Acad. Sci. USA* **2003**, *100*, 473–477.

(406) De Sarkar, S.; Sarkar, D.; Sarkar, A.; Dighal, A.; Staniek, K.; Gille, L.; Chatterjee, M. Berberine chloride mediates its antileishmanial activity by inhibiting *Leishmania* mitochondria. *Parasitol. Res*. **2019**, *118*, 335–345.

(407) Liu, Q.; Xu, X.; Zhao, M.; Wei, Z.; Li, X.; Zhang, X.; Liu, Z.; Gong, Y.; Shao, C. Berberine induces senescence of human glioblastoma cells by downregulating the EGFR-MEK-ERK signaling pathway. *Mol. Cancer Ther*. **2015**, *14*, 355–363.

(408) Dong, S. F.; Hong, Y.; Liu, M.; Hao, Y. Z.; Yu, H. S.; Liu, Y.; Sun, J. N. Berberine attenuates cardiac dysfunction in hyperglycemic and hypercholesterolemic rats. *Eur. J. Pharmacol*. **2011**, *660*, 368–374.

(409) El-Zeftawy, M.; Ghareeb, D.; ElBealy, E. R.; Saad, R.; Mahmoud, S.; Elguindy, N.; El-kott, A. F.; El-Sayed, M. Berberine chloride ameliorated PI3K/Akt-p/SIRT-1/PTEN signaling pathway in insulin resistance syndrome induced in rats. *J. Food Biochem*. **2019**, *43*, e13049.

(410) Liang, R.; Yong, X.; Duan, Y.; Tan, Y.; Zeng, P.; Zhou, Z.; Jiang, Y.; Wang, S.; Jiang, Y.; Huang, X.; et al. Potent in vitro synergism of fusidic acid (FA) and berberine chloride (BBR)

against clinical isolates of methicillin-resistant *Staphylococcus aureus* (MRSA). *World J. Microbiol. Biotechnol*. **2014**, *30*, 2861–2869.

(411) Dziedzic, A.; Wojtyczka, R. D. W.; Kubina, R. Inhibition of oral *Streptococci* growth induced by the complementary action of berberine chloride and antibacterial compounds. *Molecules* **2015**, *20*, 13705–13724.

(412) Raistrick, H.; Rice, F. A. H. 2,3-Dihydro-3,6-dihydroxy-2-methyl-4-pyrone and curvularin from *Penicillium gilmanii. J. Chem. Soc*. **1971**, 3069–3070.

(413) Rudolph, K.; Serwe, A.; Erkel, G. Inhibition of TGF-β signaling by the fungal lactones (S)-curvularin, dehydrocurvularin, oxacyclododecindione and geliellalactone. *Cytokine* **2013**, *61*, 285-296.

(414) Xie, L. W.; Ouyang, Y. C.; Zou, K.; Wang, G. H.; Chen, M. J.; Sun, H. M.; Dai, S. K.; Li, X. Isolation and difference in anti-*Staphylococcus aureus* bioactivity of curvularin derivates from fungus *Eupenicillium* sp. *Appl. Biochem. Biotechnol*. **2009**, *159*, 284–293.

(415) CDC. Antibiotic Resistance Threats in the United States, 2019; Atlanta, GA, 2019. https://doi.org/CS239559-B.

(416) 2017 National and State Healthcare-Associated Infections Progress Report; 2019.

(417) Long, K. S.; Poehlsgaard, J.; Kehrenberg, C.; Schwarz, S.; Vester, B. The Cfr rRNA methyltransferase confers resistance to phenicols, lincosamides, oxazolidinones, pleuromutilins, and streptogramin A antibiotics. *Antimicrob. Agents Chemother.* **2006**, *50*, 2500–2505.

(418) Fritz, S. A.; Hogan, P. G.; Camins, B. C.; Ainsworth, A. J.; Patrick, C.; Martin, M. S.; Krauss, M. J.; Rodriguez, M.; Burnham, C. A. D. Mupirocin and chlorhexidine resistance in *Staphylococcus aureus* in patients with community-onset skin and soft tissue infections. *Antimicrob. Agents Chemother*. **2013**, *57*, 559–568.

(419) McGuinness, W. A.; Malachowa, N.; DeLeo, F. R. Vancomycin resistance in *Staphylococcus aureus* strains. *Arch. Razi Inst*. **2017**, *90*, 107–110.

(420) Chambers, H. F. Methicillin resistance in *Staphylococci*: molecular and biochemical basis and clinical implications. *Clin. Microbiol. Rev*. **1997**, *10*, 781–791.

(421) Sabri, I.; Adwan, K.; Essawi, T. A.; Farraj, M. A. Molecular characterization of methicillin-resistant *Staphylococcus aureus* isolates in three different Arab world countries. *Eur. J. Microbiol. Immunol*. **2013**, 3, 183–187.

(422) Wilson, D. N. Ribosome-targeting antibiotics and mechanisms of bacterial resistance. *Nat. Rev. Microbiol*. **2014**, *12*, 35–48.

(423) Maracci, C.; Wohlgemuth, I.; Rodnina, M. V. Activities of the peptidyl transferase center of ribosomes lacking protein L27. *RNA* **2015**, *21*, 2047–2052.

(424) Wall, E. A.; Caufield, J. H.; Lyons, C. E.; Manning, K. A.; Dokland, T.; Christie, G. E. Specific N-terminal cleavage of ribosomal protein L27 in *Staphylococcus aureus* and related bacteria. *Mol. Microbiol*. **2015**, *95*, 258–269.

(425) Wall, E. A.; Johnson, A. L.; Peterson, D. L.; Christie, G. E. Structural modeling and functional analysis of the essential ribosomal processing protease Prp from *Staphylococcus aureus*. *Mol. Microbiol*. **2017**, *104*, 520–532.

(426) Zhang, J. H.; Chung, T. D. Y.; Oldenburg, K. R. A simple statistical parameter for use in evaluation and validation of high throughput screening assays. *J. Biomol. Screen*. **1999**, *4*, 67–73.

(427) Patel, N.; Nizami, S.; Song, L.; Mikami, M.; Hsu, A.; Hickernell, T.; Chandhanayingyong, C.; Rho, S.; Compton, J. T.; Caldwell, J. M.; et al. CA-074Me compound inhibits osteoclastogenesis via suppression of the NFATc1 and c-FOS signaling pathways. *J. Orthop. Res*. **2015**, *33*, 1474–1486.

(428) Aoyagi, T.; Miyata, S.; Nanbo, M.; Kojima, F.; Matsuzaki, M.; Ishizuka, M.; Takeuchi, T.; Umezawa, H. Biological activities of leupeptins. *J. Antibiot. (Tokyo).* **1969**, *22*, 558–568.

(429) Desai, P. V.; Patny, A.; Gut, J.; Rosenthal, P. J.; Tekwani, B.; Srivastava, A.; Avery, M. Identification of novel parasitic cysteine protease inhibitors by use of virtual screening. 2. The available chemical directory. *J. Med. Chem*. **2006**, *49*, 1576–1584.

(430) Barrett, A. J.; Kembhavi, A. A.; Brown, M. A.; Kirschke, H.; Knight, C. G.; Tamai, M.; Hanada, K. L-*trans*-Epoxysuccinyl-leucylamido(4-guanidino)butane (E-64) and its analogues as inhibitors of cysteine proteinases including cathepsins B, H and L. *Biochem. J*. **1982**, *201*, 189–198.

(431) Zhang, S.; Shi, Y.; Jin, H.; Liu, Z.; Zhang, L.; Zhang, L. Covalent complexes of proteasome model with peptide aldehyde inhibitors MG132 and MG101: docking and molecular dynamics study. *J. Mol. Model*. **2009**, *15*, 1481–1490.

(432) Kundu, S. T.; Grzeskowiak, C. L.; Fradette, J. J.; Gibson, L. A.; Rodriguez, L. B.; Creighton, C. J.; Scott, K. L.; Gibbons, D. L. TMEM106B drives lung cancer metastasis by inducing TFEB-dependent lysosome synthesis and secretion of cathepsins. *Nat. Commun*. **2018**, *9*, 2731.

(433) Kim, C. H.; Parkin, S.; Bharara, M.; Atwood, D. Linear coordination of Hg(II) by cysteamine. *Polyhedron* **2002**, *21*, 225–228.

(434) Santos, K. L.; Vento, M. A.; Wright, J. W.; Speth, R. C. The effects of para-chloromercuribenzoic acid and different oxidative and sulfhydryl agents on a novel, non-AT1, non-AT2 angiotensin binding site identified as neurolysin. *Regul. Pept*. **2013**, *184*, 104–114.

(435) Kramer, M. J.; Cleeland, R.; Grunberg, E. Mersalyl: a diuretic with antiviral properties. *Antimicrob. Agents Chemother*. **1975**, *8*, 295–299.

(436) Cortat, M. Studies on the mode of action phenylmercuric borate on *Escherichia coli*. *Experientia* **1977**, *33*, 139–140.

(437) Tschanz, C.; Prins, C. Drug rash with eosinophilia and systemic symptoms caused by topical application of mercury. *Dermatology* **2000**, *201*, 381–382.

(438) Hill, D. G.; Barnes, A. R. Compatibility of phenylmercuric acetate with cefuroxime and ceftazidime eye drops. *Int. J. Pharm*. **1997**, *147*, 127–129.

(439) Xu, Y.; Zhao, D.; Gao, C.; Zhou, L.; Pang, G.; Sun, S. *In vitro* activity of phenylmercuric acetate against ocular pathogenic fungi. *J. Antimicrob. Chemother*. **2012**, *67*, 1941–1944.

(440) Ball, L. K.; Ball, R.; Pratt, R. D. An assessment of thimerosal use in childhood vaccines. *Pediatrics* **2001**, *107*, 1147–1154.

(441) Geier, D. A.; Sykes, L. K.; Geier, M. R. A review of thimerosal (Merthiolate) and its ethylmercury breakdown product: specific historical considerations regarding safety and effectiveness. *J. Toxicol. Environ. Heal*. **2007**, *10*, 575–596.

(442) Clark, J. A.; Kasselberg, A. G.; Glick, A. D.; O'Neill, J. A. Mercury poisoning from merbromin (Mercurochrome) therapy of omphalocele. *Clin. Pediatr. (Phila).* **1982**, *21*, 445–447.

(443) Liao, W. C.; Chou, C. T.; Kuo, C. C.; Pan, C. C.; Kuo, D. H.; Shieh, P.; Cheng, J. S.; Jan, C. R.; Shaw, C. F. Effect of thimerosal on Ca^{2+} movement and apoptosis in PC3 prostate cancer cells. *Drug Dev. Res*. **2011**, *72*, 330–336.

(444) Liu, S. I.; Huang, C. C.; Huang, C. J.; Wang, B. W.; Chang, P. M.; Fang, Y. C.; Chen, W. C.; Wang, J. L.; Lu, Y. C.; Chu, S. T.; et al. Thimerosal-induced apoptosis in human SCM1 gastric cancer cells: activation of p38 MAP kinase and caspase-3 pathways without involvement of $[Ca^{2+}]_i$ elevation. *Toxicol. Sci*. **2007**, *100*, 109–117.

(445) Kuo, L.; Huang, C.; Fang, Y.; Huang, C.; Wang, J.; Lin, K.; Chu, S.; Chang, H.; Chien, J.; Su, H.; et al. Effect of thimerosal on Ca^{2+} movement and viability in human oral cancer cells. *Hum. Exp. Toxicol.* **2009**, *28*, 301–308.

APPENDIX I

High throughput screening results for ApexScreen 5040.

Table A1: Compounds in the ApexScreen 5040 Library and results of initial screen.

Plate	Well	IUPAC NAME	Inhibitor Y/N
1	A03	N-(2,2,6,6-tetramethyl(4-piperidyl))-N'-(2,2,6,6-tetramethyl(4-piperidyl))ethane-1,2-diamide	No
1	B03	1-{[(2-{[(2-hydroxynaphthyl)methyl]amino}ethyl)amino]methyl}naphthalen-2-ol	No
1	C03	pyridine-2,6-dicarbohydrazide	No
1	D03	4,5-dichloroisothiazol-3-yl piperidyl ketone	No
1	E03	ethyl 5-(ethoxycarbonyl)-2-(2,2,7-trimethyl-3-thioxo(4-1,2-dihydroquinolyliden e))-1,3-dithiolene-4-carboxylate	No
1	F03	ethyl 5-(ethoxycarbonyl)-2-(1,2,2-trimethyl-3-thioxo(4-1,2-dihydroquinolyliden e))-1,3-dithiolene-4-carboxylate	No
1	G03	ethyl 5-(ethoxycarbonyl)-2-(1,2,2,6-tetramethyl-3-thioxo(4-1,2-dihydroquinolyl idene))-1,3-dithiolene-4-carboxylate	No
1	H03	indeno[2,3-b]1,2,5-oxadiazolo[3,4-e]pyrazin-5-one	No
1	I03	ethyl 4-amino-1,2,5-oxadiazole-3-carboxylate	No
1	J03	6-[(1E)-2-(4-bromophenyl)vinyl]-5-nitropyrimidine-2,4-diol	No
1	K03	2-[(1E)-2-(4-bromophenyl)vinyl]-5-nitropyrimidine-4,6-diol	No
1	L03	1,3-dimethyl-5-(methylamino)-4,6-dinitro-3-hydrobenzimidazol-2-one	No
1	M03	ethyl 2-(2-furylcarbonylamino)-6-methyl-4,5,6,7-tetrahydrobenzo[b]thiophene-3- carboxylate	No
1	N03	2-(2-furylcarbonylamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxamide	No
1	O03	[(4-chlorophenyl)methyl]thiocarboxamidine	No
1	P03	6-methoxy-2,2,4-trimethyl-8-(triphenylmethyl)-1,2-dihydroquinoline	No
1	A04	4,4-dimethyl-4,5-dihydro-1,2-dithioleno[5,4-c]quinoline-1-thione	No
1	B04	8-methoxy-4,4-dimethyl-4,5-dihydro-1,2-dithioleno[5,4-c]quinoline-1-thione	No
1	C04	ethyl 5-(ethoxycarbonyl)-2-(2,2,6-trimethyl-3-thioxo(4-1,2-dihydroquinolyliden e))-1,3-dithiolene-4-carboxylate	No
1	D04	2-[(4,4-dimethyl-2,6-dioxocyclohexyl)(5-butyl(2-thienyl))methyl]-5,5-dimethylc yclohexane-1,3-dione	No
1	E04	3,5,7-trimethylhydroquinoxalin-2-one	No

1	F04	4-[6-(3,5-dimethylpyrazolyl)-4-morpholin-4-yl-1,3,5-triazin-2-yl]morpholine	No
1	G04	2-({[1,1-bis(hydroxymethyl)-2-hydroxyethyl]amino}methylene)-5,5-dimethylcycloh exane-1,3-dione	No
1	H04	2-amino-4-(5-butyl(2-thienyl))-7,7-dimethyl-5-oxo-4H-6,7,8-trihydrochromene-3- carbonitrile	No
1	I04	2-amino-4-(2,4-dichlorophenyl)-5,6,7,8,9-pentahydrocyclohepta[2,1-b]pyridine-3 -carbonitrile	OFF-SCALE
1	J04	2-amino-4-(5-butyl(2-thienyl))-5,6,7,8-tetrahydroquinoline-3-carbonitrile	No
1	K04	(1R,2R)-2-(2,5-dimethylphenyl)-1-(phenylcarbonyl)-10,3a-dihydropyrrolidino[1,2 -a]quinoline-3,3-dicarbonitrile	No
1	L04	methyl 2-{3-amino-2,4,4-tricyano-5-[(methoxycarbonyl)methyl]-5-methylcyclohexa -1(6),2-dienyl}acetate	Yes
1	M04	2-amino-4-(2-furyl)-3,4,5,6,7,8-hexahydronaphthalene-1,3,3-tricarbonitrile	No
1	N04	2-amino-4-(2-furyl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile	No
1	O04	2-amino-4-(3-bromophenyl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile	No
1	P04	4-hydroxy-2-methoxy-6-phenyl-2H-3,4,5,6,7,8,4a,8a-octahydro-5,7-dioxachromen-3 -yl 4-methylbenzenesulfonate	No
1	A05	2-methoxy-6-phenyl-2H-3,4,5,6,7,8,4a,8a-octahydro-5,7-dioxachromene-3,4-diol	No
1	B05	(7S,14R)-5-acetyloxy-14-(acetyloxyethyl)-2,15-dimethyltetracyclo[8.7.0.0<2,7>. 0<11,15>]heptadec-14-yl acetate	No
1	C05	morpholin-4-yl(phenylamino)methane-1-thione	No
1	D05	2-(4-nitropyrazol-3-yl)propane-1,3-dial	No
1	E05	2-(4-nitropyrazolyl)acetic acid	No
1	F05	diethyl 2,3-diacetylbutane-1,4-dioate	No
1	G05	1-(1-methylvinyl)-3-hydrobenzimidazol-2-one	No
1	H05	4-pyrrolylphenol	No
1	I05	benzo[b]furan-2-carboxamide	
1	J05	3-nitro-6-(4-nitropyrazol-3-yl)-8-hydro-3-pyrazolino[2,3-a]pyrimidin-2-one	No
1	K05	3-bromo-6-[5-(3-bromo-2-oxo(8-hydro-3-pyrazolino[2,3-a]pyrimidin-6-yl))-4-nitr opyrazol-3-yl]-8-hydro-3-pyrazolino[2,3-a]pyrimidin-2-one	No
1	L05	N'-(cyclopentylideneazamethyl)-N-(methylethyl)propane-1,3-diamide	No
1	M05	5-{[4-(methylethyl)phenyl]methylene}-2-morpholin-4-yl-1,3-thiazolin-4-one	No
1	N05	1,1,2,2,4-pentamethyl-1,2-dihydroquinoline, iodide	No
1	O05	8-methoxy-2,2,4-trimethyl-6-(triphenylmethyl)-1,2-dihydroquinoline	No

1	P05	4,4,8-trimethyl-4,5-dihydro-1,2-dithioleno[5,4-c]quinoline-1-thione	No
1	A06	8-ethoxy-4,4-dimethyl-4,5-dihydro-1,2-dithioleno[5,4-c]quinoline-1-thione	No
1	B06	3-acetyl-1,1-dichloro-2,2,7b-trimethyl-1,2,3,1a,7b-pentahydrocyclopropa[2,1-c] quinoline	No
1	C06	amino(4-methylquinazolin-2-yl)carboxamidine	No
1	D06	amino(6-methoxy-4-methylquinazolin-2-yl)carboxamidine	OFF-SCALE
1	E06	methyl 14-methoxy-10,10-dimethyl-4,5,8-tris(methoxycarbonyl)spiro[1,3-dithiole ne-2,1'-5,6-dihydrothiino[2,3-c]quinoline]-7-carboxylate	No
1	F06	2-tetradecylbutanedioic acid	No
1	G06	4-[(5-hydroxy-4-phenyl(1,2,5-oxadiazol-3-yl))diazenyl]-3-phenyl-1,2,5-oxadiazo l-2-ol	No
1	H06	methyl 4-[(5R)-5-(methoxycarbonyloxy)-2,15-dimethyl-16-oxotetracyclo[8.7.0.0<2 ,7>.0<11,15>]heptadeca-9,11-dien-14-yl]pentanoate	No
1	I06	(6S,4R)-6-acetyl-7,11-dimethyl-14-oxo-5-oxapentacyclo[8.8.0.0<2,7>.0<4,6>.0<11 ,16>]octadec-15-ene	No
1	J06	methyl 4-((16S,5R,9R)-5,9,16-trihydroxy-2,15-dimethyltetracyclo[8.7.0.0<2,7>.0 <11,15>]heptadec-14-yl)pentanoate	No
1	K06	1-((6R)-14-acetyloxy-7,11-dimethyl-5-oxapentacyclo[8.8.0.0<2,7>.0<4,6>.0<11,16 >]octadec-16-en-6-yl)(1S)ethyl acetate	No
1	L06	14-(hydroxyethyl)-2,15-dimethyltetracyclo[8.7.0.0<2,7>.0<11,15>]heptadec-7-en- 5-yl acetate	No
1	M06	(24R)-12,25-dimethyldispiro[1,3-dioxolane-4,4'-1,3-dioxolane-5',14"-tetracycl o[8.7.0.0<2,7>.0<11,15>]heptadecane]-16-en-15-one	No
1	N06	2-morpholin-4-yl-N-(1,3-thiazol-2-yl)acetamide	No
1	O06	5-bromo-2-{[(4-bromophenyl)amino]methyl}benzo[c]azolidine-1,3-dione	No
1	P06	2-[(dibenzo[b,d]furan-3-ylamino)methyl]-5-nitrobenzo[c]azolidine-1,3-dione	No
1	A07	5-bromo-2-(piperidylmethyl)benzo[c]azolidine-1,3-dione	No
1	B07	17-(2-naphthyl)-17-azapentacyclo[6.6.5.0<2,7>.0<9,14>.0<15,19>]nonadeca-2(7),3 ,5,9(14),10,12-hexaene-16,18-dione	No
1	C07	5-[(2,4-dichlorophenyl)methylene]-2-thioxo-1,3-diazolidin-4-one	No
1	D07	quinoxaline-2,3-diol	No
1	E07	dibenzo[f,h]phenanthro[9,10-b]quinoxaline	No
1	F07	(2E)-3-(N-cyclohexylcarbamoyl)prop-2-enoic acid	No
1	G07	4-(hydrazinoiminomethyl)-1,2,5-oxadiazole-3-ylamine	No

1	H07	6-(4-nitrophenyl)-1,3,5-triazine-2,4-diamine	Yes
1	I07	2-furyl-N-(1,2,4-triazol-4-yl)carboxamide	Yes
1	J07	2-((1E)-2-nitrovinyl)thiophene	No
1	K07	ethyl 4-methyl-4-nitropentanoate	No
1	L07	4-(amino(hydroxyimino)methyl)-1,2,5-oxadiazole-3-ylamine	No
1	M07	1-(9-anthryl)-2-nitroethan-1-ol	No
1	N07	4-[(3-bromophenyl)methylene]-2-phenyl-1,3-oxazolin-5-one	No
1	O07	methyl 12-ethoxy-10,10-dimethyl-4,5,8-tris(methoxycarbonyl)spiro[1,3-dithiolen e-2,1'-5,6-dihydrothiino[2,3-c]quinoline]-7-carboxylate	No
1	P07	amino(4,8-dimethylquinazolin-2-yl)carboxamidine	No
1	A08	amino(8-methoxy-4-methylquinazolin-2-yl)carboxamidine	OFF-SCALE
1	B08	ethyl 2-[(4R)-5-acetyl-3-cyano-6-methyl-4-(2-nitrophenyl)-2-1,4-dihydropyridyl thio]acetate	No
1	C08	5-amino-7-(2,4-dichlorophenyl)-2-[(2,4-dichlorophenyl)methylene]-3-oxo-4,7-dih ydro-1,3-thiazolidino[3,2-a]pyridine-6,8-dicarbonitrile	No
1	D08	2-[(3,4-dichlorophenyl)methylthio]-4-(2-thienyl)-5,6,7,8-tetrahydroquinoline-3 -carbonitrile	No
1	E08	2-amino-6-(tert-butyl)-4-phenyl-3,4,5,6,7,4a-hexahydronaphthalene-1,3,3-tricar bonitrile	No
1	F08	2,11-diacetyl-6-aminospiro[1,2,3,7,8,8a-hexahydroisoquinoline-8,4'-piperidine] -5,7,7-tricarbonitrile	No
1	G08	amino(4-imino(5-hydropyridino[1,2-a]pyrimidin-3-yl))methane-1-thione	No
1	H08	1-[3-amino-7-(tert-butyl)-4-(2-thienyl)(5,6,7,8-tetrahydrothiopheno[2,3-b]quin olin-2-yl)]-2,2-dimethylpropan-1-one	No
1	I08	2-(cyanomethylthio)-4,6-diphenylpyridine-3-carbonitrile	No
1	J08	4-((1E)-3-(3-pyridyl)-2-azaprop-1-enyl)-1-benzothiazol-2-yl-3-(trifluoromethyl)-3-pyrazolin-5-one	No
1	K08	4-((1E)-2-azanon-1-enyl)-1-benzothiazol-2-yl-3-(trifluoromethyl)-3-pyrazolin-5 -one	No
1	L08	1-(3-amino-2,4,6-tribromophenyl)pyrrolidin-2-one	No
1	M08	4-(5-benzoxazol-2-ylbenzimidazol-2-yl)phenylamine	No
1	N08	6-methyl-1-phenyl-5-prop-2-enyl-5-hydropyrazolo[5,4-d]pyrimidin-4-one	No
1	O08	[5-(4-bromophenyl)(2-furyl)]morpholin-4-ylmethane-1-thione	No
1	P08	4-{(1E)-2-[5-(1-phenyl(1,2,3,4-tetraazol-5-ylthio))(2-furyl)]-1-azavinyl}-2,3- dimethyl-1-phenyl-3-pyrazolin-5-one	No
1	A09	4-[(1E)-2-(5-benzothiazol-2-ylthio(2-furyl))-1-azavinyl]-2,3-dimethyl-1-phenyl -3-pyrazolin-5-one	No
1	B09	5-((1E)-2-(2H-benzo[3,4-d]1,3-dioxolen-5-yl)-1-azavinyl)-3-hydrobenzimidazol-2 -one	No

1	C09	5,5-dimethyl-2-{[(2-piperazinylethyl)amino]ethylidene}cyclohexane-1,3-dione	No
1	D09	2,2,3,3-tetrafluoropropyl 4-[N-(2,4-difluorophenyl)carbamoyl]butanoate	No
1	E09	N,N-diethyl[2-(2-furylcarbonylamino)(4,5,6,7-tetrahydrobenzo[b]thiophen-3-yl)] carboxamide	No
1	F09	6-[(1E)-2-(2,5-dimethoxyphenyl)vinyl]-5-nitropyrimidine-2,4-diol	No
1	G09	2-furyl-N-[6-methyl-3-(morpholin-4-ylcarbonyl)(4,5,6,7-tetrahydrobenzo[b]thiop hen-2-yl)]carboxamide	No
1	H09	ethyl 2-(2-thienylcarbonylamino)-4,5,6,7,8-pentahydrocyclohepta[2,1-b]thiophen e-3-carboxylate	No
1	I09	3-chlorobenzo[b]thiophen-2-yl indolinyl ketone	No
1	J09	N-(benzothiazol-2-ylthiomethyl)-2-furylcarboxamide	No
1	K09	({5-[3-(trifluoromethyl)phenyl]-2-furyl}methylene)methane-1,1-dicarbonitrile	No
1	L09	1-benzothiazol-2-yl-4-{[(2-thienylmethyl)amino]methylene}-3-(trifluoromethyl)- 1,2-diazolin-5-one	No
1	M09	ethyl 2-(cyclopropylcarbonylamino)-4,5,6,7,8-pentahydrocyclohepta[2,1-b]thioph ene-3-carboxylate	No
1	N09	2-benzoxazol-2-ylthio-N-(1,1,3,3-tetramethylbutyl)acetamide	No
1	O09	1-benzothiazol-2-yl-4-{[(2-morpholin-4-ylethyl)amino]methylene}-3-(trifluorome thyl)-1,2-diazolin-5-one	No
1	P09	1-benzothiazol-2-yl-4-{[(3-morpholin-4-ylpropyl)amino]ethylidene}-3-(trifluoro methyl)-1,2-diazolin-5-one	No
1	A10	1-benzothiazol-2-yl-4-[(heptylamino)ethylidene]-3-(trifluoromethyl)-1,2-diazol in-5-one	No
1	B10	N-(2H-benzo[3,4-d]1,3-dioxolen-5-yl)(3-chloro-6-fluorobenzo[b]thiophen-2-yl)ca rboxamide	No
1	C10	1-benzothiazol-2-yl-4-[(dimethylamino)methylene]-3-(trifluoromethyl)-1,2-diazo lin-5-one	No
1	D10	ethyl (3E)-4-[(5,6-dimethyl-4-oxo(3-hydrothiopheno[2,3-d]pyrimidin-2-yl))amino]-3-methyl-4-azabut-3-enoate	No
1	E10	2-(2-hydroxyphenoxy)acetic acid, sodium salt	No
1	F10	2-{[bis(phenylmethoxy)carbonyl]amino}-1-methyl-2-imidazolin-4-one	No
1	G10	2-methyl-5-[(trifluoromethyl)sulfonyl]benzothiazole	No
1	H10	ethyl 2-(4-bromo-3-chloro-2-nitroanilino)acetate	YES
1	I10	4-{(1E)-2-[1-(3-methylphenyl)(2-pyrazolin-3-yl)]-2-azavinyl}morpholine	No
1	J10	1-{[4-(2-hydroxyethyl)piperazinyl]methyl}benzo[d]azolidine-2,3-dione	No
1	K10	(6-methyl-6-azabicyclo[4.4.0]dec-2-yl)methyl 2-methylpropanoate, iodide	No

1	L10	heptyl 2-[(6-methyl-6-azabicyclo[4.4.0]dec-2-yl)methoxy]acetate, iodide	YES
1	M10	16-[(6-azabicyclo[4.4.0]dec-2-yl)methyl]-16-azatetracyclo[6.6.3.0<2,7>.0<9,14>]heptadeca-1(14),2(7),3,5,8,10,12-heptaene-15,17-dione	No
1	N10	11-(2-hydroxyethyl)-7,11-diazatricyclo[7.3.1.0<2,7>]trideca-2,4-dien-6-one	No
1	O10	1-[(6-methyl-6-azabicyclo[4.4.0]dec-2-yl)methoxy]-2-(methylpiperidyl)ethane, i odide, iodide	No
1	P10	2-(1-methyl-3-(2-pyridyl)piperidyl)-1-[(6-methyl-6-azabicyclo[4.4.0]dec-2-yl)m ethoxy]ethane, iodide, iodide	No
1	A11	1-((1E)-2-(1,3-thiazol-2-yl)-2-azavinyl)naphthalen-2-ol	No
1	B11	5-[(4-hydroxyphenyl)methylene]-2-thioxo-1,3-thiazolidin-4-one	No
1	C11	5-{[4-(dimethylamino)phenyl]methylene}-2-thioxo-1,3-thiazolidin-4-one	No
1	D11	2-oxolan-2-ylbutanedioic acid	No
1	E11	2-{2-benzimidazol-2-yl-1-[(4-methylphenyl)methyl]ethyl}benzimidazole	No
1	F11	1-(2,3-dibenzimidazol-2-ylpropyl)-2-methoxybenzene	No
1	G11	2-{2-benzimidazol-2-yl-1-[(3,5-dimethylphenyl)methyl]propyl}benzimidazole	No
1	H11	2-[3-(3,5-dimethylphenyl)-2-methylpropyl]benzimidazole	YES
1	I11	1,2-dibenzimidazol-2-ylethane-1,2-diol	No
1	J11	3-[4-(2-carboxyethyl)imidazolyl]propanoic acid	No
1	K11	5-(2-methylthioethyl)-3-prop-2-enylimidazolidin-4-one	No
1	L11	2-methoxy-1-(5-methylthio(1,3,4-oxadiazol-2-yl))benzene	No
1	M11	5-(2,4-dichlorophenyl)-2-propylthio-1,3,4-oxadiazole	No
1	N11	5-(2,4-dichlorophenyl)-2-(phenylmethylthio)-1,3,4-oxadiazole	No
1	O11	5-[(2,4-dichlorophenyl)methylthio]-1,3,4-thiadiazole-2-ylamine	No
1	P11	5-(2-chlorophenyl)-3-(methoxymethyl)-1,3,4-oxadiazoline-2-thione	No
1	A12	5-[(N-phenylcarbamoyl)amino]-1,2,3-thiadiazole-4-carboxylic acid	No
1	B12	2-[(2,4-dichlorophenyl)methylthio]-5-(2-chlorophenyl)-1,3,4-oxadiazole	No
1	C12	4,7,8-trimethoxyfurano[2,3-b]quinoline	No
1	D12	1-(4,8-dimethoxyfurano[2,3-b]quinolin-7-yloxy)-3-methylbutane-2,3-diol	No
1	E12	4-((2E)-6,7-dihydroxy-3,7-dimethyloct-2-enyloxy)hydroquinolin-2-one	No
1	F12	8-(2,3-dihydroxy-3-methylbutoxy)-4-methoxy-1-methylhydroquinolin-2-one	No
1	G12	9-methoxy-2,2-dimethyl-6-hydro-2H-pyrano[5,6-c]quinolin-5-one	No

1	H12	9-methyl-3-oxa-9-azatricyclo[3.3.1.0<2,4>]non-7-yl 3-hydroxy-2-phenylpropanoat e, bromide	No
1	I12	1,2,6,6,10,17,20-heptamethyl-12-oxo-17-[(piperidylethyl)oxycarbonyl]pentacyclo [12.8.0.0<2,11>.0<5,10>.0<15,20>]docos-13-en-7-yl acetate	No
1	J12	2-{[(4-fluorophenyl)sulfonyl]amino}-6-(methylsulfonyl)benzothiazole	No
1	K12	7,8-dioxabicyclo[3.2.1]oct-3-en-2-one	YES
1	L12	2-amino-4,5,6-trihydrocyclopenta[1,2-b]thiophene-3-carbonitrile	No
1	M12	5-(2,5-dichlorophenyl)furan-2-carbaldehyde	No
1	N12	5-amino-4-chloro-2-phenyl-2-hydropyridazin-3-one	No
1	O12	ethyl 2-amino-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate	No
1	P12	2-amino-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxamide	No
1	A13	1-methylpyrazole-5-carboxylic acid	No
1	B13	pyrazole-3-carboxylic acid	No
1	C13	4-nitropyrazole-3-carboxylic acid	No
1	D13	ethyl 2-amino-4-methyl-1,3-thiazole-5-carboxylate	No
1	E13	methyl 2-amino-6-(tert-butyl)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylat e	No
1	F13	ethyl 2-(2-amino-1,3-thiazol-4-yl)acetate	No
1	G13	ethyl 2-amino-4,5,6,7,8-pentahydrocyclohepta[1,2-b]thiophene-3-carboxylate	No
1	H13	2-amino-6-(tert-butyl)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carbonitrile	No
1	I13	4-(3,4-dichlorophenyl)-1,3-thiazole-2-ylamine	YES
1	J13	2-amino-4,5,6,7,8-pentahydrocyclohepta[1,2-b]thiophene-3-carbonitrile	No
1	K13	2-[(2,5-dimethoxyphenyl)methylene]benzo[b]thiophen-3-one	No
1	L13	N-cyclopentyl-2-(4-oxo-3-phenyl(3,5,6,7,8-pentahydrobenzo[b]thiopheno[2,3-d]py rimidin-2-ylthio))acetamide	No
1	M13	5-({6-[(5-amino-1,3,4-thiadiazol-2-ylthio)methyl]-2-pyridyl}methylthio)-1,3,4- thiadiazole-2-ylamine	YES
1	N13	5-[(4-chlorophenyl)methylthio]-1,3,4-thiadiazole-2-ylamine	No
1	O13	5-(diphenylmethylthio)-1-methyl-1,2,3,4-tetraazole	No
1	P13	2-[(2,4-dinitrophenyl)amino]ethan-1-ol	No
1	A14	2-[(5-nitro-8-quinolyl)amino]ethan-1-ol	No
1	B14	(2-aminoethyl)(2,4-dinitrophenyl)amine	No
1	C14	(4-amino(1,2,5-oxadiazol-3-yl))-N-(2-aminoethyl)carboxamide	No
1	D14	(3-aminopropyl)(4-nitrophenyl)amine	No
1	E14	(3-aminopropyl)(2-chloro-4-nitrophenyl)amine	No
1	F14		No
1	G14	(2,2-diethoxyethyl)-	No

1	H14	N-methyl-N-(pyridin-4-ylmethyl)morpholine-2-carboxamide	No
1	I14	ICRF 193	No
1	J14		No
1	K14	2-({2-[(4-chloro-2-nitrophenyl)amino]ethyl}amino)ethan-1-ol	No
1	L14	2-({2-[(2-chloro-4-nitrophenyl)amino]ethyl}amino)ethan-1-ol	No
1	M14	2-({2-[(2,4-dinitrophenyl)amino]ethyl}amino)ethan-1-ol	No
1	N14	2-[(2,4-dinitrophenyl)amino]-2-methylpropan-1-ol	No
1	O14	(2-chloro-5-nitrophenyl)pyrrolidine	No
1	P14	4-(5-chloro-2-nitrophenyl)morpholine	No
1	A15	5-morpholin-4-yl-2-nitrophenylamine	No
1	B15	(2-nitrophenyl)piperazine	No
1	C15		No
1	D15	2-nitro-5-piperazinylphenylamine	No
1	E15	1-(2-chloro-4-nitrophenyl)-4-methylpiperazine	No
1	F15	4-methyl-1-(5-nitro(8-quinolyl))piperazine	No
1	G15		No
1	H15	1-(2,4-dinitrophenyl)-3-methylpiperazine	No
1	I15	3,5-dimethyl-1-(5-nitro(8-quinolyl))piperazine	No
1	J15	5-chloro-2-nitrophenylhydrazine	No
1	K15	2-[(5-chloro-2-nitrophenyl)amino]ethan-1-ol	No
1	L15	2-[4-(5-chloro-2-nitrophenyl)piperazinyl]ethan-1-ol	No
1	M15		No
1	N15	(adamantanylethyl)(5-chloro-2-nitrophenyl)amine	No
1	O15	2-(5-chloro-2-nitrophenylthio)ethan-1-ol	No
1	P15	2-(5-nitro-8-quinolylthio)ethan-1-ol	No
1	A16	2-amino-7,7-dimethyl-5-oxo-4-(2-thienyl)-4H-6,7,8-trihydrochromene-3-carbonitr ile	No
1	B16	(9-anthrylmethylene)methane-1,1-dicarbonitrile	No
1	C16	6-amino-3-methyl-4-(4-pyridyl)-4H-pyrano[2,3-c]pyrazole-5-carbonitrile	No
1	D16	2,6-diamino-4-(4-pyridyl)-4H-thiin-3,5-dicarbonitrile	No
1	E16	2-amino-5-oxo-4-(4-pyridyl)-4H-pyrano[3,2-c]chromene-3-carbonitrile	No
1	F16	ethyl 5-(2-amino-3-cyano-7-methyl-5-oxo-4H-pyrano[3,2-c]pyran-4-yl)furan-2-car boxylate	No
1	G16	ethyl 6-amino-5-cyano-2-methyl-4-(2-thienyl)-4H-pyran-3-carboxylate	YES
1	H16	6-amino-3-methyl-4-(2-thienyl)-4H-pyrano[2,3-c]pyrazole-5-carbonitrile	YES
1	I16	2-amino-7-methyl-5-oxo-4-(4-pyridyl)-4H-pyrano[3,2-c]pyran-3-carbonitrile	No
1	J16	[(3-hydroxy-5-methylpyrazol-4-yl)-4-pyridylmethyl]methane-1,1-dicarbonitrile	No

1	K16	2-amino-7-methyl-5-oxo-4-(2-thienyl)-7-hydro-4H,8H-pyrano[3,2-c]pyran-3-carbon itrile	YES
1	L16	2,3-bis(4-methylpiperazinyl)quinoxaline	No
1	M16	2,6-dimethylmorpholin-4-yl 2-thienyl ketone	No
1	N16	N-[3-(N-methylcarbamoyl)(4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl)]-2-thienylca rboxamide	No
1	O16	2-[5-(4-methylphenyl)(1,2,3,4-tetraazolyl)]-2-(triphenylylidene)ethanenitrile	No
1	P16	3-(4-methoxyphenyl)-2-[(4-methoxyphenyl)azamethylene]-5-(2-oxo(1H-benzo[d]azol in-3-ylidene))-1,3-thiazolidin-4-one	No
1	A17	5-(1-methyl-2-oxobenzo[d]azolin-3-ylidene)-2-phenyl-1,3-thiazolidino[3,2-d]1,2 ,4-triazol-6-one	No
1	B17	5-[(2-hydroxy(3-quinolyl))methylene]-3-benzyl-2-thioxo-1,3-thiazolidin-4-one	No
1	C17	4-{5-[(2-hydroxy(3-quinolyl))methylene]-4-oxo-2-thioxo-1,3-thiazolidin-3-yl}bu tanoic acid	No
1	D17	2-[5-(1-methyl-2-oxobenzo[d]azolin-3-ylidene)-4-oxo-2-thioxo-1,3-thiazolidin-3 -yl]ethanesulfonic acid	No
1	E17	3-{[4-(difluoromethylthio)phenyl]azamethylene}-1H-benzo[d]azolin-2-one	No
1	F17	dimethoxy{2-naphthyl-5-[benzylamino](1,3-oxazol-4-yl)}phosphino-1-one	No
1	G17	(8R,8aR)-6-amino-2-propyl-8-(3-thienyl)-1,2,3,7,8,8a-hexahydroisoquinoline-5,7 ,7-tricarbonitrile	No
1	H17	4,5-dimethyl-2-[2-(3-nitro(1,2,4-triazolyl))acetylamino]thiophene-3-carboxamid e	No
1	I17	(8S,8aR)-6-amino-2-ethyl-8-(4-methylthiophenyl)-1,2,3,7,8,8a-hexahydroisoquino line-5,7,7-tricarbonitrile	No
1	J17	N-adamantanyl-2-(4-bromo-5-methyl-3-nitropyrazolyl)acetamide	No
1	K17	4-nitrophenyl 3-(trifluoromethyl)piperidinesulfonate	No
1	L17	2,4,6-trimethylphenyl [(4-morpholin-4-ylphenyl)amino]sulfonate	No
1	M17	3-(2-chlorophenyl)-1-methyl-1H-indazole	No
1	N17	N-{2,2-dimethyl-3-[(2,3,4,5,6-pentafluorophenyl)carbonylamino]propyl}(2,3,4,5, 6-pentafluorophenyl)carboxamide	No
1	O17	3-ethyl-2-methyl-4-piperazinyl-5-hydropyridino[1,2-a]benzimidazolecarbonitrile	No
1	P17	6-methyl-4-phenyl-2-thioxo-1,5,6,7,8-pentahydropyridino[3,2-c]pyridine-3-carbo nitrile	No
1	A18	2-amino-5,12-dioxospiro[4H-6,7,8-trihydrochromene-4,3'-indoline]-3-carbonitril e	No
1	B18	(4-amino(1,2,5-oxadiazol-3-yl))-N-{2-[(phenylsulfonyl)amino]ethyl}carboxamide	No
1	C18	1-nitro-4-pyrrolidinyl-2-(8-quinolylthio)benzene	No

1	D18	4-(4-methoxyphenyl)-6-phenyl-2-prop-2-ynylthiopyridine-3-carbonitrile	No
1	E18	5-(4-chlorophenyl)-7-phenyl-4,7,8-trihydro-1,2,4-triazolo[1,5-a]pyrimidine	No
1	F18	N-[3,5-bis(trifluoromethyl)phenyl]-2-pyrimidin-2-ylthioacetamide	No
1	G18	[(2,4-difluorophenyl)amino][(4-bromophenyl)amino]methane-1-thione	No
1	H18	1-(3,5-dichlorophenyl)-3-(1,2,3,4-tetrahydroquinolyl)azolidine-2,5-dione	No
1	I18		No
1	J18	(2Z)-3-[(3,4-dimethylphenyl)amino]-3-methylthio-2-azaprop-2-enenitrile	No
1	K18	{[4-(3-chlorophenyl)piperazinyl]methyl}benzotriazole	No
1	L18	1-(3,5-dichlorophenyl)-3-(4-bromophenylthio)azolidine-2,5-dione	No
1	M18	[(4-cyclohexylthio-3-nitrophenyl)methylene]methane-1,1-dicarbonitrile	No
1	N18	1-(4-fluorophenyl)-2-quinolylethan-1-one, bromide	No
1	O18	3-acetyl-1-[2-(4-fluorophenyl)-2-oxoethyl]pyridine, bromide	No
1	P18	[(1-methylindol-3-yl)methylene]methane-1,1-dicarbonitrile	No
1	A19	6-(2-thienyl)-2-thioxo-4-(trifluoromethyl)hydropyridine-3-carbonitrile	No
1	B19	[(4-aminophenyl)sulfonyl](5-ethyl(1,3,4-thiadiazol-2-yl))amine	No
1	C19	[(4-aminophenyl)sulfonyl](2,6-dimethoxypyrimidin-4-yl)amine	No
1	D19	[(4-aminophenyl)sulfonyl](6-chloropyridazin-3-yl)amine	No
1	E19	2-(1,2,2,2-tetrafluoroethyl)benzimidazole	No
1	F19	(benzimidazol-2-ylfluoromethoxy)trifluoromethane	No
1	G19	3,5-bis(ethoxycarbonyl)-2,6-dimethyl-1,4-dihydropyridine-4-carboxylic acid	No
1	H19	2-{3-[(4-amino-2-methylpyrimidin-5-yl)methyl]-4-methyl-1,3-thiazol-5-yl}ethan- 1-ol, chloride, chloride	No
1	I19	1-[(3,5-dimethylpiperidyl)sulfonyl]-4-chlorobenzene	No
1	J19	1,4-dichloro-2-[(3-methylpiperidyl)sulfonyl]benzene	No
1	K19	1-[(4-methoxyphenyl)sulfonyl]-3,5-dimethylpiperidine	No
1	L19	5-[(4-cyclohexylphenoxy)methyl]-4-methyl-1,2,4-triazole-3-thiol	No
1	M19	2-(3-ethynylphenyl)-5-(4-oxobenzo[d]1,3-oxazin-2-yl)benzo[c]azolidine-1,3-dion e	No
1	N19	2-(2-oxo-2-(1,2,3,4-tetrahydroquinolyl)ethyl)benzo[c]azoline-1,3-dione	No
1	O19	3-(1,2,3,4-tetrahydroquinolyl)benzo[d]1,2-thiazole-1,1-dione	No
1	P19	ethyl 2-[(1,1-dioxobenzo[d]1,2-thiazol-3-yl)phenylamino]acetate	No
1	A20	5-chloro-7-[(4-methylpiperazinyl)methyl]quinolin-8-ol	No
1	B20	methyl 1-(2-naphthylsulfonyl)pyrrolidine-2-carboxylate	No
1	C20	2-[(4,4-dimethyl-2,6-dioxocyclohexyl)(5-ethyl-4-nitro(2-thienyl))methyl]-5,5-d imethylcyclohexane-1,3-dione	No

1	D20	4-(2,4-dichlorophenoxy)-N-(1,2,4-triazol-4-yl)butanamide	No
1	E20	1,3-bisbenzyl-2-(4-fluorophenyl)imidazolidine	No
1	F20	4,5-diphenyl-2-(3-pyridyl)imidazole	No
1	G20	4-(4-fluorophenyl)-2-morpholin-4-yl-1,3-thiazole	No
1	H20	4-[(5-hydroxy-3-methyl-1-phenylpyrazol-4-yl)(5-methyl(2-furyl))methyl]-3-methy l-1-phenylpyrazol-5-ol	No
1	I20	1-[(2-chlorophenyl)methyl]-2-(methylsulfonyl)benzimidazole	No
1	J20	[(2,5-dichlorophenyl)sulfonyl](3-pyridylmethyl)amine	No
1	K20	1-(diphenylmethyl)-4-(phenylsulfonyl)piperazine	No
1	L20	3-(2,4-dichlorophenyl)-4-methyl-1,2,4-triazoline-5-thione	No
1	M20	6-chloro-2-(6-chloro(2H,4H-benzo[e]1,3-dioxin-8-yl))chromen-4-one	No
1	N20	1-(6-azabicyclo[4.4.0]dec-2-yl)azolidine-2,5-dione	No
1	O20	7,11-diazatricyclo[7.3.1.0<2,7>]trideca-2,4-dien-6-one	No
1	P20	3-imidazolylbutanoic acid	No
1	A21	3-(2-methylimidazolyl)propanoic acid	No
1	B21	4-[3-(3-carboxypropyl)-2-oxo-3-hydrobenzimidazolyl]butanoic acid	No
1	C21	5,6,11,12-tetrahydropyridazino[1,2-b]phthalazine-1,4-dione	No
1	D21	6-morpholin-4-yl-4-(phenylamino)-1,3,5-triazin-2-ol	No
1	E21	methyl 4,5-dinitropyrazole-3-carboxylate	No
1	F21	3-(4-nitropyrazolyl)-1H-benzo[b]1,4-diazepine	No
1	G21	5,7-dimethyl-3-nitro-8-hydro-3-pyrazolino[2,3-a]pyrimidin-2-one	No
1	H21	ethyl 5-methyl-2-(methylsulfonyloxy)-8-hydropyrazolo[1,5-a]pyrimidine-6-carbox ylate	No
1	I21	6-(4-nitropyrazol-5-yl)-8-hydropyrazolo[1,5-a]pyrimidine-3-carbonitrile	No
1	J21	ethyl 1-acetylpiperidine-4-carboxylate	No
1	K21	7-nitro-5-(pyrrolidinylmethyl)quinolin-8-ol	No
1	L21	5-[(4-methylpiperazinyl)methyl]-7-nitroquinolin-8-ol	No
1	M21	5-[(cyclohexylmethylamino)methyl]-7-nitroquinolin-8-ol	No
1	N21	7-methoxy-4,5-dihydrobenzo[e]benzothiazole-2-ylamine	No
1	O21	2-(1-bromo-2-5,6,7,8-tetrahydronaphthyloxy)acetohydrazide	No
1	P21	1-[(2-methylnaphthyl)methyl]-2-methylthiobenzimidazole	No
1	A22	4-{(hydroxyimino)[4-(4-methoxy-2-nitrophenyl)piperazinyl]methyl}-1,2,5-oxadiaz ole-3-ylamine	No
1	B22	1-(2-phenylethyl)imidazole-2-thiol	No
1	C22	4-benzyl-5-{[4-benzyl-5-sulfanyl(1,2,4-triazol-3-yl)]methyl}-1,2,4-triazole-3- thiol	No
1	D22	2-(5-amino(1,3,4-thiadiazol-2-ylthio))-N,N-dimethylacetamide	No
1	E22	2-[(2,4-dichlorophenyl)methylthio]-5-(3-bromophenyl)-1,3,4-oxadiazole	No

1	F22	[4-amino-6-(pyrimidin-2-ylthiomethyl)(1,3,5-triazin-2-yl)]phenylamine	No
1	G22	4-methoxy-1-(5-phenyl(1,3,4-thiadiazolin-2-yl))naphthalene	No
1	H22	1-phenyl-5-[(1-phenyl(1,2,3,4-tetraazol-5-ylthio))methylthio]-1,2,3,4-tetraazo le	No
1	I22	1-methyl-5-[(1-methyl(1,2,3,4-tetraazol-5-ylthio))methylthio]-1,2,3,4-tetraazo le	No
1	J22	3-(2H-benzo[3,4-d]1,3-dioxolen-5-ylmethylthio)-4-methyl-5-phenyl-1,2,4-triazol e	No
1	K22	2-(4-ethylphenyl)-4-hydroimidazo[1,2-a]pyridine	No
1	L22	2-bromo-5-(2-phenylethyl)indolo[2,3-b]quinoxaline	No
1	M22		No
1	N22	2-(3-oxo-2-hydrocyclopenta[2,3-a]benzenylidene)cyclopenta[1,2-a]benzene-1,3-di one	No
1	O22	3-[2-(3-sulfopropylthio)benzothiazol-3-yl]propanesulfonic acid	No
1	P22	di4-methoxy-2-nitrophenyl disulfide	No
Plate	**Well**	**IUPAC NAME**	**Inhibitor Y/N**
2	A03	dibenzo[c,e]1,2-dithiane-3,8-diamine	No
2	B03	3-(2-methylbenzothiazol-3-yl)propanesulfonic acid	No
2	C03	5-oxo-1-(4-sulfophenyl)-2-pyrazoline-3-carboxylic acid	No
2	D03	2-methyl-6-nitrobenzothiazole	No
2	E03	2-methyl-5-nitrobenzo[c]azoline-1,3-dione	No
2	F03	antipyrine	No
2	G03	7-methyl-2-methylthio-4-hydro-1,2,4-triazolo[1,5-a]pyrimidin-5-ol	No
2	H03	1-phenyl-1,2,3,4-tetraazole-5-thiol	No
2	I03	(2-methoxy-4-nitrophenyl)thiocarbonitrile	No
2	J03	3,3-bis[4-hydroxy-2-methyl-5-(methylethyl)phenyl]-3-hydroisobenzofuran-1-one	No
2	K03	adenosine	No
2	L03	(1E)-1-(3,4-dichlorophenyl)-2-indol-3-yl-1-azaethene	No
2	M03	4-(cyclohexylideneazamethyl)-1,2,4-triazole	No
2	N03	bis(methylethoxy)[(4-methoxyphenyl)amino]phosphino-1-one	No
2	O03	1-morpholin-4-ylbutane-1,3-dione	No
2	P03	(1E)-2-indol-3-yl-1-(3-pyridyl)-1-azaethene	No
2	A04	2-((1E)-2-(1,3-thiazol-2-yl)-2-azavinyl)-4-bromophenol	No
2	B04	(3E)-4-(2-hydroxynaphthyl)-3-azabut-3-en-1-ol	No
2	C04	2-[(1E)-2-(2,4-dichlorophenyl)-2-azavinyl]-4,6-dichlorophenol	No
2	D04	2-[(1E)-2-(4-chloro-2,5-dimethoxyphenyl)-2-azavinyl]-4,6-dichlorophenol	No
2	E04	2-[(1E)-2-(4-iodophenyl)-2-azavinyl]-4-nitrophenol	No
2	F04	(1E)-1-(3,5-dichlorophenyl)-2-(4-fluorophenyl)-1-azaethene	No

2	G04	1-[(1E,9E)-10-(2-hydroxynaphthyl)-2,9-diazadeca-1,9-dienyl]naphthalen-2-ol	No
2	H04	(3S,14S,16S,1R,2R,13R)-3-acetyl-15-oxo-17,19-dioxa-4-azapentacyclo[14.2.1.0<2, 14>.0<4,13>.0<5,10>]nonadeca-5(10),6,8,11-tetraene	No
2	I04	ethyl 2-methyl-6-(4-nitropyrazolyl)-8-hydropyrazolo[1,5-a]pyrimidine-3-carboxy late	No
2	J04	methyl (2Z)-2-cyano-3-(1-methylpyrrol-2-yl)prop-2-enoate	No
2	K04	1,2,3,4-tetrahydroquinolyl xanthen-9-yl ketone	No
2	L04	6-(indolinylcarbonyl)cyclohex-3-enecarboxylic acid	No
2	M04	4,5-dimethyl-2-{2-[5-methyl-3-(trifluoromethyl)pyrazolyl]acetylamino}thiophene -3-carboxamide	No
2	N04	(2R,3R,13R,14R)-3-(phenylcarbonyl)-17,19-dioxa-4-azapentacyclo[14.2.1.0<2,14>. 0<4,13>.0<7,12>]nonadeca-5,7(12),8,10-tetraen-15-one	No
2	O04	3,6-diamino-2-[(4-fluorophenyl)carbonyl]thiopheno[2,3-b]pyridine-5-carbonitril e	No
2	P04	ethyl 2-amino-5-oxo-4-(2-thienyl)-4H-6,7,8-trihydrochromene-3-carboxylate	No
2	A05	3-amino-6-(2-thienyl)thiopheno[2,3-b]pyridine-2-carbonitrile	No
2	B05	6-amino-4-(2,5-dimethoxyphenyl)-3-(tert-butyl)-4H-pyrano[3,2-d]pyrazole-5-carb onitrile	No
2	C05		No
2	D05	6-amino-10-ethyl-3-methylspiro[4H-pyrano[3,2-d]pyrazole-4,4'-piperidine]-5-car bonitrile	No
2	E05	2-[(3-chlorophenyl)amino]-9-methyl-4-oxo-5-hydropyridino[1,2-a]pyrimidine-3-ca rbaldehyde	No
2	F05	N-[3-(piperidylcarbonyl)(4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl)]-2-thienylca rboxamide	No
2	G05	2-(2-thienyl)-5,6,7,8-tetrahydrobenzo[b]thiopheno[2,3-d]1,3-oxazin-4-one	No
2	H05	N,N-diethyl[2-(2-thienylcarbonylamino)(4,5,6,7-tetrahydrobenzo[b]thiophen-3-yl)]carboxamide	No
2	I05	4-methyl-2-(2-morpholin-4-ylethylthio)-6-(trifluoromethyl)pyridine-3-carbonitr ile	No
2	J05	2-chloro-4-oxo-5-hydropyridino[1,2-a]pyrimidine-3-carbaldehyde	No
2	K05	4-iodo-2,3-dimethyl-1-phenyl-3-pyrazolin-5-one	No
2	L05	2-bromobenzo[b]benzo[b]thiophene	No
2	M05	4-(4-iodophenyl)-1-nitrobenzene	No
2	N05	1-[1,2-dibromo-2-(4-bromophenyl)ethyl]-2-bromobenzene	No
2	O05	2,3-dimethylquinoxaline	No
2	P05	2,3-diphenylquinoxaline	No
2	A06	2H,6H-azolino[3',4'-1,2]benzo[4,5-c]azolidine-1,3,5,7-tetraone	No
2	B06	4-bromo-1-[1-(4-bromophenyl)-2,2,2-trichloroethyl]benzene	No

2	C06	3,5-dinitropyridine-2,6-diamine	No
2	D06	4-[(1E)-1-(3-bromo-4-methoxyphenyl)-2-chlorovinyl]-2-bromo-1-methoxybenzene	No
2	E06	4-iodo-1-[2,2,2-trifluoro-1-(4-iodophenyl)-1-(trifluoromethyl)ethyl]benzene	No
2	F06	2,3-bis(3-iodophenyl)quinoxaline	No
2	G06	2,3-bis(4-bromophenyl)quinoxaline	No
2	H06	2-(2-phenylethynyl)benzo[b]benzo[b]thiophene	No
2	I06	2-chloroquinoline-3-carbaldehyde	No
2	J06	2-methoxy-5-(vinylsulfonyl)phenylamine	No
2	K06	2-amino-3-bromo-5-nitrobenzenecarbonitrile	No
2	L06	2-chloro-4-nitrophenylamine	No
2	M06	6-bromo-2-chloro-4-nitrophenylamine	No
2	N06	2,6-dibromo-4-nitrophenylamine	No
2	O06	N-[6-(acetylamino)hexyl]acetamide	No
2	P06	2,7-diiodofluoren-9-one	No
2	A07	3,4-diacetylhexane-2,5-dione	No
2	B07	3,5-bis(dimethylamino)-2-[(phenylamino)thioxomethyl]phenol	No
2	C07	2-(2-{2-[(4-methylphenyl)sulfonyloxy]ethoxy}ethoxy)ethyl 4-methylbenzenesulfon ate	No
2	D07	2-methoxy-6-methyl-5-(phenylmethoxy)-2H-3,4,5,6-tetrahydropyran-3,4-diol	No
2	E07	2-ethyl-6-methoxy-2,5-dimethyl-2H-3,4,5,6-tetrahydropyran	No
2	F07	6,6-diethylthiohexane-1,2,3,4,5-pentaol	No
2	G07	8-ethoxy-3-ethyl-8-methyl-2,7,9-trioxabicyclo[4.3.0]nonane	No
2	H07	2-((1E)-2-(2-furyl)-1-azavinyl)-5-nitrophenol	No
2	I07	2-((1E)-2-(2-furyl)-1-azavinyl)-4-nitrophenol	No
2	J07	5-[(1E)-2-(3,4-dichlorophenyl)-2-azavinyl]-2-bromofuran	No
2	K07	5-[(1E)-2-(3,4-dichlorophenyl)-2-azavinyl]-2-iodofuran	No
2	L07	3-[(1E)-2-(3,4-dichlorophenyl)-2-azavinyl]-2-chloroquinoline	No
2	M07	2-[(1E)-2-(2-hydroxy-5-nitrophenyl)-1-azavinyl]-4-nitrophenol	No
2	N07	4-((1E)-2-(2-pyridyl)-1-azavinyl)-2,3-dimethyl-1-phenyl-3-pyrazolin-5-one	No
2	O07	4-[(1E)-2-(5-bromo(2-furyl))-1-azavinyl]-2,3-dimethyl-1-phenyl-3-pyrazolin-5-o ne	No
2	P07	4-((1E)-2-indol-2-yl-1-azavinyl)-2,3-dimethyl-1-phenyl-3-pyrazolin-5-one	No
2	A08	2-[(1E)-2-(4-iodophenyl)-2-azavinyl]-4-bromophenol	No
2	B08	2-[(1E)-2-(2,5-dimethoxyphenyl)-2-azavinyl]-4-bromophenol	No
2	C08	2-[(1E)-2-(2,5-dichlorophenyl)-2-azavinyl]-4-bromophenol	No
2	D08	2-[(1E)-2-(3,5-dichlorophenyl)-2-azavinyl]-4-bromophenol	No
2	E08	2-[(1E)-2-(4-chlorophenyl)-2-azavinyl]thiophene	No
2	F08	2-[(1E)-2-(2-hydroxy-4-nitrophenyl)-2-azavinyl]-4-bromophenol	No

2	G08	2-[(1E)-2-(2-bromo-4-nitrophenyl)-2-azavinyl]-4-bromophenol	No
2	H08	2-[(1E)-2-(4-{4-[(1E)-2-(6-bromo-3-hydroxyphenyl)-1-azavinyl]phenyl}phenyl)-2- azavinyl]-4-bromophenol	No
2	I08	1-[(1E)-2-(2-chloro(3-quinolyl))-1-azavinyl]-4-chloro-2,5-dimethoxybenzene	No
2	J08	3-[(1E)-2-(2,3-dichlorophenyl)-2-azavinyl]-2-chloroquinoline	No
2	K08	2-[(1E)-2-(2-hydroxy-4-nitrophenyl)-2-azavinyl]-4,6-dibromophenol	No
2	L08	2-[(1E)-2-(4-fluorophenyl)-2-azavinyl]-4,6-dibromophenol	No
2	M08	4-[(1E)-2-(3,5-dibromo-2-hydroxyphenyl)-1-azavinyl]benzenesulfonamide	No
2	N08	2-[(1E)-2-(4-bromophenyl)-2-azavinyl]-4,6-dibromophenol	No
2	O08	2-[(1E)-2-(2-hydroxy-5-nitrophenyl)-2-azavinyl]-4,6-dibromophenol	No
2	P08	2-[(1E)-2-(4-nitrophenyl)-2-azavinyl]-4,6-dibromophenol	No
2	A09	3-[(1E)-2-(4-bromophenyl)-2-azavinyl]-2-chloroquinoline	No
2	B09	3-[(1E)-2-(2,5-dichlorophenyl)-2-azavinyl]-2-chloroquinoline	No
2	C09	2-[(1E)-2-(2,4-dichlorophenyl)-2-azavinyl]-4,6-dibromophenol	No
2	D09	2-[(1E)-2-(5-chloro(2-pyridyl))-2-azavinyl]-4,6-dibromophenol	No
2	E09	2-[(1E)-2-(2,5-dichlorophenyl)-2-azavinyl]-4,6-dibromophenol	No
2	F09	2-[(1E)-2-(3,4-dichlorophenyl)-2-azavinyl]-4,6-dibromophenol	No
2	G09	2-[(1E)-2-(3,5-dichlorophenyl)-2-azavinyl]-4,6-dibromophenol	No
2	H09	2-[(1E)-2-(3,5-dimethylphenyl)-2-azavinyl]-4,6-dibromophenol	No
2	I09	2-[(1E)-2-(2,5-dimethoxyphenyl)-2-azavinyl]-4,6-dibromophenol	No
2	J09	2-[(1E,9E)-10-(3,5-dibromo-2-hydroxyphenyl)-2,9-diazadeca-1,9-dienyl]-4,6-dibr omophenol	No
2	K09	1-[(1E)-2-(5-chloro(2-pyridyl))-2-azavinyl]naphthalen-2-ol	No
2	L09	6-[(1E)-2-(5-chloro(2-pyridyl))-2-azavinyl]-2-bromo-4-nitrophenol	No
2	M09	2-[(1E)-2-(5-chloro(2-pyridyl))-2-azavinyl]-4-bromophenol	No
2	N09	2-((1E)-2-naphthyl-1-azavinyl)-5-chloropyridine	No
2	O09	2-[(1E)-2-(4-fluorophenyl)-1-azavinyl]-5-chloropyridine	No
2	P09	2-[(1E)-2-(4-chlorophenyl)-1-azavinyl]-5-chloropyridine	No
2	A10	4-((1E)-2-(2-thienyl)-1-azavinyl)benzenesulfonamide	No
2	B10	2-[(1E,9E)-10-(3,5-dichloro-2-hydroxyphenyl)-2,9-diazadeca-1,9-dienyl]-4,6-dic hlorophenol	No
2	C10	2-((1E)-2-(2-pyridyl)-2-azavinyl)-4,6-dichlorophenol	No
2	D10	2-[(1E)-2-(2,5-dimethoxyphenyl)-2-azavinyl]-4,6-dichlorophenol	No
2	E10	2-[(1E)-2-(2,5-dichlorophenyl)-2-azavinyl]-4,6-dichlorophenol	No
2	F10	2-[(1E)-2-(3,5-dichlorophenyl)-2-azavinyl]-4,6-dichlorophenol	No
2	G10	2-[(1E)-2-(3,4-dichlorophenyl)-2-azavinyl]-4,6-dichlorophenol	No
2	H10	2-[(1E)-2-(2-hydroxy-4-nitrophenyl)-2-azavinyl]-4,6-dichlorophenol	No
2	I10	2-[(1E)-2-(4-fluorophenyl)-2-azavinyl]-4,6-dichlorophenol	No

2	J10	1-((1E)-2-(2-pyridyl)-2-azavinyl)naphthalen-2-ol	No
2	K10	2-[(1E)-2-(2-chlorophenyl)-1-azavinyl]-5-chloropyridine	No
2	L10	2-((1E)-2-(2-pyridyl)-2-azavinyl)-4-bromophenol	No
2	M10	2-[(1E)-2-(2,5-dichlorophenyl)-2-azavinyl]thiophene	No
2	N10	2-[(1E)-2-(2,4-dichlorophenyl)-2-azavinyl]thiophene	No
2	O10	2-((1E)-2-(1,3-thiazol-2-yl)-2-azavinyl)-4,6-dibromophenol	No
2	P10	2-((1E)-2-(2-pyridyl)-2-azavinyl)-4,6-dibromophenol	No
2	A11	4-chloro-1-[(3-methylpiperidyl)sulfonyl]benzene	No
2	B11	1-chloro-4-{[4-(4-fluorophenyl)piperazinyl]sulfonyl}benzene	No
2	C11	[(4-chlorophenyl)sulfonyl](2,4,5-trichlorophenyl)amine	No
2	D11	4-chloro-1-(1,2,3,4-tetrahydroquinolylsulfonyl)benzene	No
2	E11	4-chloro-1-[(4-methylpiperidyl)sulfonyl]benzene	No
2	F11	(2,5-dimethoxyphenyl)[(4-chlorophenyl)sulfonyl]amine	No
2	G11	(3-chloro-4-fluorophenyl)[(4-chlorophenyl)sulfonyl]amine	YES
2	H11	[(4-chlorophenyl)sulfonyl]cycloheptylamine	YES
2	I11	4-chloro-1-(indolinylsulfonyl)benzene	No
2	J11	(3,5-dichlorophenyl)[(4-chlorophenyl)sulfonyl]amine	YES
2	K11	N,N-bis(cyanomethyl)-2-thienylcarboxamide	No
2	L11	1-bromo-4-{[4-(4-nitrophenyl)piperazinyl]sulfonyl}benzene	No
2	M11	[(4-bromophenyl)sulfonyl](2-furylmethyl)amine	No
2	N11	1-(azaperhydroepinylsulfonyl)-4-bromobenzene	No
2	O11	4-bromo-1-[(3-methylpiperidyl)sulfonyl]benzene	No
2	P11	1-bromo-4-[(4-methylpiperazinyl)sulfonyl]benzene	No
2	A12	[(4-bromophenyl)sulfonyl](oxolan-2-ylmethyl)amine	No
2	B12	1,4-dichloro-2-{[4-(4-nitrophenyl)piperazinyl]sulfonyl}benzene	No
2	C12	[(2,5-dichlorophenyl)sulfonyl](2-methoxyethyl)amine	No
2	D12	1,4-dichloro-2-(2-1,2,3,4-tetrahydroisoquinolylsulfonyl)benzene	No
2	E12	[(2,5-dichlorophenyl)sulfonyl](2,5-dimethoxyphenyl)amine	No
2	F12	1-phenyl-4-(phenylsulfonyl)piperazine	No
2	G12	(2,4-dinitrophenyl)(phenylsulfonyl)amine	No
2	H12	(4-bromophenyl)(phenylsulfonyl)amine	YES
2	I12	diphenyl(phenylsulfonyl)amine	No
2	J12	(4-chlorophenyl)[(4-fluorophenyl)sulfonyl]amine	No
2	K12	(4-bromophenyl)[(4-fluorophenyl)sulfonyl]amine	No
2	L12	4-fluoro-1-[(4-phenylpiperazinyl)sulfonyl]benzene	No
2	M12	(3,4-dichlorophenyl)[(4-fluorophenyl)sulfonyl]amine	No
2	N12	1-fluoro-4-{[4-(4-nitrophenyl)piperazinyl]sulfonyl}benzene	No
2	O12	benzothiazol-2-yl[(4-methoxyphenyl)sulfonyl]amine	No
2	P12	2-[(4-methoxyphenyl)sulfonyl]-1,2,3,4-tetrahydroisoquinoline	No
2	A13	cycloheptyl[(4-methoxyphenyl)sulfonyl]amine	No
2	B13	[(4-methoxyphenyl)sulfonyl](2,4,5-trichlorophenyl)amine	No

2	C13	1-(morpholin-4-ylsulfonyl)-4-nitrobenzene	No
2	D13	cycloheptyl[(4-nitrophenyl)sulfonyl]amine	No
2	E13	benzothiazol-2-yl[(4-nitrophenyl)sulfonyl]amine	No
2	F13	1-(benzimidazolylsulfonyl)-4-nitrobenzene	No
2	G13	1-(benzimidazolylsulfonyl)-2-nitrobenzene	No
2	H13	7-amino-5-(2,4-dichlorophenyl)-2-[(2,4-dichlorophenyl)methylene]-3-oxo-4,5-dih ydro-1,3-thiazolidino[3,2-a]pyridine-6,8-dicarbonitrile	YES
2	I13	7-amino-5-(3-fluorophenyl)-2-[(3-fluorophenyl)methylene]-3-oxo-4,5-dihydro-1,3 -thiazolidino[3,2-a]pyridine-6,8-dicarbonitrile	No
2	J13	7-amino-5-(6-chloro-2-fluorophenyl)-2-[(6-chloro-2-fluorophenyl)methylene]-3-o xo-4,5-dihydro-1,3-thiazolidino[3,2-a]pyridine-6,8-dicarbonitrile	No
2	K13	7-amino-5-(4-fluorophenyl)-2-[(4-fluorophenyl)methylene]-3-oxo-4,5-dihydro-1,3 -thiazolidino[3,2-a]pyridine-6,8-dicarbonitrile	No
2	L13	methyl 7-amino-8-(methoxycarbonyl)-3-oxo-5-(3-pyridyl)-2-(3-pyridylmethylene)- 4,5-dihydro-1,3-thiazolidino[3,2-a]pyridine-6-carboxylate	No
2	M13	methyl 7-amino-8-(methoxycarbonyl)-3-oxo-5-(4-pyridyl)-2-(4-pyridylmethylene)- 4,5-dihydro-1,3-thiazolidino[3,2-a]pyridine-6-carboxylate	No
2	N13	methyl 7-amino-6-cyano-3-oxo-5-(4-pyridyl)-2-(4-pyridylmethylene)-4,5-dihydro- 1,3-thiazolidino[3,2-a]pyridine-8-carboxylate	No
2	O13	tert-butyl 6-amino-5-(ethoxycarbonyl)-8-oxo-2-propylspiro[4H-pyran-4,3'-indoli ne]-3-carboxylate	No
2	P13	methylethyl 6-amino-5-(ethoxycarbonyl)-8-oxo-2-propylspiro[4H-pyran-4,3'-indol ine]-3-carboxylate	No
2	A14	methylethyl 6-amino-2-methyl-8-oxo-5-(prop-2-enyloxycarbonyl)spiro[4H-pyran-4, 3'-indoline]-3-carboxylate	No
2	B14	6-amino-15-bromo-3-methyl-11-oxospiro[4H-pyrano[2,3-c]pyrazole-4,3'-indoline]- 5-carbonitrile	No
2	C14	2,6-diamino-12-oxospiro[4H-chromene-4,3'-indoline]-3-carbonitrile	No
2	D14	3-amino-19-bromo-5,16-dioxospiro[1H-pyrano[2,3-c]chromene-1,3'-indoline]-2-car bonitrile	No
2	E14	methyl 2-amino-11-bromo-5-[(2-methoxyethyl)oxycarbonyl]-6-methyl-8-oxospiro[4H -pyran-4,3'-indoline]-3-carboxylate	No
2	F14	ethyl 2-amino-11-bromo-5-[(2-methoxyethyl)oxycarbonyl]-6-methyl-8-oxospiro[4H- pyran-4,3'-indoline]-3-carboxylate	No
2	G14	methylethyl 2-amino-5-[(2-methoxyethyl)oxycarbonyl]-6-methyl-8-oxospiro[4H-pyr an-4,3'-indoline]-3-carboxylate	No
2	H14	methylethyl 6-amino-11-bromo-2-methyl-8-oxo-5-(prop-2-enyloxycarbonyl)spiro[4H -pyran-4,3'-indoline]-3-carboxylate	YES

2	I14	2-[(5-hydroxypyrazol-3-yl)methylthio]-4,6-dimethylpyridine-3-carbonitrile	No
2	J14	(1S,3aR)-2-(2-chloro-6-fluorophenyl)-1-[(4-fluorophenyl)carbonyl]-10,3a-dihydr opyrrolidino[1,2-a]quinoline-3,3-dicarbonitrile	No
2	K14	(10aS,8R,9R)-8-(phenylcarbonyl)-9-(2-thienyl)-7,10a-dihydropyrrolidino[2,1-a]i soquinoline-10,10-dicarbonitrile	No
2	L14	(2S,3S,13R,14R)-3-(phenylcarbonyl)-17,19-dioxa-4-azapentacyclo[14.2.1.0<2,14>. 0<4,13>.0<5,10>]nonadeca-5(10),6,8,11-tetraen-15-one	No
2	M14	(1S,2S,3aR)-1-(phenylcarbonyl)-2-[2-(trifluoromethyl)phenyl]-10,3a-dihydropyrr olidino[1,2-a]quinoline-3,3-dicarbonitrile	No
2	N14	(4aS,4R)-2-amino-4-(3-iodophenyl)-6-methyl-3,4,5,6,7,4a-hexahydronaphthalene-1 ,3,3-tricarbonitrile	No
2	O14	(1S,14S,2R,3R,13R,16R)-3-(adamantanylcarbonyl)-17,19-dioxa-4-azapentacyclo[14. 2.1.0<2,14>.0<4,13>.0<7,12>]nonadeca-5,7(12),8,10-tetraen-15-one	No
2	P14	(9S,10aS,8R)-8-(phenylcarbonyl)-9-(3-thienyl)-7,10a-dihydropyrrolidino[2,1-a]i soquinoline-10,10-dicarbonitrile	No
2	A15	(10aS,8R,9R)-9-(3,4-dichlorophenyl)-8-(phenylcarbonyl)-7,10a-dihydropyrrolidin o[2,1-a]isoquinoline-10,10-dicarbonitrile	No
2	B15	(8aR)-6-amino-8-(4-fluorophenyl)-2-(methylethyl)-1,2,3,7,8,8a-hexahydroisoquin oline-5,7,7-tricarbonitrile	No
2	C15	(8aR)-6-amino-2-methyl-8-[4-(methylethyl)phenyl]-1,2,3,7,8,8a-hexahydroisoquin oline-5,7,7-tricarbonitrile	No
2	D15	(8aR)-6-amino-8-(4-fluorophenyl)-2-methyl-1,2,3,7,8,8a-hexahydroisoquinoline-5 ,7,7-tricarbonitrile	No
2	E15	6-amino-3-(tert-butyl)-4-(3-methyl(2-thienyl))-4H-pyrano[2,3-c]pyrazole-5-carb onitrile	No
2	F15	6-amino-3-(tert-butyl)-4-(4-methylthiophenyl)-4H-pyrano[2,3-c]pyrazole-5-carbo nitrile	No
2	G15	6-amino-3-(tert-butyl)-4-(4-fluorophenyl)-4H-pyrano[2,3-c]pyrazole-5-carbonitr ile	No
2	H15	6-amino-3-(tert-butyl)-4-(3-pyridyl)-4H-pyrano[2,3-c]pyrazole-5-carbonitrile	No
2	I15	6-amino-4-(3-furyl)-3-phenyl-4H-pyrano[2,3-c]pyrazole-5-carbonitrile	No
2	J15	6-amino-4-(2-furyl)-3-phenyl-4H-pyrano[2,3-c]pyrazole-5-carbonitrile	No
2	K15	6-amino-4-(2,3-dichlorophenyl)-3-phenyl-4H-pyrano[2,3-c]pyrazole-5-carbonitril e	No
2	L15	1,2-dimethoxy-4-(3-phenyl(4H-pyrano[2,3-c]pyrazol-4-yl))benzene	No
2	M15	6-amino-3-phenyl-4-(3-pyridyl)-4H-pyrano[2,3-c]pyrazole-5-carbonitrile	No
2	N15	2,6-diamino-4-(5-nitro(2-thienyl))-4H-thiin-3,5-dicarbonitrile	No

2	O15	(4S,6R)-6-hydroxy-6-methyl-5-(2-methylpyridyl)-4-(3-pyridyl)-2-sulfanyl-1,4,5, 6-tetrahydropyridine-3-carbonitrile	No
2	P15	2-amino-7,7-dimethyl-4-(4-nitro(2-thienyl))-5-oxo-4H-6,7,8-trihydrochromene-3- carbonitrile	No
2	A16	6-amino-3-methyl-11-oxospiro[4H-pyrano[2,3-c]pyrazole-4,3'-indoline]-5-carboni trile	No
2	B16	6-amino-3-(tert-butyl)-11-oxospiro[4H-pyrano[2,3-c]pyrazole-4,3'-indoline]-5-c arbonitrile	No
2	C16	(8aS,8R)-6-amino-8-(3-bromophenyl)-2-benzyl-1,2,3,7,8,8a-hexahydroisoquinoline -5,7,7-tricarbonitrile	No
2	D16	4-oxo-9-propyl-2-sulfanyl-3,9-diazaspiro[5.5]undec-1-ene-1,5-dicarbonitrile	No
2	E16	9-ethyl-4-oxo-2-sulfanyl-3,9-diazaspiro[5.5]undec-1-ene-1,5-dicarbonitrile	No
2	F16	(3S,14S,16S,1R,2R,13R)-3-[(4-fluorophenyl)carbonyl]-17,19-dioxa-4-azapentacycl o[14.2.1.0<2,14>.0<4,13>.0<5,10>]nonadeca-5(10),6,8,11-tetraen-15-one	No
2	G16	(4S,4aR)-2-amino-4a-methyl-4-(3-pyridyl)-3,4,5,6,7,4a-hexahydronaphthalene-1,3 ,3-tricarbonitrile	YES
2	H16	6-amino-3-(methoxymethyl)-4-(3-methyl(2-thienyl))-4H-pyrano[2,3-c]pyrazole-5-c arbonitrile	No
2	I16	2-amino-4-(4-methylthiophenyl)-8-[(4-methylthiophenyl)methylene]-6-propyl-5,6, 7-trihydro-4H-pyrano[3,2-c]pyridine-3-carbonitrile	No
2	J16	[(3-hydroxy-5-phenylpyrazol-4-yl)-3-thienylmethyl]methane-1,1-dicarbonitrile	No
2	K16	[2-(3-hydroxy-5-methylpyrazol-4-yl)adamantan-2-yl]methane-1,1-dicarbonitrile	No
2	L16	6-(2-chloro-6-fluorophenyl)-4-hydroxy-4-phenyl-5-(2,2,2-trifluoroacetyl)-1,3-d iazaperhydroin-2-one	No
2	M16	7-phenylpyridino[2',3'-4,5]thiopheno[2,3-b]pyridine-2,4-diol	No
2	N16	7-(4-pyridyl)pyridino[2',3'-4,5]thiopheno[2,3-b]pyridine-2,4-diol	No
2	O16	N-[6-methyl-3-(morpholin-4-ylcarbonyl)(4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl)]-2-thienylcarboxamide	No
2	P16	[6-methyl-2-(2-thienylcarbonylamino)(4,5,6,7-tetrahydrobenzo[b]thiophen-3-yl)] -N,N-dipropylcarboxamide	No
2	A17	{[1-(4-nitrophenyl)-5-phenylhydropyrazin-2-ylidene]azamethyl}phenylbenzylamine	No
2	B17	[(1,6-diphenylhydropyrimidin-4-ylidene)azamethyl]phenylbenzylamine	No
2	C17	3-((1E)-3-phenyl-2-azaprop-1-enyl)-4-phenyl-1,4-thiazine	No
2	D17	2-[5-methyl-3-(trifluoromethyl)pyrazolyl]acetamide	No
2	E17	2-amino-11-chloro-6-methyl-5-(2-methylpropanoyl)-8-oxospiro[4H-pyran-4,3'-indo line]-3-carbonitrile	No

2	F17	ethyl 5-amino-6-(ethoxycarbonyl)-7-(2-furyl)-2-(2-furylmethylene)-3-oxo-4,7-di hydro-1,3-thiazolidino[3,2-a]pyridine-8-carboxylate	No
2	G17	ethyl 5-amino-6-cyano-7-(5-methyl(2-thienyl))-2-[(5-methyl(2-thienyl))methylen e]-3-oxo-4,7-dihydro-1,3-thiazolidino[3,2-a]pyridine-8-carboxylate	No
2	H17	methyl 5-amino-6-(methoxycarbonyl)-3-oxo-7-(3-pyridyl)-2-(3-pyridylmethylene)- 4,7-dihydro-1,3-thiazolidino[3,2-a]pyridine-8-carboxylate	YES
2	I17	{[4-((1E)-2-(2-furyl)-1-azavinyl)phenyl]sulfonyl}(6-methoxypyrimidin-4-yl)amin e	No
2	J17	N-[1-(2-bromoethyl)-2-oxoindolin-3-yl]acetamide	No
2	K17	(6-methoxy-2-hydrobenzo[b]furan-3-ylidene)azamethyl 2-chloroacetate	No
2	L17	1,4-diphenyl-3-(phenylazamethylene)-1,2,4-triazoline	No
2	M17		No
2	N17		No
2	O17	1,3-dimethyl-1,3,4,6,3a,6a-hexahydro-1,3,4,6-tetraazapentalene-2,5-dione	No
2	P17	4-(dimethylamino)-2,3-dimethyl-1-phenyl-3-pyrazolin-5-one	No
2	A18	4,5-diacetyloxy-6-(acetyloxymethyl)-2-prop-2-enyloxy-2H-3,4,5,6-tetrahydropyra n-3-yl acetate	No
2	B18	2-methoxy-6-[(triphenylmethoxy)methyl]-2H-3,4,5,6-tetrahydropyran-3,4,5-triol	No
2	C18	3-(2H-benzo[d]1,3-dioxolan-5-yl)(2Z)-2-(aminothioxomethyl)prop-2-enenitrile	No
2	D18	2-(acetylamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylic acid	No
2	E18	4-indol-3-ylbutanoic acid	No
2	F18	2,15-dimethyl-14-oxotetracyclo[8.7.0.0<2,7>.0<11,15>]heptadec-7-en-5-yl acetat e	No
2	G18		No
2	H18	ethyl 2-amino-1,3-thiazole-4-carboxylate	YES
2	I18	(3S,4S,6S,5R)-5-[(4S,5S,2R,3R,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)(2H-3,4,5, 6-tetrahydropyran-2-yloxy)]-6-(hydroxymethyl)-2H-3,4,5,6-tetrahydropyran-2,3,4 -triol	No
2	J18	2-[(5S,2R,3R,4R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yloxy]-6-{[(2S,4S,3R, 5R,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)(2H-3,4,5,6-tetrahydropyran-2-yloxy)] methyl}(4S,5S,2R,3R,6R)-2H-3,4,5,6-tetrahydropyran-3,4,5-triol	No
2	K18	10-methylacridine-3,6-diamine, chloride, chloride	No
2	L18	[6-chloro-4-(ethylamino)(1,3,5-triazin-2-yl)]ethylamine	No
2	M18	4-methylphenyl di4-methylphenyl phosphate	No
2	N18	3-(3-oxoisobenzofuranylidene)pentane-2,4-dione	No

2	O18	14-(1,5-dimethylhexyl)-2,15-dimethyltetracyclo[8.7.0.0<2,7>.0<11,15>]heptadec- 7-en-5-ol	No
2	P18	1-[4,6-bis(2-chloroethoxy)(1,3,5-triazin-2-yloxy)]-2-chloroethane	No
2	A19	1-acetyl-4-[2-oxo-1-(3-oxoisobenzofuranylidene)propyl]benzene	No
2	B19	methoxy-N-(5-propylthiobenzimidazol-2-yl)carboxamide	No
2	C19	(2S)-2-(5,6-dichloro-1,3-dioxobenzo[c]azolin-2-yl)-3-methylbutanoic acid	No
2	D19	3-(5-{[4-(dimethylamino)phenyl]methylene}-4-oxo-2-thioxo-1,3-thiazolidin-3-yl) thiolane-1,1-dione	No
2	E19	2-{5-[(2-hydroxy(3-quinolyl))methylene]-4-oxo-2-thioxo-1,3-thiazolidin-3-yl}ac etic acid	No
2	F19	5-({9-methyl-4-oxo-2-[(2-phenylethyl)amino](5-hydropyridino[1,2-a]pyrimidin-3- yl)}methylene)-3-(phenylethyl)-2-thioxo-1,3-thiazolidin-4-one	No
2	G19	3-methyl-5-[(9-methyl-4-oxo-2-piperidyl(5-hydropyridino[1,2-a]pyrimidin-3-yl)) methylene]-2-thioxo-1,3-thiazolidin-4-one	No
2	H19	N-(4-fluorophenyl)-2-[4-methyl-5-(trifluoromethyl)(1,2,4-triazol-3-ylthio)]ace tamide	YES
2	I19	2-(hydroxyimino)-3-methylhydroquinoxaline	No
2	J19	indolo[2,3-e]1,2,3,4-tetraazolo[1,5-b]1,2,4-triazine	No
2	K19	6-bromo-2-[(6-nitrobenzimidazol-2-yl)methylthio]benzimidazole	No
2	L19	5-(4,6-dimethylpyrimidin-2-ylthio)-4-nitrobenzo[c]1,2,5-thiadiazole	No
2	M19	5-({1-[2-(2-fluorophenoxy)ethyl]indol-3-yl}methylene)-2-thioxo-1,3-thiazolidin -4-one	No
2	N19	ethyl 6-[4-methoxy-2-methyl-5-(methylethyl)phenyl]-4-methyl-2-thioxo-1,3,6-tri hydropyrimidine-5-carboxylate	No
2	O19	6-amino-10-methyl-3-phenylspiro[4H-pyrano[2,3-c]pyrazole-4,4'-piperidine]-5-ca rbonitrile	No
2	P19	[(3-amino-5-imino(1,2-diazolin-4-ylidene))azamethyl](4-methoxyphenyl)amine	No
2	A20	N-(2H,3H-benzo[e]1,4-dioxin-6-yl)-2-(4-methyl(1,2,4-triazol-3-ylthio))acetamid e	No
2	B20	1-cyclohexylthio-2-(1,3-dithiolan-2-yl)-4-nitrobenzene	No
2	C20	(3-amino(1H-1,2,4-triazol-5-yl))(4-chlorophenyl)amine	No
2	D20	((1E)-2-{5-[(3,4-dimethylphenyl)amino](1H-1,2,4-triazol-3-yl)}-2-azavinyl)dime thylamine	No
2	E20	4-((1E)-2-(2-thienyl)-1-azavinyl)phenyl 4-chlorobenzenesulfonate	No
2	F20	{[4-((2Z)-3-phenylprop-2-enyl)piperazinyl]methyl}benzotriazole	No
2	G20	4-bromo-6-methoxy-2-{[(5-methylisoxazol-3-yl)amino]methyl}phenol	No
2	H20	acridine-3,6-diamine	No
2	I20	3-nitro-1-(pyrrolidinylsulfonyl)benzene	No

2	J20	(phenylamino){2-[(phenylamino)thioxomethyl]hydrazino}methane-1-thione	TES
2	K20	1-chloro-2-(morpholin-4-ylsulfonyl)-4-nitrobenzene	No
2	L20	5-chloro-7-nitroquinolin-8-ol	No
2	M20	methyl(phenylsulfonyl)-8-quinolylamine	No
2	N20	5-chlorobenzothiazole-2-thiol	No
2	O20	acenaphthen-5-yl(methylsulfonyl)amine	No
2	P20	[(3,4-dimethoxyphenyl)amino]methylthiomethane-1-thione	No
2	A21		No
2	B21	(4-chloro-2-nitrophenyl)cyclohexylamine	No
2	C21	1,4-bis(4-chloro-2-nitrophenyl)piperazine	No
2	D21	cyclohexyl(2-nitrophenyl)amine	No
2	E21		No
2	F21	1,4-bis(2-chloro-4-nitrophenyl)piperazine	No
2	G21	7-(tert-butyl)-3-methyl-2-sulfanyl-3,5,6,7,8-pentahydrobenzo[b]thiopheno[2,3-d]pyrimidin-4-one	No
2	H21	4-(4-bromophenyl)-2-morpholin-4-yl-1,3-thiazole	No
2	I21	1-(4-nitrophenyl)pyrrolidin-2-one	No
2	J21	4-(3-chloro-4-nitrophenyl)morpholine	No
2	K21		No
2	L21	1-(morpholin-4-ylmethyl)-4-phenyl-1,2,3,4-tetraazoline-5-thione	No
2	M21	4,5,6,7-tetrahydrobenzothiazole-2-ylamine	No
2	N21	2-chloro-1-indolinylethan-1-one	No
2	O21	methyl 7-(methoxycarbonyl)-2,6-dimethylfurano[2',3'-5,4]benzo[b]furan-3-carbox ylate	No
2	P21	methyl 1-(phenylsulfonyl)pyrrolidine-2-carboxylate	No
2	A22	3-(tert-butyl)-5-chloro-6-methyl-1,3,5,6-tetrahydropyrimidine-2,4-dione	No
2	B22		No
2	C22	6-methyl-3-(phenyldiazenyl)-2-pyridylamine	No
2	D22	2-pyridyl-1-(2-thienyl)ethan-1-one, iodide	No
2	E22	8-bromopurine-6-ylamine	No
2	F22	3-chloro-4-morpholin-4-ylphenylamine	No
2	G22	[3,4-diacetyloxy-5-(6-hydroxypurin-9-yl)oxolan-2-yl]methyl acetate	No
2	H22	1,8-dihydroxy-2,4,5,7-tetranitroanthracene-9,10-dione	No
2	I22	[3,4-diacetyloxy-5-(2-amino-6-oxohydropurin-9-yl)oxolan-2-yl]methyl acetate	No
2	J22	5-(2-amino-6-sulfanylpurin-9-yl)-2-(hydroxymethyl)oxolane-3,4-diol	No
2	K22	5-hexyl-2,3-diphenyl-1,2,3,4-tetraazole, chloride	No
2	L22	3,7-diamino-10H-dibenzo[b,e]thiin-5,5-dione	No

2	M22	8-(4-amino-2-oxohydropyrimidinyl)-3-hydroxy-6-(hydroxymethyl)-2,4,7-trioxa-3-p hosphabicyclo[3.3.0]octan-3-one	No
2	N22	3-[(4-cyclohexylphenoxy)methyl]-4-methyl-1-(morpholin-4-ylmethyl)-1,2,4-triazo line-5-thione	No
2	O22	1-(tert-butyl)-5-nitrobenzimidazole	No
2	P22	(2-oxo-2-(2-thienyl)ethyl)thiocarbonitrile	No
Plate	**Well**	**IUPAC NAME**	**Inhibitor Y/N**
3	A03	5-undecyl-1,3,4-thiadiazole-2-ylamine	No
3	B03	3,4-diphenyl-1-(piperidylmethyl)-1,2,4-triazoline-5-thione	No
3	C03	2-[(2,6-dichlorophenyl)methylthio]benzoxazole	No
3	D03	2-amino-6-(aminocarbonylamino)hexanoic acid	No
3	E03	5-phenyl-4-benzyl-1,2,4-triazole-3-thiol	No
3	F03	(2-chloroethyl)(phenylsulfonyl)amine	No
3	G03	purine-2,6-diamine	No
3	H03	2-(2-pyridyl)quinoline	No
3	I03	[4-(N,N-dimethylcarbamoyl)piperazinyl]-N,N-dimethylcarboxamide	No
3	J03	4,7-dimethylpyridino[3,2-h]quinoline, oxamethane	No
3	K03	5-nitro-3-hydrobenzimidazol-2-one	No
3	L03	2-(2-amino-6-oxohydropurin-9-yl)-4-phenylcarbonyloxy-5-(phenylcarbonyloxymethy l)oxolan-3-yl benzoate	No
3	M03	bis(5-chloro-3-methyl-1-phenylpyrazol-4-yl)diazene	No
3	N03	2,2-dimethyl-5-nitrobenzo[d]1,3-dioxolene	No
3	O03	5-(2-phenylethyl)-4-benzyl-1,2,4-triazole-3-thiol	No
3	P03	1-(phenylsulfonyl)pyrrolidine-2-carboxylic acid	No
3	A04	1-phenylbenzimidazole-2-thiol	No
3	B04	(5-nitro-2-phenyl-1,3-dioxan-5-yl)methan-1-ol	No
3	C04	5-(2,5-dioxo-1-phenylazolidin-3-yl)-4-methyl-2-phenyl-6,7,3a,7a-tetrahydroisoi ndole-1,3-dione	No
3	D04	2-ethylthiobenzimidazole	No
3	E04	5-acetyl-2-amino-4-methyl-1,3-thiazole	No
3	F04	4-[(2-methylpiperidyl)sulfonyl]phenylamine	No
3	G04	[2-hydroxy-1-(hydroxymethyl)-isopropyl](phenylsulfonyl)amine	No
3	H04		No
3	I04	4-((1Z)-2-nitrovinyl)-1,2-dimethoxybenzene	No
3	J04	4-phenyl-5-(phenoxymethyl)-1,2,4-triazole-3-thiol	No
3	K04	2-chloro-N-(2-furylmethyl)acetamide	No
3	L04	di2-nitro-4-(trifluoromethyl)phenyl disulfide	No
3	M04	(methylsulfonyl)indoline	No
3	N04	5-(phenoxymethyl)-4-prop-2-enyl-1,2,4-triazole-3-thiol	No
3	O04	4-benzoxazol-2-yl-2,6-dichlorophenylamine	No

3	P04	2,6-dibromo-4-(6-methylbenzothiazol-2-yl)phenylamine	No
3	A05	[5-(2,4-dichlorophenyl)-2-furyl]methan-1-ol	No
3	B05	methyl 2-amino-4-methyl-1,3-thiazole-5-carboxylate	No
3	C05	3-(1,3-oxazolino[4,5-b]pyridin-2-yl)phenylamine	No
3	D05	3-(5,7-dimethylbenzoxazol-2-yl)-4-chlorophenylamine	No
3	E05	3-benzoxazol-2-yl-4-chlorophenylamine	No
3	F05	4-chloro-3-(5-chlorobenzoxazol-2-yl)phenylamine	No
3	G05	5-(5,7-dimethylbenzoxazol-2-yl)-2-methylphenylamine	No
3	H05	2-methyl-5-(5-methylbenzoxazol-2-yl)phenylamine	No
3	I05	2-methyl-5-(6-methylbenzoxazol-2-yl)phenylamine	No
3	J05	4-(5-chlorobenzoxazol-2-yl)phenylamine	No
3	K05	2-(4-chlorophenyl)benzoxazole-5-ylamine	No
3	L05	2-(2,4-dichlorophenyl)benzoxazole-5-ylamine	No
3	M05	2-(2,5-dichlorophenyl)benzoxazole-5-ylamine	No
3	N05	2-(3,4-dichlorophenyl)benzoxazole-5-ylamine	No
3	O05	2-(5-bromo-2-chlorophenyl)benzoxazole-5-ylamine	No
3	P05	2-naphthylbenzoxazole-5-ylamine	YES
3	A06	2-phenyl-2-hydrobenzotriazole-5-ylamine	No
3	B06	2-(4-methoxyphenyl)-2-hydrobenzotriazole-5-ylamine	No
3	C06	2-(4-ethoxyphenyl)-2-hydrobenzotriazole-5-ylamine	No
3	D06	2-(3-chlorophenyl)-2-hydrobenzotriazole-5-ylamine	No
3	E06	2-(4-chlorophenyl)-2-hydrobenzotriazole-5-ylamine	No
3	F06	4-amino-2-(5-chlorobenzoxazol-2-yl)phenol	No
3	G06	2-(4-phenylphenyl)benzoxazole-5-ylamine	No
3	H06	2-(4-fluorophenyl)-2-hydrobenzotriazole-5-ylamine	No
3	I06	2-(4-bromophenyl)-2-hydrobenzotriazole-5-ylamine	No
3	J06	2-naphthyl-2-hydrobenzotriazole-5-ylamine	No
3	K06	2-(3,5-dichloro-4-methoxyphenyl)benzoxazole-5-ylamine	No
3	L06	2-chloro-N-(5-ethyl(1,3,4-thiadiazol-2-yl))acetamide	No
3	M06	2-chloro-N-(1,3-thiazol-2-yl)acetamide	No
3	N06	2-chloro-N-[4-(2-chloroacetylamino)(1,2,5-oxadiazol-3-yl)]acetamide	No
3	O06	(4-bromophenyl)[(4-chlorophenyl)sulfonyl]amine	No
3	P06	benzothiazol-2-yl[(4-chlorophenyl)sulfonyl]amine	No
3	A07	1-[3-(dimethylamino)prop-1-ynyl]cyclohexan-1-ol	No
3	B07	4-(diethylamino)-1,1-diphenylbut-2-yn-1-ol	No
3	C07	(2-(1,3-dioxolan-4-ylidene)ethyl)diethylmethylamine, iodide	No
3	D07	4-[2-(methylpiperidyl)ethylidene]-1,3-dioxolane, iodide	No
3	E07	trimethyl[2-(3-methyl(2-furyl))ethyl]amine, iodide	No
3	F07	[2-(5-hexadecyl-5-methyl(1,3-dioxolan-4-ylidene))ethyl]trimethylamine, iodide	No

3	G07	[2-(5-hexyl-5-methyl(1,3-dioxolan-4-ylidene))ethyl]trimethylamine, iodide	No
3	H07	[2-(5,5-dimethyl(1,3-dioxolan-4-ylidene))ethyl]trimethylamine, iodide	No
3	I07	trimethyl[2-(5-methyl-5-phenyl(1,3-dioxolan-4-ylidene))ethyl]amine, iodide	No
3	J07	trimethyl[2-(5-methyl-5-vinyl(1,3-dioxolan-4-ylidene))ethyl]amine, iodide	No
3	K07	3-(2,3,3-trimethyl-3-hydroindolyl)propanenitrile, bromide	No
3	L07	(4-{(1E)-2-[4-(2-amino(1,3-thiazol-4-yl))phenyl]-2-azavinyl}phenyl)dimethylami ne	No
3	M07	(1E)-1-acridin-9-yl-2-phenyl-1-azaethene	No
3	N07	2-((1E)-2-phenyl-1-azavinyl)-1,3-thiazole	No
3	O07	2-[(1E)-2-(4-chlorophenyl)-1-azavinyl]-1,3-thiazole	No
3	P07	2-((1E)-2-(2-furyl)-1-azavinyl)-4-phenyl-1,3-thiazole	No
3	A08	2-((1E)-2-(2-furyl)-1-azavinyl)-1,3-thiazole	No
3	B08	[4-((1E)-2-(1,3-thiazol-2-yl)-2-azavinyl)phenyl]dimethylamine	No
3	C08	8-((1E)-2-acridin-9-yl-2-azavinyl)-2H,4H-benzo[e]1,3-dioxin	No
3	D08	2-((1E)-2-(2H,4H-benzo[e]1,3-dioxin-8-yl)-1-azavinyl)-1,3-thiazole	No
3	E08	5-(2H-benzo[d]1,3-dioxolan-5-ylmethylene)-1,3-dihydropyrimidine-2,4,6-trione	No
3	F08	5-(2-furylmethylene)-1,3-dihydropyrimidine-2,4,6-trione	No
3	G08	2-[2-(diethylamino)-isopropyl]benzo[c]azoline-1,3-dione	YES
3	H08	2-(2-morpholin-4-ylethyl)benzo[c]azoline-1,3-dione	No
3	I08	{[4-((1E)-2-(2H-benzo[3,4-d]1,3-dioxolan-5-yl)-1-azavinyl)phenyl]sulfonyl}-1,3 -thiazol-2-ylamine	No
3	J08	({4-[(1E)-2-(6-nitro(2H-benzo[3,4-d]1,3-dioxolan-5-yl))-1-azavinyl]phenyl}sulf onyl)-1,3-thiazol-2-ylamine	No
3	K08	3-(6-oxo-7,11-diazatricyclo[7.3.1.0<2,7>]trideca-2,4-dien-11-yl)propanisothioc yanate	No
3	L08	1-[2-(4-methoxyphenoxy)ethyl]indole-3-carbaldehyde	No
3	M08	({1-[2-(2-fluorophenoxy)ethyl]indol-3-yl}methylene)methane-1,1-dicarbonitrile	No
3	N08	1-ethyl-2-[(6-nitrobenzimidazol-2-yl)methylthio]benzimidazole	No
3	O08	4,6-dimethyl-2-[(1-methylbenzimidazol-2-yl)methylthio]pyrimidine	No
3	P08	6-methyl-2-[(1-methylbenzimidazol-2-yl)methylthio]benzimidazole	YES
3	A09	2-(2,4-dichlorophenyl)-7-methyl-1,2,3,5,6,7,8-heptahydropyrimidino[5',4'-4,5]t hiopheno[2,3-c]pyridin-4-one	No
3	B09	N-[(5-bromo-2-oxo(1H-benzo[d]azolin-3-ylidene))azamethyl]-3-pyridylcarboxamide	No

3	C09	methyl 4-(6-bromo(2H-benzo[d]1,3-dioxolan-5-yl))-2,7,7-trimethyl-5-oxo-1,4,6,7 ,8-pentahydroquinoline-3-carboxylate	No
3	D09	methylethyl 4-(6-bromo(2H-benzo[d]1,3-dioxolan-5-yl))-2-methyl-5-oxo-1,4,6,7,8 -pentahydroquinoline-3-carboxylate	No
3	E09	cyclohexyl 2,7,7-trimethyl-5-oxo-4-(3,4,5-trimethoxyphenyl)-1,4,6,7,8-pentahyd roquinoline-3-carboxylate	No
3	F09	2-methoxyethyl 4-(6-bromo(2H-benzo[d]1,3-dioxolen-5-yl))-2,7,7-trimethyl-5-oxo -1,4,6,7,8-pentahydroquinoline-3-carboxylate	No
3	G09	4-(3-iodophenyl)-1,3,4-trihydrobenzo[h]quinolin-2-one	No
3	H09	propyl 3a,8b-dihydroxy-2-methyl-4-oxoindano[2,1-d]2-pyrroline-3-carboxylate	No
3	I09	4-(6-bromo-2H-benzo[d]1,3-dioxolen-5-yl)-1,3,4-trihydrobenzo[h]quinolin-2-one	YES
3	J09	ethyl 4-methyl-2-oxo-6-(2-thienyl)-1,3,6-trihydropyrimidine-5-carboxylate	No
3	K09	4-(4-iodophenyl)-1,3,4-trihydrobenzo[h]quinolin-2-one	No
3	L09	1-(2-iodophenyl)-1,2,4-trihydrobenzo[f]quinolin-3-one	No
3	M09	3-bromo-7-methyl-5-phenyl-8-hydro-3-pyrazolino[2,3-a]pyrimidin-2-one	No
3	N09	2-amino-4-(2-furyl)-7,7-dimethyl-5-oxo-4H-6,7,8-trihydrochromene-3-carbonitril e	No
3	O09	4-(chloromethyl)-1-[4-(chloromethyl)phenylthio]benzene	No
3	P09	2-(6,7-dimethoxy-3,4-dihydroisoquinolyl)ethanenitrile	No
3	A10	4-[(dimethylamino)methylene]-3-methyl-1-phenyl-1,2-diazolin-5-one	No
3	B10	[(dimethylamino)sulfonyl](3-nitrophenyl)amine	No
3	C10	1-morpholin-4-yl-2-(morpholin-4-ylsulfonyl)-4-nitrobenzene	No
3	D10	1-(2,4-dinitrophenyl)-5-ethoxy-3-methylpyrazole	No
3	E10	3,7-dibromobenzo[b]benzo[b]thiophene	No
3	F10	5-nitrospiro[benzo[d]1,3-dioxolene-2,1'-cyclopentane]	No
3	G10	3-methylthio-4,5-diphenyl-1,2,4-triazole	No
3	H10	1-(2,4-dihydrobenzothiazol-2-ylthio)-2,4-dinitrobenzene	No
3	I10	1-(azaethylidene)-2-(hydroxyimino)-5,6,7,8,4a,8a-hexahydronaphthalene	No
3	J10	2-methoxydibenzo[b,e]thiin-10-one	No
3	K10	(cyclohexylamino)(2-pyridylamino)methane-1-thione	No
3	L10	3-phenyl-4-hydroisoxazol-5-one	No
3	M10	3-(4-decyloxyphenyl)-4-prop-2-enyl-1,2,4-triazoline-5-thione	No
3	N10	1-(3-fluorophenyl)-4,4,6-trimethyl-1,3,4-trihydropyridine-2-thione	No
3	O10	5-[3,5-bis(trifluoromethoxy)phenyl]furan-2-carbaldehyde	No
3	P10	5,6,7,8,10-pentahydroacridin-9-one	No
3	A11	1-acetyl-5-bromoindoline	No
3	B11		No

3	C11		No
3	D11	methylbeta-carboline	No
3	E11	4-oxopyran-2,6-dicarboxylic acid	No
3	F11	[5-(4-amino-2-oxohydropyrimidinyl)-3,4-dihydroxyoxolan-2-yl]methyl dihydrogen phosphate, sodium salt, sodium salt	No
3	G11	2-(6-aminopurin-9-yl)-4-hydroxy-5-(hydroxymethyl)oxolan-3-yl dihydrogen phosph ate	No
3	H11	[5-(2,4-dioxo(1,3-dihydropyrimidinyl))-3,4-dihydroxyoxolan-2-yl]methyl dihydro gen phosphate, sodium salt, sodium salt	No
3	I11	4-methyl-7-[3,4,5-trihydroxy-6-(hydroxymethyl)(2H-3,4,5,6-tetrahydropyran-2-yl oxy)]chromen-2-one	No
3	J11	6-(hydroxymethyl)-2-(4-nitrophenoxy)-2H-3,4,5,6-tetrahydropyran-3,4,5-triol	No
3	K11	4-(1,3-thiazol-2-yldiazenyl)benzene-1,3-diol	No
3	L11	[5-(4-amino-2-oxohydropyrimidinyl)-3,4-dihydroxyoxolan-2-yl]methyl dihydrogen phosphate	No
3	M11	[5-(4-amino-2-oxohydropyrimidinyl)-3-hydroxyoxolan-2-yl]methyl dihydrogen phos phate	No
3	N11	7-hydroxy-6-methoxy-8-[3,4,5-trihydroxy-6-(hydroxymethyl)(2H-3,4,5,6-tetrahydr opyran-2-yl)oxy]chromen-2-one	No
3	O11	[5-(2-amino-6-oxohydropurin-9-yl)-3,4-dihydroxyoxolan-2-yl]methyl dihydrogen p hosphate	No
3	P11	1-fluoro-13,14,17-trihydroxy-14-(2-hydroxyacetyl)-2,15-dimethyltetracyclo[8.7. 0.0<2,7>.0<11,15>]heptadeca-3,6-dien-5-one	YES
3	A12	2-(2,4-dioxo(1,3-dihydropyrimidinyl))-4-phenylcarbonyloxy-5-(phenylcarbonyloxy methyl)oxolan-3-yl benzoate	No
3	B12	[3,4-diacetyloxy-5-(2,4-dioxo(1,3-dihydropyrimidinyl))oxolan-2-yl]methyl aceta te	No
3	C12	2,15-dimethyltetracyclo[8.7.0.0<2,7>.0<11,15>]heptadec-6-ene-5,14,17-trione	No
3	D12	14-((1R)-1,5-dimethylhexyl)(1S,2S,11S,10R,14R,15R)-2,15-dimethyltetracyclo[8.7 .0.0<2,7>.0<11,15>]heptadecan-5-ol	No
3	E12	14-((1R)-1,5-dimethylhexyl)(1S,10S,11S,2R,14R,15R)-5-butoxy-2,15-dimethyltetra cyclo[8.7.0.0<2,7>.0<11,15>]heptadec-7-ene	No
3	F12	15-methyltetracyclo[8.7.0.0<2,7>.0<11,15>]heptadeca-2(7),3,5-triene-5,14-diol	No
3	G12	3-phenyl-2-thioxo-1,3-diazolidin-4-one	No
3	H12	3-(5,6-dimethylbenzoxazol-2-yl)-4-chlorophenylamine	No
3	I12	2-(3-iodophenyl)benzoxazole-5-ylamine	No
3	J12	2-(4-iodophenyl)benzoxazole-5-ylamine	No
3	K12	2-[4-(tert-butyl)phenyl]benzoxazole-5-ylamine	No
3	L12	4-(5,7-dichlorobenzoxazol-2-yl)phenylamine	YES
3	M12	2-((1E)-2-nitroprop-1-enyl)thiophene	No

3	N12	4-iodo-2,5-dioctyloxybenzaldehyde	No
3	O12	5-(morpholin-4-ylmethyl)-7-nitroquinolin-8-ol	No
3	P12	6-amino-4-(3,4-dichlorophenyl)-2-[(3,4,5-trimethoxyphenyl)methylthio]pyridine- 3,5-dicarbonitrile	No
3	A13	2-(2-(2H-benzo[3,4-d]1,3-dioxolen-5-yl)-2-oxoethylthio)-4-amino-6-methylthiopy rimidine-5-carbonitrile	No
3	B13	methylethyl (2Z)-3-(2-bromo(3-thienyl))-2-cyanoprop-2-enoate	No
3	C13	(2E)-3-(3-furyl)-2-(methylthiocarbonyl)prop-2-enenitrile	No
3	D13	3,5-bis{[4-(tert-butyl)phenyl]methylene}-4-(2-methyl-1-azapropylidene)-2H-6-hy dropyran	No
3	E13	4-(azaethylidene)-3,5-bis{[4-(tert-butyl)phenyl]methylene}-2H-6-hydropyran	No
3	F13	ethyl (2Z)-3-(2-bromo(3-thienyl))-2-cyanoprop-2-enoate	No
3	G13	{[(3-chloro-4-fluorophenyl)amino]methylene}methane-1,1-dicarbonitrile	No
3	H13	{[(2,5-difluorophenyl)amino]methylene}methane-1,1-dicarbonitrile	No
3	I13	2-methoxyethyl (2E)-3-[(2-bromo(4-pyridyl))amino]-2-cyanoprop-2-enoate	No
3	J13	(2E)-2-(aminothioxomethyl)-3-[(3,4-dimethoxyphenyl)amino]prop-2-enenitrile	No
3	K13	(2E)-2-[(4-bromophenyl)carbonyl]-3-[2-(4-bromophenyl)-2-oxoethylthio]-3-(cyano methylthio)prop-2-enenitrile	No
3	L13	ethyl (2Z)-2-cyano-3-[(2-methyl(1,3-oxazol-5-yl))amino]prop-2-enoate	No
3	M13	{[(2,5-dichlorophenyl)amino]methylene}methane-1,1-dicarbonitrile	No
3	N13	(2E)-2-(aminothioxomethyl)-3-[(3-chloro(2-pyridyl))amino]prop-2-enenitrile	No
3	O13	methyl 2-(5-acetyl-3-cyano-6-methyl-4-(2-thienyl)-2-1,4-dihydropyridylthio)ace tate	No
3	P13	{[(3,4-dimethoxyphenyl)amino]methylene}methane-1,1-dicarbonitrile	No
3	A14	(2E)-3-(2-(2H-benzo[d]1,3-dioxolen-5-yl)-2-oxoethylthio)-2-(2H-benzo[3,4-d]1,3 -dioxolen-5-ylcarbonyl)-3-(cyanomethylthio)prop-2-enenitrile	No
3	B14	ethyl (2E)-2-cyano-3-(isothiazol-3-ylamino)prop-2-enoate	No
3	C14	5-amino-2-methoxy-7-[3-methoxy-4-(methylethoxy)phenyl]-7H-pyrano[3,2-d]imidazo le-6-carbonitrile	No
3	D14	4-amino-2-(2-furyl)-7,7-dimethyl-5-oxo-6,7,8-trihydro-2H-benzo[1,2-e]thiin-3-c arbonitrile	No
3	E14	6-amino-4-(3-bromophenyl)-2-sulfanyl-1,4-dihydropyridine-3,5-dicarbonitrile	No
3	F14	(2Z)-2-cyano-3-(3-methylpyrrol-2-yl)prop-2-enedithioic acid	No

3	G14	5-amino-7-(4-hydroxyphenyl)-2-methyl-7H-pyrano[3,2-d]imidazole-6-carbonitrile	No
3	H14	(4R,4aR)-2-amino-4-(4-chlorophenyl)-4a-methyl-1,4,5,6,7,4a-hexahydronaphthalen e-1,1,3-tricarbonitrile	No
3	I14	2-amino-6-(methylethyl)-4-(3-pyridyl)-8-(3-pyridylmethyl)-5,6-dihydro-4H-pyran o[3,2-c]pyridine-3-carbonitrile	No
3	J14	5-amino-2-methyl-7-[4-(methylethyl)phenyl]-7H-pyrano[3,2-d]imidazole-6-carboni trile	No
3	K14	1-(2-pyridyl)-3-(2-thienylmethylthio)-5,6,7,8-tetrahydroisoquinoline-4-carboni trile	No
3	L14	(8S,8aR)-6-amino-8-(3,4-difluorophenyl)-2-(methylethyl)-1,2,3,5,8,8a-hexahydro isoquinoline-5,5,7-tricarbonitrile	No
3	M14	(8S,8aR)-7-amino-2-methyl-8-phenyl-1,2,3,5,8,8a-hexahydroisoquinoline-5,5,6-tr icarbonitrile	No
3	N14	2-amino-4-(4-methoxyphenyl)-8-[(4-methoxyphenyl)methyl]-6-methyl-5,6-dihydro-4 H-pyrano[3,2-c]pyridine-3-carbonitrile	No
3	O14	5-aminospiro[2,4,7,7a-tetrahydroindene-7,1'-cyclohexane]-4,4,6-tricarbonitrile	No
3	P14	ethyl 4-[((1E)-2-cyano-1-vinylthio-2-azavinyl)amino]-3-oxobutanoate	No
3	A15	2-amino-4-(2,5-difluorophenyl)-5-oxo-4H-6,7,8-trihydrochromene-3-carbonitrile	No
3	B15	6-(aminocyanomethylene)hydropyridine-2,3,5-tricarbonitrile	No
3	C15	2-amino-4-(3-methyl(2-thienyl))-8-oxo-4H-5,6,7-trihydrochromene-3-carbonitrile	No
3	D15	2-amino-4-(4-fluorophenyl)-8-[(4-fluorophenyl)methyl]-6-(methylethyl)-5,6-dihy dro-4H-pyrano[3,2-c]pyridine-3-carbonitrile	No
3	E15	(3S,2R)-5-amino-3-(4-chlorophenyl)-12-methyl-12-azatricyclo[7.2.1.0<2,7>]dodec a-4,7-diene-4,6,6-tricarbonitrile	No
3	F15	(1S,2S,3R,3aR)-3-[(4-bromophenyl)carbonyl]-2-phenyl-10,3a-dihydropyrrolidino[1 ,2-a]quinoline-1,3-dicarbonitrile	No
3	G15	2-amino-5-oxo-4-[2-(trifluoromethyl)phenyl]-4H-pyrano[2,3-b]chromene-3-carboni trile	No
3	H15	(8S,8aR)-6-amino-8-(3-bromophenyl)-2-(methylethyl)-1,2,3,5,8,8a-hexahydroisoqu inoline-5,5,7-tricarbonitrile	No
3	I15	5-amino-2-methyl-7-(3,4,5-trimethoxyphenyl)-4,7-dihydro-1,3-oxazolo[5,4-b]pyri dine-6-carbonitrile	No
3	J15	5-amino-7-(3,5-dimethoxyphenyl)-2-methyl-4,7-dihydro-1,3-oxazolo[5,4-b]pyridin e-6-carbonitrile	No
3	K15	4-amino-2-(3-methyl-2-oxobutylthio)-6-methylthiopyrimidine-5-carbonitrile	No
3	L15	4-(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)-2-amino-5-oxo-4H-pyrano[2,3-b]chromene-3 -carbonitrile	No
3	M15	4-(2-amino-3-nitro-5-oxo-4H-pyrano[3,2-c]chromen-4-yl)benzenecarbonitrile	No

3	N15	3-(methylethyl)-4-oxo-2-sulfanyl-3,9-diazaspiro[5.5]undec-1-ene-1,5-dicarbonit rile	No
3	O15	(4S,4aR)-2-amino-6-(tert-butyl)-4-[4-methoxy-3-(methylethoxy)phenyl]-1,4,5,6,7 ,4a-hexahydronaphthalene-1,1,3-tricarbonitrile	No
3	P15	(3aS,1R,2R,3R)-1-[(4-bromophenyl)carbonyl]-3-(phenylcarbonyl)-10,3a-dihydropyr rolidino[1,2-a]quinoline-2,3-dicarbonitrile	No
3	A16	2,6-diamino-4-(3-pyridyl)-4H-chromene-3-carbonitrile, chloride	No
3	B16	methyl 1-acetyl-3-carbamoyl-1-cyano-2-(3-thienyl)-1,2,3,8a-tetrahydroindolizin e-6-carboxylate	No
3	C16	(4S,4aR)-2-amino-6-(tert-butyl)-4-(4-chlorophenyl)-1,4,5,6,7,4a-hexahydronapht halene-1,1,3-tricarbonitrile	No
3	D16	(8R,8aR)-6-amino-8-(2-fluorophenyl)-2-methyl-1,2,3,5,8,8a-hexahydroisoquinolin e-5,5,7-tricarbonitrile	No
3	E16	4-(2-furyl)-6-methyl-2-(3,3,3-trifluoro-2-oxopropylthio)pyridine-3-carbonitril e	No
3	F16	6-amino-7-bromo-8-(4-cyanophenyl)-2-(methylethyl)-1,2,3,5,8,8a-hexahydroisoqui noline-5,5-dicarbonitrile	No
3	G16	2,6-dimethyl-4-(2-pyridylmethylthio)pyridine-3-carbonitrile	No
3	H16	2-amino-4-(3-iodophenyl)-1,4,5,6,7,8-hexahydronaphthalene-1,1,3-tricarbonitril e	No
3	I16	6-amino-2-ethyl-8-(1-ethyl(4-piperidylidene))-1,2,3,5,8a-pentahydroisoquinolin e-5,5,7-tricarbonitrile	No
3	J16	ethyl 11-amino-12-cyano-8-(methoxymethyl)spiro[2H-3,4,5,6-tetrahydropyran-4,7' -4,7-dihydroimidazo[5,4-b]pyridine]-10-carboxylate	No
3	K16	2,6-diamino-4-(3,5-dimethoxyphenyl)-4H-pyran-3,5-dicarbonitrile	No
3	L16	5-amino-7-(3-chloro-5-methyl-1-phenylpyrazol-4-yl)-2-methyl-4-phenyl-4,7-dihyd ro-1,3-oxazolo[5,4-b]pyridine-6-carbonitrile	No
3	M16	(8S,9S,10aR)-8-(3,5-dimethoxyphenyl)-9-(tert-butyl)-7,10a-dihydropyrrolidino[2 ,1-a]isoquinoline-10,10-dicarbonitrile	No
3	N16	2-amino-16-bromo-5,12-dioxospiro[4H-6,7,8-trihydrochromene-4,3'-indoline]-3-ca rbonitrile	No
3	O16	5-amino-12-methyl-3-[2-(trifluoromethyl)phenyl]-12-azatricyclo[7.2.1.0<2,7>]do deca-2(7),5-diene-4,4,6-tricarbonitrile	No
3	P16	tert-butyl 11-amino-12-cyano-8-(trifluoromethyl)spiro[2H-3,4,5,6-tetrahydropyr an-4,7'-4,7-dihydroimidazo[5,4-b]pyridine]-10-carboxylate	No
3	A17	1-amino-5-methyl(6,7,8,9-tetrahydrothiopheno[2,3-c]isoquinolin-2-yl) 2-thienyl ketone	No
3	B17	2-amino-1-benzyl-4-(3-pyridyl)-8-(3-pyridylmethylene)-1,4,7-trihydro-5H-pyrano [4,3-b]pyridine-3-carbonitrile	No
3	C17	6-amino-2,11-dimethylspiro[1,2,3,4,5,8-hexahydroisoquinoline-8,4'-piperidine]- 5,5,7-tricarbonitrile	No

3	D17	(1S,2S,3aR)-1-(3,5-dimethoxyphenyl)-2-(tert-butyl)-10,3a-dihydropyrrolidino[1, 2-a]quinoline-3,3-dicarbonitrile	No
3	E17	4,6-diamino-2-(2-thienyl)-2H-thiin-3,5-dicarbonitrile	No
3	F17	5-amino-7-(2,4-diethoxyphenyl)-2-methyl-4,7-dihydro-1,3-oxazolo[5,4-b]pyridine -6-carbonitrile	No
3	G17	(2E)-2-amino-3-(2-methyl-1-phenylimidazol-4-yl)prop-2-enenitrile	No
3	H17	9-[2-(4-fluorophenyl)-2-oxoethylthio]-7-oxo-10-azaspiro[4.5]dec-8-ene-6,8-dica rbonitrile	No
3	I17	2-[2-(diethylamino)-2-thioxoethylthio]-4-(2-furyl)-6-phenylpyridine-3-carbonit rile	No
3	J17	3,5-diaminothiopheno[3,2-b]thiophene-2,6-dicarbonitrile	No
3	K17	4-methyl-6-(3-pyridyl)-2-thioxohydropyridine-3-carbonitrile	No
3	L17	[(3,5-dimethoxyphenyl)methylene]methane-1,1-dicarbonitrile	No
3	M17	1-(3-methoxyphenyl)-2-(6-methoxyquinolyl)ethan-1-one, bromide	No
3	N17	(2E)-2-(aminothioxomethyl)-3-{[2-chloro-5-(trifluoromethyl)phenyl]amino}prop-2 -enenitrile	No
3	O17	1-(2-fluoro-4-methoxyphenyl)-2-quinolylethan-1-one, bromide	No
3	P17	(4R,4aR)-2-amino-6-(tert-butyl)-4-(2,4,5-trimethoxyphenyl)-1,4,5,6,7,4a-hexahy dronaphthalene-1,1,3-tricarbonitrile	No
3	A18	(1S,3R,3aR)-3-(phenylcarbonyl)-10,3a-dihydropyrrolidino[1,2-a]quinoline-1,3-di carbonitrile	No
3	B18	1-[(3,4-dichlorophenyl)methyl]-4-(4-fluorophenyl)-6-phenyl-2-thioxohydropyridi ne-3-carbonitrile	No
3	C18	6-amino-2-methyl-8-[4-(methylethyl)phenyl]-1,2,3,5,8,8a-hexahydroisoquinoline- 5,5,7-tricarbonitrile	No
3	D18	6-amino-2-(methylethyl)-8-phenyl-1,2,3,5,8,8a-hexahydroisoquinoline-5,5,7-tric arbonitrile	No
3	E18	6-amino-2-(methylethyl)-8-[2-(trifluoromethyl)phenyl]-1,2,3,5,8,8a-hexahydrois oquinoline-5,5,7-tricarbonitrile	No
3	F18	2,9-diamino-4,7-bis(4-chlorophenyl)-4H,7H-chromeno[6,7-g]chromene-3,8-dicarbon itrile	No
3	G18	4,6-diamino-2-(3,5-dimethoxyphenyl)-2H-thiin-3,5-dicarbonitrile	YES
3	H18	2-amino-4-(3,4-dimethoxyphenyl)-8-[(3,4-dimethoxyphenyl)methyl]-6-methyl-5,6-d ihydro-4H-pyrano[3,2-c]pyridine-3-carbonitrile	No
3	I18	1-[3-amino-4-(5-chloro(2-thienyl))-6-(2-thienyl)thiopheno[2,3-b]pyridin-2-yl]- 2,2,2-trifluoroethan-1-one	No
3	J18	3,5-bis(2-furylmethylene)-1-methylazaperhydroin-4-one, bromide	No
3	K18	2-amino-4-[(5-bromo(2-thienyl))carbonyl]-5-(prop-2-enylamino)thiophene-3-carbo nitrile	No
3	L18	5-amino-7-(4-butoxy-3-propylphenyl)-2-methoxy-4,7-dihydro-1,3-oxazolo[5,4-b]py ridine-6-carbonitrile	No
3	M18	5-amino-2-methoxy-7-[4-(methylethoxy)-3-propylphenyl]-4,7-dihydro-1,3-oxazolo[5,4-b]pyridine-6-carbonitrile	No

3	N18	ethyl 5-amino-6-cyano-2-propylspiro[4,7-dihydro-1,3-oxazolo[5,4-b]pyridine-7,4 '-piperidine]-4-carboxylate	No
3	O18	3-(methylethyl)-5-({2-[methylbenzylamino]-4-oxo(5-hydropyridino[1,2-a]pyrimidi n-3-yl)}methylene)-2-thioxo-1,3-thiazolidin-4-one	No
3	P18	5-({2-[methylbenzylamino]-4-oxo(5-hydropyridino[1,2-a]pyrimidin-3-yl)}methylen e)-3-(2-phenylethyl)-2-thioxo-1,3-thiazolidin-4-one	No
3	A19	1,2,3,12-tetrahydro-7H,8H,9H,10H,11H-azaperhydroepino[1,2-a]benzo[b]thiopheno[2,3-d]pyrimidine-4,13-dione	No
3	B19	3-{N-[3-(ethoxycarbonyl)-4,5-dimethyl-2-thienyl]carbamoyl}propanoic acid	No
3	C19		No
3	D19		No
3	E19		No
3	F19		No
3	G19	2-(4-bromo-5-methyl-3-nitropyrazolyl)acetic acid	No
3	H19	2-(3,5-dimethyl-4-nitropyrazolyl)acetic acid	No
3	I19	methyl 5-(methoxycarbonyl)-2,6-dioxotricyclo[3.3.1.1<3,7>]decanecarboxylate	No
3	J19	methyl 2,6-dioxo-3,5,7-tris(methoxycarbonyl)tricyclo[3.3.1.1<3,7>]decanecarbox ylate	No
3	K19	2-[(4-fluorophenyl)(1,3-thiazol-2-ylamino)methyl]-3-hydroxy-6-(hydroxymethyl)p yran-4-one	No
3	L19	3-hydroxy-6-(hydroxymethyl)-2-[(4-phenylpiperazinyl)methyl]pyran-4-one	No
3	M19	4-[(2-furylmethyl)amino]-3-hydroxythiolane-1,1-dione	No
3	N19	ethyl 6-methyl-2-[(methylsulfonyl)amino]-4,5,6,7-tetrahydrobenzo[b]thiophene-3 -carboxylate	No
3	O19	methyl 3-(methoxycarbonyl)-2-(2,2,2-trifluoroacetylamino)-4,5,6-trihydrocyclop enta[3,2-b]thiophene-4-carboxylate	No
3	P19	3-(4-oxo-3-hydroquinazolin-2-yl)-4,10-dihydro-2-pyrrolino[1,2-a]quinazoline-2, 5-dione	No
3	A20	2-methylpropyl 6-(6-bromo(2H-benzo[d]1,3-dioxolan-5-yl))-3,4-dimethyl-2-oxo-1, 3,6-trihydropyrimidine-5-carboxylate	No
3	B20	ethyl 3-methyl-4H-benzo[e]1,4-thiazine-2-carboxylate	No
3	C20	2-chloro-N-[3-cyano-5-(N-cyclohexyl-N-ethylcarbamoyl)-4-methyl(2-thienyl)]acet amide	No
3	D20	[4-cyano-3-methyl-5-(2-thienylcarbonylamino)(2-thienyl)]-N-cyclohexyl-N-ethylc arboxamide	No
3	E20	ethyl 5-(azaperhydroepinylcarbonyl)-4-methyl-2-(2-thienylcarbonylamino)thiophe ne-3-carboxylate	No
3	F20	2-amino-4-naphthyl-5-oxo-4H-pyrano[3,2-c]chromene-3-carbonitrile	No

3	G20	2-(4-methylthiophenyl)-1,2,3,5,6,7,8-heptahydrobenzo[b]thiopheno[2,3-d]pyrimid in-4-one	No
3	H20	oxolan-2-ylmethyl 4-methyl-6-(4-methylphenyl)-2-oxo-1,3,6-trihydropyrimidine-5 -carboxylate	No
3	I20	2-(6-bromo-2H-benzo[d]1,3-dioxolan-5-yl)-1,2,3,5,6,7,8-heptahydrobenzo[b]thiop heno[2,3-d]pyrimidin-4-one	No
3	J20	2-(3,4,5-trimethoxyphenyl)-1,2,3,5,6,7,8-heptahydrobenzo[b]thiopheno[2,3-d]pyr imidin-4-one	No
3	K20	2-(2H-benzo[3,4-d]1,3-dioxolan-5-yl)-1,2,3,5,6,7,8-heptahydrobenzo[b]thiopheno [2,3-d]pyrimidin-4-one	No
3	L20	2-[4-(dimethylamino)phenyl]-1,2,3,5,6,7,8-heptahydrobenzo[b]thiopheno[2,3-d]py rimidin-4-one	No
3	M20	prop-2-enyl 6-(6-bromo(2H-benzo[d]1,3-dioxolan-5-yl))-3-ethyl-4-methyl-2-oxo-1 ,3,6-trihydropyrimidine-5-carboxylate	No
3	N20	(2E)but-2-enyl 6-(2H-benzo[3,4-d]1,3-dioxolan-5-yl)-4-methyl-2-oxo-1,3,6-trihy dropyrimidine-5-carboxylate	No
3	O20	2-amino-4-(3,4-dimethoxyphenyl)-6-methoxypyridine-3,5-dicarbonitrile	No
3	P20	2-(3-methyl-2-thienyl)-1,2,3,5,6,7,8-heptahydrobenzo[b]thiopheno[2,3-d]pyrimid in-4-one	No
3	A21	4-phenyl-2-hydrophthalazin-1-one	No
3	B21	4-phenyl-2-(2-phenylethyl)-2-hydrophthalazin-1-one	No
3	C21	7-nitro-2-(2-thienyl)benzo[d]1,3-oxazin-4-one	No
3	D21	ethyl 6-methyl-2-(2-morpholin-4-ylacetylamino)-4,5,6,7-tetrahydrobenzo[b]thiop hene-3-carboxylate	No
3	E21	ethyl 2-(2-azaperhydroepinylacetylamino)-4,5,6-trihydrocyclopenta[2,1-b]thioph ene-3-carboxylate	No
3	F21	ethyl 6-methyl-2-(2-piperidylacetylamino)-4,5,6,7-tetrahydrobenzo[b]thiophene- 3-carboxylate	No
3	G21	ethyl 2-(2-morpholin-4-ylacetylamino)-4,5,6-trihydrocyclopenta[2,1-b]thiophene -3-carboxylate	YES
3	H21	ethyl 2-(2-morpholin-4-ylacetylamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-ca rboxylate	No
3	I21	6-(2-furyl)-1-phenylpyrazolo[5,4-d]1,3-oxazin-4-one	No
3	J21	ethyl 2-(adamantanylcarbonylamino)-3-(ethoxycarbonyl)-4,5,6,7-tetrahydrothioph eno[2,3-c]pyridine-6-carboxylate	No
3	K21	ethyl 3-(ethoxycarbonyl)-2-(propanoylamino)-4,5,6,7-tetrahydrothiopheno[2,3-c] pyridine-6-carboxylate	No
3	L21	ethyl 3-(ethoxycarbonyl)-2-(2-thienylcarbonylamino)-4,5,6,7-tetrahydrothiophen o[2,3-c]pyridine-6-carboxylate	No
3	M21	ethyl 2-(2-chloroacetylamino)-3-(ethoxycarbonyl)-4,5,6,7-tetrahydrothiopheno[2 ,3-c]pyridine-6-carboxylate	No
3	N21	3-{N-[3,6-bis(ethoxycarbonyl)-4,5,6,7-tetrahydrothiopheno[2,3-c]pyridin-2-yl]c arbamoyl}propanoic acid	No

3	O21	ethyl 3-(ethoxycarbonyl)-2-(2,2,2-trifluoroacetylamino)-4,5,6,7-tetrahydrothio pheno[2,3-c]pyridine-6-carboxylate	No
3	P21	ethyl 2-(adamantanylcarbonylamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carbo xylate	No
3	A22	[2-(2-furylcarbonylamino)-6-methyl(4,5,6,7-tetrahydrobenzo[b]thiophen-3-yl)]-N ,N-dipropylcarboxamide	No
3	B22	(2-amino(4,5,6-trihydrocyclopenta[1,2-b]thiophen-3-yl))-N-naphthylcarboxamide	No
3	C22	2-(2-chlorophenyl)-5,6,7-trihydrocyclopenta[1,2-d]1,3-oxazino[4,5-b]thiophen-4 -one	No
3	D22	ethyl 2-(2-furylcarbonylamino)-4,5,6-trihydrocyclopenta[2,1-b]thiophene-3-carb oxylate	No
3	E22	N-(4-bromophenyl)[2-(2-thienylcarbonylamino)(4,5,6-trihydrocyclopenta[1,2-b]th iophen-3-yl)]carboxamide	No
3	F22	2-(4-bromophenyl)-5,6,7,8-tetrahydrobenzo[b]thiopheno[2,3-d]1,3-oxazin-4-one	No
3	G22	2-phenylbenzo[d]1,3-oxazin-4-one	No
3	H22	3-amino-2-phenyl-3-hydroquinazolin-4-one	No
3	I22	2-(2-fluorophenyl)benzo[d]1,3-oxazin-4-one	No
3	J22	2-(2-pyridyl)benzo[d]1,3-oxazin-4-one	No
3	K22	2-(2-furyl)-3-hydroquinazolin-4-one	No
3	L22	2-(2-furyl)-3-phenyl-3-hydroquinazolin-4-one	No
3	M22	3-amino-2-(2-furyl)-3-hydroquinazolin-4-one	No
3	N22	ethyl 2-amino-6-methyl-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate	No
3	O22	7-methyl-2-(2-thienyl)-5,6,7,8-tetrahydrobenzo[b]thiopheno[2,3-d]1,3-oxazin-4- one	No
3	P22	3-phenyl-2-(trifluoromethyl)-3-hydroquinazolin-4-one	No
Plate	**Well**	**IUPAC NAME**	**Inhibitor Y/N**
4	A03	2-methyl-3-(2-pyridyl)-3-hydroquinazolin-4-one	No
4	B03	3-(5-bromo(2-pyridyl))-2-(3-pyridyl)-3-hydroquinazolin-4-one	No
4	C03	N-[3-(morpholin-4-ylcarbonyl)-4,5,6,7,8-pentahydrocyclohepta[2,1-d]thiophen-2- yl]acetamide	No
4	D03	N-[3-(N,N-dipropylcarbamoyl)-4,5,6,7,8-pentahydrocyclohepta[2,1-d]thiophen-2-y l]acetamide	No
4	E03	ethyl 2-(acetylamino)-4,5,6,7,8-pentahydrocyclohepta[2,1-b]thiophene-3-carboxy late	No
4	F03	2-(acetylamino)-4,5,6,7,8-pentahydrocyclohepta[2,1-b]thiophene-3-carboxamide	No
4	G03	2-methyl-5,6,7,8,9-pentahydrocyclohepta[1,2-d]1,3-oxazino[4,5-b]thiophen-4-one	No
4	H03	2-(2-fluorophenyl)-5,6,7,8,9-pentahydrocyclohepta[1,2-d]1,3-oxazino[4,5-b]thio phen-4-one	No

4	I03	7,8,9,10,11,13-hexahydrocyclohepta[2,1-d]piperidino[1',2'-1,2]pyrimidino[4,5-b]thiophen-12-one	No
4	J03	1,2,3,4,5,13-hexahydro-8H,9H,10H,11H,12H-azaperhydroepino[1',2'-1,2]pyrimidino [4,5-b]cyclohepta[1,2-d]thiophen-14-one	No
4	K03	2-(2-thienylcarbonylamino)-4,5,6,7,8-pentahydrocyclohepta[2,1-b]thiophene-3-ca rboxylic acid	No
4	L03	(2-amino(4,5,6,7,8-pentahydrocyclohepta[1,2-b]thiophen-3-yl))-N-methylcarboxam ide	No
4	M03	(2-amino(4,5,6,7,8-pentahydrocyclohepta[1,2-b]thiophen-3-yl))-N-ethylcarboxami de	No
4	N03	ethyl 2-[(2,2,3,3-tetramethylcyclopropyl)carbonylamino]-4,5,6-trihydrocyclopen ta[2,1-b]thiophene-3-carboxylate	No
4	O03	(2,2,3,3-tetramethylcyclopropyl)-N-(3,4,5-tribromophenyl)carboxamide	No
4	P03	1-(4-bromophenyl)-2-(3-bromopyridyl)ethan-1-one, bromide	No
4	A04	2-(2-amino-4-methylpyridyl)-1-(4-bromophenyl)ethan-1-one, bromide	No
4	B04	1-(4-bromophenyl)-2-pyridylethan-1-one, bromide	No
4	C04	2-(hydroxymethyl)-1-[(4-methylphenyl)sulfonyl]pyrrolidine	No
4	D04	1-phenylpyrazolidin-3-one	No
4	E04	({4-[(1E)-2-(3,5-dibromo-2-hydroxyphenyl)-1-azavinyl]phenyl}sulfonyl)(6-methox ypyridazin-3-yl)amine	No
4	F04	({4-[(1E)-2-(3,5-dichloro-2-hydroxyphenyl)-1-azavinyl]phenyl}sulfonyl)aminocar boxamidine	No
4	G04	({4-[(1E)-2-(3,5-dibromo-2-hydroxyphenyl)-1-azavinyl]phenyl}sulfonyl)aminocarb oxamidine	No
4	H04	4-{(1E)-2-[4-(dimethylamino)phenyl]-1-azavinyl}benzenesulfonamide	No
4	I04	[((1E)-2-(2-furyl)-1-azaprop-1-enyl)amino]aminomethane-1-thione	No
4	J04	[((1E)-2-(2-thienyl)-1-azaprop-1-enyl)amino]aminomethane-1-thione	No
4	K04	[((1E)-2-naphthyl-1-azaprop-1-enyl)amino]aminomethane-1-thione	No
4	L04	{[(1E)-2-(4-bromophenyl)-1-azaprop-1-enyl]amino}aminomethane-1-thione	No
4	M04	{[(1E)-2-(4-chlorophenyl)-1-azaprop-1-enyl]amino}aminomethane-1-thione	No
4	N04	({(1E)-2-[4-(2-methylpropyl)phenyl]-1-azaprop-1-enyl}amino)aminomethane-1-thio ne	No
4	O04	6-[(1E)-2-(3,5-dichlorophenyl)-2-azavinyl]-4-bromo-2-nitrophenol	No
4	P04	6-[(1E)-2-(2,5-dichlorophenyl)-2-azavinyl]-4-bromo-2-nitrophenol	No
4	A05	6-[(1E)-2-(4-nitrophenyl)-2-azavinyl]-4-bromo-2-nitrophenol	No
4	B05	6-[(1E)-2-(4-bromophenyl)-2-azavinyl]-4-bromo-2-nitrophenol	No
4	C05	6-[(1E)-2-(4-iodophenyl)-2-azavinyl]-4-bromo-2-nitrophenol	No
4	D05	6-[(1E)-2-(4-hydroxyphenyl)-2-azavinyl]-4-bromo-2-nitrophenol	No

4	E05	4-[(1E)-2-(5-iodo(2-furyl))-2-azavinyl]-2,3-dimethyl-1-phenyl-3-pyrazolin-5-on e	No
4	F05	2-[(1E)-2-(6-ethoxybenzothiazol-2-yl)-2-azavinyl]-4,6-dibromophenol	No
4	G05	5-[(1Z)-2-(4-nitrophenyl)-2-azavinyl]-2-bromofuran	No
4	H05	{[(1E)-2-(4-fluorophenyl)-1-azaprop-1-enyl]amino}aminomethane-1-thione	No
4	I05	2-{(1E)-2-[(aminothioxomethyl)amino]-1-methyl-2-azavinyl}benzene-1,4-diol	No
4	J05	6-((1E)-2-{4-[(1E)-2-(5-bromo-2-hydroxy-3-nitrophenyl)-1-azavinyl]phenyl}-2-az avinyl)-4-bromo-2-nitrophenol	No
4	K05	6-[(1E,9E)-10-(5-bromo-2-hydroxy-3-nitrophenyl)-2,9-diazadeca-1,9-dienyl]-4-br omo-2-nitrophenol	No
4	L05	6-[(1E,5E)-6-(5-bromo-2-hydroxy-3-nitrophenyl)-2,5-diazahexa-1,5-dienyl]-4-bro mo-2-nitrophenol	No
4	M05	6-[(1E)-2-(5-chloro(2-pyridyl))-2-azavinyl]-4-bromo-2-nitrophenol	No
4	N05	6-[(1E)-2-(2-hydroxy-5-nitrophenyl)-2-azavinyl]-4-bromo-2-nitrophenol	No
4	O05	6-[(1E)-2-(2-hydroxy-4-nitrophenyl)-2-azavinyl]-4-bromo-2-nitrophenol	No
4	P05	8-[(1Z)-2-(4-nitrophenyl)-1-azavinyl]-3-bromo-5,6,7,8,9-pentahydro-4aH-carbazo le	No
4	A06	6-cyclohexyl-2,3,4,9-tetrahydro-4aH-carbazol-1-one	No
4	B06		No
4	C06		No
4	D06		No
4	E06	6-bromo-1,2,3,4,9-pentahydro-4aH-carbazolylamine	No
4	F06		No
4	G06		No
4	H06		No
4	I06		No
4	J06	6-bromo-9-ethyl-2,3,4,9-tetrahydro-4aH-carbazol-1-one	No
4	K06		No
4	L06		No
4	M06		No
4	N06		No
4	O06	6-(4-methoxyphenoxy)-2,3,4,9-tetrahydro-4aH-carbazol-1-one	No
4	P06		No
4	A07	{[(6-cyclohexyl(2,3,4,9-tetrahydro-4aH-carbazolylidene))azamethyl]amino}(pheny lamino)methane-1-thione	No
4	B07		No
4	C07		No
4	D07	ethyl 2-(4-morpholin-4-yl-1,2,5-thiadiazol-3-yloxy)acetate	No

4	E07	4-morpholin-4-yl-1,2,5-thiadiazol-3-ol	No
4	F07	3-chloro-4-morpholin-4-yl-1,2,5-thiadiazole	No
4	G07	3-(4-amino(1,2,5-oxadiazol-3-yl))-2-imino-1,3-thiazolidin-4-one	No
4	H07	2-imino-3-(1,3-thiazol-2-yl)-1,3-thiazolidin-4-one	YES
4	I07	6-methyl-4H,8H-1,2,5-oxadiazolo[3,4-b]1,4-diazepin-5-one	No
4	J07	4,7-dihydro-1,2,5-oxadiazolo[3,4-b]pyrazine-5,6-dione	No
4	K07	5-{[5-(3,4-dichlorophenyl)(2-furyl)]methylene}-2-thioxo-1,3-thiazolidin-4-one	No
4	L07	oxolan-2-ylmethyl 6-(6-bromo(2H-benzo[d]1,3-dioxolen-5-yl))-4-methyl-2-oxo-1,3 ,6-trihydropyrimidine-5-carboxylate	No
4	M07	methylpropyl 3a,8b-dihydroxy-2-methyl-4-oxoindano[2,1-d]2-pyrroline-3-carboxyl ate	No
4	N07	pentyl 6-(6-bromo(2H-benzo[d]1,3-dioxolen-5-yl))-4-methyl-2-oxo-1,3,6-trihydro pyrimidine-5-carboxylate	No
4	O07	cyclopentyl 2-methyl-5-oxo-4-(2-thienyl)-1,4,6,7,8-pentahydroquinoline-3-carbo xylate	No
4	P07	2-methoxyethyl 2,7,7-trimethyl-5-oxo-4-(2-thienyl)-1,4,6,7,8-pentahydroquinoli ne-3-carboxylate	No
4	A08	cyclohexyl 2,7,7-trimethyl-5-oxo-4-(4-pyridyl)-1,4,6,7,8-pentahydroquinoline-3 -carboxylate	No
4	B08	methylethyl 2-methyl-5-oxo-4-(2-thienyl)-1,4,6,7,8-pentahydroquinoline-3-carbo xylate	No
4	C08	methylethyl 2,7,7-trimethyl-5-oxo-4-(2-thienyl)-1,4,6,7,8-pentahydroquinoline- 3-carboxylate	No
4	D08	2-phenoxyethyl 3-methyl-4H-benzo[e]1,4-thiazine-2-carboxylate	No
4	E08	cyclohexyl 2,7,7-trimethyl-5-oxo-4-(2-thienyl)-1,4,6,7,8-pentahydroquinoline-3 -carboxylate	No
4	F08	propyl 4-(6-bromo(2H-benzo[d]1,3-dioxolan-5-yl))-2,7,7-trimethyl-5-oxo-1,4,6,7 ,8-pentahydroquinoline-3-carboxylate	No
4	G08	methyl 4-ethyl-2-(3-{N-[4-ethyl-3-(methoxycarbonyl)-5-methyl(2-thienyl)]carbam oyl}-2,2,3,3-tetrafluoropropanoylamino)-5-methylthiophene-3-carboxylate	No
4	H08	(6-azabicyclo[4.4.0]dec-2-yl)methan-1-ol	No
4	I08	ethyl 6-(4-nitropyrazol-3-yl)-8-hydropyrazolo[1,5-a]pyrimidine-3-carboxylate	No
4	J08	morpholin-4-yl 3-nitropyrazol-5-yl ketone	No
4	K08	[2,6-dinitro-4-(trifluoromethyl)phenyl]{2-[(4-chloro-2-nitrophenyl)amino]ethyl }amine	No
4	L08	[2,6-dinitro-4-(trifluoromethyl)phenyl](2,2,6,6-tetramethyl(4-piperidyl))amine	No
4	M08	[2,6-dinitro-4-(trifluoromethyl)phenyl]{2-[(2,3,4,5,6-pentachlorophenyl)amino] ethyl}amine	No
4	N08	1-[2,6-dinitro-4-(trifluoromethyl)phenyl]-4-(4-fluorophenyl)piperazine	No

4	O08	N-{4-[(3,6-dichlorobenzo[b]thiophen-2-yl)carbonylamino]-1,2,5-oxadiazol-3-yl}a cetamide	No
4	P08	adamantanyl-N-[4-(adamantanylcarbonylamino)(1,2,5-oxadiazol-3-yl)]carboxamide	No
4	A09	N-[4-(2-imino-4-oxo-1,3-thiazolidin-3-yl)-1,2,5-oxadiazol-3-yl]carboxamide	No
4	B09	N-(4-amino-1,2,5-oxadiazol-3-yl)acetamide	No
4	C09	2-imino-5-[(2-methylindol-3-yl)methylene]-3-(1,3-thiazol-2-yl)-1,3-thiazolidin -4-one	No
4	D09	4-[(3-adamantanyl-1-phenylpyrazol-4-yl)methylene]-3-methyl-1-phenyl-1,2-diazol in-5-one	No
4	E09	5-{[3-(4-fluorophenyl)pyrazol-4-yl]methylene}-2-imino-3-(1,3-thiazol-2-yl)-1,3 -thiazolidin-4-one	No
4	F09	5-{[4-(dimethylamino)phenyl]methylene}-2-imino-3-(1,3-thiazol-2-yl)-1,3-thiazo lidin-4-one	No
4	G09	5-[(3-adamantanyl-1-phenylpyrazol-4-yl)methylene]-2-imino-3-(1,3-thiazol-2-yl) -1,3-thiazolidin-4-one	No
4	H09	2-imino-5-[(1-phenyl-3-(2-thienyl)pyrazol-4-yl)methylene]-3-(1,3-thiazol-2-yl) -1,3-thiazolidin-4-one	No
4	I09	3-(4-amino(1,2,5-oxadiazol-3-yl))-2-imino-5-[(2-methylindol-3-yl)methylene]-1, 3-thiazolidin-4-one	No
4	J09	3-(4-amino(1,2,5-oxadiazol-3-yl))-2-imino-5-(phenylmethylene)-1,3-thiazolidin- 4-one	No
4	K09	3-(4-amino(1,2,5-oxadiazol-3-yl))-5-{[3-(4-fluorophenyl)pyrazol-4-yl]methylene }-2-imino-1,3-thiazolidin-4-one	No
4	L09	3-(4-amino(1,2,5-oxadiazol-3-yl))-5-{[3-(4-chlorophenyl)pyrazol-4-yl]methylene }-2-imino-1,3-thiazolidin-4-one	No
4	M09	5-[(3-adamantanyl-1-phenylpyrazol-4-yl)methylene]-3-(4-amino(1,2,5-oxadiazol-3 -yl))-2-imino-1,3-thiazolidin-4-one	No
4	N09	3-(4-amino(1,2,5-oxadiazol-3-yl))-2-imino-5-[(4-methoxyphenyl)methylene]-1,3-t hiazolidin-4-one	No
4	O09	2-(3-benzimidazol-2-ylpropyl)benzimidazole	No
4	P09	2-methyl-1,3-dinonylimidazole, bromide	YES
4	A10	2-benzimidazol-2-ylethanenitrile	No
4	B10	5,6-dimethyl-1,3-dinonylbenzimidazole, bromide	YES
4	C10	3,7-dimethyl-1-nonyl-1,3,7-trihydropurine-2,6-dione	No
4	D10	1-nonyl-2-[3-(1-nonylbenzimidazol-2-yl)propyl]benzimidazole	No
4	E10	1,3-dimethyl-7-nonyl-1,3,7-trihydropurine-2,6-dione	No
4	F10	6-amino-3-methylspiro[4H-pyrano[2,3-c]pyrazole-4,4'-thiane]-5-carbonitrile	No
4	G10	12-amino-9-methylspiro[2H-3,4,5,6-tetrahydropyran-4,4'-4H-pyrano[2,3-c]pyrazol e]-11-carbonitrile	YES
4	H10	6-amino-3-propylspiro[4H-pyrano[2,3-c]pyrazole-4,4'-thiane]-5-carbonitrile	YES

4	I10	6-amino-3-(methoxymethyl)spiro[4H-pyrano[2,3-c]pyrazole-4,4'-thiane]-5-carboni trile	No
4	J10	6-amino-3-(methoxymethyl)-10-methylspiro[4H-pyrano[2,3-c]pyrazole-4,4'-piperid ine]-5-carbonitrile	No
4	K10	2-hydroxy-7,7,11-trimethyl-5-oxospiro[1,4,6,7,8-pentahydroquinoline-4,4'-piper idine]-3-carbonitrile	No
4	L10	2-hydroxy-7,7-dimethyl-11-(methylethyl)-5-oxospiro[1,4,6,7,8-pentahydroquinoli ne-4,4'-piperidine]-3-carbonitrile	YES
4	M10	6-phenyl-2-thioxo-4-(trifluoromethyl)hydropyridine-3-carbonitrile	No
4	N10	6-(2-thienyl)-2-thioxo-4-(trifluoromethyl)pyran-3-carbonitrile	No
4	O10	6-chloro-3-hydrobenzoxazol-2-one	No
4	P10	4,5-dihydroxynaphthalene-2,7-disulfonic acid	No
4	A11	2-cyclopent-2-enylpropanedioic acid	No
4	B11	2-hydroxy-5-sulfobenzoic acid, hydrate, hydrate	No
4	C11		No
4	D11	4-{[4-(2-aminoethyl)piperazinyl]methyl}-3,5-bis(tert-butyl)phenol	No
4	E11	3,3,5,5-tetramethylmorpholine	No
4	F11	2,3,3-trimethyl-3H-pyrrolo[3,2-h]quinoline	No
4	G11	5-nitro-2-(trifluoromethyl)benzimidazole	No
4	H11	5-[(2E,4E)-5-(phenylamino)penta-2,4-dienylidene]-2-thioxo-1,3-thiazolidin-4-on e	No
4	I11	3-butyl-5-(1-ethyl(2-hydroquinolylidene))-2-thioxo-1,3-thiazolidin-4-one	No
4	J11	1-(3-methyl-3-hydrobenzothiazol-2-ylidene)acetone	No
4	K11	1,3-dimethyl-5-[2-(1-methylpyrrolidin-2-ylidene)ethylidene]-2-thioxo-1,3-diazo lidin-4-one	No
4	L11	5-(5-chloro-3-ethyl(3-hydrobenzothiazol-2-ylidene))-3-methyl-2-thioxo-1,3-thia zolidin-4-one	No
4	M11	N-(bicyclo[2.2.1]hept-2-ylethyl)-2-(4-bromo-5-methyl-3-nitropyrazolyl)acetamid e	No
4	N11	2-[2-(4-bromo-5-methyl-3-nitropyrazolyl)acetylamino]-6-methyl-4,5,6,7-tetrahyd robenzo[b]thiophene-3-carboxamide	No
4	O11	tert-butyl 6-amino-5-cyano-10-methylspiro[4H-pyrano[2,3-c]pyrazole-4,4'-piperi dine]-3-carboxylate	No
4	P11	methyl 6-(6-bromo(2H-benzo[d]1,3-dioxolen-5-yl))-4-methyl-2-oxo-1,3,6-trihydro pyrimidine-5-carboxylate	No
4	A12	7-(2,3-dihydro-4H,5H,6H-azepin-7-yl)-2,5-diphenyl-4-imidazolino[1,2-b]3-pyrazo lin-6-one, bromide	No
4	B12	(2S)-4-oxo-1-(1,1,2,2-tetramethyl-1-silapropyl)azetidine-2-carboxylic acid	No
4	C12	3,4-bis(diphenylmethyl)-1,2,5-oxadiazol-2-ol	No
4	D12	4-(5,7-dimethylbenzoxazol-2-yl)phenylamine	No
4	E12	(methylsulfonyl)(2-phenoxyethyl)amine	No
4	F12		No

4	G12	(benzimidazol-2-ylmethoxy)benzene	No
4	H12	4-(hydroxyimino)-3-methyl-1-phenyl-1,2-diazolin-5-one	No
4	I12	2,3,4,7,3a-pentahydrobenzimidazole-2-carboxylic acid, hydrate, hydrate	No
4	J12	methyl quinoline-2-carboxylate	No
4	K12	6-???-2,3-dihydrophthalazine-1,4-dione	No
4	L12	5-(3-fluorophenyl)-4-phenyl-1,2,4-triazole-3-thiol	No
4	M12	2-[1,3-bisbenzylimidazolidin-2-yl]-4,6-dichlorophenol	No
4	N12	3-methyl-4-(2-oxo(1H-benzo[d]azolin-3-ylidene))-1-phenyl-1,2-diazolin-5-one	No
4	O12	2-(4-oxo-3-phenyl-3,5,6,7,8-pentahydropentaleno[2,1-d]pyrimidin-2-ylthio)aceta mide	No
4	P12	2-[1,3-bisbenzylimidazolidin-2-yl]furan	No
4	A13	adamantanyl-N-{[(prop-2-enylamino)thioxomethyl]amino}carboxamide	No
4	B13	5-(4-nitrophenyl)-1H-1,2,4-triazole-3-thiol	No
4	C13	spiro[3H-benzo[e]1,3-oxazaperhydroine-2,1'-cyclohexane]-4-one	No
4	D13	spiro[1,2,3,5,6,7,8-heptahydroquinazoline-2,1'-cyclohexane]-4-one	No
4	E13	4-amino-3-ethyl-2-thioxo-1,3-thiazoline-5-carboxamide	No
4	F13	5-ethoxy-3-methyl-1-(4-nitrophenyl)pyrazole	No
4	G13	4-(4-nitrophenyl)-1,3-dioxan-5-ol	No
4	H13	1,3,5-trihydrofurano[3,4-d]pyrimidine-2,4,7-trione	No
4	I13	2-(4-chlorophenyl)-5-methyl-5-pentyl-1,2,4-triazolidine-3-thione	No
4	J13	6-nitro-8-hydropyrazolo[1,5-a]pyrimidine-3-carbonitrile	No
4	K13	N-(3,4-dichlorophenyl)-2-(1-methyl(1,2,3,4-tetraazol-5-ylthio))acetamide	No
4	L13	N-(3-chloro-4-fluorophenyl)-2-(1-methyl(1,2,3,4-tetraazol-5-ylthio))acetamide	No
4	M13	4-(1,3-dithiolan-2-yl)-1-methoxy-2-nitrobenzene	No
4	N13	2-(1,3-dithiolan-2-yl)-1-(2-furylmethylthio)-4-nitrobenzene	No
4	O13	cyclododecylideneazamethyl 4-fluorobenzoate	No
4	P13	N-(3,5-dichlorophenyl)-2-(1-methylimidazol-2-ylthio)acetamide	No
4	A14	1-(4-fluorophenyl)azolidine-2,5-dione	No
4	B14	1-(2,4-difluorophenyl)azolidine-2,5-dione	No
4	C14	N-(4-fluorophenyl)-2-(1-methylimidazol-2-ylthio)acetamide	No
4	D14	N-(4-fluorophenyl)-2-(4-methyl(1,2,4-triazol-3-ylthio))acetamide	No
4	E14	(benzotriazolylmethyl)(2,4-dimethoxyphenyl)amine	No
4	F14	N-(2H-benzo[d]1,3-dioxolan-5-yl)-2-[4-methyl-5-(trifluoromethyl)(1,2,4-triazol -3-ylthio)]acetamide	No
4	G14	3-(2,5-difluorophenyl)-2-methyl-3-hydroquinazolin-4-one	YES
4	H14	(benzotriazolylmethyl)(2,3,4-trifluorophenyl)amine	No
4	I14	(benzotriazolylbutyl)(3,4-difluorophenyl)amine	No

4	J14	N-(2,5-difluorophenyl)-2-(5-methyl(1,3,4-thiadiazol-2-ylthio))acetamide	No
4	K14	N-(2,5-difluorophenyl)-2-(4-methyl(1,2,4-triazol-3-ylthio))acetamide	No
4	L14	3-(2-methylpropyl)-2-thioxo-1,3-dihydroquinazolin-4-one	No
4	M14	1-(4-bromophenyl)-3-[4-(4-fluorophenyl)piperazinyl]azolidine-2,5-dione	No
4	N14	N-(3-chloro-4-fluorophenyl)-2-[4-methyl-5-(trifluoromethyl)(1,2,4-triazol-3-yl thio)]acetamide	No
4	O14	2-((1E)-2-phenylvinyl)benzo[d]1,3-oxazin-4-one	No
4	P14	3-amino-2-(2-thienyl)-3-hydroquinazolin-4-one	No
4	A15	2-[3-(trifluoromethyl)phenyl]benzo[d]1,3-oxazin-4-one	No
4	B15	(benzotriazolylmethyl)(3,4-dichlorophenyl)amine	No
4	C15	5-(5-bromo(2-thienyl))-2-(4-chlorophenyl)-1,3-thiazole	No
4	D15	5-(4-chloro-3-methylphenyl)-2-(4-chlorophenyl)-1,3-thiazole	No
4	E15	4-(2H-benzo[d]1,3-dioxolen-5-yl)-6-amino-3-methyl-4H-pyrano[3,2-d]pyrazole-5-c arbonitrile	No
4	F15	7-(4-chlorophenyl)-2-methylthio-5-phenyl-4,7,8-trihydro-1,2,4-triazolo[1,5-a]p yrimidine	No
4	G15	(1S,4aS,10aR)-6-hydroxy-1,4a-dimethyl-1,2,3,4,9,10,10a,4a-octahydrophenanthren ecarboxylic acid	No
4	H15	5-hydroxy-2-(hydroxymethyl)pyran-4-one	No
4	I15	5-hydroxy-15-methyltetracyclo[8.7.0.0<2,7>.0<11,15>]heptadeca-2(7),3,5-trien-1 4-one	No
4	J15	{4-[(1E)-2-(4-morpholin-4-ylphenyl)-2-azavinyl]phenyl}dimethylamine	No
4	K15	5-[(1E)-2-(4-morpholin-4-ylphenyl)-2-azavinyl]-2-nitrothiophene	No
4	L15	[(2-bromophenyl)amino](phenylamino)methane-1-thione	No
4	M15	8-bromo-1,3-dimethyl-7-(2-oxopropyl)-1,3,4,5,7-pentahydropurine-2,6-dione	No
4	N15	4-[(1Z)-2-(2-chlorophenyl)-2-hydroxy-1-azavinyl]-1,2-dimethyl-3-phenyl-3-pyraz olin-5-one	No
4	O15	1-(4-chlorophenyl)-4-hydroimidazo[1,5-a]pyridine	No
4	P15	N-[(2-hydroxyindol-3-ylidene)azamethyl]acetamide	No
4	A16	8,9-dibromo-4-(4-bromophenyl)-4-azatricyclo[5.2.1.0<2,6>]decane-3,5-dione	No
4	B16	(2-bromophenyl)(phenylsulfonyl)amine	No
4	C16	5-{[(5-chloro-2-hydroxyphenyl)amino]methylene}-1,3-dihydropyrimidine-2,4,6-tri one	No
4	D16	[5-(2,4-dichlorophenyl)-2-thioxo-1,3,4-oxadiazolin-3-yl]methan-1-ol	No
4	E16	6-[(3-hydroxypropyl)amino]-5-nitro-3-hydrobenzimidazol-2-one	No
4	F16	3-[(4-methylpiperazinyl)carbonyl]bicyclo[2.2.1]hept-5-ene-2-carboxylic acid	No
4	G16	1H-1,2,4-triazol-5-yl[(4-chlorophenyl)methyl]amine	No

4	H16	3-(2-1,2,3,4-tetrahydroisoquinolylcarbonyl)bicyclo[2.2.1]hept-5-ene-2-carboxyl ic acid	No
4	I16	4-indol-3-ylbutanamide	No
4	J16	2-[(1E)-2-(2-methoxybenzo[3,4-b]benzo[d]furan-3-yl)-2-azavinyl]-4-bromophenol	No
4	K16	2-[(2-oxo-1H-benzo[d]azolidin-3-ylidene)azamethyl]-3a,7a-dihydroisoindole-1,3- dione	No
4	L16	2-(4-bromophenyl)-3-(4-methoxyphenyl)-1,3-oxazolidine-4-thione	No
4	M16	2-(4-bromophenyl)-3-phenyl-1,3-oxazolidine-4-thione	No
4	N16	2,3-bis(4-bromophenyl)-1,3-oxazolidine-4-thione	No
4	O16	(3-pyridylmethyl)(2-thienylsulfonyl)amine	No
4	P16	5-[(3-bromophenyl)methylthio]-1-naphthyl-1,2,3,4-tetraazole	No
4	A17	4-[(4-methylphenyl)sulfonyl]-1-[(2-thioxo(3-hydrobenzothiazol-3-yl))methyl]pip erazine	No
4	B17	(2H-benzo[3,4-d]1,3-dioxolen-5-ylmethyl)(2-naphthylsulfonyl)amine	No
4	C17	6-[(5-methyl(2-furyl))methylene]-3-(4-methylphenyl)-1,3-thiazolidino[2,3-c]1,2 ,4-triazol-5-one	No
4	D17	3-{[(4-ethoxyphenyl)amino]methyl}-5-(2-furyl)-1,3,4-oxadiazoline-2-thione	No
4	E17	2-(1,3-dioxobenzo[c]azolin-2-yl)-N-[(1,1-dioxobenzo[d]1,2-thiazolin-3-yl)(2-cy anoethyl)amino]acetamide	No
4	F17	1-prop-2-enyl-5-({3-[(1-prop-2-enyl(1,2,3,4-tetraazol-5-ylthio))methyl]phenyl} methylthio)-1,2,3,4-tetraazole	No
4	G17	2-methyl-5-[(5-phenyl(1,3,4-oxadiazol-2-yl))methylthio]-1,3,4-thiadiazole	No
4	H17	3-methyl-6-nitro-3-hydroquinazolin-4-one	No
4	I17	ethyl 2-amino-5-(N,N-diethylcarbamoyl)-4-methylthiophene-3-carboxylate	No
4	J17	adamantanyl-N-(2-hydroxyethyl)carboxamide	No
4	K17	1-(cyclohexylideneazamethoxy)-4-nitrobenzene	No
4	L17	1-(methylsulfonyl)-5-nitroindoline	No
4	M17	8-nitro-1,2,3,4-tetrahydrobenzo[d]benzo[1,2-b]furan	No
4	N17	2-amino-4,5-dimethylthiophene-3-carboxamide	No
4	O17	(4-methoxyphenyl)purin-6-ylamine	No
4	P17	methyl 1-(2-furylmethyl)-2-methyl-5-oxo-2-pyrroline-3-carboxylate	No
4	A18	1,4-bis(methylsulfonyl)piperazin-2-one	No
4	B18	4-[(4-bromophenyl)methylene]-3-(2-fluorophenyl)isoxazol-5-one	No
4	C18	3-(4-bromophenyl)-4-[(4-methylphenyl)methylene]isoxazol-5-one	No
4	D18	4-((2Z)-2-bromo-3-phenylprop-2-enylidene)-3-(3-methylphenyl)isoxazol-5-one	No
4	E18	4-[(2,4-dichlorophenyl)methylene]-3-(4-bromophenyl)isoxazol-5-one	No
4	F18	4-((2E)-3-phenylprop-2-enylidene)-3-(4-bromophenyl)isoxazol-5-one	No
4	G18	4-(phenylmethylene)-3-(4-phenylphenyl)isoxazol-5-one	No

4	H18	4-{[4-(dimethylamino)phenyl]methylene}-3-(3-iodophenyl)isoxazol-5-one	YES
4	I18	4-[(2,4-dichlorophenyl)methylene]-3-(3-iodophenyl)isoxazol-5-one	No
4	J18	4-((2E)-3-phenylprop-2-enylidene)-3-(3-iodophenyl)isoxazol-5-one	No
4	K18	3-(2,4-dichlorophenyl)-4-[(2-bromophenyl)methylene]isoxazol-5-one	No
4	L18	3-(2,4-dichlorophenyl)-4-[(3-iodophenyl)methylene]isoxazol-5-one	No
4	M18	4-((2E)-3-phenylprop-2-enylidene)-3-(2,4-dichlorophenyl)isoxazol-5-one	No
4	N18	3-(2-fluorophenyl)-4-[(2-fluorophenyl)methylene]isoxazol-5-one	No
4	O18	4-[(3-bromophenyl)methylene]-3-(2-fluorophenyl)isoxazol-5-one	No
4	P18	3-(4-nitrophenyl)-4-(3-pyridylmethylene)isoxazol-5-one	No
4	A19	4-[(2-hydroxyphenyl)methylene]-3-(3-iodophenyl)isoxazol-5-one	No
4	B19	3-(3,4-dimethoxyphenyl)-4-[(4-methoxyphenyl)methylene]isoxazol-5-one	No
4	C19	4-((2E)-3-phenylprop-2-enylidene)-3-(2-thienyl)isoxazol-5-one	No
4	D19	4-[(3-iodophenyl)methylene]-3-(2-thienyl)isoxazol-5-one	No
4	E19	4-((2Z)-2-bromo-3-phenylprop-2-enylidene)-3-(2-thienyl)isoxazol-5-one	No
4	F19	4-(2-furylmethylene)-3-(2-thienyl)isoxazol-5-one	No
4	G19	3-(4-chloro-3-nitrophenyl)-4-(3-pyridylmethylene)isoxazol-5-one	No
4	H19	4-[(2,4-dichlorophenyl)methylene]-3-naphthylisoxazol-5-one	No
4	I19	4-{[4-(dimethylamino)phenyl]methylene}-3-naphthylisoxazol-5-one	No
4	J19	3-phenyl-4-({[3-(trifluoromethyl)phenyl]amino}methylene)isoxazol-5-one	No
4	K19	3-phenyl-4-(piperidylmethylene)isoxazol-5-one	No
4	L19	3-(2-furyl)-4-(2-furylmethylene)isoxazol-5-one	No
4	M19	3-(2-furyl)-4-(naphthylmethylene)isoxazol-5-one	No
4	N19	4-[(4-bromophenyl)methylene]-3-(3,4,5-trimethoxyphenyl)isoxazol-5-one	No
4	O19	4-{[4-(methylethyl)phenyl]methylene}-3-(4-methyl-3-nitrophenyl)isoxazol-5-one	No
4	P19	4-(benzo[e]1,4-dioxin-2-ylmethylene)-3-(4-bromophenyl)isoxazol-5-one	No
4	A20	4-((2E)-3-phenylprop-2-enylidene)-3-(3-chlorophenyl)isoxazol-5-one	No
4	B20	4-(benzo[e]1,4-dioxin-2-ylmethylene)-3-(2-chlorophenyl)isoxazol-5-one	No
4	C20	2-[(2-cyanoethyl)methylamino]-N-(1,3-thiazol-2-yl)acetamide	No
4	D20	2-[(2-cyanoethyl)methylamino]-N-(5-ethyl(1,3,4-thiadiazol-2-yl))acetamide	No
4	E20	5-ethyl-2-ethylthiothiophene-3-carboxylic acid	No
4	F20	4-bromo-5-ethylthiopheno[3,2-d]isothiazole	No
4	G20	3-acetyl-5-[1-(4-acetyl-5-ethylthio(2-thienyl))-1-methylpropyl]-2-ethylthiothi ophene	No

4	H20	3-((1E)-2-cyclohexyl-2-azavinyl)-5-[(dimethylamino)methyl]thiophene-2-thiol	No
4	I20	2,3-bis(ethylsulfonyl)thiophene	No
4	J20	2,4-dinitro-1-(2-thienylthio)benzene	No
4	K20	2,5-bis(ethylsulfonyl)thiophene	No
4	L20	2,5-bis(methylsulfonyl)thiophene	No
4	M20	3-acetyl-5-ethyl-2-ethylthiothiophene	No
4	N20	{[5-ethylthio-4-((hydroxyimino)methyl)(2-thienyl)]methyl}dimethylamine	No
4	O20	2-ethyl-5-ethylthio-4-formylthiophene-3-carboxylic acid	No
4	P20	5-methyl-2-(methylsulfonyl)thiophene-3-carboxylic acid, hydrate	No
4	A21	5-methyl-2-methylthiothiophene-3-carboxamide	No
4	B21	2-acetyl-5-methylthiothiophene	No
4	C21	(hydroxyimino)(5-methyl-2-methylthio(3-thienyl))methane	No
4	D21	5-ethyl-3-ethylthiothiophene-2-carboxylic acid	No
4	E21	3-((hydroxyimino)methyl)-5-methyl-2-(methylsulfonyl)thiophene	No
4	F21	5-ethylthiopheno[2,3-b]thiophene-2-carboxylic acid	No
4	G21	[4-(hydroxymethyl)-2,5-dimethylthio-3-thienyl]methan-1-ol	No
4	H21	[(5-ethyl-2-ethylthio-3-thienyl)methylene]methane-1,1-dicarbonitrile	No
4	I21	5-(4-nitrophenyl)-3-(3-pyridyl)-1,2,4-oxadiazole	No
4	J21	5-(4-bromophenyl)-3-(3-pyridyl)-1,2,4-oxadiazole	No
4	K21	4-methoxy-1-(3-(3-pyridyl)(1,2,4-oxadiazol-5-yl))benzene	No
4	L21	3-(4-bromophenyl)-5-(2,2,3,3-tetramethylcyclopropyl)-1,2,4-oxadiazole	No
4	M21	N-(4-amino(1,2,5-oxadiazol-3-yl))-2-(4,6-dimethylpyrimidin-2-ylthio)acetamide	No
4	N21		No
4	O21	ethyl (2Z)-3-{[4-(acetylamino)(1,2,5-oxadiazol-3-yl)]amino}but-2-enoate	No
4	P21	N-[4-(acetylamino)(1,2,5-oxadiazol-3-yl)]-2,2,2-trifluoroacetamide	No
4	A22	(3,6-dichlorobenzo[b]thiophen-2-yl)-N-{4-[(3,6-dichlorobenzo[b]thiophen-2-yl)c arbonylamino](1,2,5-oxadiazol-3-yl)}carboxamide	No
4	B22	ethyl 2-[N-(4-amino-1,2,5-oxadiazol-3-yl)acetylamino]acetate	No
4	C22	5-amino-7-(4-methoxyphenyl)-2,6,7,7a-tetrahydroindene-4,6,6-tricarbonitrile	No
4	D22	[(2,4,6-trimethylphenyl)methylene]methane-1,1-dicarbonitrile	No
4	E22	{[3-(methoxymethyl)-2,4,6-trimethylphenyl]methylene}methane-1,1-dicarbonitrile	No
4	F22	2,6-diamino-4-(2,4,6-trimethylphenyl)-4H-thiin-3,5-dicarbonitrile	No
4	G22	(2E)-2-(aminothioxomethyl)-3-(2,4,6-trimethylphenyl)prop-2-enenitrile	No
4	H22	[(2,4,6-triethylphenyl)methylene]methane-1,1-dicarbonitrile	No

4	I22	6-amino-4-(2,4-dimethylphenyl)-3-methyl-4H-pyrano[3,2-d]pyrazole-5-carbonitril e	No
4	J22	2,6-diamino-4-(2,4-dimethylphenyl)-4H-thiin-3,5-dicarbonitrile	No
4	K22	2,6-diamino-4-[3-(methoxymethyl)-2,4,6-trimethylphenyl]-4H-thiin-3,5-dicarboni trile	No
4	L22	2-amino-4-[3-(dichloromethyl)-2,4,6-trimethylphenyl]-7,7-dimethyl-5-oxo-4H-6,7 ,8-trihydrochromene-3-carbonitrile	No
4	M22	7-amino-2,4-dioxo-5-(2,4,6-trimethylphenyl)-1,3-dihydro-5H-pyrano[2,3-d]pyrimi dine-6-carbonitrile	No
4	N22	8-amino-6-(2,4,6-trimethylphenyl)-2,3,4,5,6,7,5a-heptahydrobenzo[1,2-a][7]annu lene-7,7,9-tricarbonitrile	No
4	O22	5-amino-7-(2,4-dimethylphenyl)-2,7a-dihydroindene-4,6-dicarbonitrile	No
4	P22	[(3-{[3-(2,2-dicyanovinyl)-2,4,6-trimethylphenyl]methyl}-2,4,6-trimethylphenyl)methylene]methane-1,1-dicarbonitrile	No
Plate	**Well**	**IUPAC NAME**	**Inhibitor Y/N**
5	A03	{[3-(ethoxymethyl)-2,4,6-trimethylphenyl]methylene}methane-1,1-dicarbonitrile	No
5	B03	2-(2,5-diethoxyphenyl)-1-benzyl-10,3a-dihydropyrrolidino[1,2-a]quinoline-3,3-d icarbonitrile	No
5	C03	[(1Z)-2-(5-{(1Z)-1-methyl-2-[(4-nitrophenyl)amino]-2-azavinyl}(2-thienyl))-3-c hloro-1-azaprop-1-enyl](4-nitrophenyl)amine	No
5	D03	5-amino-7-(2,5-diethoxyphenyl)-2,6,7,7a-tetrahydroindene-4,6,6-tricarbonitrile	No
5	E03	2-amino-4-(2,5-diethoxyphenyl)-3,4,5,6,7,4a-hexahydronaphthalene-1,3,3-tricarb onitrile	No
5	F03	2,6-diamino-4-(2,5-diethoxyphenyl)-4H-thiin-3,5-dicarbonitrile	No
5	G03	ethyl 6-amino-5-cyano-2-methyl-4-(2,4,6-trimethyl-3,5-dinitrophenyl)-4H-pyran- 3-carboxylate	No
5	H03	[(2,3,5,6-tetramethylphenyl)methylene]methane-1,1-dicarbonitrile	No
5	I03	(2E)-2-(aminothioxomethyl)-3-(2,3,5,6-tetramethylphenyl)prop-2-enenitrile	No
5	J03	(hydroxyimino)[3-(methoxymethyl)-2,4,6-trimethylphenyl]methane	No
5	K03	(hydroxyimino)[2,4,6-triethyl-3-((hydroxyimino)methyl)phenyl]methane	No
5	L03	{[3-(2,2-dicyanovinyl)-2,4,6-trimethylphenyl]methylene}methane-1,1-dicarbonitr ile	No
5	M03	2-amino-4-(4-methoxyphenyl)-3,4,5,6,7,4a-hexahydronaphthalene-1,3,3-tricarboni trile	No
5	N03	6-amino-4-(2,5-diethoxyphenyl)-3-methyl-4H-pyrano[3,2-d]pyrazole-5-carbonitril e	No
5	O03	2-amino-4-(2,4-dimethoxyphenyl)-3,4,5,6,7,4a-hexahydronaphthalene-1,3,3-tricar bonitrile	No
5	P03	5-(2-thienyl)pentanoic acid	No

5	A04	5-amino-7-(2,4-dimethoxyphenyl)-2,6,7,7a-tetrahydroindene-4,6,6-tricarbonitril e	No
5	B04	3-amino-7-hydroxy-8aH-chromene-4-carbonitrile	No
5	C04	N-(3,4-dichlorophenyl)(cyclohexylamino)carboxamide	No
5	D04	[(5-methyl-2-thienyl)methylene]methane-1,1-dicarbonitrile	No
5	E04	methyl (2E)-2-cyano-3-(5-methyl(2-thienyl))prop-2-enoate	No
5	F04	[(5-ethyl-2-thienyl)methylene]methane-1,1-dicarbonitrile	No
5	G04	ethyl (2E)-2-cyano-3-(5-ethyl(2-thienyl))prop-2-enoate	No
5	H04	2-amino-4-(4-bromo(2-thienyl))-3,4,5,6,7,4a-hexahydronaphthalene-1,3,3-tricarb onitrile	No
5	I04	ethyl 4-(4-bromo(2-thienyl))-2,7,7-trimethyl-5-oxo-1,4,6,7,8-pentahydroquinoli ne-3-carboxylate	No
5	J04	ethyl 6-amino-4-(4-bromo(2-thienyl))-5-cyano-2-methyl-4H-pyran-3-carboxylate	YES
5	K04	2-amino-4-(2,4-dichlorophenyl)-3,4,5,6,7,4a-hexahydronaphthalene-1,3,3-tricarb onitrile	No
5	L04	[(2,4-dichlorophenyl)methylene]methane-1,1-dicarbonitrile	No
5	M04	5-amino-7-(2,4,6-trimethylphenyl)-2,6,7,7a-tetrahydroindene-4,6,6-tricarbonitr ile	No
5	N04	2-(acetylamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxamide	No
5	O04	(2E)-3-(4-bromo(2-thienyl))-2-cyanoprop-2-enamide	No
5	P04		No
5	A05	methyl (2E)-2-cyano-3-(5-ethyl(2-thienyl))prop-2-enoate	No
5	B05	ethyl (2E)-3-(5-butyl-4-nitro(2-thienyl))-2-cyanoprop-2-enoate	No
5	C05	methyl (2E)-3-(5-butyl-4-nitro(2-thienyl))-2-cyanoprop-2-enoate	No
5	D05	5-methyl-3-nitropyrazole-4-carboxylic acid	No
5	E05	4-bromo-5-methyl-1,3-dinitropyrazole	No
5	F05	3-methyl-1,4-dinitropyrazole	No
5	G05	N-(3-cyano(4,5,6-trihydrocyclopenta[1,2-d]thiophen-2-yl))(3-nitropyrazol-5-yl) carboxamide	YES
5	H05	ethyl (2E)-3-(4-bromo(2-thienyl))-2-cyanoprop-2-enoate	No
5	I05	5-bromothiophene-2-carboxylic acid	No
5	J05	ethyl (2E)-3-(5-bromo(2-thienyl))-2-cyanoprop-2-enoate	No
5	K05	(hydroxyimino){3-[(5-((hydroxyimino)methyl)-3-{[3-((hydroxyimino)methyl)-2,4,6 -trimethylphenyl]methyl}-2,4,6-trimethylphenyl)methyl]-2,4,6-trimethylphenyl}m ethane	No
5	L05	(2E)-2-(aminothioxomethyl)-3-(5-bromo(2-thienyl))prop-2-enenitrile	No
5	M05	1-(2,5-dimethyl(3-thienyl))-2-chloroethan-1-one	No
5	N05	4-(dichloromethyl)-2,3,5,6-tetramethylbenzaldehyde	No
5	O05	6-amino-4-(2,5-dimethylphenyl)-3-methyl-4H-pyrano[3,2-d]pyrazole-5-carbonitril e	No
5	P05	(hydroxyimino)[4-((hydroxyimino)methyl)-2,3,5,6-tetramethylphenyl]methane	No

5	A06	{[4-(dichloromethyl)-2,3,5,6-tetramethylphenyl]methylene}methane-1,1-dicarboni trile	No
5	B06	2,5-bis(oxolan-2-ylmethylene)cyclopentan-1-one	No
5	C06	3-(2H-benzo[3,4-d]1,3-dioxolen-5-yl)(2Z)-2-(2-pyridyl)prop-2-enenitrile	No
5	D06	(2Z)-3-(2,6-dichlorophenyl)-2-(2-pyridyl)prop-2-enenitrile	No
5	E06	7-chloro-1-cyclopropyl-6-fluoro-4-oxohydroquinoline-3-carboxylic acid	No
5	F06	3,4,5,6-tetraphenyl-7-(phenylcarbonyl)-3H,6H-azocin-2-one	No
5	G06	2,5-bis[(2,5-dimethoxyphenyl)methylene]cyclopentan-1-one	No
5	H06	(2E)-3-(2H-benzo[3,4-d]1,3-dioxolan-5-yl)-2-(4-methylphenyl)prop-2-enenitrile	YES
5	I06	(2E)-3-(2H-benzo[3,4-d]1,3-dioxolan-5-yl)-2-(2,4-dichlorophenyl)prop-2-enenitr ile	No
5	J06	5-(2H-benzo[2,3-d]1,3-dioxolan-4-ylmethylene)-2-(2H-benzo[2,3-d]1,3-dioxolen-4 -ylmethylene)cyclopentan-1-one	No
5	K06	2-(2H-benzo[3,4-d]1,3-dioxolan-5-ylmethylene)-3,4-dihydronaphthalen-1-one	No
5	L06	3-(2H-benzo[3,4-d]1,3-dioxolan-5-ylmethylene)-5-(2H-benzo[3,4-d]1,3-dioxolen-5 -ylmethylene)-1-methylazaperhydroin-4-one	No
5	M06	6-(4-bromophenyl)-2-ethoxy-4-(4-methylphenyl)pyridine-3-carbonitrile	No
5	N06	3-(2H-benzo[3,4-d]1,3-dioxolan-5-ylmethylene)-5-(2H-benzo[3,4-d]1,3-dioxolen-5 -ylmethylene)-1-(methylethyl)azaperhydroin-4-one	No
5	O06	6-(2H-benzo[3,4-d]1,3-dioxolan-5-ylmethylene)-2-(2H-benzo[3,4-d]1,3-dioxolen-5 -ylmethylene)-4-(tert-butyl)cyclohexan-1-one	No
5	P06	3-[2-(2-(2H-benzo[3,4-d]1,3-dioxolan-5-yl)(1Z)-2-cyanovinyl)phenyl]-2-(2H-benz o[3,4-d]1,3-dioxolen-5-yl)(2Z)prop-2-enenitrile	No
5	A07	6-(4-bromophenyl)-4-(4-chlorophenyl)-2-methoxypyridine-3-carbonitrile	OFFSCALE
5	B07	2-methoxy-4,6-diphenylpyridine-3-carbonitrile	OFFSCALE
5	C07	4,6-bis(4-chlorophenyl)-2-methoxypyridine-3-carbonitrile	No
5	D07	6-(4-bromophenyl)-2-methoxy-4-(4-methylphenyl)pyridine-3-carbonitrile	YES
5	E07	4-(3,4-dichlorophenyl)-6-(4-chlorophenyl)-2-methoxypyridine-3-carbonitrile	OFFSCALE
5	F07	ethyl 3,5-dimethyl-4-(2-methylpropyl)pyrrole-2-carboxylate	No
5	G07	ethyl 5-{[5-(ethoxycarbonyl)-3-ethyl-4-methylpyrrol-2-yl]methyl}-4-ethyl-3-met hylpyrrole-2-carboxylate	No
5	H07		No
5	I07	N-[6-methyl-3-(piperidylcarbonyl)(4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl)]-2- thienylcarboxamide	No
5	J07	(2E)-3-(4-ethylphenyl)-2-(6-methylbenzimidazol-2-yl)prop-2-enenitrile	No

5	K07	5-[(1E,3E)-4-(4-morpholin-4-ylphenyl)-4-azabuta-1,3-dienyl]-2H-benzo[d]1,3-dio xolane	No
5	L07	N-[(1-methyl-2-oxobenzo[d]azolin-3-ylidene)azamethyl]-2-thienylcarboxamide	No
5	M07	2-thienyl-N-[(2,4,6-trioxo(1,3-dihydropyrimidin-5-ylidene))azamethyl]carboxami de	No
5	N07	2-(2H-benzo[3,4-d]1,3-dioxolen-5-yl)-7-(tert-butyl)-1,2,3,5,6,7,8-heptahydrobe nzo[b]thiopheno[2,3-d]pyrimidin-4-one	No
5	O07	7-(tert-butyl)-2-(5-bromo-2-hydroxyphenyl)-1,2,3,5,6,7,8-heptahydrobenzo[b]thi opheno[2,3-d]pyrimidin-4-one	No
5	P07	7-(tert-butyl)-2-(2-furyl)-1,2,3,5,6,7,8-heptahydrobenzo[b]thiopheno[2,3-d]pyr imidin-4-one	No
5	A08	N-((1Z)-2-(2-furyl)-1-azaprop-1-enyl)-2-(2-thienyl)acetamide	No
5	B08	N-[(5,7-dibromo-2-oxo(1H-benzo[d]azolin-3-ylidene))azamethyl]-2-(5-phenyl(1,2, 3,4-tetraazol-2-yl))acetamide	No
5	C08	2-[(6-nitrobenzimidazol-2-yl)methylthio]hydroquinazolin-4-one	No
5	D08	1-{(1Z)-2-[3-chloro-5-methoxy-4-(phenylmethoxy)phenyl]-1-azavinyl}-1,2,3,4-tet raazole-5-ylamine	No
5	E08	7-(tert-butyl)-2-(2-thienyl)-1,2,3,5,6,7,8-heptahydrobenzo[b]thiopheno[2,3-d]p yrimidin-4-one	No
5	F08	7-(tert-butyl)-2-(4-methylphenyl)-1,2,3,5,6,7,8-heptahydrobenzo[b]thiopheno[2, 3-d]pyrimidin-4-one	No
5	G08	2-((1E)-2-(2H-benzo[d]1,3-dioxolen-5-yl)vinyl)-5,6-dimethyl-1,2,3-trihydrothio pheno[2,3-d]pyrimidin-4-one	No
5	H08	2H-benzo[3,4-d]1,3-dioxolan-5-yl-N-{[1-(naphthylmethyl)-2-oxobenzo[d]azolin-3- ylidene]azamethyl}carboxamide	No
5	I08	4-(2H-benzo[3,4-d]1,3-dioxolan-5-ylmethylene)-3-(4-bromophenyl)isoxazol-5-one	No
5	J08	[(5-amino(1,2,4-dithiazolin-3-ylidene))azamethyl]phenylamine	No
5	K08	N-[5-(tert-butyl)(1,3,4-thiadiazol-2-yl)]-N-methyl(methylamino)carboxamide	No
5	L08	3-amino-1-phenyl-1,2,4-triazoline-5-thione	No
5	M08	N-(5-ethylthio(1,3,4-thiadiazol-2-yl))hexyloxycarboxamide	No
5	N08	5-methylthio-1-phenyl-1,2,4-triazole-3-ylamine	No
5	O08	5-octylthio-1-phenyl-1,2,4-triazole-3-ylamine	No
5	P08	bis(4-methyl-2-pyridyl)diazene	No
5	A09	1-(4-chlorophenoxy)-3,3-dimethyl-1-(1,2,4-triazol-4-yl)butan-2-one	No
5	B09	2-(2,4-dichlorophenyl)-4-propyl-2-(1,2,4-triazolylmethyl)-1,3-dioxolane	No
5	C09	3-(methoxy(hydroxyphosphoryl))propanohydrazide	No
5	D09	2-[bis(phosphonomethyl)amino]acetic acid	No
5	E09	{(3E)-4-[(2,4-dinitrophenyl)amino]-1,1,3-trimethyl-4-azabut-3-enyl}diethoxypho sphino-1-one	No

5	F09	[(3E)-1,3-dimethyl-4-(phenylamino)-4-azabut-3-enyl]dimethoxyphosphino-1-one	No
5	G09	bis(2-chloro-3-pyridyl)diazene	No
5	H09	bis(5-bromo-2-pyridyl)diazene	No
5	I09	3-(tert-butyl)-5,6-dimethyl-1,3-dihydropyrimidine-2,4-dione	No
5	J09	methyl 4-amino-3,5,6-trichloropyridine-2-carboxylate	No
5	K09	(4,6-dichloro(1,3,5-triazin-2-yl))methylamine	No
5	L09	N-benzimidazol-2-ylmethoxycarboxamide	No
5	M09	9-hydroxyfluorene-9-carboxylic acid	No
5	N09	(3-(hydroxyimino)-1,1-dimethylbutyl)dimethoxyphosphino-1-one	No
5	O09	benzylpurin-6-ylamine	No
5	P09	[(dibutoxycarbonyl)methoxy]-N-(3,4-dichlorophenyl)carboxamide	No
5	A10	3-benzimidazol-2-ylpropan-1-ol	No
5	B10	2-chloro-N-(2-pyridyl)acetamide	No
5	C10	2-chloro-N-pyrimidin-2-ylacetamide	No
5	D10	ethyl 4-amino-2-methylthio-1,3-thiazole-5-carboxylate	No
5	E10	ethyl 2-[4-amino-5-(N-(1,3-thiazol-2-yl)carbamoyl)-1,3-thiazol-2-ylthio]acetat e	No
5	F10	2-[4-amino-5-(N-(1,3-thiazol-2-yl)carbamoyl)(1,3-thiazol-2-ylthio)]-N-(4-bromo phenyl)acetamide	No
5	G10	2-[4-amino-5-(N-(1,3-thiazol-2-yl)carbamoyl)(1,3-thiazol-2-ylthio)]-N-[4-(dime thylamino)phenyl]acetamide	No
5	H10	2-(4-amino-5-{N-[4-(dimethylamino)phenyl]carbamoyl}(1,3-thiazol-2-ylthio))-N-(1,3-thiazol-2-yl)acetamide	No
5	I10	2-(4-amino-5-{N-[4-(dimethylamino)phenyl]carbamoyl}(1,3-thiazol-2-ylthio))-N-[4-(dimethylamino)phenyl]acetamide	No
5	J10	(4-amino-2-thioxo(1,3-thiazolin-5-yl))-N-[4-(dimethylamino)phenyl]carboxamide	YES
5	K10	2-{3-[4-(dimethylamino)phenyl]-5-oxo-1,3-thiazolidin-2-ylidene}-2-azaethanenit rile	No
5	L10	4-oxohydroquinoline-3-carboxylic acid	No
5	M10	N,N-diethyl(4-oxo(3-hydroquinolyl))carboxamide	No
5	N10	3-(piperidylcarbonyl)hydroquinolin-4-one	No
5	O10	N-butyl(2-oxoimidazolidinyl)carboxamide	No
5	P10	(2-oxoimidazolidinyl)-N,N-dipropylcarboxamide	No
5	A11	N-(tert-butyl)-N-(2-cyanoethyl)(2-oxoimidazolidinyl)carboxamide	No
5	B11	N-cyclohexyl(2-oxoimidazolidinyl)carboxamide	No
5	C11	N-(3-chlorophenyl)(2-oxoimidazolidinyl)carboxamide	No
5	D11	N-(3,4-dichlorophenyl)(2-oxoimidazolidinyl)carboxamide	No
5	E11	N-(2,4-dichlorophenyl)(2-oxoimidazolidinyl)carboxamide	No
5	F11	2-[(2-oxoimidazolidinyl)carbonylamino]acetic acid	No
5	G11		No
5	H11	2-(2-thienylcarbonylamino)acetic acid	No

5	I11	N-(4-amino(1,2,5-oxadiazol-3-yl))-2-(1-phenyl(1,2,3,4-tetraazol-5-ylthio))acet amide	No
5	J11	N-(4-amino(1,2,5-oxadiazol-3-yl))-2-naphthylthioacetamide	No
5	K11	(2Z)-2-(aminothioxomethyl)-3-(4-bromo(2-thienyl))prop-2-enenitrile	No
5	L11	2-amino-4-(2,5-dimethylphenyl)-3,4,5,6,7,4a-hexahydronaphthalene-1,3,3-tricarb onitrile	No
5	M11	[(5-butyl-2-thienyl)methylene]methane-1,1-dicarbonitrile	No
5	N11	9-(5-butyl(2-thienyl))-3,3,6,6-tetramethyl-2,3,4,5,6,7-hexahydroxanthene-1,8-d ione	No
5	O11	4-{[(4-formyl-2,3,5,6-tetramethylphenyl)methoxy]methyl}-2,3,5,6-tetramethylben zaldehyde	No
5	P11	6-amino-8-(2,5-dimethylphenyl)-2-methyl-1,2,3,8a-tetrahydroisoquinoline-5,7-di carbonitrile	OFFSCALE
5	A12	2-amino-4-(2,4-dimethylphenyl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile	OFFSCALE
5	B12	2-amino-4-(5-bromo(2-thienyl))-5-oxo-4H-6,7,8-trihydrochromene-3-carbonitrile	No
5	C12	2-amino-4-(5-butyl(2-thienyl))-5,6,7,8,9-pentahydrocyclohepta[2,1-b]pyridine-3 -carbonitrile	No
5	D12	2-amino-4-(2,4,6-trimethyl-3-nitrophenyl)-5,6,7,8,9-pentahydrocyclohepta[1,2-b]pyridine-3-carbonitrile	No
5	E12	2-amino-4-(2,5-dimethylphenyl)-5,6,7,8,9-pentahydrocyclohepta[1,2-b]pyridine-3 -carbonitrile	OFFSCALE
5	F12	2-amino-4-(5-butyl(2-thienyl))-5,6,7,4a-tetrahydronaphthalene-1,3-dicarbonitri le	No
5	G12	2-amino-4-[4-(dimethylamino)phenyl]-5,6,7,8,9-pentahydrocyclohepta[1,2-b]pyrid ine-3-carbonitrile	No
5	H12	2-(2,4-dichlorophenyl)-1-(phenylcarbonyl)-10,3a-dihydropyrrolidino[1,2-a]quino line-3,3-dicarbonitrile	No
5	I12	4-[(2,4-dichlorophenyl)methylene]-3-phenylisoxazol-5-one	No
5	J12	4-[(5-bromo(2-thienyl))methylene]-3-phenylisoxazol-5-one	YES
5	K12	4-[(4-bromo(2-thienyl))methylene]-3-phenylisoxazol-5-one	No
5	L12	2-amino-4-(4-fluorophenyl)-5,6,7,8,9-pentahydrocyclohepta[1,2-b]pyridine-3-car bonitrile	No
5	M12	2-(4-fluorophenyl)-3-(phenylcarbonyl)-10,3a-dihydropyrrolidino[1,2-a]quinoline -1,1-dicarbonitrile	No
5	N12	2-amino-4-(4-fluorophenyl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile	No
5	O12	2-amino-4-(4-fluorophenyl)-3,4,5,6,7,4a-hexahydronaphthalene-1,3,3-tricarbonit rile	No
5	P12	6-amino-4-(4-fluorophenyl)-3-methyl-4H-pyrano[3,2-d]pyrazole-5-carbonitrile	No
5	A13	(2Z)-2-cyano-3-(5-methyl(2-furyl))prop-2-enamide	No
5	B13	[(5-methyl-2-furyl)methylene]methane-1,1-dicarbonitrile	No

5	C13	2-amino-4-(5-methyl(2-furyl))-5-oxo-4H-6,7,8-trihydrochromene-3-carbonitrile	No
5	D13	(2Z)-2-(aminothioxomethyl)-3-(5-methyl(2-furyl))prop-2-enenitrile	No
5	E13	methyl (2Z)-2-cyano-3-(5-methyl(2-furyl))prop-2-enoate	No
5	F13	ethyl (2Z)-2-cyano-3-(5-methyl(2-furyl))prop-2-enoate	No
5	G13	7-amino-5-(4-fluorophenyl)-2,4-dioxo-1,3-dihydro-5H-pyrano[2,3-d]pyrimidine-6- carbonitrile	No
5	H13	methylethyl (2Z)-2-cyano-3-(5-methyl(2-furyl))prop-2-enoate	No
5	I13	4-(2H-benzo[3,4-d]1,3-dioxolan-5-yl)-2-amino-5-oxo-4H-6,7,8-trihydrochromene-3 -carbonitrile	No
5	J13	4-[(4-fluorophenyl)methylene]-3-phenylisoxazol-5-one	No
5	K13	4-[(1-methylpyrrol-2-yl)methylene]-3-phenylisoxazol-5-one	No
5	L13	3-phenyl-4-(3-pyridylmethylene)isoxazol-5-one	No
5	M13	ethyl (2Z)-2-cyano-3-(1-methylpyrrol-2-yl)prop-2-enoate	No
5	N13	methylethyl (2Z)-2-cyano-3-(1-methylpyrrol-2-yl)prop-2-enoate	No
5	O13	(2Z)-2-(aminothioxomethyl)-3-(1-methylpyrrol-2-yl)prop-2-enenitrile	No
5	P13	(2Z)-2-cyano-3-(1-methylpyrrol-2-yl)prop-2-enamide	No
5	A14	[(1-methylpyrrol-2-yl)methylene]methane-1,1-dicarbonitrile	No
5	B14	2-amino-4-(2,4,6-trimethylphenyl)-5,6,7,8,9,10-hexahydrocycloocta[2,1-b]pyridi ne-3-carbonitrile	No
5	C14	4-(2H-benzo[3,4-d]1,3-dioxolan-5-yl)-2-amino-5,6,7,8,9,10-hexahydrocycloocta[2 ,1-b]pyridine-3-carbonitrile	No
5	D14	2-amino-4-(5-butyl(2-thienyl))-5,6,7,8,9,10-hexahydrocycloocta[2,1-b]pyridine- 3-carbonitrile	No
5	E14	2,6-diamino-4-(5-methyl(2-furyl))-4H-thiin-3,5-dicarbonitrile	No
5	F14	2-amino-4-(5-bromo(2-thienyl))-5,6,7,8,9,10-hexahydrocycloocta[2,1-b]pyridine- 3-carbonitrile	No
5	G14	2-amino-4-(4-fluorophenyl)-5,6,7,8,9,10-hexahydrocycloocta[1,2-b]pyridine-3-ca rbonitrile	No
5	H14	1-(phenylcarbonyl)-2-(3-pyridyl)-10,3a-dihydropyrrolidino[1,2-a]quinoline-3,3- dicarbonitrile	No
5	I14	2-amino-4-(4-hydroxyphenyl)-5,6,7,8,9-pentahydrocyclohepta[1,2-b]pyridine-3-ca rbonitrile	OFFSCALE
5	J14	2-(4-hydroxyphenyl)-1-(phenylcarbonyl)-10,3a-dihydropyrrolidino[1,2-a]quinolin e-3,3-dicarbonitrile	No
5	K14	6-amino-3-methyl-1-phenyl-4-(2-pyridyl)-4H-pyrano[3,2-d]pyrazole-5-carbonitril e	No
5	L14	(2E)-2-(aminothioxomethyl)-3-(3-pyridyl)prop-2-enenitrile	No
5	M14	2-amino-4-(3-pyridyl)-5,6,7,8,9-pentahydrocyclohepta[1,2-b]pyridine-3-carbonit rile	No
5	N14	4-(2H-benzo[3,4-d]1,3-dioxolan-5-yl)-2-amino-5,6,7,8-tetrahydroquinoline-3-car bonitrile	No

5	O14	4-(2H-benzo[3,4-d]1,3-dioxolan-5-yl)-2-amino-5,6,7,8,9-pentahydrocyclohepta[2, 1-b]pyridine-3-carbonitrile	No
5	P14	2-amino-6-hydroxy-4-(3-pyridyl)-4H-chromene-3-carbonitrile	No
5	A15	7-amino-2,4-dioxo-5-(3-pyridyl)-1,3-dihydro-5H-pyrano[2,3-d]pyrimidine-6-carbo nitrile	No
5	B15	2-[(4,4-dimethyl-2,6-dioxocyclohexyl)(5-methyl(2-thienyl))methyl]-5,5-dimethyl cyclohexane-1,3-dione	No
5	C15	2-[(4,4-dimethyl-2,6-dioxocyclohexyl)(5-ethyl(2-thienyl))methyl]-5,5-dimethylc yclohexane-1,3-dione	No
5	D15	2-[(4,4-dimethyl-2,6-dioxocyclohexyl)(4-bromo-5-methyl(2-thienyl))methyl]-5,5- dimethylcyclohexane-1,3-dione	No
5	E15	2-[(4,4-dimethyl-2,6-dioxocyclohexyl)(4-bromo-5-ethyl(2-thienyl))methyl]-5,5-d imethylcyclohexane-1,3-dione	No
5	F15	3,3,6,6-tetramethyl-9-(5-methyl(2-thienyl))-2,3,4,5,6,7-hexahydroxanthene-1,8- dione	No
5	G15	2,6-diamino-4-(5-methyl(2-thienyl))-4H-thiin-3,5-dicarbonitrile	No
5	H15	2,6-diamino-4-(5-ethyl(2-thienyl))-4H-thiin-3,5-dicarbonitrile	No
5	I15	2,6-diamino-4-(4-bromo-5-methyl(2-thienyl))-4H-thiin-3,5-dicarbonitrile	No
5	J15	2,6-diamino-4-(4-bromo-5-ethyl(2-thienyl))-4H-thiin-3,5-dicarbonitrile	No
5	K15	methyl 6-amino-5-cyano-2-methyl-4-(2-thienyl)-4H-pyran-3-carboxylate	No
5	L15	methyl 6-amino-5-cyano-4-(5-ethyl(2-thienyl))-2-methyl-4H-pyran-3-carboxylate	No
5	M15	methyl 6-amino-4-(4-bromo-5-methyl(2-thienyl))-5-cyano-2-methyl-4H-pyran-3-car boxylate	YES
5	N15	methyl 6-amino-4-(4-bromo-5-ethyl(2-thienyl))-5-cyano-2-methyl-4H-pyran-3-carb oxylate	No
5	O15	ethyl 6-amino-5-cyano-2-methyl-4-(5-methyl(2-thienyl))-4H-pyran-3-carboxylate	No
5	P15	ethyl 6-amino-5-cyano-4-(5-ethyl(2-thienyl))-2-methyl-4H-pyran-3-carboxylate	No
5	A16	2-amino-4-(5-ethyl(2-thienyl))-5-oxo-4H-6,7,8-trihydrochromene-3-carbonitrile	No
5	B16	2-amino-4-(4-bromo-5-methyl(2-thienyl))-5-oxo-4H-6,7,8-trihydrochromene-3-carb onitrile	No
5	C16	2-amino-4-(4-bromo-5-ethyl(2-thienyl))-5-oxo-4H-6,7,8-trihydrochromene-3-carbo nitrile	No
5	D16	2-amino-4-(5-methyl-4-nitro(2-thienyl))-5-oxo-4H-6,7,8-trihydrochromene-3-carb onitrile	No
5	E16	2-amino-7,7-dimethyl-4-(5-methyl(2-thienyl))-5-oxo-4H-6,7,8-trihydrochromene-3 -carbonitrile	No
5	F16	2-amino-4-(5-ethyl(2-thienyl))-7,7-dimethyl-5-oxo-4H-6,7,8-trihydrochromene-3- carbonitrile	No

5	G16	2-amino-4-(4-bromo-5-methyl(2-thienyl))-7,7-dimethyl-5-oxo-4H-6,7,8-trihydroch romene-3-carbonitrile	No
5	H16	2-amino-4-(4-bromo-5-ethyl(2-thienyl))-7,7-dimethyl-5-oxo-4H-6,7,8-trihydrochr omene-3-carbonitrile	No
5	I16	ethyl 6-amino-4-(4-bromo-5-methyl(2-thienyl))-5-cyano-2-methyl-4H-pyran-3-carb oxylate	No
5	J16	ethyl 6-amino-4-(4-bromo-5-ethyl(2-thienyl))-5-cyano-2-methyl-4H-pyran-3-carbo xylate	No
5	K16	2-amino-7,7-dimethyl-4-(5-methyl-4-nitro(2-thienyl))-5-oxo-4H-6,7,8-trihydroch romene-3-carbonitrile	No
5	L16	2-amino-4-(5-butyl-4-nitro(2-thienyl))-7,7-dimethyl-5-oxo-4H-6,7,8-trihydrochr omene-3-carbonitrile	No
5	M16	6-amino-3-methyl-4-(5-methyl(2-thienyl))-4H-pyrano[3,2-d]pyrazole-5-carbonitri le	No
5	N16	6-amino-4-(5-ethyl(2-thienyl))-3-methyl-4H-pyrano[3,2-d]pyrazole-5-carbonitril e	No
5	O16	6-amino-4-(4-bromo-5-methyl(2-thienyl))-3-methyl-4H-pyrano[3,2-d]pyrazole-5-ca rbonitrile	No
5	P16	6-amino-4-(4-bromo-5-ethyl(2-thienyl))-3-methyl-4H-pyrano[3,2-d]pyrazole-5-car bonitrile	No
5	A17	2-amino-4-(2-thienyl)-3,4,5,6,7,4a-hexahydronaphthalene-1,3,3-tricarbonitrile	No
5	B17	3-amino-5-(5-methyl(2-thienyl))bicyclo[4.4.0]dec-1(10)-ene-2,4,4-tricarbonitri le	No
5	C17	methyl 2,7,7-trimethyl-5-oxo-4-(2-thienyl)-1,4,6,7,8-pentahydroquinoline-3-car boxylate	No
5	D17	methyl 4-(5-ethyl(2-thienyl))-2,7,7-trimethyl-5-oxo-1,4,6,7,8-pentahydroquinol ine-3-carboxylate	No
5	E17	methyl 4-(4-bromo-5-methyl(2-thienyl))-2,7,7-trimethyl-5-oxo-1,4,6,7,8-pentahy droquinoline-3-carboxylate	No
5	F17	methyl 4-(4-bromo-5-ethyl(2-thienyl))-2,7,7-trimethyl-5-oxo-1,4,6,7,8-pentahyd roquinoline-3-carboxylate	No
5	G17	ethyl 2,7,7-trimethyl-4-(5-methyl(2-thienyl))-5-oxo-1,4,6,7,8-pentahydroquinol ine-3-carboxylate	No
5	H17	ethyl 4-(5-ethyl(2-thienyl))-2,7,7-trimethyl-5-oxo-1,4,6,7,8-pentahydroquinoli ne-3-carboxylate	No
5	I17	ethyl 4-(4-bromo-5-methyl(2-thienyl))-2,7,7-trimethyl-5-oxo-1,4,6,7,8-pentahyd roquinoline-3-carboxylate	No
5	J17	ethyl 4-(4-bromo-5-ethyl(2-thienyl))-2,7,7-trimethyl-5-oxo-1,4,6,7,8-pentahydr oquinoline-3-carboxylate	No
5	K17	ethyl 2,7,7-trimethyl-4-(5-methyl-4-nitro(2-thienyl))-5-oxo-1,4,6,7,8-pentahyd roquinoline-3-carboxylate	No
5	L17	methyl 2-methyl-5-oxo-4-(2-thienyl)-1,4,6,7,8-pentahydroquinoline-3-carboxylat e	No
5	M17	methyl 4-(4-bromo-5-methyl(2-thienyl))-2-methyl-5-oxo-1,4,6,7,8-pentahydroquin oline-3-carboxylate	No

5	N17	methyl 4-(4-bromo-5-ethyl(2-thienyl))-2-methyl-5-oxo-1,4,6,7,8-pentahydroquino line-3-carboxylate	No
5	O17	methyl 2-methyl-4-(5-methyl-4-nitro(2-thienyl))-5-oxo-1,4,6,7,8-pentahydroquin oline-3-carboxylate	No
5	P17	ethyl 2-methyl-5-oxo-4-(2-thienyl)-1,4,6,7,8-pentahydroquinoline-3-carboxylate	No
5	A18	ethyl 2-methyl-4-(5-methyl(2-thienyl))-5-oxo-1,4,6,7,8-pentahydroquinoline-3-c arboxylate	No
5	B18	ethyl 4-(5-ethyl(2-thienyl))-2-methyl-5-oxo-1,4,6,7,8-pentahydroquinoline-3-ca rboxylate	No
5	C18	ethyl 4-(4-bromo-5-methyl(2-thienyl))-2-methyl-5-oxo-1,4,6,7,8-pentahydroquino line-3-carboxylate	No
5	D18	ethyl 4-(4-bromo-5-ethyl(2-thienyl))-2-methyl-5-oxo-1,4,6,7,8-pentahydroquinol ine-3-carboxylate	No
5	E18	ethyl 2-amino-4-(4-bromo-5-methyl(2-thienyl))-5-oxo-4H-6,7,8-trihydrochromene- 3-carboxylate	No
5	F18	ethyl 6-amino-3-methyl-4-(2-thienyl)-4H-pyrano[3,2-d]pyrazole-5-carboxylate	No
5	G18	2-amino-4-(4-bromo-5-methyl(2-thienyl))-5,6,7,8-tetrahydroquinoline-3-carbonit rile	No
5	H18	2-amino-4-(4-bromo-5-ethyl(2-thienyl))-5,6,7,8-tetrahydroquinoline-3-carbonitr ile	No
5	I18	2-amino-4-(5-methyl-4-nitro(2-thienyl))-5,6,7,8-tetrahydroquinoline-3-carbonit rile	No
5	J18	2-amino-4-(5-ethyl-4-nitro(2-thienyl))-5,6,7,8-tetrahydroquinoline-3-carbonitr ile	No
5	K18	2-amino-4-(5-butyl-4-nitro(2-thienyl))-5,6,7,8-tetrahydroquinoline-3-carbonitr ile	No
5	L18	2-amino-4-(5-methyl(2-thienyl))-5,6,7,8,9-pentahydrocyclohepta[2,1-b]pyridine- 3-carbonitrile	No
5	M18	2-amino-4-(5-ethyl(2-thienyl))-5,6,7,8,9-pentahydrocyclohepta[2,1-b]pyridine-3 -carbonitrile	OFFSCALE
5	N18	2-amino-4-(4-bromo-5-ethyl(2-thienyl))-5,6,7,8,9-pentahydrocyclohepta[2,1-b]py ridine-3-carbonitrile	No
5	O18	2-amino-4-(4-bromo-5-methyl(2-thienyl))-5,6,7,8,9-pentahydrocyclohepta[2,1-b]p yridine-3-carbonitrile	No
5	P18	2-amino-4-(4-bromo-5-butyl(2-thienyl))-5,6,7,8,9-pentahydrocyclohepta[2,1-b]py ridine-3-carbonitrile	No
5	A19	2-amino-4-(5-ethyl-4-nitro(2-thienyl))-5,6,7,8,9,10-hexahydrocycloocta[2,1-b]p yridine-3-carbonitrile	No
5	B19	(2Z)-2-(aminothioxomethyl)-3-(2-thienyl)prop-2-enenitrile	No
5	C19	(2Z)-2-(aminothioxomethyl)-3-(5-methyl(2-thienyl))prop-2-enenitrile	No
5	D19	(2Z)-2-cyano-3-(5-methyl(2-thienyl))prop-2-enamide	No
5	E19	methylethyl (2Z)-2-cyano-3-(5-ethyl(2-thienyl))prop-2-enoate	No
5	F19	(2Z)-2-(aminothioxomethyl)-3-(5-ethyl(2-thienyl))prop-2-enenitrile	No

5	G19	(2Z)-2-cyano-3-(5-ethyl(2-thienyl))prop-2-enamide	No
5	H19	methylethyl (2Z)-3-(4-bromo-5-methyl(2-thienyl))-2-cyanoprop-2-enoate	No
5	I19	(2Z)-2-(aminothioxomethyl)-3-(4-bromo-5-methyl(2-thienyl))prop-2-enenitrile	No
5	J19	(2Z)-3-(4-bromo-5-methyl(2-thienyl))-2-cyanoprop-2-enamide	No
5	K19	methyl (2Z)-3-(4-bromo-5-ethyl(2-thienyl))-2-cyanoprop-2-enoate	No
5	L19	ethyl (2Z)-3-(4-bromo-5-ethyl(2-thienyl))-2-cyanoprop-2-enoate	No
5	M19	methylethyl (2Z)-3-(4-bromo-5-ethyl(2-thienyl))-2-cyanoprop-2-enoate	No
5	N19	(2Z)-2-(aminothioxomethyl)-3-(4-bromo-5-ethyl(2-thienyl))prop-2-enenitrile	No
5	O19	(2Z)-3-(4-bromo-5-ethyl(2-thienyl))-2-cyanoprop-2-enamide	No
5	P19	ethyl (2Z)-2-cyano-3-(5-methyl-4-nitro(2-thienyl))prop-2-enoate	No
5	A20	methylethyl (2Z)-2-cyano-3-(5-methyl-4-nitro(2-thienyl))prop-2-enoate	No
5	B20	(2Z)-2-(aminothioxomethyl)-3-(5-methyl-4-nitro(2-thienyl))prop-2-enenitrile	No
5	C20	(2Z)-2-cyano-3-(5-methyl-4-nitro(2-thienyl))prop-2-enamide	No
5	D20	[(5-methyl-4-nitro-2-thienyl)methylene]methane-1,1-dicarbonitrile	No
5	E20	methyl (2Z)-2-cyano-3-(5-ethyl-4-nitro(2-thienyl))prop-2-enoate	No
5	F20	ethyl (2Z)-2-cyano-3-(5-ethyl-4-nitro(2-thienyl))prop-2-enoate	No
5	G20	(2Z)-2-(aminothioxomethyl)-3-(5-ethyl-4-nitro(2-thienyl))prop-2-enenitrile	No
5	H20	methylethyl (2Z)-3-(5-butyl-4-nitro(2-thienyl))-2-cyanoprop-2-enoate	No
5	I20	(2Z)-2-(aminothioxomethyl)-3-(5-butyl-4-nitro(2-thienyl))prop-2-enenitrile	No
5	J20	5-[(5-butyl-4-nitro-2-thienyl)methylene]-1,3-dihydropyrimidine-2,4,6-trione	No
5	K20	5-[(5-methyl-2-thienyl)methylene]-1,3-dihydropyrimidine-2,4,6-trione	No
5	L20	4-(4-bromophenyl)-2-(phenylazamethylene)-1,3-thiazoline	No
5	M20	5-(4-methoxyphenyl)-1,3-thiazolin-2-imine	No
5	N20	4-(2H,3H-benzo[3,4-e]1,4-dioxin-6-yl)-1,3-thiazolin-2-imine, bromide	No
5	O20	4-(2,4,6-trimethylphenyl)-1,3-thiazolin-2-imine, bromide	No
5	P20	2-{2-[(1,1-dioxobenzo[d]1,2-thiazolin-3-yl)amino]ethoxy}ethyl 5-oxo-1-phenylpy rrolidine-3-carboxylate	No
5	A21	N-methyl-N-phenyl-2-(pyrrolidinylthioxomethylthio)acetamide	No
5	B21	[2-(4-amino(1,2,5-oxadiazol-3-yloxy))ethyl]phenylamine	No
5	C21	4-(5,6-dimethylbenzoxazol-2-yl)phenylamine	No
5	D21	2-(2-chloro-5-iodophenyl)benzoxazole-5-ylamine	No
5	E21	4,5-diphenylimidazole-2-thiol	No

5	F21	4-[2,2,2-trifluoro-1-(4-hydroxyphenyl)-1-(trifluoromethyl)ethyl]phenol	No
5	G21	5-(2-chlorophenyl)-1H-1,2,4-triazole-3-thiol	No
5	H21	5-(3-methylbutyl)-1,3,4-thiadiazole-2-ylamine	No
5	I21	4-(nitromethyl)-2-hydrophthalazin-1-one	No
5	J21	3,4-dimethoxybenzenesulfonamide	No
5	K21	5-methylthio-1-phenyl-1,2,3,4-tetraazole	No
5	L21	adamantanylmethylamine, chloride	No
5	M21	6-hydroxy-1,4-dimethyl-2-oxohydropyridine-3-carbonitrile	No
5	N21	5-phenyl-1,3,4-oxadiazole-2-ylamine	No
5	O21	benzimidazol-2-ylphenylmethan-1-ol	No
5	P21	3-[(3-chlorophenyl)azamethylene]-1H-benzo[d]azolidin-2-one	No
5	A22	(2,4-dinitrophenyl)methylamine	No
5	B22	5-(4-methoxyphenyl)-1,3,4-oxadiazole-2-ylamine	No
5	C22	(2,4-dinitrophenyl)piperidine	No
5	D22	3,3,6,6-tetramethyl-2,3,4,5,6,7-hexahydroacridine-1,8-dione	No
5	E22	methoxy-N-(1,3-thiazol-2-yl)carboxamide	No
5	F22	9-(4-pyridylmethyl)acridine	No
5	G22	1-(phenylsulfonyl)-1,2,3,4-tetrahydroquinoline	No
5	H22	di6-nitrobenzothiazol-2-yl disulfide	No
5	I22	[(4-iodophenyl)amino](methylamino)methane-1-thione	No
5	J22	(methylamino)morpholin-4-ylmethane-1-thione	No
5	K22	1-(1H,3H-naphtho[1,2-e]1,3-oxazin-2-yl)-2-ethoxybenzene	No
5	L22	N-(2H-benzo[d]1,3-dioxolan-5-yl)adamantanylcarboxamide	No
5	M22	2-[4-oxo-5-(phenylmethylene)-2-thioxo(1,3-thiazolidin-3-yl)]-N-(4-oxo-2-thioxo (1,3-thiazolidin-3-yl))acetamide	No
5	N22	cyclohexyl-N-(1,3-thiazol-2-yl)carboxamide	No
5	O22	amino-N-[(4-aminophenyl)sulfonyl]amide, hydrate	No
5	P22	benzo[b]furan-2-carboxylic acid	No
Plate	**Well**	**IUPAC NAME**	**Inhibitor Y/N**
6	A03	2-acetyl-3,6-dimethyl-7-oxo-1,3-thiazolino[3,2-b]1,2,4-triazine	No
6	B03	2-(5,7-dichloro-8-quinolyloxy)ethan-1-ol	No
6	C03	({[7-(1,6-dihydroxy-3-methyl-5-(methylethyl)-7-oxo-8-{[(sulfenamoylmethyl)amin o]methylene}(2-naphthyl))-3,8-dihydroxy-6-methyl-4-(methylethyl)-2-oxonaphthyl idene]methyl}amino)methanesulfenamide	No
6	D03	5-(indol-3-ylmethylene)-1-phenyl-1,3-dihydropyrimidine-2,4,6-trione	No
6	E03	5-[(1-methylindol-3-yl)methylene]-1-phenyl-1,3-dihydropyrimidine-2,4,6-trione	No
6	F03	1-(4-bromophenyl)-5-(indol-3-ylmethylene)-1,3-dihydropyrimidine-2,4,6-trione	No

6	G03	7-[(1E)-2-(4-ethylphenyl)vinyl]-6-nitro-4-hydro-1,2,4-triazolo[1,5-a]pyrimidin -5-ol	No
6	H03	5-[5-((hydroxyimino)methyl)-2-furyl]-2H-benzo[c]azoline-1,3-dione	No
6	I03	4-(2-thienyl)-2-hydrophthalazin-1-one	No
6	J03	4-amino-3-prop-2-enyl-2-thioxo-1,3-thiazoline-5-carboxamide	No
6	K03	2-(2-thienyl)-1,3-thiazolidine-4-carboxylic acid	No
6	L03	(2H,3H-benzo[e]1,4-dioxin-6-ylsulfonyl){4-[(1,3-thiazol-2-ylamino)sulfonyl]phe nyl}amine	No
6	M03	3-methyl-7-benzylazolino[3,4-d]1,2,4-triazino[3,4-b]1,3-thiazoline-4,6,8-trion e	No
6	N03	2-[(1E)-2-(5-nitro(2-thienyl))-1-azavinyl]-4,5-dimethylthiophene-3-carboxamide	No
6	O03	2-{[(6-methyl-5-oxo-4H-1,2,4-triazin-3-yl)amino]azamethylene}propanedioic acid	No
6	P03	(3-(2-furyl)pyrazol-5-yl)-N-[(2-oxo(1H-benzo[d]azolin-3-ylidene))azamethyl]car boxamide	No
6	A04	1,3-dimethyl-5-nitro-3-hydrobenzimidazol-2-one	No
6	B04	(indol-3-ylmethyl)dimethylamine	No
6	C04	7-methoxy-1-methyl-3,4-dihydrobeta-carboline	No
6	D04	4-[(6,7-dimethoxyisoquinolyl)methyl]-1,2-dimethoxybenzene	No
6	E04	2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-3-methoxychromen-4-one, oxamethane, oxam ethane, oxamethane	No
6	F04	(phenylamino)-N-(1,2,3-thiadiazol-5-yl)carboxamide	YES
6	G04	2-(2-benzoxazol-2-ylthioethylthio)benzoxazole	No
6	H04	1,1,2-triphenylethane-1,2-diol	No
6	I04	hydroxy-2-pyridylmethanesulfonic acid	No
6	J04	4-nitroquinolin-1-ol	No
6	K04	2-aminohexanedioic acid	YES
6	L04		No
6	M04	2-amino-3-(oxyphosphinyloxyphosphinyl)propanoic acid	No
6	N04	3,4,5,6-tetrahydroxy-2H-3,4,5,6-tetrahydropyran-2-carboxylic acid	No
6	O04	3-oxo-3-piperidylpropanenitrile	No
6	P04	1-[(3,4-dimethoxyphenyl)methyl]-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydroisoqu inoline	No
6	A05	3-(pyrrolylmethyl)pyridine	No
6	B05	2-methyl-4,9,10-trihydrobenzo[d]1,3-oxazolo[5,4-a][7]annulen-4-ol	No
6	C05	methyl 2-oxopyran-5-carboxylate	No
6	D05	1H-1,2,3-triazole-4,5-dicarboxylic acid	No
6	E05	N-(4-methyl-1,3-thiazol-2-yl)acetamide	No
6	F05	(3S,4S,2R,5R)-3,4-bis(phenylmethoxy)-5-[(phenylmethoxy)methyl]oxolan-2-yl 4-ni trobenzoate	No
6	G05	2H-naphtho[2,3-c]azoline-1,3-dione	No
6	H05	(4S)-2-[(4S)-4-benzyl(1,3-oxazolin-2-yl)]-4-benzyl-1,3-oxazoline	No

6	I05	N-((3S)-5-oxo(3-2,3,4-trihydrofuryl))(phenylmethoxy)carboxamide	No
6	J05	2-(6-chloropurin-9-yl)-2H-3,4,5,6-tetrahydropyran	No
6	K05	1-methylpyridine-3-carboxylic acid, chloride	No
6	L05	1-[(4S,2R,3R,5R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-1,3-dihydropyrimi dine-2,4-dione	No
6	M05	1,5-diaminoanthracene-9,10-dione	No
6	N05	6,7-dimethoxy-1-methyl-1,2,3,4-tetrahydroisoquinoline	No
6	O05	hexadecanoic acid	No
6	P05	(1S,2S,4S,7S,9S,12S,16S,8R,13R,26R)-7,9,13,23-tetramethyl-5-oxaspiro[pentacycl o[10.8.0.0<2,9>.0<4,8>.0<13,18>]icosane-6,6'-piperidine]-18-en-16-ol	No
6	A06	indeno[2,3-e]1,2,3,4-tetraazolo[1,5-b]1,2,4-triazin-10-one	No
6	B06	2-[(4-hydroxy-3-methylphenyl)(3-methyl-4-oxocyclohexa-2,5-dienylidene)methyl]b enzenesulfonic acid	No
6	C06	3-(2-aminoethyl)-5-methoxyindole-2-carboxylic acid	No
6	D06	2-[6-((2S)-2-hydroxy-2-phenylethyl)(6S,2R)-1-methyl(2-piperidyl)]-1-phenyletha n-1-one	No
6	E06	methyl 5-methyl-1-(2-methylpropyl)-2-oxo-3-(2-thienylmethylene)azoline-4-carbo xylate	No
6	F06	(methylsulfonyl)(4-{4-[(methylsulfonyl)methyl]phenoxy}phenyl)amine	No
6	G06	3-phenyl-2-(phenylazamethylene)-1,3-thiazolidin-4-one	No
6	H06	5-imino-1,2,4-dithiazolidine-3-thione	No
6	I06	{[4-(tert-butyl)phenyl]piperidylmethyl}phenylphosphinopiperidyl-1-one	No
6	J06	ethyl 2-(acetylamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate	No
6	K06	5-[(4-methylphenyl)methylthio]-1,3,4-thiadiazole-2-ylamine	No
6	L06	2H,3H-benzo[3,4-e]1,4-dioxan-6-yl(2-naphthylsulfonyl)amine	No
6	M06	2-furyl-N-{[(methylamino)thioxomethyl]amino}carboxamide	No
6	N06	4-chloro-1-(methylsulfonyl)benzene	No
6	O06	N-(2-hydroxyethyl)-N'-(2-hydroxyethyl)propane-1,3-diamide	No
6	P06	amino(4-chlorophenyl)[(4-chlorophenyl)azamethylene]-1-ol	No
6	A07	(4-hydroxy-3-methoxyphenyl)thiocarbonitrile	No
6	B07	3-hydroxy-3-(2-oxocyclohexyl)indolin-2-one	No
6	C07	4-[(2,5-dimethoxyphenyl)sulfonyl]morpholine	No
6	D07	(3-nitrophenyl)pyrrolidine	No
6	E07	adamantanyl-N-(2-hydroxypropyl)carboxamide	No
6	F07	1-bromo-4-(methylsulfonyl)benzene	No
6	G07	2-(3-nitrophenyl)isoindoline	No
6	H07	2-(acetylamino)-3-methylpentanoic acid	No
6	I07	(2,4-dinitrophenyl)(3-morpholin-4-ylpropyl)amine	No
6	J07		No

6	K07	1-chloro-4-(ethylsulfonyl)benzene	No
6	L07	1-(3-nitrophenyl)pyrrole-2-carbaldehyde	No
6	M07	4-(5,5-dimethyl-1,3-dioxan-2-yl)phenol	No
6	N07	methyl 2-cyano-2-(2-oxo(1H-benzo[d]azolidin-3-ylidene))acetate	No
6	O07	3-{[(4-chlorophenyl)sulfonyl](2-cyanoethyl)amino}propanenitrile	No
6	P07	5-amino-2-[(4-aminophenyl)amino]benzenesulfonic acid	No
6	A08	(methylamino)(phenylamino)methane-1-thione	No
6	B08	[(4-chlorophenyl)amino](methylamino)methane-1-thione	No
6	C08	[(4-bromophenyl)amino](methylamino)methane-1-thione	No
6	D08	(2E)-3-(2,4-dichlorophenyl)-2-(4-chlorophenyl)prop-2-enenitrile	No
6	E08	[(4-bromophenyl)amino](ethylamino)methane-1-thione	No
6	F08	(ethylamino)[(4-iodophenyl)amino]methane-1-thione	No
6	G08	(ethylamino)[(4-fluorophenyl)amino]methane-1-thione	No
6	H08	(ethylamino)morpholin-4-ylmethane-1-thione	No
6	I08	[(3-methoxyphenyl)amino](methylamino)methane-1-thione	No
6	J08	[(4-methoxyphenyl)amino](methylamino)methane-1-thione	No
6	K08	[(4-fluorophenyl)amino](methylamino)methane-1-thione	No
6	L08	(methylamino)piperidylmethane-1-thione	No
6	M08	[(2-chlorophenyl)amino](phenylamino)methane-1-thione	No
6	N08	[(4-fluorophenyl)amino](phenylamino)methane-1-thione	YES
6	O08	[(tert-butyl)amino](phenylamino)methane-1-thione	No
6	P08	(phenylamino)piperidylmethane-1-thione	No
6	A09	3-(4-chlorophenyl)-4-methyl-1-(2-1,2,3,4-tetrahydroisoquinolylmethyl)-1,2,4-tr iazoline-5-thione	No
6	B09	3-butoxy-1-piperidylpropan-2-ol	No
6	C09	3-butoxy-1-pyrrolidinylpropan-2-ol	No
6	D09	4-amino-3-(5-aminobenzimidazol-2-yl)phenol	No
6	E09	1-morpholin-4-yl-2-(3-pyridyl)ethane-1-thione	No
6	F09	1-azaperhydroepinyl-3-phenoxypropan-2-ol	No
6	G09	5-benzimidazol-2-ylthiofuran-2-carbaldehyde	No
6	H09	2,3-dihydrobenzo[d]furan-2-yl(2,3-dihydrobenzo[d]furan-2-ylmethoxy)methan-1-ol	No
6	I09	2-(3-methylthio(1,2,4-thiadiazol-5-ylthio))-N-(4-nitrophenyl)acetamide	No
6	J09	N-(4-nitrophenyl)-2-(1,3-thiazolin-2-ylthio)acetamide	No
6	K09	3-hydroxy-3-(2-oxopropyl)indolin-2-one	No
6	L09	3-nitro-5,6,7,8,9-pentahydro-4aH-carbazole	No
6	M09	3,6-bis(3,5-dimethylpyrazolyl)-1,2,4,5-tetraazine	No
6	N09	4-carbamoyl-5-hydroxy-1,2,5-oxadiazole-3-carboxylic acid	No
6	O09	N-[2-hydroxy-4-(methoxycarbonylamino)(1,2,5-oxadiazol-3-yl)]methoxycarboxamide	No
6	P09	bis(4-phenyl-1,2,5-oxadiazol-3-yl)diazene	No

6	A10	2-hydroxy-1,2,5-oxadiazole-3,4-dicarboxamide	No
6	B10	8-hydroxy-15-(hydroxyimino)-8-azadispiro[5.2.5.1]pentadec-10-en-7-one	No
6	C10		No
6	D10	dimethyl[4-(5-methyl-5-nitro(1,3-dioxan-2-yl))phenyl]amine	No
6	E10	3,9-bis(2-bromophenyl)-2,4,8,10-tetraoxaspiro[5.5]undecane	No
6	F10	ethyl 5-amino-4-cyano-3-methylthiophene-2-carboxylate	No
6	G10	ethyl 5-(acetylamino)-4-cyano-3-methylthiophene-2-carboxylate	YES
6	H10	ethyl 5-(acetylamino)-4-cyano-3-methylthiophene-2-carboxylate, potassium salt	YES
6	I10	ethyl 2-[2-amino-6,8-dibromo-3-(ethoxycarbonyl)(4H-chromen-4-yl)]-2-cyanoaceta te	No
6	J10	(3-methylphenyl){6-[(3-methylphenyl)amino](1,2,5-oxadiazolo[3,4-e]pyrazin-5-yl)}amine	No
6	K10	5,6-dipyrrolidinyl-1,2,5-oxadiazolo[3,4-b]pyrazine	No
6	L10	(3,4-dichlorophenyl){6-[(3,4-dichlorophenyl)amino](1,2,5-oxadiazolo[3,4-e]pyra zin-5-yl)}amine	No
6	M10	(4-chlorophenyl){6-[(4-chlorophenyl)amino](1,2,5-oxadiazolo[3,4-e]pyrazin-5-yl)}amine	No
6	N10	(4-fluorophenyl){6-[(4-fluorophenyl)amino](1,2,5-oxadiazolo[3,4-e]pyrazin-5-yl)}amine	YES
6	O10	(4-bromophenyl)(6-chloro(1,2,5-oxadiazolo[3,4-e]pyrazin-5-yl))amine	YES
6	P10		No
6	A11	(3-chloroquinoxalin-2-yl)(phenylsulfonyl)amine	No
6	B11	(3-morpholin-4-ylquinoxalin-2-yl)(phenylsulfonyl)amine	No
6	C11	indolo[2,3-b]quinoxaline	No
6	D11	2-fluoroindolo[2,3-b]quinoxaline	No
6	E11	5-acetyl-2-fluoroindolo[2,3-b]quinoxaline	No
6	F11	3,7-dibromoindolo[2,3-b]pyridino[3,2-e]pyrazine	No
6	G11	2-methylindolo[2,3-b]quinoxaline	No
6	H11	5-(2-hydroxy-1,3-dioxo-2-hydrocyclopenta[3,4-a]benzen-2-yl)-1,3,5-trihydropyri midine-2,4,6-trione, hydrate	No
6	I11	phenyl({3-[(phenylamino)azamethylene](2-hydrocyclopenta[3,2-a]benzenylidene)}a zamethyl)amine	No
6	J11	2-(2-furylmethylene)cyclopenta[1,2-a]benzene-1,3-dione	No
6	K11	2-[(5-methyl-2-furyl)methylene]cyclopenta[1,2-a]benzene-1,3-dione	No
6	L11	2-(4-quinolylmethylene)cyclopenta[1,2-a]benzene-1,3-dione	No
6	M11	2-(indol-3-ylmethylene)cyclopenta[1,2-a]benzene-1,3-dione	No
6	N11	3-(indol-3-ylmethylene)benzo[b]pyran-2,4-dione	YES
6	O11	11-phenylindeno[2,3-e]indeno[3,2-b]pyridine-10,12-dione	No
6	P11	11-(3-bromophenyl)indeno[2,3-e]indeno[3,2-b]pyridine-10,12-dione	No
6	A12	1-phenylbenzo[c]1,3-thiazolino[3,4-a]azoline-3,5-dione	No

6	B12	2-(3-(hydroxyimino)-2-hydrocyclopenta[2,3-a]benzenylidene)cyclopenta[1,2-a]ben zene-1,3-dione	No
6	C12	1,2,5-oxadiazolo[3,4-b]pyrazine-5,6-diamine	No
6	D12	ethyl 2-amino-4-methyl-5-(piperidylcarbonyl)thiophene-3-carboxylate	No
6	E12	ethyl 3a,8b-dihydroxy-2-methyl-4-oxoindano[2,1-d]2-pyrroline-3-carboxylate	No
6	F12	ethyl 2-amino-4-methyl-5-(morpholin-4-ylcarbonyl)thiophene-3-carboxylate	No
6	G12	methyl 7-(2H-benzo[3,4-d]1,3-dioxolan-5-yl)-5-methyl-3-oxo-4,7-dihydro-2H-1,3- thiazolidino[3,2-a]pyrimidine-6-carboxylate	No
6	H12	hexyl 6-(6-bromo(2H-benzo[d]1,3-dioxolan-5-yl))-4-methyl-2-oxo-1,3,6-trihydrop yrimidine-5-carboxylate	No
6	I12	11-indol-3-yl-3,3-dimethyl-2,3,4-trihydro-5H,10H,11H-benzo[b]benzo[2,1-f]1,4-d iazepin-1-one	No
6	J12	3-(3,3-dimethyl-1-oxo-2,3,4-trihydro-5H,10H,11H-benzo[b]benzo[2,1-f]1,4-diazep in-11-yl)chromen-4-one	No
6	K12	3-(3,3-dimethyl-1-oxo(2,3,4-trihydro-5H,10H,11H-benzo[b]benzo[2,1-f]1,4-diazep in-11-yl))-6-chlorochromen-4-one	No
6	L12	(4R)-2-(4-oxochromen-3-yl)-1,3-thiazolidine-4-carboxylic acid	No
6	M12	(4R)-2-[4-(trifluoromethyl)phenyl]-1,3-thiazolidine-4-carboxylic acid	No
6	N12	11-(4-bromophenyl)-3-phenyl-2,3,4-trihydro-5H,10H,11H-benzo[b]benzo[2,1-f]1,4- diazepin-1-one	YES
6	O12		No
6	P12	4-(5-bromo-2-fluorophenyl)-1,3,4-trihydrobenzo[h]quinolin-2-one	No
6	A13	({2-[dithiocarboxy(2-thienylmethyl)amino]ethyl}(2-thienylmethyl)amino)methaned ithioic acid, sodium salt, sodium salt	No
6	B13	2-[(tert-butyl)sulfonyl]-1,3-dibromo-5-methylbenzene	No
6	C13	[(2,6-dibromo-4-methylphenyl)sulfonyl]diethylamine	No
6	D13	2,2,6,6-tetramethyl-3-(2-thienylmethylene)azaperhydroin-4-one	No
6	E13	7-(4-methyl-1,3-thiazol-2-ylthio)heptanoic acid	No
6	F13		No
6	G13	(methylphenylamino)(phenylmethylthio)methane-1-thione	No
6	H13	2-{[2-(2-thienyl)-3-(2-thienylmethyl)imidazolidinyl]methyl}thiophene	No
6	I13	1,8-dichloro-15-oxahexacyclo[6.6.4.1<15,18>.0<1,17>.0<2,7>.0<9,14>]nonadeca-2(7),3,5,9(14),10,12-hexaene-16,19-dione	No
6	J13	1-{[(2-{[(2-oxopropylthio)thioxomethyl](2-thienylmethyl)amino}ethyl)(2-thienyl methyl)amino]thioxomethylthio}acetone	No
6	K13	3-[(tert-butyl)sulfonyl]-2-(methylsulfonyl)thiophene	No
6	L13	2-(2-aminophenylthio)-5-(ethylsulfonyl)-3-nitrothiophene	No
6	M13	2,5-bis(tert-butylthio)thiophene	No

6	N13	(methylphenylamino)(2-thienylmethylthio)methane-1-thione	YES
6	O13	[methyl(2-thienylmethyl)amino](2-thienylmethylthio)methane-1-thione	YES
6	P13	4-bromo-2-(4-bromo(2-thienyl))thiophene	No
6	A14	6-butylthio-2-phenyl-4-hydroimidazo[1,2-a]pyridine, bromide	No
6	B14	5-[1-methyl-1-benzylpyrrolidin-2-yl]-2-pyridylamine, iodide	No
6	C14	(tert-butoxy)-N-(5-methyl(2-thienyl))carboxamide	No
6	D14	ethoxy-N-(5-methyl(2-thienyl))carboxamide	No
6	E14	3-[(1Z)-2-(4-oxo-3-phenyl(3-hydroquinazolin-2-yl))vinyl]-6-chlorochromen-4-one	No
6	F14	5-{[5-(4-iodophenyl)(2-furyl)]methylene}-3-methyl-2-thioxo-1,3-thiazolidin-4-o ne	No
6	G14	1,2,3,9,9a-pentahydrocyclopenta[2,1-b]quinolin-3-ol, chloride	No
6	H14	7-acetyloxy-2-(3,4-diacetyloxyphenyl)-4-oxochromen-5-yl acetate	No
6	I14	2-(3,4-diacetyloxyphenyl)-4-oxo-7-[3,4,5-triacetyloxy-6-(acetyloxymethyl)(2H-3 ,4,5,6-tetrahydropyran-2-yloxy)]chromen-5-yl acetate	YES
6	J14	3,7-diacetyloxy-2-(3,4-diacetyloxyphenyl)-4-oxochromen-5-yl acetate	No
6	K14	2-(3,4-dihydroxyphenyl)-5,7-dihydroxychromen-4-one	No
6	L14	2-(3,4-dihydroxyphenyl)-5-hydroxy-7-[3,4,5-trihydroxy-6-(hydroxymethyl)(2H-3,4 ,5,6-tetrahydropyran-2-yloxy)]chromen-4-one	No
6	M14	(2S)-5,7-dihydroxy-2-phenylchroman-4-one	YES
6	N14	2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxychromen-4-one	YES
6	O14	7-((2R)-2,3-dihydroxy-3-methylbutoxy)-6-methylchromen-2-one	No
6	P14		YES
6	A15	2-(3,4-dihydroxyphenyl)-5,7-dihydroxy-3-{3,4,5-trihydroxy-6-[(3,4,5-trihydroxy -6-methyl(2H-3,4,5,6-tetrahydropyran-2-yloxy))methyl](2H-3,4,5,6-tetrahydropyr an-2-yloxy)}chromen-4-one	No
6	B15	methyl(2-oxa-6-azatricyclo[4.2.1.0<3,7>]non-8-yl)amine	No
6	C15	5-hydroxy-3-(4-methoxyphenyl)-7-[3,4,5-trihydroxy-6-(hydroxymethyl)(2H-3,4,5,6 -tetrahydropyran-2-yloxy)]chromen-4-one	No
6	D15	7-hydroxy-3-(4-methoxyphenyl)chromen-4-one	No
6	E15	xanthen-9-one	No
6	F15	7,8-dihydroxy-6-methoxychromen-2-one	No
6	G15	7-hydroxy-6-methoxy-3-(2-oxochromen-7-yloxy)chromen-2-one	No
6	H15	8-hydroxy-6-methoxy-7-(3-methylbut-2-enyloxy)chromen-2-one	No
6	I15	4-((1S,2S,7S,11S,16S,5R,9R,10R,14R,15R)-5,9,16-trihydroxy-2,15-dimethyltetracy clo[8.7.0.0<2,7>.0<11,15>]heptadec-14-yl)pentanoic acid	No

6	J15	ethyl 4-((1S,2S,7S,11S,16S,5R,9R,10R,14R,15R)-5,9,16-trihydroxy-2,15-dimethylt etracyclo[8.7.0.0<2,7>.0<11,15>]heptadec-14-yl)pentanoate	No
6	K15	methyl 4-((1S,2S,11S,16S,5R,7R,10R,14R,15R)-5,16-dihydroxy-2,15-dimethyltetrac yclo[8.7.0.0<2,7>.0<11,15>]heptadec-14-yl)pentanoate	No
6	L15	ethyl 4-((1S,2S,11S,16S,5R,7R,10R,14R,15R)-5,16-dihydroxy-2,15-dimethyltetracy clo[8.7.0.0<2,7>.0<11,15>]heptadec-14-yl)pentanoate	No
6	M15	5,9,13-trimethyl-3-oxatricyclo[8.3.0.0<2,6>]trideca-9,12-diene-4,11-dione	No
6	N15	6-methoxy-2-oxo-3-(2-oxochromen-7-yloxy)chromen-7-yl acetate	YES
6	O15	{3,4,5-triacetyloxy-6-[5-acetyloxy-3-(4-methoxyphenyl)-4-oxochromen-6-yloxy]-2 H-3,4,5,6-tetrahydropyran-2-yl}methyl acetate	No
6	P15	5-(6-acetyloxy-3,5,7-trimethoxy-4-oxochromen-2-yl)-2-methoxyphenyl acetate	No
6	A16	1-(3-hydroxyphenyl)-2-(methylamino)ethan-1-ol	No
6	B16	5-[(3,4,5-trimethoxyphenyl)methyl]pyrimidine-2,4-diamine	No
6	C16	[(4-aminophenyl)sulfonyl](5-methylisoxazol-3-yl)amine	No
6	D16	[2-(diphenylmethoxy)ethyl]dimethylamine	YES
6	E16	(1S,11S,14S)-17-hydroxy-14-(2-hydroxyacetyl)-2,15-dimethyltetracyclo[8.7.0.0<2 ,7>.0<11,15>]heptadeca-3,6-dien-5-one	No
6	F16	2-amino-9-[(2-hydroxyethoxy)methyl]hydropurin-6-one	No
6	G16	(1S,2S,19S,12R)-12,19-difluoro-11-hydroxy-8-(2-hydroxyacetyl)-6,6,9,13-tetrame thyl-5,7-dioxapentacyclo[10.8.0.0<2,9>.0<4,8>.0<13,18>]icosa-14,17-dien-16-one	No
6	H16	1-(2,4-dichlorophenyl)-1-[(2,4-dichlorophenyl)methoxy]-2-imidazolylethane	No
6	I16		No
6	J16	1-cyclopropyl-6-fluoro-4-oxo-7-piperazinylhydroquinoline-3-carboxylic acid	No
6	K16	3,8-dimethoxy-4-(methoxycarbonyl)-1,2,3,4,5,11,14,14a,4a,5a-decahydrobenzo[3,4 -g]indolo[2,3-a]quinolizin-2-yl 3,4,5-trimethoxybenzoate	No
6	L16	3-[(methylethyl)amino]-1-naphthyloxypropan-2-ol	No
6	M16	2-((2S,10S,11S,13S,15S,17S,1R,14R)-1-fluoro-17-hydroxy-2,13,15-trimethyl-5-oxo -14-propanoyloxytetracyclo[8.7.0.0<2,7>.0<11,15>]heptadeca-3,6-dien-14-yl)-2-o xoethyl propanoate	No
6	N16	1,3-dimethyl-1,3,7-trihydropurine-2,6-dione	No
6	O16	(2S)-2-[(4-{[(2-amino-4-oxohydropteridin-6-yl)methyl]amino}phenyl)carbonylamin o]pentanedioic acid	No
6	P16		No

6	A17	4-((2E)-3-phenylprop-2-enyl)-1-[bis(4-fluorophenyl)methyl]piperazine	No
6	B17	2-(2-methyl-5-nitroimidazolyl)ethan-1-ol	No
6	C17	1-(ethylsulfonyl)-2-(2-methyl-5-nitroimidazolyl)ethane	No
6	D17	[(2-amino-3,5-dibromophenyl)methyl]cyclohexylmethylamine	No
6	E17	(2S,5R,6R)-6-(2-amino-2-phenylacetylamino)-3,3-dimethyl-7-oxo-4-thia-1-azabicy clo[3.2.0]heptane-2-carboxylic acid	No
6	F17	7-acetyloxy-6-methoxy-2-oxochromen-8-yl acetate	No
6	G17	2-{[4-(tert-butyl)-2,6-dimethylphenyl]methyl}-2-imidazoline	No
6	H17	2-(2-hydroxy-1-methyleneethyl)-8,9-dimethoxy-1,2-dihydrochromano[3,4-b]furano[2,3-h]chroman-6-one	No
6	I17	2-[1-(bromomethyl)vinyl]-8,9-dimethoxy-1,2-dihydrochromano[3,4-b]furano[2,3-h] chroman-6-one	No
6	J17	2-(2-hydroxy-1-methyleneethyl)-8,9-dimethoxy-1,2-dihydro-12H-chromeno[3,4-b]fu rano[2,3-h]chromen-6-one	No
6	K17	((7aS,1R)perhydropyrrolizinyl)methyl 2,3-dihydroxy-2-(methylethyl)butanoate	No
6	L17	(7S,7aS)-7-hydroxy-3,5,6,7,7a-pentahydropyrrolizinyl 2-hydroxy-3-methoxy-2-(me thylethyl)butanoate	No
6	M17	4-hydroxy-1-methyl-2-oxohydropyridine-3-carbonitrile	No
6	N17	4-methoxy-1-methyl-2-oxohydropyridine-3-carbonitrile	No
6	O17	3-cyano-1-methyl-2-oxo-4-hydropyridyl acetate	No
6	P17	4-{(1E)-2-[3-(trifluoromethyl)phenyl]-2-azavinyl}phenyl methylsulfonate	No
6	A18	4-((1E)-2-(2H-benzo[3,4-d]1,3-dioxolan-5-yl)-1-azavinyl)phenyl 4-butylbenzenes ulfonate	No
6	B18	[4-(2H-benzo[3,4-d]1,3-dioxolen-5-ylmethyl)piperazinyl](cyclohexylamino)methan e-1-thione	No
6	C18	2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9-hexadecafluoro-N-(4-methyl(1,3-thiazol-2-yl))n onanamide	No
6	D18	2,2,3,3,4,4,5,5,6,6,7,7-dodecafluoro-N-(1,3-thiazol-2-yl)heptanamide	No
6	E18	6-chloro-2,2,3,3,4,4,5,5,6,6-decafluoro-N-(4-methyl(1,3-thiazol-2-yl))hexanami de	No
6	F18	9-chloro-2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9-hexadecafluoro-N-(4-methyl(1,3-thiazo l-2-yl))nonanamide	No
6	G18	methyl 4-(methoxycarbonyl)-3-methyl-5-(2,2,3,3,4,4,5,5,5-nonafluoropentanoylam ino)thiophene-2-carboxylate	No
6	H18	ethyl 5-(N,N-diethylcarbamoyl)-2-(2,2,3,3,4,4,4-heptafluorobutanoylamino)-4-me thylthiophene-3-carboxylate	No
6	I18	methylethyl 3-methyl-4-[(methylethyl)oxycarbonyl]-5-(2,2,3,3,4,4,5,5,5-nonaflu oropentanoylamino)thiophene-2-carboxylate	No
6	J18	5-({3-[(4-iodophenoxy)methyl]-4-methoxyphenyl}methylene)-2-thioxo-1,3-thiazoli din-4-one	No
6	K18	2-amino-3-(2,5-difluorophenyl)propanoic acid	No

6	L18	4-[(4-fluorophenyl)methylene]-2-phenyl-1,3-oxazolin-5-one	No
6	M18	N-[4-(acetylamino)(1,2,5-oxadiazol-3-yl)]-2-(4,6-diaminopyrimidin-2-ylthio)ace tamide	No
6	N18	2-[5-(carbamoylmethylthio)-1,3,4-thiadiazol-2-ylthio]acetamide	No
6	O18	2-(8-quinolylthio)acetamide	No
6	P18	2-benzothiazol-2-ylthioacetamide	No
6	A19	N-(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)(3-chloro-6-nitrobenzo[b]thiophen-2-yl)ca rboxamide	No
6	B19	4-bromo-3-nitropyrazol-5-yl 4-(4-fluorophenyl)piperazinyl ketone	No
6	C19	(4-bromo-3-nitropyrazol-5-yl)-N-(3-cyano(4,5,6,7,8-pentahydrocyclohepta[1,2-d] thiophen-2-yl))carboxamide	YES
6	D19	(4-bromo-3-nitropyrazol-5-yl)-N-(3-cyano(4,5,6-trihydrocyclopenta[1,2-d]thioph en-2-yl))carboxamide	No
6	E19	N-butyl-2-(4-nitropyrazolyl)acetamide	No
6	F19	1-[(2,4-dichlorophenyl)methyl]-3-nitro-1,2,4-triazole	No
6	G19	4-chloro-5-methyl-1,3-dinitropyrazole	No
6	H19	1-cyclopentyloxy-4-[5-(4-cyclopentyloxy-3-methoxyphenyl)(1,3-thiazolo[5,4-d]1, 3-thiazol-2-yl)]-2-methoxybenzene	No
6	I19	2,5-bis(4-ethylphenyl)-1,3-thiazolo[5,4-d]1,3-thiazole	No
6	J19	4-(methylethoxy)-1-{5-[4-(methylethoxy)phenyl](1,3-thiazolo[5,4-d]1,3-thiazol- 2-yl)}benzene	No
6	K19	4-[5-(3,4-dimethoxyphenyl)(1,3-thiazolo[5,4-d]1,3-thiazol-2-yl)]-1,2-dimethoxy benzene	No
6	L19	2,5-bis(4-bromophenyl)-1,3-thiazolo[5,4-d]1,3-thiazole	No
6	M19	(4-{5-[4-(dimethylamino)phenyl](1,3-thiazolo[5,4-d]1,3-thiazol-2-yl)}phenyl)di methylamine	No
6	N19	4-[5-(4-hydroxy-3-methoxyphenyl)(1,3-thiazolo[5,4-d]1,3-thiazol-2-yl)]-2-metho xyphenol	No
6	O19	2,5-bis(1,3-diphenylpyrazol-4-yl)-1,3-thiazolo[5,4-d]1,3-thiazole	No
6	P19	4-[5-(4-hydroxy-3,5-dimethoxyphenyl)(1,3-thiazolo[5,4-d]1,3-thiazol-2-yl)]-2,6 -dimethoxyphenol	No
6	A20	1,2,3-trimethoxy-5-[5-(3,4,5-trimethoxyphenyl)(1,3-thiazolo[5,4-d]1,3-thiazol- 2-yl)]benzene	No
6	B20	2-(6-chloro-2-fluorophenyl)-5-(2-chloro-6-fluorophenyl)-1,3-thiazolo[5,4-d]1,3 -thiazole	No
6	C20	2,5-di(2-thienyl)-1,3-thiazolo[5,4-d]1,3-thiazole	No
6	D20	2,5-bis(4-fluorophenyl)-1,3-thiazolo[5,4-d]1,3-thiazole	No
6	E20	2,5-bis(4-chlorophenyl)-1,3-thiazolo[5,4-d]1,3-thiazole	No
6	F20	2,5-bis(2,4-dichlorophenyl)-1,3-thiazolo[5,4-d]1,3-thiazole	No
6	G20	N-[4-(2-imino-4-oxo-1,3-thiazolidin-3-yl)-1,2,5-oxadiazol-3-yl]acetamide	No
6	H20	5-amino-7-(4-chlorophenyl)-2-[(4-chlorophenyl)methylene]-3-oxo-4,7-dihydro-1,3 -thiazolidino[3,2-a]pyridine-6,8-dicarbonitrile	No

6	I20	5-amino-7-(4-bromophenyl)-2-[(4-bromophenyl)methylene]-3-oxo-4,7-dihydro-1,3-t hiazolidino[3,2-a]pyridine-6,8-dicarbonitrile	No
6	J20	5-amino-7-(5-bromo-2-hydroxyphenyl)-2-[(5-bromo-2-hydroxyphenyl)methylene]-3-o xo-4,7-dihydro-1,3-thiazolidino[3,2-a]pyridine-6,8-dicarbonitrile	No
6	K20	5-amino-3-oxo-7-(3,4,5-trimethoxyphenyl)-2-[(3,4,5-trimethoxyphenyl)methylene] -4,7-dihydro-1,3-thiazolidino[3,2-a]pyridine-6,8-dicarbonitrile	No
6	L20	5-amino-7-(4-hydroxyphenyl)-2-[(4-hydroxyphenyl)methylene]-3-oxo-4,7-dihydro-1 ,3-thiazolidino[3,2-a]pyridine-6,8-dicarbonitrile	No
6	M20	5-amino-7-(2,4-dihydroxyphenyl)-2-[(2,4-dihydroxyphenyl)methylene]-3-oxo-4,7-d ihydro-1,3-thiazolidino[3,2-a]pyridine-6,8-dicarbonitrile	No
6	N20	5-amino-7-(4-hydroxy-3,5-dimethoxyphenyl)-2-[(4-hydroxy-3,5-dimethoxyphenyl)me thylene]-3-oxo-4,7-dihydro-1,3-thiazolidino[3,2-a]pyridine-6,8-dicarbonitrile	No
6	O20	5-amino-7-(4-fluorophenyl)-2-[(4-fluorophenyl)methylene]-3-oxo-4,7-dihydro-1,3 -thiazolidino[3,2-a]pyridine-6,8-dicarbonitrile	No
6	P20	3-(4-amino(1,2,5-oxadiazol-3-yl))-5-[(4-fluorophenyl)methylene]-2-imino-1,3-th iazolidin-4-one	No
6	A21	N-[4-(acetylamino)(1,2,5-oxadiazol-3-yl)]-2-(3-amino(1H-1,2,4-triazol-5-ylthio))acetamide	No
6	B21	5-[(4-ethoxy-2-nitrophenyl)amino]-2-(hydroxymethyl)oxolane-3,4-diol	No
6	C21	2-[(4-fluorophenyl)methylthio]-4-phenyl-5,6,7-trihydrocyclopenta[1,2-b]pyridin e-3-carbonitrile	No
6	D21	6-amino-3-(methoxymethyl)-4-(3,4,5-trimethoxyphenyl)-4H-pyrano[2,3-c]pyrazole- 5-carbonitrile	No
6	E21	6-amino-4-(3-furyl)-3-methyl-4H-pyrano[3,2-d]pyrazole-5-carbonitrile	No
6	F21	8-({2-[4-(tert-butyl)phenoxy]ethyl}amino)-1,3,7-trimethyl-1,3,7-trihydropurine -2,6-dione	No
6	G21	N-(5-ethyl(1,3,4-thiadiazol-2-yl))-2,2,3,3,4,4,5,5,5-nonafluoropentanamide	No
6	H21	4-[8-(methylethyl)-3,4,5,3a,9b-pentahydrocyclopenta[1,2-c]quinolin-4-yl]benzoi c acid	No
6	I21	5-{[5-(4-iodophenyl)(2-furyl)]methylene}-3-benzyl-2-thioxo-1,3-thiazolidin-4-o ne	No
6	J21	2-[3-(carboxymethyl)adamantanyl]acetic acid	No
6	K21	4-phenyl-2-(4-phenyl(2-pyridyl))pyridine	No
6	L21	1-cyclohexylazoline-2,5-dione	No
6	M21	3-amino-2-thioxo-1,3-thiazolidin-4-one	No
6	N21	5-imino-4,6-dihydro-3H-1,2,3-triazolo[5,4-d]pyrimidin-7-one	No
6	O21	methyl (2S)-2-amino-5-{[imino(nitroamino)methyl]amino}pentanoate, chloride	No

6	P21	(2R)-2-amino-3-methyl-3-sulfanylbutanoic acid	No
6	A22	2-methylbenzo[d]1,3-oxazin-4-one	No
6	B22	2-(benzimidazol-2-ylmethylthio)-6-ethoxybenzothiazole	No
6	C22	3-amino-5-[(4-methoxyphenyl)methylene]-2-thioxo-1,3-thiazolidin-4-one	No
6	D22	5-[(5-iodo-2-furyl)methylene]-1,3-thiazolidine-2,4-dione	No
6	E22	5-({5-[3-(trifluoromethyl)phenyl]-2-furyl}methylene)-1,3-thiazolidine-2,4-dion e	No
6	F22	2-[5-(2-furylmethylene)-4-oxo-2-thioxo-1,3-thiazolidin-3-yl]acetic acid	No
6	G22	3-amino-3-thioxo-2-(triphenylylidene)propanenitrile	No
6	H22	4-((1E)-3-cyclohexylthio-3-oxoprop-1-enyl)benzenecarbonitrile	No
6	I22	4-((1E)-2-(2-thienyl)-1-azavinyl)phenyl 4-fluorobenzenesulfonate	No
6	J22	4-((1E)-2-(2-thienyl)-1-azavinyl)phenyl 2,5-dichlorobenzenesulfonate	No
6	K22	(2E)-3-(2-chlorophenyl)-2-phenylprop-2-enenitrile	No
6	L22	(2E)-3-naphthyl-2-phenylprop-2-enenitrile	No
6	M22	(2Z)-2-(4-bromophenyl)-3-naphthylprop-2-enenitrile	No
6	N22	(2Z)-3-(2,4-dichlorophenyl)-2-(4-bromophenyl)prop-2-enenitrile	No
6	O22	10-{3-[4-(4-phenyl(1,3-thiazol-2-yl))piperazinyl]propyl}-2-(trifluoromethyl)ph enothiazine	No
6	P22	3-(4-chlorophenyl)-5-fluoren-9-ylthio-4-benzyl-1,2,4-triazole	No
Plate	**Well**	**IUPAC NAME**	**Inhibitor Y/N**
7	A03	2-[3-(2-oxo-2-piperidylethylthio)quinoxalin-2-ylthio]-1-piperidylethan-1-one	No
7	B03	2,5-bis((2E)-3-phenylprop-2-enylthio)-1,3,4-thiadiazole	No
7	C03	2-(5-(2-furyl)(1,3,4-oxadiazol-2-ylthio))-N,N-dimethylacetamide	No
7	D03	3-(4-methoxyphenyl)-4-benzyl-1-[(4-phenylpiperidyl)methyl]-1,2,4-triazoline-5- thione	No
7	E03	phenyl({2-[4-phenyl-5-benzyl(1,2,4-triazol-3-ylthio)]ethyl}sulfonyl)amine	No
7	F03	4,5,6-trimethoxy-7-[(1-phenyl(1,2,3,4-tetraazol-5-ylthio))methyl]-3-hydroisobe nzofuran-1-one	No
7	G03	6-amino-2-(dicyanomethyl)-4-(3,4-dimethoxyphenyl)-1,4-dihydropyridine-3,5-dica rbonitrile	No
7	H03	2-[(1E)-2-(4-chlorophenyl)-1-cyanovinyl]-4-amino-6-(cyanomethyl)pyrimidine-5-c arbonitrile	No
7	I03	3-hydroxy-1-methyl-3-(5-methyl-2-oxocyclohexyl)indolin-2-one	No
7	J03	5,7-dibutyl-2-phenyl-8-hydropyrazolo[1,5-a]pyrimidine	No
7	K03	3-[(4-hydroxyphenyl)diazenyl]-5-(methylsulfonyl)-1H-1,2,4-triazole	No
7	L03	1-[(2,4-dichlorophenyl)methyl]-5-methyl-1,2,3,4-tetraazole	No
7	M03	5-(4-methoxyphenyl)-2-(morpholin-4-ylmethyl)-4-benzyl-1,2,4-triazolidine-3-thi one	No

7	N03	2-(6-ethoxybenzothiazol-2-ylthio)-1-(5-methyl(2-thienyl))ethan-1-one	No
7	O03	4-methoxy-1-(4-phenyl-5-{[4-(1,1,2,2-tetrafluoroethoxy)phenyl]methoxy}(1,2,4-t riazol-3-yl))benzene	No
7	P03	(dimethylamino)bis(2-phenylhydrazino)phosphino-1-one	No
7	A04	3-{[(4-chlorophenyl)methylthio]methyl}-1,2,4-triazolin-5-one	No
7	B04	5-[(2-chlorophenyl)methylthio]-1,3,4-thiadiazole-2-thiol	No
7	C04	5-(3,4-dimethoxyphenyl)-1,3,4-oxadiazole-2-thiol	No
7	D04	5-(naphthylmethyl)-1,3,4-oxadiazole-2-thiol	No
7	E04	4-(4-fluorophenyl)-1,3-thiazole-2-thiol	No
7	F04	[2-(5-methyl(2-furyl))-2-oxoethyl]thiocarbonitrile	No
7	G04	5,6-dimethyl-4-phenyl-1,3,4-thiadiazine-2-thiol	YES
7	H04	11-{[(dimethylamino)sulfonyl]amino}undecanoic acid	YES
7	I04	1,1,1-trichloro-3-(1-methylbenzimidazol-2-yl)propan-2-ol	No
7	J04	5-(2-furyl)-4-methyl-1,2,4-triazole-3-thiol	No
7	K04	5-[(4-fluorophenyl)methylene]-1,3-thiazolidine-2,4-dione	No
7	L04	5-(2-oxo(1H-benzo[d]azolin-3-ylidene))-2-thioxo-1,3-thiazolidin-4-one	No
7	M04	5-(2H-benzo[3,4-d]1,3-dioxolen-5-ylmethylene)-1,3-thiazolidine-2,4-dione	No
7	N04	6-methyl-1H-1,2,4-triazolino[4,5-b]1,2,4-triazin-7-one	No
7	O04	(2Z)-2-methyl-3-[(6-methyl-5-oxo(4H-1,2,4-triazin-3-yl))amino]-3-azaprop-2-eno ic acid	No
7	P04	2-[4-(methylethyl)phenyl]-1,3-thiazolidine-4-carboxylic acid	No
7	A05	2-(3,5-dioxo-2H,4H-1,2,4-triazin-6-ylthio)ethyl hydroxysulfonate	No
7	B05	2-(3,5-dioxo-2H,4H-1,2,4-triazin-6-ylthio)ethanenitrile	No
7	C05	3-(4-methoxyphenoxy)-4-oxochromen-7-yl 2,2-dimethylpropanoate	No
7	D05	4-benzothiazol-2-ylthiobutanoic acid	No
7	E05	methylethyl 2-[(3,5-dioxo-2H,4H-1,2,4-triazin-6-yl)amino]propanoate	No
7	F05	5-(1-hexyl-2-oxobenzo[d]azolidin-3-ylidene)-1,3-thiazolidine-2,4-dione	No
7	G05	2,5-dioxoazolidinyl 6-(1,3-dioxobenzo[c]azolidin-2-yl)hexanoate	No
7	H05	2-[((1E)-1-methyl-3-oxobut-1-enyl)amino]propanoic acid	No
7	I05	5-bromo-1-methylbenzo[d]azoline-2,3-dione	No
7	J05	2-(cyclohexylamino)-3-hydropyrimidin-4-one	No
7	K05	5-{[2-(dimethylamino)ethyl]amino}-6-methyl-2H-1,2,4-triazin-3-one	No
7	L05	2,5-dioxoazolidinyl 2-(1,3-dioxobenzo[c]azolidin-2-yl)-3-methylbutanoate	No
7	M05	6-(phenylmethylthio)-5-thioxo-2H,4H-1,2,4-triazin-3-one	No
7	N05	methyl 2-[(3,5-dioxo-2H,4H-1,2,4-triazin-6-yl)amino]propanoate	No
7	O05	1-(2,3-dichlorophenyl)-3-chloro-4-(prop-2-enylamino)azoline-2,5-dione	No

7	P05	1-(2,4-dichlorophenyl)-3,4-dichloroazoline-2,5-dione	No
7	A06	1-(2,5-dichlorophenyl)-3,4-dichloroazoline-2,5-dione	No
7	B06	1-(3,4-dichlorophenyl)-3,4-dichloroazoline-2,5-dione	No
7	C06	1-(3,4-dichlorophenyl)azoline-2,5-dione	No
7	D06	3-methyl-2-(quinazolin-4-ylamino)butanoic acid	No
7	E06	6,6-dihydroxy-1,3,6-trihydropyrimidine-2,4,5-trione	No
7	F06	1-(4-chlorophenyl)-3,4-dimethylpyrano[5,6-d]pyrazol-6-one	No
7	G06	4-(6-chloropyridazin-3-yl)morpholine	No
7	H06	1,3,7-trimethyl-8-pyrrolidinyl-1,3,7-trihydropurine-2,6-dione	No
7	I06	2-[2-(4-chlorophenoxy)ethylthio]pyrimidine-4,6-diamine	No
7	J06	2-butylthio-6-methylhydropyrimidin-4-one	No
7	K06	2-(6-methyl-4-oxohydropyrimidin-2-ylthio)acetamide	No
7	L06	[imino(phenylamino)methyl]phenylamine	No
7	M06	3-nitro-1-[(2,4,6-trimethylphenyl)sulfonyl]-1,2,4-triazole	No
7	N06	N-{(1Z)-1-[(4-methylquinazolin-2-yl)amino]-3-oxo-2-azapent-1-enyl}propanamide	OFFSCALE
7	O06	5-[(2,4-dichlorophenoxy)methyl](2-furyl) 4-bromopyrazolyl ketone	No
7	P06	5-[(2,5-dichlorophenoxy)methyl]furan-2-carbohydrazide	No
7	A07	5-[(4-iodophenoxy)methyl](2-furyl) pyrrolidinyl ketone	No
7	B07	4-(2-furylcarbonyl)piperazinyl 5-(indan-5-yloxymethyl)(2-furyl) ketone	No
7	C07	5-(indan-5-yloxymethyl)furan-2-carbohydrazide	No
7	D07	{5-[(2,5-dichlorophenoxy)methyl](2-furyl)}-N-cyclopentylcarboxamide	No
7	E07	N-cyclooctyl{5-[(2,3,5,6-tetrafluorophenoxy)methyl](2-furyl)}carboxamide	No
7	F07	N-cyclooctyl[5-(indan-5-yloxymethyl)(2-furyl)]carboxamide	No
7	G07	6-bromo-2-(5-chloro(2-thienyl))quinoline-4-carboxylic acid	YES
7	H07	5-[(4-fluorophenoxy)methyl]furan-2-carbohydrazide	No
7	I07	6-bromo-2-(2-furyl)quinoline-4-carboxylic acid	YES
7	J07	6-bromo-2-[4-(methylethoxy)phenyl]quinoline-4-carboxylic acid	No
7	K07	2-(2H-benzo[3,4-d]1,3-dioxolen-5-yl)-6-bromoquinoline-4-carboxylic acid	No
7	L07	6-bromo-2-(5-methyl(2-thienyl))quinoline-4-carboxylic acid	No
7	M07	6-bromo-2-(4-ethylphenyl)quinoline-4-carboxylic acid	No
7	N07	2-(2-chlorophenyl)quinoline-4-carboxylic acid	No
7	O07	2-(2-thienylsulfonyl)thiophene	No
7	P07	ethyl 2-(4-methyl-1,3-thiazol-2-ylthio)acetate	No
7	A08	2-{[methyl(2-thienylmethyl)amino]thioxomethylthio}ethan-1-ol	No
7	B08	2-(phenylsulfonyl)thiophene	No
7	C08	3-(phenylsulfonyl)thiophene	No
7	D08	2-(tert-butylthio)-1,3-dibromobenzene	No

7	E08	3-(tert-butylthio)thiophene-2,5-dicarboxylic acid	No
7	F08	1-methoxy-4-(2-thienylthio)benzene	No
7	G08	8-bromo-1,2,3,4,10-pentahydropyridino[1,2-a]benzimidazole	No
7	H08	5-ethylthio-2-(5-ethylthio(2-thienyl)thio)thiophene	No
7	I08	(2-thienylmethyl){2-[(2-thienylmethyl)amino]ethyl}amine	No
7	J08	5-(tert-butylthio)-2-(2,4-dinitrophenylthio)thiophene	No
7	K08	2,5-bis(2,2,6,6-tetramethyl-4-1,2,5,6-tetrahydropyridyl)thiophene	No
7	L08	(N-cyclohexylcarbamoyl)methyl acetate	No
7	M08	2-amino-2-(hydroxyimino)-N-(4-sulfamoylphenyl)acetamide	No
7	N08	2-(2-piperidylacetylamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxamide	No
7	O08	[(4R,5R)-5-(N,N-dimethylcarbamoyl)-2,2-dimethyl(1,3-dioxolan-4-yl)]-N,N-dimeth ylcarboxamide	No
7	P08	2-(2-morpholin-4-ylacetylamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxam ide	No
7	A09	2-[2-(phenylamino)-2-thioxoacetylamino]-4,5,6-trihydrocyclopenta[1,2-b]thiophe ne-3-carboxamide	No
7	B09	2-[2-(diethylamino)acetylamino]-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxam ide	No
7	C09	4-methyl-1-(4,5,6,7-tetrahydroindolylethoxy)benzene	No
7	D09	1-(ethynylcyclohexyloxy)-1-(2-phenylpyrrolyl)ethane	No
7	E09	1-[(2-(2-thienyl)pyrrolyl)ethoxy]prop-2-yne	No
7	F09	1-[(2-phenylpyrrolyl)ethoxy]prop-2-yne	No
7	G09	[(4-chlorophenyl)sulfonyl](2,2,2-trichloro-1-hydroxyethyl)amine	No
7	H09	(phenylsulfonyl)(2,2,2-trichloro-1-hydroxyethyl)amine	No
7	I09	(phenylsulfonyl)(2,2,2-trichloro-1-methoxyethyl)amine	No
7	J09	2-amino-4-propyl-1,3-thiazine-6-thione	No
7	K09	3,3-dimethyl-2-phenyl-1-pyrrolin-5-ol	No
7	L09	4-chloro-1-{[2-(trichloromethyl)(1,3-oxazolidin-3-yl)]sulfonyl}benzene	No
7	M09	2,2-dimethyl-3H-benzo[e]1,3-oxazin-4-one	No
7	N09	1-(methylethoxy)-1-(2-phenylpyrrolyl)ethane	No
7	O09	diethyl{4-[(2-phenylpyrrolyl)ethoxy]but-2-ynyl}amine	No
7	P09	(2Z)-4-hydroxy-4-methyl-3-pyrazolylpent-2-enenitrile	No
7	A10	2-amino-4-phenyl-1,3-thiazine-6-thione	No
7	B10	4-(2,2-dichlorovinyl)-1,3-thiazole-2-ylamine	No
7	C10	6-(2,2-dichlorovinyl)-4-methylpyran-2-one	No
7	D10	6-(2,2-dichlorovinyl)-4-ethyl-3-methylpyran-2-one	No
7	E10	4-chloro-2-{[(4-methylphenyl)sulfonyl]ethyl}benzenisocyanide	No
7	F10	2-imino-5-[(3-methyl(2-thienyl))methylene]-1,3-thiazolidin-4-one	No
7	G10	N-{4-[(3-chlorobenzo[b]thiophen-2-yl)carbonylamino]-1,2,5-oxadiazol-3-yl}aceta mide	No
7	H10	N-(5-methyl(1,3,4-thiadiazol-2-yl))-2-thienylcarboxamide	No

7	I10	[(4-chlorophenyl)sulfonyl](6-methoxybenzothiazol-2-yl)amine	No
7	J10	4-(2,4-dichlorophenoxy)-N-(methoxycarbonylamino)butanamide	No
7	K10	N-(2-cyclohex-1-enylethyl)-N'-(2-cyclohex-1-enylethyl)pentane-1,5-diamide	No
7	L10	1-(3,5-dichlorophenyl)azoline-2,5-dione	No
7	M10	5-(dimethylamino)-6-methylpyrimidine-2,4-diol	No
7	N10	(2E)-3-[N-(1,3-dioxobenzo[c]azolin-2-yl)carbamoyl]prop-2-enoic acid	No
7	O10	ethyl (2E)-3-(N-(1,3-thiazol-2-yl)carbamoyl)prop-2-enoate	No
7	P10	ethyl (2E)-3-[N-(3-carbamoyl-4,5-dimethyl(2-thienyl))carbamoyl]prop-2-enoate	No
7	A11	(2E)-4-[4-((2E)-3-carboxyprop-2-enoyl)piperazinyl]-4-oxobut-2-enoic acid	No
7	B11	ethyl (2E)-3-[N-(2-cyclohex-1-enylethyl)carbamoyl]prop-2-enoate	No
7	C11	bisbenzylhydroxylamine	No
7	D11	3-(4-pyridyl)-4,5-dihydro-2H-benzo[g]indazole, methanesulfonic acid	No
7	E11	2-phenylbenzoxazole	No
7	F11	6-phenylphenanthridine-3,8-diamine	No
7	G11	(1S,5S,10S,11S,14S,15S,2R)-14-acetyl-2,15-dimethyltetracyclo[8.7.0.0<2,7>.0<11 ,15>]heptadec-7-en-5-yl acetate	No
7	H11	6,8,9-trichloro-3,4,5,3a,9b-pentahydrocyclopenta[1,2-c]quinoline-4-carboxylic acid	No
7	I11	3-[4-((1E)-2-(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)-2-azavinyl)phenoxy]thietane	No
7	J11	1-(2-phenyl-1,2,3-triazol-4-yl)butane-1,2,3,4-tetraol	No
7	K11	3-chlorobenzo[b]thiophen-2-yl 4-methylpiperazinyl ketone	No
7	L11	1-(5-nitro-1,2,3,4-tetraazol-2-yl)acetone	No
7	M11	2-[2-amino-5-(4-chlorophenyl)-6-(trifluoromethyl)pyrimidin-4-yl]-5-[(4-chlorop henyl)methoxy]phenol	No
7	N11	5-[(4-chlorophenyl)methoxy]-2-[5-(4-chlorophenyl)pyrimidin-4-yl]phenol	No
7	O11	2-[2-amino-5-(2-methyl(1,3-thiazol-4-yl))pyrimidin-4-yl]-4-ethyl-5-methoxyphen ol	No
7	P11	2-(2-amino-5-(1,3-thiazol-4-yl)pyrimidin-4-yl)-5-methoxyphenol	No
7	A12	5-[2-amino-5-(2-methyl(1,3-thiazol-4-yl))-6-(trifluoromethyl)pyrimidin-4-yl]-2 H-benzo[d]1,3-dioxolan-4-ol	No
7	B12	5-[2-methyl-5-(2-methyl(1,3-thiazol-4-yl))-6-(trifluoromethyl)pyrimidin-4-yl]- 2H-benzo[d]1,3-dioxolan-4-ol	No
7	C12	5-[2-amino-5-(2-methyl(1,3-thiazol-4-yl))pyrimidin-4-yl]-2H-benzo[d]1,3-dioxol an-4-ol	No
7	D12	5-[2-methyl-5-(2-methyl(1,3-thiazol-4-yl))pyrimidin-4-yl]-2H-benzo[d]1,3-dioxo lan-4-ol	No

7	E12	5-methoxy-4-methyl-2-[2-methyl-5-(2-methyl(1,3-thiazol-4-yl))-6-(trifluorometh yl)pyrimidin-4-yl]phenol	No
7	F12	3-[5-(1-ethyl-2-oxobenzo[d]azolin-3-ylidene)-4-oxo-2-thioxo-1,3-thiazolidin-3- yl]thiolane-1,1-dione	No
7	G12	3,5,6,7,8-pentahydrobenzo[b]thiopheno[2,3-d]pyrimidin-4-one	No
7	H12	(2E)-2-benzothiazol-2-yl-3-[5-(4-fluorophenyl)(2-furyl)]prop-2-enenitrile	No
7	I12	(2E)-2-benzothiazol-2-yl-3-[5-(3-bromophenyl)(2-furyl)]prop-2-enenitrile	No
7	J12	6-methyl-2-(4-methylphenyl)-4-hydroimidazo[1,2-a]pyridine	No
7	K12	{[4-(6-chloro-4-hydroimidazo[1,2-a]pyridin-2-yl)phenyl]sulfonyl}azaperhydroepi ne	YES
7	L12	4-(4-fluorophenyl)-2-(phenylazamethylene)-3-(3-pyridylmethyl)-1,3-thiazoline	No
7	M12	6-chloro-2-(4-fluorophenyl)-4-hydroimidazo[1,2-a]pyridine	No
7	N12	3,4-diphenyl-2-(phenylazamethylene)-1,3-thiazoline	No
7	O12	(2Z)-3-[5-(4-bromophenyl)(2-furyl)]-2-(phenylsulfonyl)prop-2-enenitrile	No
7	P12	4-(4-oxo-2-thioxo-1,3-thiazolidin-3-yl)butanoic acid	No
7	A13	5-[(3-methyl(2-thienyl))methylene]-2-piperidyl-1,3-thiazolin-4-one	No
7	B13	4-phenyl-2-(phenylazamethylene)-3-(2-phenylethyl)-1,3-thiazoline	No
7	C13	2-fluoro-1-methoxy-4-[3-phenyl-2-(phenylazamethylene)(1,3-thiazolin-4-yl)]benz ene	No
7	D13	4-phenyl-2-(phenylazamethylene)-3-benzyl-1,3-thiazoline	No
7	E13	1-[3-(dimethylamino)propyl]-5-(2-furyl)-3-hydroxy-4-(2-thienylcarbonyl)-3-pyrr olin-2-one	No
7	F13	(2E)-2-cyano-3-(3-methyl(2-thienyl))-N-(2-piperidylethyl)prop-2-enamide	No
7	G13	1-[2-(dimethylamino)ethyl]-5-(2-furyl)-3-hydroxy-4-(2-thienylcarbonyl)-3-pyrro lin-2-one	No
7	H13	2-(2-methylpropyl)-5-morpholin-4-yl-1,3-oxazole-4-carbonitrile	No
7	I13	1-[4-cyano-2-(2-methylpropyl)-1,3-oxazol-5-yl]piperidine-4-carboxamide	No
7	J13	8-methyl-2-(4-methylphenyl)-4-hydroimidazo[1,2-a]pyridine	No
7	K13	7-(4-methoxyphenyl)-2-oxobenzo[3,4-d]1,3-oxathiolan-5-yl (2E)-3-(4-methoxyphen yl)prop-2-enoate	No
7	L13	methyl 4-methyl-2-oxo-6-(2-thienyl)-1,3,6-trihydropyrimidine-5-carboxylate	No
7	M13	4-chlorophenylthio 2-furyl ketone	No
7	N13	2-(2,6-dimethylmorpholin-4-yl)-5-(5-bromo-2-oxo-1-prop-2-enylbenzo[d]azolin-3- ylidene)-1,3-thiazolin-4-one	No
7	O13	1-benzylbenzimidazole-2-ylamine	No

7	P13	5-{[2-(cyclohexylmethylamino)-4-oxo(5-hydropyridino[1,2-a]pyrimidin-3-yl)]meth ylene}-3-(oxolan-2-ylmethyl)-2-thioxo-1,3-thiazolidin-4-one	No
7	A14	2-(cyclohexylmethylamino)-4-oxo-5-hydropyridino[1,2-a]pyrimidine-3-carbaldehyd e	No
7	B14	2-(3-methylpiperidyl)-4-oxo-5-hydropyridino[1,2-a]pyrimidine-3-carbaldehyde	No
7	C14	3-hydroxy-1-(2-morpholin-4-ylethyl)-5-(2-thienyl)-4-(2-thienylcarbonyl)-3-pyrr olin-2-one	No
7	D14	5-[(oxolan-2-ylmethyl)amino]-2-phenyl-1,3-oxazole-4-carbonitrile	OFFSCALE
7	E14	4-bromophenyl 2-(4-fluorophenoxy)acetate	No
7	F14	5-(2-furyl)-4-(2-furylcarbonyl)-3-hydroxy-1-(3-morpholin-4-ylpropyl)-3-pyrroli n-2-one	No
7	G14	1-[3-(dimethylamino)propyl]-5-(2-furyl)-4-(2-furylcarbonyl)-3-hydroxy-3-pyrrol in-2-one	No
7	H14	1-[3-(dimethylamino)propyl]-4-(2-furylcarbonyl)-3-hydroxy-5-(2-thienyl)-3-pyrr olin-2-one	No
7	I14	1-[3-(dimethylamino)propyl]-4-(2-furylcarbonyl)-3-hydroxy-5-(5-methyl(2-furyl))-3-pyrrolin-2-one	No
7	J14	4-(2-furylcarbonyl)-3-hydroxy-5-(5-methyl(2-furyl))-1-(2-morpholin-4-ylethyl)- 3-pyrrolin-2-one	No
7	K14	5-(2-furyl)-4-(2-furylcarbonyl)-3-hydroxy-1-(2-morpholin-4-ylethyl)-3-pyrrolin -2-one	No
7	L14	3-hydroxy-1-(3-morpholin-4-ylpropyl)-5-(2-thienyl)-4-(2-thienylcarbonyl)-3-pyr rolin-2-one	No
7	M14	1-[3-(dimethylamino)propyl]-3-hydroxy-5-(2-thienyl)-4-(2-thienylcarbonyl)-3-py rrolin-2-one	No
7	N14	4-{[4-(6-chloro-4-hydroimidazo[1,2-a]pyridin-2-yl)phenyl]sulfonyl}morpholine	No
7	O14	5-(2H-chromen-3-ylmethylene)-2-morpholin-4-yl-1,3-thiazolin-4-one	No
7	P14	3-(2H-chromen-3-yl)(2Z)-2-cyano-N-cyclohexylprop-2-enamide	No
7	A15	(2E)-N-(1,1-dioxothiolan-3-yl)-2-cyano-3-(2-methyl(2H-chromen-3-yl))prop-2-ena mide	No
7	B15	3-(2H-chromen-3-yl)(2Z)-N-(1,1-dioxothiolan-3-yl)-2-cyanoprop-2-enamide	No
7	C15	3-(2H-chromen-3-yl)(2Z)-2-cyano-N-prop-2-enylprop-2-enamide	No
7	D15	7-(4-methoxyphenyl)-2-oxobenzo[3,4-d]1,3-oxathiolen-5-yl 3,4,5-trimethoxybenzo ate	No
7	E15	1-[2-(tert-butyl)-4-cyano-1,3-oxazol-5-yl]piperidine-4-carboxamide	No
7	F15	3-(5-{[2-(cyclohexylmethylamino)-4-oxo(5-hydropyridino[1,2-a]pyrimidin-3-yl)]m ethylene}-4-oxo-2-thioxo-1,3-thiazolidin-3-yl)thiolane-1,1-dione	No
7	G15	3-((1E)-3-(3-pyridyl)-2-azaprop-1-enyl)-7-methyl-2-[(3-pyridylmethyl)amino]-5- hydropyridino[1,2-a]pyrimidin-4-one	No

7	H15	5-[(2-morpholin-4-yl-4-oxo(5-hydropyridino[1,2-a]pyrimidin-3-yl))methylene]-3- (oxolan-2-ylmethyl)-2-thioxo-1,3-thiazolidin-4-one	No
7	I15	3-((1E)-3-(2-furyl)-2-azaprop-1-enyl)-2-[(2-furylmethyl)amino]-5-hydropyridino [1,2-a]pyrimidin-4-one	No
7	J15	2-ethyl-5-morpholin-4-yl-1,3-oxazole-4-carbonitrile	No
7	K15	3-(oxolan-2-ylmethyl)-5-{[4-oxo-2-(prop-2-enylamino)(5-hydropyridino[1,2-a]pyr imidin-3-yl)]methylene}-2-thioxo-1,3-thiazolidin-4-one	No
7	L15	5-[(9-methyl-4-oxo-2-pyrrolidinyl(5-hydropyridino[1,2-a]pyrimidin-3-yl))methyl ene]-3-(oxolan-2-ylmethyl)-2-thioxo-1,3-thiazolidin-4-one	No
7	M15	3-ethyl-5-[(9-methyl-4-oxo-2-pyrrolidinyl(5-hydropyridino[1,2-a]pyrimidin-3-yl))methylene]-2-thioxo-1,3-thiazolidin-4-one	No
7	N15	3-(methylethyl)-5-[(9-methyl-4-oxo-2-pyrrolidinyl(5-hydropyridino[1,2-a]pyrimi din-3-yl))methylene]-2-thioxo-1,3-thiazolidin-4-one	No
7	O15	3-butyl-5-[(9-methyl-4-oxo-2-pyrrolidinyl(5-hydropyridino[1,2-a]pyrimidin-3-yl))methylene]-2-thioxo-1,3-thiazolidin-4-one	No
7	P15	2-(methylethyl)-5-morpholin-4-yl-1,3-oxazole-4-carbonitrile	No
7	A16	prop-2-enyl 4-methyl-2-(2-thienylcarbonylamino)-1,3-thiazole-5-carboxylate	No
7	B16	prop-2-enyl 2-(2-furylcarbonylamino)-4-methyl-1,3-thiazole-5-carboxylate	No
7	C16	2-methoxyethyl 6-cyclohex-3-enyl-4-methyl-2-oxo-1,3,6-trihydropyrimidine-5-car boxylate	No
7	D16	2-methoxyethyl 4-methyl-6-(3-methyl(2-thienyl))-2-oxo-1,3,6-trihydropyrimidine -5-carboxylate	No
7	E16	2-(1-methyl-2-oxobenzo[d]azolin-3-ylidene)-1,3-thiazolidino[3,2-a]benzimidazol -3-one	No
7	F16	ethyl 4-methyl-6-(3-methyl(2-thienyl))-2-oxo-1,3,6-trihydropyrimidine-5-carbox ylate	No
7	G16	ethyl 4-methyl-6-(5-methyl(2-furyl))-2-oxo-1,3,6-trihydropyrimidine-5-carboxyl ate	No
7	H16	methylethyl 6-cyclohex-3-enyl-4-methyl-2-oxo-1,3,6-trihydropyrimidine-5-carbox ylate	No
7	I16	methylethyl 4-methyl-6-(5-methyl(2-furyl))-2-oxo-1,3,6-trihydropyrimidine-5-ca rboxylate	No
7	J16	methylethyl 4-methyl-6-(3-methyl(2-thienyl))-2-oxo-1,3,6-trihydropyrimidine-5- carboxylate	No
7	K16	2H,3H-benzo[e]1,4-dioxin-2-yl-N-[3-(N-ethylcarbamoyl)(4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl)]carboxamide	No
7	L16	2H,3H-benzo[e]1,4-dioxin-2-yl-N-{3-[N-(oxolan-2-ylmethyl)carbamoyl](4,5,6,7-te trahydrobenzo[b]thiophen-2-yl)}carboxamide	No

7	M16	2-(2H,3H-benzo[e]1,4-dioxin-2-ylcarbonylamino)-4,5,6,7-tetrahydrobenzo[b]thiop hene-3-carboxamide	No
7	N16	6,8-dichloro-2-nitro-9,10-dihydrophenanthrene-9-carbonitrile	No
7	O16	1,4-dichloro-6-nitro-9,10-dihydrophenanthrene-9-carbonitrile	No
7	P16	1-(4-bromophenyl)-2-phenylpropane-1,3-dicarbonitrile	No
7	A17	1-(4-bromophenyl)-2-(4-chlorophenyl)propane-1,3-dicarbonitrile	No
7	B17	6-bromo-2,3-dimethoxy-9,10-dihydrophenanthrene-9-carbonitrile	YES
7	C17	7-methoxy-2-nitro-9,10-dihydrophenanthrene-9-carbonitrile	No
7	D17	2-bromo-6-fluoro-9,10-dihydrophenanthrene-9-carbonitrile	No
7	E17	3-(3,4-dichlorophenyl)-1-(4-chlorophenyl)-3-(2-oxocyclooctyl)propan-1-one	No
7	F17	3-(3,4-dichlorophenyl)-1-(4-chlorophenyl)-3-(2-oxocycloheptyl)propan-1-one	No
7	G17	5-[(4-iodophenoxy)methyl]furan-2-carboxylic acid	No
7	H17	5-(indan-5-yloxymethyl)furan-2-carboxylic acid	No
7	I17	2-chloro-3-[(2-morpholin-4-ylethyl)amino]naphthalene-1,4-dione	No
7	J17	N-(2H,3H-benzo[3,4-e]1,4-dioxin-6-yl)-2-[4-(4-fluorophenyl)piperazinyl]acetami de	No
7	K17	2,4,6-tris[(4-fluorophenyl)methylthio]-1,3,5-triazine	No
7	L17	5-(3-chlorophenyl)-3-(2-naphthyl)-1-phenyl-2-pyrazoline	No
7	M17	3-(3-chloro-1,2,4-triazolyl)adamantanecarboxylic acid	No
7	N17	N-(3-cyano(3,4,5,6,7-pentahydrobenzo[b]thiophen-2-yl))-3-pyridylcarboxamide	No
7	O17	4-azaperhydroepinyl-7-bromo-5-nitrobenzo[c]1,2,5-thiadiazole	No
7	P17	3-(3,4-dichlorophenyl)-2-(purin-6-ylthiomethyl)-3-hydroquinazolin-4-one	No
7	A18	8-ethoxy-3,10-dihydrobenzo[g]pteridine-2,4-dione	No
7	B18	5-((2E)-3-phenylprop-2-enylidene)-2-thioxo-1,3-thiazolidin-4-one	No
7	C18	5-(indolinylmethylene)-1-benzyl-1,3-dihydropyrimidine-2,4,6-trione	No
7	D18	1-(4-fluorophenyl)-5-[(phenylamino)methylene]-1,3-dihydropyrimidine-2,4,6-trio ne	No
7	E18	4-piperazinyl-2,6-dipiperidyl-1,3,5-triazine	No
7	F18	[1-(4-ethoxyphenyl)-2,5-dimethylpyrrol-3-yl]morpholin-4-ylmethane-1-thione	No
7	G18	2-phenyl-4-(2-phenylquinazolin-4-ylthio)quinazoline	No
7	H18	2-{4-[3-(4-methyl(1,2,4-triazol-3-ylthio))-4-nitrophenyl]piperazinyl}ethan-1-o l	No
7	I18	4-[3-(cyclopropylamino)-4-nitrophenyl]-1-(phenylsulfonyl)piperazine	No
7	J18	1-(2-naphthylsulfonyl)-4-(4-nitro-3-pyrrolidinylphenyl)piperazine	No
7	K18	4-(3-morpholin-4-yl-4-nitrophenyl)-1-(phenylsulfonyl)piperazine	No
7	L18	4-chloro-1-{[4-(3-morpholin-4-yl-4-nitrophenyl)piperazinyl]sulfonyl}benzene	No

7	M18	4-[3-(cyclopropylamino)-4-nitrophenyl]-1-(2-naphthylsulfonyl)piperazine	No
7	N18	1-(2-naphthylsulfonyl)-4-(4-nitro-3-piperidylphenyl)piperazine	No
7	O18	4-(3-morpholin-4-yl-4-nitrophenyl)-1-(2-naphthylsulfonyl)piperazine	No
7	P18	1-(2-naphthylsulfonyl)-4-(5-nitro(8-quinolyl))piperazine	No
7	A19	{2,2-dimethyl-3-[(5-nitro(8-quinolyl))amino]propyl}[(4-bromophenyl)sulfonyl]am ine	No
7	B19	{3-[(4-chloro-2-nitrophenyl)amino]propyl}(methylsulfonyl)amine	No
7	C19	2-[(8-nitro-5-quinolyl)amino]ethan-1-ol	No
7	D19	(2-chloro-4-nitrophenyl)(3-morpholin-4-ylpropyl)amine	No
7	E19	8-[(2-hydroxy-2-phenylethyl)amino]-1,3,7-trimethyl-1,3,7-trihydropurine-2,6-di one	No
7	F19	1-{[3-(4-bromophenyl)-1,2,4-oxadiazol-5-yl]methyl}indole-3-carbaldehyde	No
7	G19	1-{[3-(diphenylmethyl)-1,2,4-oxadiazol-5-yl]methyl}indole-3-carbaldehyde	No
7	H19	(hydroxyimino)(4-methylphenyl)methylamine	No
7	I19	(4-bromophenyl)(hydroxyimino)methylamine	No
7	J19	5-({1-[2-(2-fluorophenoxy)ethyl]indol-3-yl}methylene)-1-(2-furylmethyl)-1,3-di hydropyrimidine-2,4,6-trione	No
7	K19	3-cyclohexyl-5-(indol-3-ylmethylene)-2-(phenylazamethylene)-1,3-thiazolidin-4- one	No
7	L19	N-benzothiazol-2-yl(3-chlorobenzo[b]thiophen-2-yl)carboxamide	No
7	M19	5-(3-methoxyphenyl)-1,3,4-oxadiazole-2-thiol	No
7	N19	4-[(5-(2-furyl)-1,3,4-oxadiazol-2-ylthio)methyl]benzoic acid	No
7	O19	2-cyano-2-(1-methyl-2-oxobenzo[d]azolin-3-ylidene)acetamide	No
7	P19	1-[(3,4-dichlorophenyl)sulfonyl]pyrrolidine-2-carboxylic acid	No
7	A20	5-(naphthyloxymethyl)-4-phenyl-1,2,4-triazole-3-thiol	No
7	B20	3-[(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)methyl]-1-methyl-3-hydrobenzimidazole-2- thione	No
7	C20	2-methylthio-3-phenyl-3,5,6,7-tetrahydrocyclopenta[2,1-d]pyrimidino[4,5-b]thio phen-4-one	No
7	D20	2-methyl-5-[(2,4,6-trimethylphenyl)methylthio]-1,3,4-thiadiazole	No
7	E20	3-[(4-nitrophenylthio)methyl]-1,2,4-triazolin-5-one	No
7	F20	11-[(2-fluorophenyl)methyl]spiro[1,2,3-trihydroquinazoline-2,3'-indoline]-4,12 -dione	No
7	G20	3-(4-methoxyphenyl)-1-(morpholin-4-ylmethyl)-1,2,4-triazoline-5-thione	No
7	H20	N-(1,3-thiazol-2-yl)-2-[6-(trifluoromethyl)benzothiazol-2-ylthio]acetamide	No
7	I20	N-(tert-butyl)-2-[5-(1,3,7-trimethyl-2,6-dioxo(1,3,7-trihydropurin-8-ylthio))(1,2,4-triazolyl)]acetamide	No
7	J20	N'-(2-cyclohex-1-enylethyl)-N-cyclohexylethane-1,2-diamide	No
7	K20	N'-(2-cyclohex-1-enylethyl)-N-(2-furylmethyl)ethane-1,2-diamide	No

7	L20	2-bromo-4-[5-(3-bromo-4-methoxyphenyl)(1,3-thiazolo[5,4-d]1,3-thiazol-2-yl)]-1 -methoxybenzene	No
7	M20	N-(2-cyclohex-1-enylethyl)-N'-(2-methoxyethyl)ethane-1,2-diamide	No
7	N20	phenyl(4-phenyl-5-sulfanyl(1,2,4-triazol-3-yl))methan-1-ol	No
7	O20	2-[(3-methyl(2-furyl))carbonylamino]-4-methylthiobutanoic acid	No
7	P20	4-(benzoxazol-2-ylthiomethyl)-3-chlorobenzenecarbonitrile	No
7	A21	4-(4,6-dimethylpyrimidin-2-ylthio)-3,5-dinitrobenzoic acid, azamethane	No
7	B21	1-(4-fluorophenoxy)-4-nitro-2-(trifluoromethyl)benzene	No
7	C21	dimethyl[(2-methylthiobenzothiazol-6-yl)sulfonyl]amine	No
7	D21	3-chloro-4-(2-pyridylthiomethyl)benzenecarbonitrile	No
7	E21	5-(2-methyl(3-furyl))-4-phenyl-1,2,4-triazole-3-thiol	No
7	F21	2-[(2-bromophenyl)methyl]-5-phenyl-1,2,3,4-tetraazole	No
7	G21	N,N-dimethyl-3-oxo-2-(2-phenyl(1,2,3,4-tetraazol-5-ylthio))butanamide	No
7	H21	1,3-dinitro-2-(4-phenylimidazol-2-ylthio)-5-(trifluoromethyl)benzene	No
7	I21	(5-bromo(2-pyridyl))(ethylsulfonyl)amine	No
7	J21	(2H-benzo[3,4-d]1,3-dioxolen-5-ylmethyl)(benzo[3,4-d]benzo[b]furan-2-ylsulfony l)amine	No
7	K21	2-[(4-phenylpiperidyl)sulfonyl]dibenzo[b,d]furan	No
7	L21	2,5-bis[4-(tert-butyl)phenyl]-1,3-thiazolo[5,4-d]1,3-thiazole	No
7	M21	2-{[1-(2-phenylethyl)benzimidazol-2-yl]methylthio}benzoxazole	No
7	N21	3-amino-2-[(4-fluoronaphthyl)methylthio]-3-hydroquinazolin-4-one	No
7	O21	1-(3,5-dichlorophenyl)-8-(tert-butyl)-4-thia-1-azaspiro[4.5]decan-2-one	No
7	P21	2-[2-(4-methoxyphenoxy)ethyl]-6-{1-[2-(4-methoxyphenoxy)ethyl]-2,5-dioxoazolid in-3-yl}-4-methyl-6,7-dihydroisoindole-1,3-dione	No
7	A22	1-[1,3-dimethyl-2,4,6-trioxo-5-(2-(4-pyridyl)ethyl)-1,3,5-trihydropyrimidin-5- yl]cyclohexanecarbonitrile	No
7	B22	1-(4-methylpentyl)-5-(pyrrol-2-ylmethylene)-1,3-dihydropyrimidine-2,4,6-trione	No
7	C22	1,3-dimethyl-5-(2-thienylmethyl)-1,3,5-trihydropyrimidine-2,4,6-trione	No
7	D22	3-(2,4-dichlorophenyl)-5-[(2-chlorophenyl)methylthio]-4-methyl-1,2,4-triazole	No
7	E22	5-(benzimidazolylmethyl)-4-phenyl-1,2,4-triazole-3-thiol	No
7	F22	6-[(2-chlorophenyl)methyl]-5-phenylspiro[1,3,4-thiadiazoline-2,3'-indoline]-7- one	No
7	G22	1-[(2,6-dichlorophenyl)methyl]-3-{[(hydrazinothioxomethyl)amino]azamethylene}b enzo[d]azolin-2-one	No
7	H22	2-(4-methylphenyl)-1-thia-3,4-diazaspiro[4.5]dec-2-ene	No
7	I22	4-methoxy-1-[5-(4-methylphenyl)(1,3,4-thiadiazolin-2-yl)]benzene	No
7	J22	2-(4-fluorophenyl)-5-(4-methylphenyl)-1,3,4-thiadiazoline	No

7	K22	10-ethyl-5-(4-methylphenyl)spiro[1,3,4-thiadiazoline-2,3'-indoline]-7-one	No
7	L22	3,5-dimethyl-1-[(4-methylphenyl)thioxomethyl]-4-(2-methylpropyl)-2-pyrazolin-5 -ol	No
7	M22	2-[5-(4-methylphenyl)-1,3,4-thiadiazolin-2-yl]thiophene	No
7	N22	3-ethyl-5-hydroxy-5-(trifluoromethyl)(2-pyrazolinyl) 4-pyridyl ketone	No
7	O22	3-benzyl-2-thioxo-1,3-thiazolino[4,5-d]pyrimidin-7-ol	No
7	P22	N-benzo[3,4-b]benzo[d]furan-3-ylmorpholin-4-ylcarboxamide	No
Plate	**Well**	**IUPAC NAME**	**Inhibitor Y/N**
8	A03	3-(4-bromophenyl)-5-(methylsulfonyl)-1H-1,2,4-triazole	No
8	B03	2-[(2-fluorophenyl)methylthio]-3-methyl-3,4a,8a-trihydroquinazolin-4-one	No
8	C03	N'-(2-cyclohex-1-enylethyl)-N-(2-methylpropyl)ethane-1,2-diamide	No
8	D03	N-(3-{[5-(acetylamino)-1H-1,2,4-triazol-3-ylthio]methylthio}-1H-1,2,4-triazol- 5-yl)acetamide	No
8	E03	8-nitro-5-(1-phenyl(1,2,3,4-tetraazol-5-ylthio))quinoline	No
8	F03	1-methyl-5-methylthio-3-(4-nitrophenyl)-1,2,4-triazole	No
8	G03	N-[(1,1-dioxobenzo[d]1,2-thiazol-3-yl)amino]-2-naphthylacetamide	No
8	H03	1-[5-(4-methylphenyl)-1,3,4-thiadiazolin-2-yl]pentane-1,2,3,4-tetraol	No
8	I03	N-(2,4-dichlorophenyl)[(4-chlorophenyl)amino]carboxamide	No
8	J03	3-[N-(3-carbamoyl-4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl)carbamoyl]propanoic acid	YES
8	K03	2,6-dimethyl-4-(4-pyridyl)hepta-1,6-dien-4-ylamine	No
8	L03	4-(2,6-diprop-2-enyl-2-1,2,5,6-tetrahydropyridyl)hepta-1,6-dien-4-ol	No
8	M03	2,6-bis(2-methylprop-2-enyl)-1-benzyl-1,2,5,6-tetrahydropyridine	No
8	N03	2-[2,6-bis(2-methylpropyl)piperidyl]ethan-1-ol	YES
8	O03		No
8	P03	(2S,6R)-2,6-bis(2-methylprop-2-enyl)-1,2,5,6-tetrahydropyridine	No
8	A04	(2S,6S)-1-acetyl-2,6-diprop-2-enyl-1,2,5,6-tetrahydropyridine	No
8	B04	ethyl 4-cyano-3-methyl-5-(2,2,2-trifluoroacetylamino)thiophene-2-carboxylate	No
8	C04	N-(3-cyano(4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl))-2,2,2-trifluoroacetamide	No
8	D04	(2E)-4-indolinyl-4-oxobut-2-enoic acid	No
8	E04	(2E)-3-{N-[3-(methoxycarbonyl)(4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl)]carbam oyl}prop-2-enoic acid	No
8	F04	(2S,6S)-1-acetyl-4-methyl-2,6-diprop-2-enyl-1,2,5,6-tetrahydropyridin	No
8	G04	2,3-bis(2-methylprop-2-enyl)-1,2,3,4-tetrahydroquinoxaline	No
8	H04	4-{[(2,6-dichloro-4-nitrophenyl)amino]azamethylene}-1-[4-(tert-butyl)(1,3-thia zol-2-yl)]-3-methyl-1,2-diazolin-5-one	No
8	I04	N-[4-(indolinylsulfonyl)phenyl](phenylamino)carboxamide	No

8	J04	4,6-diphenyl-2-(phenylmethylthio)pyridine-3-carbonitrile	YES
8	K04	11,11-dimethyl-10-(2-methylprop-2-enyl)-9-azatricyclo[6.2.2.0<2,7>]dodeca-2(7) ,3,5-triene	No
8	L04	2-(3-quinolyl)quinoline	No
8	M04	2-(acetylamino)-4,5-dimethylthiophene-3-carboxamide	No
8	N04	[(4-chlorophenyl)amino]-N-(3-cyano(4,5,6-trihydrocyclopenta[1,2-d]thiophen-2-y l))carboxamide	No
8	O04	4,4,10,10-tetramethyl-1,3,7,9-tetraazaspiro[5.5]undecane-2,8-dione	No
8	P04	1,3,4,6-tetramethyl-1,3,4,6,3a,6a-hexahydro-1,3,4,6-tetraazapentalene-2,5-dion e	No
8	A05	1,3-diacetyl-4,6-diethyl-2,5-dioxo-1,3,4,6,3a,6a-hexahydro-1,3,4,6-tetraazapen talene	No
8	B05	6-amino-3-methylspiro[4H-pyrano[3,2-d]pyrazole-4,1'-cyclohexane]-5-carbonitril e	No
8	C05	methyl 2-(propanoylamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate	YES
8	D05	3-[N-(2,6-dimethoxypyrimidin-4-yl)carbamoyl]propanoic acid	No
8	E05	3-amino-1-(4-fluorophenyl)-1H-benzo[f]chromene-2-carbonitrile	No
8	F05	2-amino-7,7-dimethyl-5,12-dioxospiro[4H-6,7,8-trihydrochromene-4,3 indoline]- 3-carbonitrile	No
8	G05	3-amino-5,6,7-trihydrocyclopenta[2,1-e]thiopheno[2,3-b]pyridine-2-carbonitrile	No
8	H05	3-amino-5,6,7,8-tetrahydrothiopheno[2,3-b]quinoline-2-carbonitrile	No
8	I05	2-methylthio-5,6,7,8,9-pentahydrocyclohepta[2,1-b]pyridine-3-carbonitrile	No
8	J05	2-[(6-hydroxy-4,4-dimethyl-2-oxocyclohex-1(6)-enyl)-2-thienylmethyl]-5,5-dimet hylcyclohexane-1,3-dione	No
8	K05	(3-chlorobenzo[b]thiophen-2-yl)-N-(2-furylcarbonylamino)carboxamide	No
8	L05	naphthalene-2,3-diamine	No
8	M05	3-amino-2-thioxo-1,3-dihydroquinazolin-4-one	No
8	N05	5-[(tert-butyl)sulfonyl]thiophene-2-carboxylic acid	No
8	O05	(tert-butylthio)naphthalene	No
8	P05	2,5-bis[(tert-butyl)sulfonyl]thiophene	No
8	A06	(2-thienylmethyl){4-[(2-thienylmethyl)amino]phenyl}amine	No
8	B06	5-(ethylsulfonyl)-2-(2-naphthylamino)-3-nitrothiophene	No
8	C06	methyl 2-(4-bromo-5-methyl-3-nitropyrazolyl)acetate	No
8	D06	2-(4-chloro-5-methyl-3-nitropyrazolyl)acetamide	No
8	E06	ethyl 2-(3,5-dimethyl-4-nitropyrazolyl)acetate	No
8	F06	2-(5-methyl-3-nitropyrazolyl)acetic acid	No
8	G06	2-(2-thienylthio)butanedioic acid	No
8	H06	5-(tert-butylthio)thiophene-2-carboxylic acid	No
8	I06	6-bromo-2-phenyl-4-hydroimidazo[1,2-a]pyridine	No

8	J06	2-[(2,5-dimethoxyphenyl)sulfonyl]-1,4-dimethoxybenzene	No
8	K06	4-[(3,4-dimethoxyphenyl)sulfonyl]-1,2-dimethoxybenzene	No
8	L06	2-[(2,5-dimethoxyphenyl)sulfonyl]-3,6-dimethoxybenzoic acid	No
8	M06	4-bromo-3-nitropyrazole-5-carboxylic acid	No
8	N06	[(3,4-dichlorophenyl)amino]-N-{2-[N-(3,4-dichlorophenyl)carbamoyloxy]ethyl}car boxamide	No
8	O06	N-(6-acetyl(2H-benzo[d]1,3-dioxolen-5-yl))[4-(1H-1,2,3-triazol-4-ylthiomethyl) phenyl]carboxamide	No
8	P06	(hydroxyimino)(6-methoxybenzothiazol-2-yl)methylamine	No
8	A07	2-[2-amino-5-(2-methyl(1,3-thiazol-4-yl))-6-(trifluoromethyl)pyrimidin-4-yl]-4 -ethyl-5-methoxyphenol	No
8	B07	4-ethyl-5-methoxy-2-[2-methyl-5-(2-methyl(1,3-thiazol-4-yl))-6-(trifluoromethy l)pyrimidin-4-yl]phenol	No
8	C07	(2E)-3-[N-(2-oxoazaperhydroepin-3-yl)carbamoyl]prop-2-enoic acid	No
8	D07	3-[(2-oxoazaperhydroepin-3-yl)amino]-1-phenylazolidine-2,5-dione	No
8	E07	1-(4-bromophenyl)-3-[(2-oxoazaperhydroepin-3-yl)amino]azolidine-2,5-dione	No
8	F07	3-(4,5-diphenylimidazolyl)-1-phenothiazin-10-ylpropan-2-ol	No
8	G07	ethyl (6-oxo-5,11,4b-trihydro-12H,4bH-benzo[e]quinazolino[1,2-c]1,3-oxazin-5-y loxy)formate	No
8	H07	7-bromo-5-nitro-4-piperidylbenzo[c]1,2,5-thiadiazole	No
8	I07	4-(3,4-dichlorophenyl)-1-(2-bromo-4,5-dimethylphenyl)-3,5-dimethylpyrazole	No
8	J07	(4-methyl(1,2,5-oxadiazol-3-yl))(phenylsulfonyl)amine	No
8	K07	3-(2-benzothiazol-2-ylthioethoxy)-1-methoxybenzene	No
8	L07	6-methyl-2-(trifluoromethyl)benzimidazole	No
8	M07	1-methyl-2-(phenylmethylthio)benzimidazole	No
8	N07	2-methoxy-1-[2-(1-methylbenzimidazol-2-ylthio)ethoxy]benzene	No
8	O07	1-(3-bromophenyl)-4-(2-oxo(1H-benzo[d]azolin-3-ylidene))-1,2-diazolidine-3,5-d ione	No
8	P07	5-{[5-(2,4-dichlorophenyl)(2-furyl)]methylene}-2-thioxo-1,3-diazolidin-4-one	No
8	A08	5-{5-[(4-oxo-2-thioxo-1,3-thiazolidin-5-ylidene)methyl]-2-furyl}-2H-benzo[c]az olidine-1,3-dione	No
8	B08	prop-2-enyl 4-{5-[(5-oxo-2-thioxo-1,3-diazolidin-4-ylidene)methyl]-2-furyl}ben zoate	No
8	C08	2-amino-7-methyl-4-hydro-1,2,4-triazolo[1,5-a]pyrimidin-5-ol	No
8	D08	1-(3,4-dichlorophenyl)-4-(methylethylidene)-1,2-diazolidine-3,5-dione	No
8	E08	2-[(2-phenoxyethyl)sulfonyl]benzimidazole	No
8	F08	N-cyclohexyl-2-[2-(trifluoromethyl)benzimidazolyl]acetamide	No
8	G08	5-{[1-benzylbenzimidazol-2-yl]methylthio}-1,3,4-thiadiazole-2-ylamine	No
8	H08	[3-(tert-butyl)pyrazol-5-yl]-N-[(5-bromo-1-methyl-2-oxobenzo[d]azolin-3-yliden e)azamethyl]carboxamide	No

8	I08	3-[2-(4-fluorophenyl)-2-oxoethyl]-3-hydroxy-1-prop-2-ynylindolin-2-one	No
8	J08	N-[(5-bromo-2-oxo(1H-benzo[d]azolin-3-ylidene))azamethyl](3-chlorobenzo[b]thio phen-2-yl)carboxamide	No
8	K08	(3-chlorobenzo[b]thiophen-2-yl)-N-[(1-ethyl-2-oxobenzo[d]azolin-3-ylidene)azam ethyl]carboxamide	No
8	L08	5-[(3-bromo-5-methoxy-4-prop-2-ynyloxyphenyl)methylene]-2-thioxo-1,3-thiazolid in-4-one	No
8	M08	2H,3H-benzo[e]1,4-dioxin-2-yl-N-[(1-butyl-2-oxobenzo[d]azolin-3-ylidene)azamet hyl]carboxamide	No
8	N08	2-methoxy-1-{2-[2-(methylethylthio)benzimidazolyl]ethoxy}benzene	No
8	O08	2-[1-benzylbenzimidazol-2-ylthio]ethan-1-ol	No
8	P08	2-{2-[2-(2-fluorophenoxy)ethylthio]benzimidazolyl}ethan-1-ol	No
8	A09	2-(benzimidazol-2-ylmethylthio)-1-phenylbenzimidazole	No
8	B09	4-methyl-1-(2-purin-6-ylthioethoxy)benzene	No
8	C09	[2-(6-bromobenzimidazol-2-ylthio)ethoxy]benzene	No
8	D09	N-(2-furylmethyl)-2-[2-(trifluoromethyl)benzimidazolyl]acetamide	No
8	E09	2-oxo-2-(4-phenylphenyl)ethyl 1,2,3-trihydrocyclopenta[2,1-b]quinoline-9-carbo xylate	No
8	F09	(2Z)-2-(aminothioxomethyl)-3-(4-pyridyl)prop-2-enenitrile	No
8	G09	ethyl (2E)-2-cyano-3-(1-methylimidazol-2-yl)prop-2-enoate	No
8	H09	methyl (2E)-2-cyano-3-(1-methylimidazol-2-yl)prop-2-enoate	No
8	I09	ethyl 4-(5-ethyl(2-thienyl))-2,7,7-trimethyl-5-oxo-4H-6,7,8-trihydrochromene-3 -carboxylate	No
8	J09	ethyl 2-amino-4-(4-bromo-5-ethyl(2-thienyl))-7,7-dimethyl-5-oxo-4H-6,7,8-trihy drochromene-3-carboxylate	No
8	K09	2,6-diamino-4-(2,4,6-triethylphenyl)-4H-thiin-3,5-dicarbonitrile	No
8	L09	(2E)-2-(aminothioxomethyl)-3-(5-butyl(2-thienyl))prop-2-enenitrile	No
8	M09	2-amino-4-(2,4-dimethoxyphenyl)-5,6,7,8-tetrahydroquinoline-3-carbonitrile	OFFSCALE
8	N09	6-amino-4-(4-bromophenyl)-3-methyl-4H-pyrano[3,2-d]pyrazole-5-carbonitrile	No
8	O09	2-amino-4-(4-bromophenyl)-3,4,5,6,7,4a-hexahydronaphthalene-1,3,3-tricarbonitr ile	No
8	P09	2-amino-4-(3-bromophenyl)-5,6,7,8,9-pentahydrocyclohepta[2,1-b]pyridine-3-carb onitrile	YES
8	A10	2-amino-4-(3-bromophenyl)-5,6,7,8,9,10-hexahydrocycloocta[2,1-b]pyridine-3-car bonitrile	OFFSCALE
8	B10	ethyl 2-(adamantanylcarbonylamino)-4,5,6,7,8-pentahydrocyclohepta[2,1-b]thioph ene-3-carboxylate	No
8	C10	({5-[(4-bromophenylthio)methyl]-2,4-dimethylphenyl}methylene)methane-1,1-dicar bonitrile	No
8	D10	({4-[(4-bromophenoxy)methyl]-5-methyl-2-thienyl}methylene)methane-1,1-dicarbon itrile	No

8	E10	({3-[(4-fluorophenoxy)methyl]-2,4,6-trimethylphenyl}methylene)methane-1,1-dica rbonitrile	No
8	F10	1,2,3,4-tetrahydroisoquinolinecarboxylic acid	No
8	G10		No
8	H10	3-(1,1-dimethylpyrrolidin-2-yl)-5-bromo-2-pyridylamine, iodide	No
8	I10	(9aR)-4,8-diacetyl-1,3-dihydroxy-2,9a-dimethyl-7,9-dioxo-8,9a-dihydrobenzo[2,1 -d]benzo[b]furan	No
8	J10	((2E)-3-phenylprop-2-enyl)piperazine	No
8	K10	6-amino-5-fluoro-3-hydropyrimidin-2-one	YES
8	L10	(2E)-3-dodecylthioprop-2-enoic acid	No
8	M10	1-ethylthio-2-(3-propyl-2-(2-thienyl)pyrrolyl)ethane	No
8	N10	2,2,2-trifluoro-1-(5-(2-thienyl)pyrrol-2-yl)ethan-1-one	No
8	O10	2-(2-(4,5,6,7-tetrahydroindolyl)ethylthio)acetamide	No
8	P10	2-(hydroxymethyl)-5-[(3-nitrophenyl)amino]oxolane-3,4-diol	No
8	A11	4-(benzo[f]benzimidazol-2-ylmethyl)morpholine	No
8	B11	methyl (2Z)-2-cyano-3-(5-methyl-4-nitro(2-thienyl))prop-2-enoate	No
8	C11	2-{N-[6-(1,1-dimethylpropyl)-3-(ethoxycarbonyl)-4,5,6,7-tetrahydrobenzo[b]thio phen-2-yl]carbamoyl}cyclohexanecarboxylic acid	No
8	D11	N-(2-hydroxyphenyl)phenothiazin-10-ylcarboxamide	No
8	E11	4-(bicyclo[2.2.1]hept-5-en-2-ylmethyl)-1-{[2-(trifluoromethyl)phenyl]methyl}pi perazine	No
8	F11	N-[(1E)-2-(3,4-dimethoxyphenyl)-1-azaprop-1-enyl]-2-fluoren-9-ylthioacetamide	No
8	G11	2-(2-{[(cyclohexylamino)thioxomethyl]amino}ethyl)isoindolin-1-one	No
8	H11	5-(tert-butyl)-7-(1,1,2,2,3,3,3-heptafluoropropyl)-2-phenyl-8-hydropyrazolo[1, 5-a]pyrimidine	No
8	I11	6-hydroxy-5-{[6-hydroxy-1-(4-methylpentyl)-2,4-dioxo(1,3-dihydropyrimidin-5-yl)]-2-pyridylmethyl}-1-(4-methylpentyl)-1,3-dihydropyrimidine-2,4-dione	No
8	J11	diethyl{4-[5-(4-methylphenyl)(1,3,4-thiadiazolin-2-yl)]phenyl}amine	No
8	K11	2-(4-cyclohexylphenyl)-2-methyl-5-(4-methylphenyl)-1,3,4-thiadiazoline	No
8	L11	2-methyl-2-[2-methyl-5-(4-methylphenyl)(1,3,4-thiadiazolin-2-yl)]-5-(4-methylp henyl)-1,3,4-thiadiazoline	No
8	M11	2-[(1E)-2-amino-2-(4-amino(1,2,5-oxadiazol-3-yl))-1-azavinyloxy]-1-piperidylet han-1-one	No
8	N11	8-[4-(methylethyl)phenyl]-2,4,6-triphenyl-1-thia-3,4,6,7-tetraazaspiro[4.5]dec a-2,7-diene	No
8	O11	3-{[(2,4-dichlorophenyl)methyl]sulfonyl}-1H-1,2,4-triazole-5-ylamine	No
8	P11	2-[(4-phenylpiperazinyl)sulfonyl]dibenzo[b,d]furan	No
8	A12	spiro[2,3-dihydroperimidine-2,1'-cycloheptane]	No
8	B12	(6Z,4E)-7-amino-3,3,4-trimethyl-7-(4-methylphenyl)-5,6-diazahepta-4,6-dien-2-o ne, iodide	No

8	C12	N-{[(cyclohexylamino)thioxomethyl]amino}-2-thienylcarboxamide	No
8	D12	1-[(1E)-2-(1-hexyl(2-pyridyl))vinyl]-2,3,4-trimethoxybenzene, iodide	No
8	E12	3-[5-(5-bromo-2-oxo(1H-benzo[d]azolidin-3-ylidene))-4-oxo-2-thioxo-1,3-thiazol idin-3-yl]propanoic acid	No
8	F12	3-amino-2-methyl-3,5,6,7-tetrahydrocyclopenta[2,1-d]pyrimidino[4,5-b]thiophen- 4-one	No
8	G12	methyl 4-(ethoxycarbonyl)-3-methyl-5-{[(2,4,6-trioxo(1,3-dihydropyrimidin-5-yl idene))azamethyl]amino}thiophene-2-carboxylate	No
8	H12	5-methyl-5-(4-methylphenyl)-1,3-diazolidine-2,4-dione	No
8	I12	2,7-dihydroxyxanthen-9-one	No
8	J12	3-[3-(3,6-dibromocarbazol-9-yl)-2-hydroxypropyl]-1,3-thiazolidine-2,4 dione	YES
8	K12	[((1E)-1,2-diphenyl-2-azavinyl)amino](phenylamino)methane-1-thione	No
8	L12	3-(3-carbazol-9-yl-2-hydroxypropyl)-5-(phenylmethylene)-1,3-thiazolidine-2,4-d ione	No
8	M12	2-[3-(3,6-dibromocarbazol-9-yl)-2-hydroxypropyl]-2-hydrobenzo[d]isothiazole-1, 1,3-trione	No
8	N12	3-[3-(3,6-dichlorocarbazol-9-yl)-2-hydroxypropyl]-1,8,8-trimethyl-3-azabicyclo [3.2.1]octane-2,4-dione	No
8	O12	3-(3,6-dichlorocarbazol-9-yl)-1-(4-bromo-3,5-dimethylpyrazolyl)propan-2-ol	No
8	P12	3-(5,6,7-trihydrocyclopenta[1,2-d]pyrimidino[4,5-b]thiophen-4-ylamino)propan-1 -ol	No
8	A13	(2E)-3-phenyl-3-{[(phenylamino)thioxomethyl]amino}-1-(phenylsulfonyl)-2-azapro p-2-ene	No
8	B13	(2E)-3-({[(4-bromophenyl)amino]thioxomethyl}amino)-3-phenyl-1-(phenylsulfonyl) -2-azaprop-2-ene	No
8	C13	7-hydroxy-3-(4-methoxyphenoxy)chromen-4-one	No
8	D13	7,9-dibromo-5-hydro-3H,4H-pyridino[2,1-c]1,2,4-thiadiazine-2,2-dion	No
8	E13	5-{[(2-imino-4-methyl-1,3-thiazolin-5-ylidene)azamethyl]amino}benzene-1,3-dica rboxylic acid	No
8	F13	3-amino-2-methyl-3-hydroquinazolin-4-one	No
8	G13	methyl 2-(acetylamino)-3-(methoxycarbonyl)-4,5,6-trihydrocyclopenta[3,2-b]thio phene-4-carboxylate	YES
8	H13	6-[5-(5-bromo-2-oxo(1H-benzo[d]azolin-3-ylidene))-4-oxo-2-thioxo-1,3-thiazolid in-3-yl]hexanoic acid	No
8	I13	methyl 2-(butoxycarbonylamino)-4,5,6-trihydrocyclopenta[2,1-b]thiophene-3-carb oxylate	No
8	J13	2-(7-methyl-4-oxo-3,5,6,7,8-pentahydrobenzo[b]thiopheno[2,3-d]pyrimidin-3-yl)a cetic acid	No
8	K13	2-(5,6,7,8-tetrahydrobenzo[b]thiopheno[3,2-e]pyrimidin-4-ylthio)propanoic acid	No
8	L13	N-(2-furylmethyl)morpholin-4-ylcarboxamide	YES

8	M13	ethyl 2-((2E)-3-(2-thienyl)prop-2-enoylamino)-4,5,6,7,8-pentahydrocyclohepta[2 ,1-b]thiophene-3-carboxylate	No
8	N13	2H,3H-benzo[3,4-e]1,4-dioxin-6-yl(5,6-dimethylthiopheno[3,2-e]pyrimidin-4-yl)a mine	No
8	O13	2-({2-[4-(tert-butyl)phenyl]quinazolin-4-yl}amino)ethan-1-ol	No
8	P13	4-(4-amino-3-methoxyphenylthio)-2-methoxyphenylamine	No
8	A14	2-(tert-butyl)-4-[5-(tert-butyl)-4-hydroxy-2-methylphenylthio]-5-methylphenol	No
8	B14	(4-(2-hydrobenzotriazol-2-yl)phenyl)(methylethyl)amine	No
8	C14	2-{4-[(methylethyl)amino]phenyl}-2-hydrobenzotriazol-1-ol	No
8	D14	4-chloro-2-(5-chloro-2-hydroxyphenylthio)phenol	No
8	E14	[3,5-bis(tert-butyl)phenyl]{[3,5-bis(tert-butyl)phenyl]methylthio}methane	No
8	F14	6-{[2-hydroxy-5-methyl-3-(methylcyclohexyl)phenyl]methyl}-4-methyl-2-(methylcy clohexyl)phenol	No
8	G14	1-[3,5-bis(tert-butyl)-4-hydroxyphenyl]-2-(hydroxyamino)-2-methylpropan-1-one	No
8	H14	6-hexyl-2-[(3-hexyl-2-hydroxy-5-methylphenyl)methyl]-4-methylphenol	No
8	I14	1-(phenyldiazenyl)naphthalen-2-ol	No
8	J14	3-(tert-butyl)-2-{1-[6-(tert-butyl)-2-hydroxy-4-methylphenyl]-isopropyl}-5-met hylphenol	No
8	K14	2,6-bis(tert-butyl)-4-{3-[3,5-bis(tert-butyl)-4-hydroxyphenyl]-1-methylpropyl} phenol	No
8	L14	(cyclohexylamino)morpholin-4-ylmethane-1-thione	No
8	M14	2-cyclohexyl-4-(3-cyclohexyl-4-hydroxy-5-methylphenylthio)-6-methylphenol	No
8	N14	(dicyclohexylamino)(butylamino)methane-1-thione	No
8	O14	(dicyclohexylamino)(cyclohexylamino)methane-1-thione	No
8	P14	(dicyclohexylamino)[(1,1-dimethylhexyl)amino]methane-1-thione	No
8	A15	bis(cyclohexylamino)methane-1-thione	No
8	B15	2-[6-(2-hydroxyphenyl)-2-phenylpyrimidin-4-yl]phenol	No
8	C15	2-(2,6-diphenylpyrimidin-4-yl)phenol	No
8	D15	2-(4,6-diphenylpyrimidin-2-yl)phenol	No
8	E15	(butylamino)morpholin-4-ylmethane-1-thione	No
8	F15	(diethylamino)(cyclohexylamino)methane-1-thione	No
8	G15	3-benzothiazol-2-ylthiopropanenitrile	No
8	H15	11-chlorotricyclo[6.2.1.0<2,7>]undeca-2(7),3,5-trien-9-yl (diethylamino)sulfon ate	No
8	I15	2,6-bis(tert-butyl)-4-[(dimethylamino)methyl]phenol	No
8	J15	N-(4-oxo-2-thioxo-1,3-dihydroquinazolin-3-yl)acetamide	No
8	K15	1-(2-imino-1,3-thiazino[3,2-a]benzimidazol-4-yl)cyclohexan-1-ol	No
8	L15	4-(1-hydroxy-isopropyl)-1,3-thiazino[3,2-a]benzimidazol-2-one	YES

8	M15	2-chloro-4-nitroimidazole	No
8	N15	(2S)-6-{[(4,4-dimethyl-2,6-dioxocyclohexylidene)ethyl]amino}-2-[(fluoren-9-ylm ethoxy)carbonylamino]hexanoic acid	No
8	O15	(3S)-3-[(fluoren-9-ylmethoxy)carbonylamino]-3-(prop-2-enyloxycarbonyl)propanoi c acid	No
8	P15	(2S)-2-[(fluoren-9-ylmethoxy)carbonylamino]-4-methylthiobutanoic acid	No
8	A16	2-[(2,5-dimethoxyphenyl)methylene]-7-bromopyridino[3',2'-5,4]imidazo[2,1-b]1,3 -thiazolidin-3-one	No
8	B16	4-[(1E)-2-(1-ethylindol-3-yl)-1-azavinyl]-2,3-dimethyl-1-phenyl-3-pyrazolin-5- one	No
8	C16	2-(2-phenyl-1-azaethylidene)-3-benzyl-5-(phenylmethylene)-1,3-thiazolidin-4-on e	No
8	D16	5-{5-[(5-oxo-2-thioxo-1,3-diazolidin-4-ylidene)methyl]-2-furyl}-3-hydroisobenz ofuran-1-one	No
8	E16	methyl 4-{5-[(5-oxo-2-thioxo-1,3-diazolidin-4-ylidene)methyl]-2-furyl}benzoate	No
8	F16	5-{[5-(4-bromophenyl)(2-furyl)]methylene}-2-thioxo-1,3-diazolidin-4-one	No
8	G16	2-methylquinazoline-4-thiol	No
8	H16	6,7-dimethyl-2-[(6-nitro(2H-benzo[3,4-d]1,3-dioxolen-5-yl))methylene]-1,3-thia zolidino[3,2-a]benzimidazol-3-one	YES
8	I16	5,6-diazaperhydroepinyl-1,2,5-oxadiazolo[3,4-b]pyrazine	No
8	J16	4-({6-[(3-chlorophenyl)amino](1,2,5-oxadiazolo[3,4-e]pyrazin-5-yl)}amino)-2,3- dimethyl-1-phenyl-3-pyrazolin-5-one	No
8	K16	5-[(5,5-dimethyl-3-oxocyclohexylidene)azamethyl]-3-hydrobenzimidazol-2-one	No
8	L16	6-methyl-2-[(1-methylbenzimidazol-2-yl)methylthio]hydropyrimidin-4-one	No
8	M16	3,6-bis(2-furylmethylene)-1,4-diazaperhydroine-2,5-dione	No
8	N16	7-bromopyridino[2,3-b]pyrazine-2,3-diol	No
8	O16	5,6-diamino-3-hydrobenzimidazol-2-one	No
8	P16	3-amino-1-phenylpyrazol-5-ol	No
8	A17	2-(benzimidazol-2-ylmethylthio)-6-phenylhydropyrimidin-4-one	No
8	B17	1-{[2-((1E)-2-phenylvinyl)-5-(methylamino)(1,3-oxazol-4-yl)]sulfonyl}-4-chloro benzene	YES
8	C17		No
8	D17	6-(3-chlorophenyl)-9-phenyl-6H,10aH-benzo[e]2-pyrazolino[1,5-c]1,3-oxazine	No
8	E17	1,6-dibromonaphthalen-2-ol	No
8	F17	[4-((1E)-2-indol-3-yl-1-azavinyl)phenyl]diethylamine	No
8	G17	N-benzothiazol-2-yl-2-(1,3-dimethyl-2,6-dioxo(1,3,7-trihydropurin-7-yl))acetam ide	No

8	H17	(phenylamino)[(1-phenyl-1-prop-2-enylbut-3-enyl)amino]methane-1-thione	No
8	I17	2-[(1E)-2-(4-chloro-3-nitrophenyl)-2-azavinyl]-5-methylfuran	No
8	J17	2-(2-(2H-benzo[3,4-d]1,3-dioxolen-5-yl)-2-oxoethylthio)-4,6-dimethylpyridine-3 -carbonitrile	YES
8	K17	[(4-{(1E)-2-[4-(dimethylamino)phenyl]-1-azavinyl}phenyl)sulfonyl](4-fluorophen yl)amine	No
8	L17	3-({2-[(2-oxo-1H-benzo[d]azolin-3-ylidene)azamethyl]phenyl}azamethylene)-1H-be nzo[d]azolin-2-one	No
8	M17	(4-bromophenyl)(methylsulfonyl)amine	No
8	N17	[4-(dimethylamino)phenyl]morpholin-4-ylmethane-1-thione	No
8	O17	(2R)-3-(tert-butoxy)-2-[(fluoren-9-ylmethoxy)carbonylamino]propanoi acid	No
8	P17	3,5,7-trihydroxy-2-(4-hydroxyphenyl)chromen-4-one	No
8	A18	2-[6-(acetylamino)benzothiazol-2-ylthio]-N-(1,3-thiazol-2-yl)acetamid	No
8	B18	(2-methoxybenzo[3,4-b]benzo[d]furan-3-yl)[(4-methoxynaphthyl)sulfonyl]amine	No
8	C18	N-(5-chloro(2-pyridyl))[1-(naphthylsulfonyl)pyrrolidin-2-yl]carboxamide	No
8	D18	3-(3-bromophenyl)-5-methylspiro[1,3-thiazolidine-2,3'-indoline]-4,7-dione	No
8	E18	1-[(2,5-dimethoxyphenyl)(2-hydroxynaphthyl)methyl]naphthalen-2-ol	No
8	F18	7-[(4-phenylpiperazinyl)methyl]spiro[1,3-dioxane-2,3'-indoline]-8-one	No
8	G18	N-[4-({[(4,6-dimethylpyrimidin-2-yl)amino]iminomethyl}amino)phenyl]acetamide	No
8	H18	phenyl 4,4,6,8-tetramethyl-1-thioxo(4,5-dihydro-1,2-dithioleno[5,4-c]quinolin- 5-yl) ketone	No
8	I18	2-benzoxazol-2-ylthio-1-carbazol-9-ylethan-1-one	No
8	J18	(4-amino(1,2,5-oxadiazol-3-yl))-N-[(1-ethyl-2-oxobenzo[d]azolidin-3-ylidene)az amethyl]carboxamide	No
8	K18	N-[(1-ethyl-2-oxobenzo[d]azolidin-3-ylidene)azamethyl]-6-(2-oxo(1,3-diazaperhy droin-4-yl))hexanamide	YES
8	L18	(5-nitro(2-furyl))-N-[(2-oxo(1H-benzo[d]azolidin-3-ylidene))azamethyl]carboxam ide	No
8	M18	(4-amino(1,2,5-oxadiazol-3-yl))-N-[(2-oxo(1H-benzo[d]azolidin-3-ylidene))azame thyl]carboxamide	No
8	N18	2-furyl-N-[(2-oxo(1H-benzo[d]azolidin-3-ylidene))azamethyl]carboxamide	No
8	O18	(5-chloro(2-thienyl))-N-[(2-oxo(1H-benzo[d]azolidin-3-ylidene))azamethyl]carbo xamide	No
8	P18	(2Z)-2-(aminothioxomethyl)-3-(2,5-dimethyl(3-thienyl))prop-2-enenitrile	No
8	A19	[(2,5-dimethyl-3-thienyl)methylene]methane-1,1-dicarbonitrile	No
8	B19	methyl (2E)-3-(2,5-dimethyl(3-thienyl))-2-cyanoprop-2-enoate	No

8	C19	(2E)-3-(2,5-dimethyl(3-thienyl))-2-cyanoprop-2-enamide	No
8	D19	ethyl (2E)-3-(2,5-dimethyl(3-thienyl))-2-cyanoprop-2-enoate	No
8	E19	methylethyl (2E)-3-(2,5-dimethyl(3-thienyl))-2-cyanoprop-2-enoate	No
8	F19	[(2-ethylthio-5-methyl-3-furyl)methylene]methane-1,1-dicarbonitrile	No
8	G19	N-(4-bromo-2-fluorophenyl)[(methylpropyl)amino]carboxamide	No
8	H19	N-(2-chloro(3-pyridyl))[(3-fluorophenyl)amino]carboxamide	YES
8	I19	N-(2-chloro(3-pyridyl))[(4-chlorophenyl)amino]carboxamide	No
8	J19	[(4-fluorophenyl)amino]-N-(1,3,4-thiadiazol-2-yl)carboxamide	No
8	K19	N-(2-chloro(3-pyridyl))[(4-fluorophenyl)amino]carboxamide	No
8	L19	[(4-fluorophenyl)amino]-N-(5-methylisoxazol-3-yl)carboxamide	No
8	M19	[(2-nitrophenyl)amino]-N-(1,3,4-thiadiazol-2-yl)carboxamide	No
8	N19	[(tert-butyl)amino]-N-(2-chloro(3-pyridyl))carboxamide	No
8	O19	[(tert-butyl)amino]-N-(5-methylisoxazol-3-yl)carboxamide	No
8	P19	[(tert-butyl)amino]-N-(1,3,4-thiadiazol-2-yl)carboxamide	No
8	A20	[(tert-butyl)amino]-N-(4-methyl(1,3-thiazol-2-yl))carboxamide	No
8	B20	[(3-chlorophenyl)amino]-N-(4-methoxyphenyl)carboxamide	No
8	C20	N-(5-methylisoxazol-3-yl)-5-(2-thienyl)pentanamide	No
8	D20	2-amino-4-(4-bromo(2-thienyl))-7,7-dimethyl-5-oxo-4H-6,7,8-trihydrochromene-3- carbonitrile	No
8	E20	2,6-diamino-4-(2,5-dimethylphenyl)-4H-thiin-3,5-dicarbonitrile	No
8	F20	4-(2H-benzo[3,4-d]1,3-dioxolan-5-ylmethylene)-3-phenylisoxazol-5-one	No
8	G20	[3-((hydroxyimino)methyl)-2,4,6-trimethylphenyl]methan-1-ol	No
8	H20	6-amino-4-(4-bromo(2-thienyl))-3-methyl-4H-pyrano[2,3-c]pyrazole-5 carbonitril e	No
8	I20	2,6-diamino-4-(4-bromo(2-thienyl))-4H-pyran-3,5-dicarbonitrile	No
8	J20	[3-(chloromethyl)-2,4,6-trimethylphenyl](hydroxyimino)methane	No
8	K20	5-benzo[b]thiophen-2-yl-1,3,4-oxathiazolin-2-one	No
8	L20	5-(4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl)-1,3,4-oxathiazolin-2-one	No
8	M20	N-[3-(2-oxo-1,3,4-oxathiazolin-5-yl)-4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl]a cetamide	No
8	N20	phenyl-N-(2-(1,3-thiazolin-2-ylthio)acetyl)carboxamide	No
8	O20	1-(2-phenoxyacetyl)imidazolidin-2-one	No
8	P20	N-[2-(3-methylthio(1,2,4-thiadiazol-5-ylthio))acetyl]benzamide	No
8	A21	(5-bromo(2-furyl))-N-(4-iodophenyl)carboxamide	No
8	B21	ethyl 2-[2-(5-methyl-1,3,4-thiadiazol-2-ylthio)acetylamino]-4,5,6-trihydrocycl openta[2,1-b]thiophene-3-carboxylate	No
8	C21	N-(3-cyano(4,5,6-trihydrocyclopenta[1,2-d]thiophen-2-yl))-2-(5-methyl(1,3,4-th iadiazol-2-ylthio))acetamide	No
8	D21	methyl 2-(2-pyrimidin-2-ylthioacetylamino)-4,5,6-trihydrocyclopenta[2,1-b]thio phene-3-carboxylate	No
8	E21	N-benzothiazol-2-ylcyclopropylcarboxamide	No

8	F21	[3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropyl]-N-(3-cyano(4,5,6-trihydrocyclo penta[1,2-d]thiophen-2-yl))carboxamide	No
8	G21	(1,5-dimethylpyrrol-2-yl)(hydroxyimino)methylamine	No
8	H21	2-[2-(5-methyl-1,3,4-thiadiazol-2-ylthio)acetylamino]-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxamide	No
8	I21	2-(2-benzoxazol-2-ylthioacetylamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-car boxamide	No
8	J21	cyclopentylideneazamethyl 3-chlorobenzo[b]thiophene-2-carboxylate	No
8	K21	methyl 2-(3-nitro-1,2,4-triazolyl)acetate	No
8	L21	N-(3-cyano(4,5,6-trihydrocyclopenta[1,2-d]thiophen-2-yl))-2-(4-methyl(1,2,4-tr iazol-3-ylthio))acetamide	No
8	M21	(2,4-dinitrophenyl)(2-morpholin-4-ylethyl)amine	No
8	N21	[1-(4-amino(1,2,5-oxadiazol-3-yl))-5-methyl(1,2,3-triazol-4-yl)]-N-[(4-bromo-1 -methylpyrazol-3-yl)carbonylamino]carboxamide	No
8	O21	ethyl 4-amino-2-hydroxy-1,2,5-oxadiazole-3-carboxylate	No
8	P21	2-(3-bromo-4-fluorophenyl)-1,3-thiazolidine-4-carboxylic acid	No
8	A22	2-(2-furyl)-1,3-thiazolidine-4-carboxylic acid	No
8	B22	2-cyclohex-3-enyl-1,3-thiazolidine-4-carboxylic acid	No
8	C22	2-(4-fluorophenyl)-1,3-thiazolidine-4-carboxylic acid	No
8	D22	2-(2,4-difluorophenyl)-1,3-thiazolidine-4-carboxylic acid	No
8	E22	2-[2-(trifluoromethyl)phenyl]-1,3-thiazolidine-4-carboxylic acid	No
8	F22	2-cyclohexyl-1,3-thiazolidine-4-carboxylic acid	No
8	G22	4-[4-???-5-(methoxymethyl)-1,2,3-triazolyl]-1,2,5-oxadiazole-3-ylamine	No
8	H22	{[4-???-1-(4-amino(1,2,5-oxadiazol-3-yl))(1,2,3-triazol-5-yl)]methyl}diethylam ine	No
8	I22	4-[4-???-5-(indolinylmethyl)-1,2,3-triazolyl]-1,2,5-oxadiazole-3-ylamine	No
8	J22	{[4-???-1-(4-amino(1,2,5-oxadiazol-3-yl))(1,2,3-triazol-5-yl)]methyl}phenylami ne	No
8	K22	4-(4-???-5-methyl-1,2,3-triazolyl)-1,2,5-oxadiazole-3-ylamine	No
8	L22	4-(4-???-5-phenyl-1,2,3-triazolyl)-1,2,5-oxadiazole-3-ylamine	No
8	M22	4-[4-???-5-(morpholin-4-ylmethyl)-1,2,3-triazolyl]-1,2,5-oxadiazole-3-ylamine	No
8	N22	4-{4-???-5-[(4-methylpiperazinyl)methyl]-1,2,3-triazolyl}-1,2,5-oxadiazole-3-y lamine	No
8	O22	4-[4-???-5-(piperidylmethyl)-1,2,3-triazolyl]-1,2,5-oxadiazole-3-ylamine	No
8	P22	ethyl 2-(2-(1,3-thiazolin-2-ylthio)acetylamino)-4,5,6-trihydrocyclopenta[2,1-b]thiophene-3-carboxylate	No
Plate	**Well**	**IUPAC NAME**	**Inhibitor Y/N**

9	A03	methylethyl 2-{[3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropyl]carbonylamino}-4 ,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate	No
9	B03	5-bromo(2-furyl) indolinyl ketone	No
9	C03	N-cycloheptylcyclopropylcarboxamide	No
9	D03	N-(2,4-dibromophenyl)-2,2-dichloroacetamide	No
9	E03	4-(2,4-dinitrophenyl)-1,4-diazabicyclo[4.3.0]nonane	No
9	F03	N-[(1,3-dimethylpyrazol-4-yl)methyl](5-bromo(2-furyl))carboxamide	No
9	G03	N-(4-bromo-2-fluorophenyl)-2-(1,3-thiazolin-2-ylthio)acetamide	No
9	H03	4-chloro-1-methylpyrazol-3-yl 2-1,2,3,4-tetrahydroisoquinolyl ketone	No
9	I03	[(1E)-2-methyl-3-(5-nitro(1,2,3,4-tetraazol-2-yl))-1-azaprop-1-enyl](2,4,6-tri chlorophenyl)amine	No
9	J03	(4-nitropyrazolyl)-N-prop-2-enylcarboxamide	No
9	K03	(4-chloropyrazolyl)-N-ethylcarboxamide	No
9	L03	methyl 4-bromo-3,5-dimethylpyrazolecarboxylate	No
9	M03	(ethylamino)(3-methylpyrazolyl)methane-1-thione	No
9	N03	4,6-dimethylbenzothiazole-2-ylamine	No
9	O03	2-cyano-N-(2-furylmethyl)acetamide	No
9	P03	4-chlorophenyl 2-oxopyran-5-carboxylate	No
9	A04	N-(2,4-dioxo(1,3-dihydropyrimidin-5-yl))-2,2-dimethylpropanamide	No
9	B04	N-(1,3-thiazol-2-yl)dodecanamide	No
9	C04	N-(2,4-dioxo(1,3-dihydropyrimidin-5-yl))(4-bromophenyl)carboxamide	No
9	D04	N-(5-{[1,3-dioxo-2-(4-pyridylcarbonylamino)benzo[c]azolidin-5-yl]carbonyl}-1,3 -dioxobenzo[c]azolin-2-yl)-4-pyridylcarboxamide	No
9	E04	5-nitro-2-[(4-oxobenzo[d]1,3-oxazin-2-yl)methyl]benzo[c]azolidine-1,3-dione	No
9	F04	6-bromo-2-(4-phenylphenyl)benzo[d]1,3-oxazin-4-one	No
9	G04	2-nonyl-6-(2-nonyl-4-oxobenzo[d]1,3-oxazin-6-yl)benzo[d]1,3-oxazin-4-one	No
9	H04	1-[6-(2,5-dioxoazolidinyl)hexyl]azolidine-2,5-dione	No
9	I04	2-(3-fluorophenyl)benzo[d]1,3-oxazin-4-one	No
9	J04	6-bromo-2-(3-fluorophenyl)benzo[d]1,3-oxazin-4-one	No
9	K04	2-(4-fluorophenyl)-6-methylbenzo[d]1,3-oxazin-4-one	No
9	L04	N-[4-(acetylamino)(1,2,5-oxadiazol-3-yl)]-2-(1,3-thiazolin-2-ylthio)acetamide	No
9	M04	(4,6-dimethylpyrimidin-2-yl)[2-benzyl-1-azabut-1-enyl]amine	No
9	N04	(4,6-dimethylpyrimidin-2-yl)(2-phenyl-1-azapent-1-enyl)amine	No
9	O04	4,6-dimethylpyrimidine-2-ylhydrazine	No
9	P04	5-(4-fluorophenyl)pyrazole-4-carbaldehyde	No
9	A05	9-ethylcarbazole-3-ylamine	No
9	B05	9-ethylcarbazole	No

9	C05	1,3-dimethyl-7-{2-oxo-2-[4-benzylpiperazinyl]ethyl}-1,3,7-trihydropurine-2,6-d ione	No
9	D05	(4-pyridylmethyl){[2,4,6-tris(methylethyl)phenyl]sulfonyl}amine	No
9	E05	4-(2H-benzo[3,4-d]1,3-dioxolen-5-ylmethyl)-1-(phenylsulfonyl)piperazine	No
9	F05	4-(2-{[(4-chlorophenyl)sulfonyl]amino}ethyl)benzenesulfonamide	No
9	G05	[(4-methoxyphenyl)sulfonyl][6-(methylsulfonyl)benzothiazol-2-yl]amine	No
9	H05	4-({4-[(1E)-2-(4-methylthiophenyl)-1-azavinyl]phenyl}sulfonyl)morpholine	No
9	I05	2,6-diamino-4-(3-bromo-4-fluorophenyl)-4H-thiin-3,5-dicarbonitrile	No
9	J05	2,6-diamino-4-(5-bromo-2-methoxyphenyl)-4H-thiin-3,5-dicarbonitrile	No
9	K05	1-chloro-4-{[4-(4-nitrophenyl)piperazinyl]sulfonyl}benzene	No
9	L05	2-[(1E)-2-(2,6-dichlorophenyl)-1-azavinyl]-4,5,6-trihydrocyclopenta[1,2-b]thio phene-3-carbonitrile	No
9	M05	(3-chlorobenzo[b]thiophen-2-yl)-N-(3-cyano(4,5,6-trihydrocyclopenta[1,2-d]thio phen-2-yl))carboxamide	No
9	N05	ethyl 3-(ethoxycarbonyl)-2-(2-furylcarbonylamino)-4,5,6,7-tetrahydrothiopheno[2,3-c]pyridine-6-carboxylate	No
9	O05	N-(tert-butyl)-2-(1,3,7-trimethyl-2,6-dioxo(1,3,7-trihydropurin-8-ylthio))acet amide	No
9	P05	2-pyrimidin-2-ylthio-1-[4-(2-pyrimidin-2-ylthioacetyl)piperazinyl]ethan-1-one	No
9	A06	5-(3-bromophenyl)-1-methyl-1,3,5,11-tetrahydroindeno[2,3-e]pyrimidino[4,5-b]py ridine-2,4,6-trione	No
9	B06	8-[2-(4-methoxyphenoxy)ethylthio]purine-6-ylamine	No
9	C06	adamantanyl-N-(2,3-dimethyl-5-oxo-1-phenyl(3-pyrazolin-4-yl))-N-methylcarboxam ide	No
9	D06	5-(morpholin-4-ylsulfonyl)-3-hydrobenzimidazol-2-one	No
9	E06	ethyl 4-methyl-5-(pyrrolidinylcarbonyl)-2-(2-thienylcarbonylamino)thiophene-3- carboxylate	No
9	F06	4-hydroxy-3-[3-(4-hydroxy-4,5,5-trimethyl-2-oxo(1,3-oxazolidin-3-yl))propyl]-4 ,5,5-trimethyl-1,3-oxazolidin-2-one	No
9	G06	N-adamantanyl[1-(phenylsulfonyl)pyrrolidin-2-yl]carboxamide	No
9	H06	5-nitro-2-(4-pyridyl)benzimidazole	No
9	I06	4-amino-1,2,5-oxadiazole-3-carboxylic acid	No
9	J06	4-methoxy-1,2,5-oxadiazole-3-ylamine	No
9	K06	(1S,2S,5S,7S,11S,10R,14R,15R)-5,7,11-trihydroxy-15-methyl-14-(5-oxo(3-2-hydrof uryl))tetracyclo[8.7.0.0<2,7>.0<11,15>]heptadecane-2-carbaldehyde	No
9	L06	4-({4-[(methylsulfonyl)amino]phenyl}sulfonyl)morpholine	No
9	M06	1-(2H-benzo[3,4-d]1,3-dioxolan-5-yl)-5-[(5-piperidyl(2-furyl))methylene]-1,3-d ihydropyrimidine-2,4,6-trione	No

9	N06	5-{[2-(1H-1,2,4-triazol-5-ylthiomethyl)phenyl]methylthio}-1H-1,2,4-triazole	No
9	O06	(4-fluorophenyl)({4-[(phenylsulfonyl)amino]phenyl}sulfonyl)amine	No
9	P06	3-(2-hydroxyethyl)-2-thioxo-1,3-dihydroquinazolin-4-one	No
9	A07	2-(2-oxopropylthio)-3-hydroquinazolin-4-one	No
9	B07	1-(adamantanylcarbonyl)imidazolidin-2-one	No
9	C07	1-[(4-methylphenyl)methyl]-3-nitro-1,2,4-triazole	No
9	D07	1-[(2,6-dichlorophenyl)methyl]-3-nitro-1,2,4-triazole	No
9	E07	4-[(4-nitroimidazolyl)methyl]benzenecarbonitrile	No
9	F07	1-[(2,6-dichlorophenyl)methyl]-4-nitroimidazole	No
9	G07	(2,5-dichloro(3-thienyl))-N-[(2-oxo(1H-benzo[d]azolidin-3-ylidene))azamethyl]c arboxamide	No
9	H07	N-[(2-oxo(1H-benzo[d]azolidin-3-ylidene))azamethyl](5-(2-thienyl)(2-thienyl))c arboxamide	No
9	I07	N-[(1-methyl-2-oxobenzo[d]azolidin-3-ylidene)azamethyl]-6-(2-oxo(1,3-diazaperh ydroin-4-yl))hexanamide	No
9	J07	(4-amino(1,2,5-oxadiazol-3-yl))-N-[(1-methyl-2-oxobenzo[d]azolidin-3-ylidene)a zamethyl]carboxamide	No
9	K07	2-furyl-N-[(1-methyl-2-oxobenzo[d]azolidin-3-ylidene)azamethyl]carboxamide	No
9	L07	N-[6-(methylsulfonyl)benzothiazol-2-yl]-2-morpholin-4-ylacetamide	No
9	M07	ethyl 2-[(5-bromo-2-furyl)carbonylamino]-4,5,6-trihydrocyclopenta[2,1-b]thioph ene-3-carboxylate	No
9	N07	6-amino-3-methyl-4-(2,3,4,5,6-pentafluorophenyl)-4H-pyrano[3,2-d]pyrazole-5-ca rbonitrile	YES
9	O07	propyl 2-(4-chlorobutanoylamino)-6-methyl-4,5,6,7-tetrahydrobenzo[b]thiophene- 3-carboxylate	YES
9	P07	2-[(1E)-2-(4-chlorophenyl)-1-azavinyl]-4,5,6,7-tetrahydrobenzo[b]thiophene-3-c arbonitrile	No
9	A08	2-((1E)-2-(2-furyl)-1-azavinyl)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carbonit rile	No
9	B08	5-[(1E)-2-(3,4,5-trimethoxyphenyl)-1-azavinyl]-1,2,3-trimethoxybenzene	No
9	C08	2-[(1E)-2-(5-nitro(2-furyl))-1-azavinyl]-4,5,6,7-tetrahydrobenzo[b]thiophene-3 -carbonitrile	No
9	D08	2-[(1E)-2-(4-bromophenyl)-1-azavinyl]-4,5,6,7-tetrahydrobenzo[b]thiophene-3-ca rbonitrile	No
9	E08	2-[(1E)-2-(2-bromophenyl)-1-azavinyl]-4,5,6,7-tetrahydrobenzo[b]thiophene-3-ca rbonitrile	No
9	F08	2-[(1E)-2-(5-methyl(2-furyl))-1-azavinyl]-4,5,6,7-tetrahydrobenzo[b]thiophene- 3-carbonitrile	No
9	G08	2-[(1E)-2-(2-fluorophenyl)-1-azavinyl]-4,5,6,7-tetrahydrobenzo[b]thiophene-3-c arbonitrile	No
9	H08	N-(cyclohexylcarbonylamino)octanamide	No

9	I08	N-benzothiazol-2-yl(1-methylpyrazol-5-yl)carboxamide	No
9	J08	((1E)-2-(2-pyridyl)-1-azaprop-1-enyl)(2,4,6-trichlorophenyl)amine	No
9	K08	N-((1E)-3-benzotriazolyl-2-methyl-1-azaprop-1-enyl)indol-3-ylcarboxamide	No
9	L08	N-[(1E)-2-methyl-3-(5-nitro(1,2,3,4-tetraazol-2-yl))-1-azaprop-1-enyl]indol-3- ylcarboxamide	No
9	M08	5-(benzothiazol-2-ylthiomethyl)furan-2-carbohydrazide	YES
9	N08	N-[(1E)-2-methyl-3-(5-nitro(1,2,3,4-tetraazol-2-yl))-1-azaprop-1-enyl][1-(4-am ino(1,2,5-oxadiazol-3-yl))-4-methyl(1,2,3-triazol-5-yl)]carboxamide	No
9	O08	2-(4-bromo-5-methyl-3-nitropyrazolyl)-N-[2-(4-nitropyrazolyl)acetylamino]aceta mide	No
9	P08	4-bromopyrazolyl 2-chloro-4,5-difluorophenyl ketone	No
9	A09	4-chloro-3,5-dimethylpyrazolyl 1-methylpyrazol-3-yl ketone	No
9	B09	3,5-dimethylpyrazolyl 1-methyl-4-nitropyrazol-3-yl ketone	No
9	C09	1-methyl-4-nitropyrazol-3-yl pyrazolyl ketone	No
9	D09	4-methoxy-3-(1,3-thiazolin-2-ylthiomethyl)benzaldehyde	No
9	E09	4-[(1E)-2-(4-methoxyphenyl)-1-azavinyl]-1,2,5-oxadiazole-3-ylamine	No
9	F09	3-(4-methoxyphenyl)-5-(2-oxo(1H-benzo[d]azolin-3-ylidene))-2-thioxo-1,3-thiazo lidin-4-one	No
9	G09	3-(4-chlorophenyl)-5-[(4-methylpiperazinyl)methylene]-2-thioxo-1,3-thiazolidin -4-one	No
9	H09	3-(4-methoxyphenyl)-5-[(4-methylpiperazinyl)methylene]-2-thioxo-1,3-thiazolidi n-4-one	No
9	I09	[(diethylamino)amino](cyclohexylamino)methane-1-thione	No
9	J09	(cyclohexylamino)(2-phenylhydrazino)methane-1-thione	No
9	K09	2,4,6-tris(tert-butyl)phenol	No
9	L09	1-[(2,5-dioxoazolinyl)disulfanyl]azoline-2,5-dione	No
9	M09	2,6-bis(tert-butyl)-4-[(2-hydroxyethoxy)methyl]phenol	No
9	N09	2-(tert-butyl)-4-[3-(tert-butyl)-4-hydroxy-5-methylphenylthio]-6-methylphenol	No
9	O09	[(dibutylamino)amino](phenylamino)methane-1-thione	No
9	P09	2,6-bis(tert-butyl)-4-[3,5-bis(tert-butyl)-4-hydroxyphenyl]phenol	No
9	A10	(cyclohexylamino)(morpholin-4-ylamino)methane-1-thione	No
9	B10	2,6-bis(tert-butyl)-4-{[3,5-bis(tert-butyl)-4-hydroxyphenyl]-2-furylmethyl}phe nol	No
9	C10	2,6-bis{[3,5-bis(tert-butyl)-4-hydroxyphenyl]methyl}-4-(tert-butyl)phenol	No
9	D10	2,6-bis{[3,5-bis(tert-butyl)-4-hydroxyphenyl]methyl}-4-ethylphenol	No
9	E10	1-(2-hydroxynaphthylthio)naphthalen-2-ol	No
9	F10	4-(2,4-dihydroxyphenylthio)benzene-1,3-diol	No
9	G10	6-{[3,5-bis(tert-butyl)-4-hydroxyphenyl]methyl}-2-(tert-butyl)-4-chlorophenol	No

9	H10	6-(tert-butyl)-2-{[3-(tert-butyl)-5-bromo-2-hydroxyphenyl]disulfanyl}-4-bromop henol	No
9	I10	2,6-bis(tert-butyl)-4-{[3-(tert-butyl)-2-hydroxy-5-methylphenyl]methyl}phenol	No
9	J10	2-(tert-butyl)-4-[(4-hydroxy-3,5-dimethylphenyl)methyl]-6-methylphenol	No
9	K10	2,6-bis(tert-butyl)-4-({[3,5-bis(tert-butyl)-4-hydroxyphenyl]methoxy}methyl)ph enol	No
9	L10	2,4-bis(tert-butyl)-6-{[3,5-bis(tert-butyl)-2-hydroxyphenyl]methyl}phenol	No
9	M10	6-(tert-butyl)-2-[3-(tert-butyl)-5-chloro-2-hydroxyphenylthio]-4-chlorophenol	No
9	N10	2-[1-(2-hydroxy-3,5-dimethylphenyl)-3-methylbutyl]-4,6-dimethylphenol	No
9	O10	methyl 2,3,5,6-tetrafluoro-4-{[2,3,5,6-tetrafluoro-4-(methoxycarbonyl)phenyl]s ulfonyl}benzoate	No
9	P10	4-((1E)-2-(2-furyl)-1-azavinyl)phenol	No
9	A11	2,6-bis(tert-butyl)-4-[(2-{[3,5-bis(tert-butyl)-4-hydroxyphenyl]methylthio}eth ylthio)methyl]phenol	No
9	B11	4-(1,1-dimethylhexyl)-2-[5-(1,1-dimethylhexyl)-2-hydroxyphenylthio]phenol	No
9	C11	2-(tert-butyl)-4-{[5-(tert-butyl)-4-hydroxy-2-methylphenyl]sulfinyl}-5-methylp henol	No
9	D11	(2-naphthylsulfonyl)spiro[benzo[3,4-d]1,3-dioxolene-2,1'-cyclohexane]-5-ylamin e	No
9	E11	2-(3-amino-1H-1,2,4-triazol-5-yl)acetic acid	No
9	F11	2-(5-amino-1,2,3,4-tetraazolyl)acetic acid	No
9	G11	5-[(5-methyl(2-furyl))methylene]-4-thioxo-1,3-thiazolidin-2-one	No
9	H11	N-adamantanyl-4-[4-oxo-5-(2-thienylmethylene)-2-thioxo(1,3-thiazolidin-3-yl)]b utanamide	No
9	I11	2-[5-(1-methyl-2-oxobenzo[d]azolin-3-ylidene)-4-oxo-2-thioxo(1,3-thiazolidin-3 -yl)]-4-methylthiobutanoic acid	No
9	J11	2-[5-(5-bromo-2-oxo(1H-benzo[d]azolin-3-ylidene))-4-oxo-2-thioxo(1,3-thiazolid in-3-yl)]-4-methylthiobutanoic acid	YES
9	K11	(4R)-4-((1S,2S,7S,11S,5R,9R,10R,14R,15R)-5,9-dihydroxy-2,15-dimethyltetracyclo [8.7.0.0<2,7>.0<11,15>]heptadec-14-yl)pentanoic acid	No
9	L11	4-chloro-7-nitrobenzo[c]1,2,5-oxadiazole	No
9	M11	(2S,3S)-2-[(2S,3S)-3-(4-hydroxy-3-methoxyphenyl)-2-(hydroxymethyl)(2H,3H-benzo [e]1,4-dioxin-6-yl)]-3,5,7-trihydroxychroman-4-one	No
9	N11	[4-((1E)-2-benzothiazol-2-ylvinyl)phenyl]dimethylamine	No
9	O11	1-chloroanthracene-9,10-dione	No
9	P11	1,5-dichloroanthracene-9,10-dione	No
9	A12	1-hydroxy-3,11-dioxa-7,9-diazatricyclo[4.3.1.1<2,5>]undecan-8-one	No

9	B12	(6-methyl-6-azabicyclo[4.4.0]dec-2-yl)methyl 2-methoxyacetate, iodide	No
9	C12	quinoxaline-6-carboxylic acid	No
9	D12	ethyl 2-(2-furylcarbonylamino)-4-methyl-5-(pyrrolidinylcarbonyl)thiophene-3-ca rboxylate	No
9	E12	3,4-diphenyl-1-xanthen-9-yl-1,2,4-triazoline-5-thione	No
9	F12	3-[4-chloro-3-(trifluoromethyl)phenyl]-2-thioxo-1,3-thiazolidin-4-one	No
9	G12	5-[(4-fluorophenyl)methoxy]-4-methyl-2-[5-(2-methyl(1,3-thiazol-4-yl))-2-pheny l-6-(trifluoromethyl)pyrimidin-4-yl]phenol	No
9	H12	5-(2-oxo-1-prop-2-enylbenzo[d]azolin-3-ylidene)-3-propyl-2-thioxo-1,3-thiazoli din-4-one	No
9	I12	2-amino-6-(4-bromophenyl)-4-(4-methoxyphenyl)pyridine-3-carbonitrile	No
9	J12	N'-dodecyl-N-(3-morpholin-4-ylpropyl)ethane-1,2-diamide	No
9	K12	7-bromo-4-(4-nitrophenyl)-3,4,5,3a,9b-pentahydrocyclopenta[1,2-c]quinoline	YES
9	L12	{[4-(4-bromophenoxy)phenyl]sulfonyl}piperidine	No
9	M12	3-[4-(naphthylcarbonyl)piperazinyl]benzo[d]1,2-thiazole-1,1-dione	No
9	N12	bis(2-methylpropyl)({2-[(cycloheptylideneazamethyl)amino]-5-nitrophenyl}sulfon yl)amine	No
9	O12	1-[(cycloheptylideneazamethyl)amino]-4-nitro-2-(piperidylsulfonyl)benzene	No
9	P12	1-{[4-(4-fluorophenyl)piperazinyl]methyl}-3-(2-naphthylazamethylene)benzo[d]az olin-2-one	No
9	A13	5-(2H-benzo[3,4-d]1,3-dioxolan-5-ylmethyl)-1,3-dimethyl-5-(2-(4-pyridyl)ethyl) -1,3,5-trihydropyrimidine-2,4,6-trione	No
9	B13	6-hydroxy-5-[(6-hydroxy-4-oxo-1-phenyl-2-thioxo(1,3-dihydropyrimidin-5-yl))-2- pyridylmethyl]-1-phenyl-2-thioxo-1,3-dihydropyrimidin-4-one	No
9	C13	1,2-dimethoxy-4-(5,6,7,8,12-pentahydrobenzo[h]1,2,4-triazolo[5,1-b]quinazolin- 7-yl)benzene	No
9	D13	2-[2-(2-indolinyl-2-oxoethylthio)benzothiazol-6-yl]benzo[c]azoline-1,3-dione	No
9	E13	N-(2,5-dimethoxyphenyl)-2-(1,3-dimethyl-2,6-dioxo(1,3,7-trihydropurin-7-yl))ac etamide	No
9	F13	[(4-{[(4-fluorophenyl)sulfonyl]amino}phenyl)sulfonyl](4-methylpyrimidin-2-yl)a mine	No
9	G13	[(4-{[(phenylamino)thioxomethyl]amino}phenyl)sulfonyl]piperidine	No
9	H13	4-methoxy-1-(9-phenyl(6H,10aH-benzo[e]2-pyrazolino[1,5-c]1,3-oxazin-6-yl))benz ene	No
9	I13	5,5-dimethyl-2-[({4-[(4-methylpiperidyl)sulfonyl]phenyl}amino)azamethylene]cyc lohexane-1,3-dione	No

9	J13	11-phenyl-2,3,4,11,10a-pentahydrobenzo[1',2'-1,2]cyclopenta[3,4-b]quinoline-1, 10-dione	No
9	K13	N-cyclohexyl(6-ethoxy-2,2,4-trimethyl(1,2,3,4-tetrahydroquinolyl))carboxamide	No
9	L13	(4,6-dimethylpyrimidin-2-yl)[imino(naphthylamino)methyl]amine	YES
9	M13	(4,6-dimethylpyrimidin-2-yl)[imino(2-naphthylamino)methyl]amine	No
9	N13	(4,6-dimethylpyrimidin-2-yl){imino[(2-methyl-4-nitrophenyl)amino]methyl}amine	No
9	O13	(4,6-dimethylpyrimidin-2-yl){imino[(2-methyl-5-nitrophenyl)amino]methyl}amine	No
9	P13	(4,6-dimethylpyrimidin-2-yl){imino[(4-methyl-3-nitrophenyl)amino]methyl}amine	No
9	A14	2-[(6-ethoxy-4-methylquinazolin-2-yl)amino]-5,6-dimethylhydropyrimidin-4-one	No
9	B14	4-[(4,4,7,8-tetramethyl-4,5-dihydro-1,2-dithioleno[5,4-c]quinolinylidene)azame thyl]benzenesulfonamide	No
9	C14	11-(3,4-dimethoxyphenyl)-11H-benzo[b]indeno[1,2-e]1,4-thiazepin-12-ol	No
9	D14	1,2,2,4-tetramethyl-7-(1,2,2,4-tetramethyl(4-1,2,3,4-tetrahydroquinolyl))-1,2- dihydroquinoline	YES
9	E14	1-methyl-5-phenyl-1,3,5,11-tetrahydroindeno[2,3-e]pyrimidino[4,5-b]pyridine-2, 4,6-trione	No
9	F14	1-methyl-5-(4-methylphenyl)-1,3,5,11-tetrahydroindeno[2,3-e]pyrimidino[4,5-b]p yridine-2,4,6-trione	No
9	G14	5-(4-chlorophenyl)-1-methyl-1,3,5,11-tetrahydroindeno[2,3-e]pyrimidino[4,5-b]p yridine-2,4,6-trione	No
9	H14	5-(4-bromophenyl)-1-methyl-1,3,5,11-tetrahydroindeno[2,3-e]pyrimidino[4,5-b]py ridine-2,4,6-trione	YES
9	I14	5-(2,4-dichlorophenyl)-1-methyl-1,3,5,11-tetrahydroindeno[2,3-e]pyrimidino[4,5 -b]pyridine-2,4,6-trione	No
9	J14	4-phenylphenyl 4,4,6-trimethyl-1-thioxo(4,5-dihydro-1,2-dithioleno[5,4-c]quino lin-5-yl) ketone	No
9	K14	(4,6-dimethylpyrimidin-2-yl){imino[(4-propoxyphenyl)amino]methyl}amine	No
9	L14	(3Z)-4-[(2,4-difluorophenyl)amino]-4-[(4,6-dimethylpyrimidin-2-yl)amino]-3-aza but-3-en-2-one	YES
9	M14	2-(1H-1,2,4-triazol-5-ylthio)-1-(8-methoxy-4,4-dimethyl-1-thioxo(4,5-dihydro-1 ,2-dithioleno[5,4-c]quinolin-5-yl))ethan-1-one	No
9	N14		No
9	O14	4-prop-2-enyl-3-(3-pyridyl)-1,2,4-triazoline-5-thione	No
9	P14	1-benzothiazol-2-yl-4-[(propylamino)propylidene]-3-(trifluoromethyl)-1,2-diazo lin-5-one	No
9	A15	3-(2-bromophenyl)-4-prop-2-enyl-1,2,4-triazoline-5-thione	No
9	B15	1-[(4-chloro-2-methylphenyl)azamethylene]-8-ethoxy-4,4-dimethyl-4,5-dihydro-1, 2-dithioleno[5,4-c]quinoline	No

9	C15	2-propoxy-1-[(4,4,7,8-tetramethyl(4,5-dihydro-1,2-dithioleno[5,4-c]quinolinyli dene))azamethyl]benzene	No
9	D15	indolinyl 2-thienyl ketone	No
9	E15	2-(1,3-dioxobenzo[c]azolin-2-yl)-N-(1,2,4-triazol-4-yl)propanamide	No
9	F15	3-ethyl-6,8-dimethyl-4-methylene-1,3-dihydroquinazolin-2-one	No
9	G15	3-(4-methylpyrimidin-2-ylthio)-1-(2-naphthyl)azolidine-2,5-dione	No
9	H15	(2Z)-3-[(4,6-dimethylpyrimidin-2-yl)amino]-3-[(3-nitrophenyl)amino]-1-phenothi azin-10-yl-2-azaprop-2-en-1-one	No
9	I15	5-(4-chlorophenyl)-1,3,4-oxadiazole-2-thiol	YEA
9	J15	2-benzimidazol-2-yl-2-(2-oxo(1H-benzo[d]azolidin-3-ylidene))ethanenitrile	No
9	K15	1-phenyl-3-(2-pyridylthio)azolidine-2,5-dione	No
9	L15	11-(2-furyl)-2,3,4,5,11-pentahydroindeno[3,2-b]quinoline-1,10-dione	No
9	M15	3-methoxy-2-thioxo-1,3-dihydroquinazolin-4-one	No
9	N15	3-(phenylmethoxy)-2-(phenylmethylthio)-3-hydroquinazolin-4-one	No
9	O15	methyl 2-(pyrazol-3-ylcarbonylamino)acetate	No
9	P15		No
9	A16	1-methyl-3-phenyl-2-thioxo-1,3-dihydroquinazolin-4-one	No
9	B16	3-phenyl-2-sulfanyl-3-hydroquinazolin-4-one	No
9	C16	3-phenyl-2-prop-2-ynylthio-3-hydroquinazolin-4-one	No
9	D16	3-phenyl-2-prop-2-enylthio-3-hydroquinazolin-4-one	No
9	E16	(2-{[(tert-butyl)amino]thioxomethylthio}ethoxy)-N-butylcarboxamide	No
9	F16	N-butyl{2-[(cyclohexylamino)thioxomethylthio]ethoxy}carboxamide	No
9	G16	N-butyl{2-[(propylamino)thioxomethylthio]ethoxy}carboxamide	No
9	H16	2-[(adamantan-2-ylideneazamethyl)amino]-3-phenyl-3-hydroquinazolin-4-one	No
9	I16	2-{[(2-oxo(3a,7a-dihydroindol-3-ylidene))azamethyl]amino}-3-phenyl-3-hydroquin azolin-4-one	No
9	J16	methyl 3-bromo-2-oxopyran-5-carboxylate	No
9	K16	4-phenyl-4,10-dihydro-1,2,3,4-tetraazolo[1,5-a]quinazolin-5-one	YES
9	L16	(1Z)-3,3-dichloro-1-phenyl-2-piperidyl-1-azaprop-1-ene	No
9	M16	2-methylthio-5,6,7-trihydrocyclopenta[2,1-b]pyridine-3-carbonitrile	OFFSCALE
9	N16	(1E)-2-(2-chloro-5-nitrophenyl)-1-(4-iodophenyl)-1-azaethene	No
9	O16	4-hydroxyquinoline-2-carboxylic acid	No
9	P16	2-hydrazino-3-phenyl-3-hydroquinazolin-4-one	No
9	A17	7-methyl-4H,6H,8H,9H,12H,16H-1,3-dioxoleno[4''',5'''-3'',4'']benzo[1'',2''-8', 9']azecino[5',4'-2,1]benzo[4,5-d]1,3-dioxolan-15-one	No
9	B17	(1,3,3-trimethyl-6-azabicyclo[3.2.1]oct-6-yl)-N-{4-[(1,3,3-trimethyl-6-azabicy clo[3.2.1]oct-6-yl)carbonylamino]phenyl}carboxamide	No
9	C17	2-(hydroxyimino)-1,2-diphenylethan-1-ol	No
9	D17	[(5-morpholin-4-yl-2-furyl)methylene]methane-1,1-dicarbonitrile	No

9	E17	4-[(2,4-dinitrophenyl)amino]phenol	No
9	F17	1-methylbenzo[d]1,3-oxazine-2,4-dione	No
9	G17	(1S,10S,11S,15S,2R,14R)-14-hydroxy-14-(2-hydroxyacetyl)-2,15-dimethyltetracycl o[8.7.0.0<2,7>.0<11,15>]heptadeca-3,6-diene-5,17-dione	YES
9	H17	2-((1S,5S)-6,6-dimethylbicyclo[3.1.1]hept-2-en-2-yl)ethan-1-ol	YES
9	I17	3-hydroisoindolylamine	YES
9	J17	6-bromo-8-quinolylamine	YES
9	K17	11-prop-2-enylspiro[1,2,3-trihydroquinazoline-2,3'-indoline]-4,12-dione	No
9	L17	1-(2H-benzo[3,4-d]1,3-dioxolen-5-yl)-2-(4-methyl(1,2,4-triazol-3-ylthio))ethan -1-one	No
9	M17	3-(3,3,7,8-tetramethyl-1-oxo-2,3,4-trihydro-5H,10H,11H-benzo[b]benzo[2,1-f]1,4 -diazepin-11-yl)chromen-4-one	No
9	N17	methyl 4-aminopyrazole-3-carboxylate	No
9	O17	4-chloro-2,5-dimethoxybenzenesulfonamide	No
9	P17	3-(2-furyl)-4-methyl-1-[(4-methylpiperidyl)methyl]-1,2,4-triazoline-5-thione	No
9	A18	3-(2-furyl)-4-methyl-1-(piperidylmethyl)-1,2,4-triazoline-5-thione	No
9	B18	spiro[1,2,3-trihydroquinazoline-2,3'-indoline]-4,12-dione	No
9	C18	2-(acetylamino)-N-cyclopropyl-3-indol-3-ylpropanamide	No
9	D18	2-(2-oxopropyl)-2-hydrobenzo[d]isothiazole-1,1,3-trione	No
9	E18	methyl 5-(methoxycarbonyl)-4-(2-thienyl)-1-(2-thienylmethyl)-1,4-dihydropyridi ne-3-carboxylate	No
9	F18	3-(2-thienyl)-11-(3-thienyl)-2,3,4-trihydro-5H,10H,11H-benzo[b]benzo[2,1-f]1,4 -diazepin-1-one	No
9	G18	3-hydroxy-3-(2-oxocyclooctyl)indolin-2-one	YES
9	H18	6-methyl-2-[(2,4,6-trimethylphenyl)methylthio]pyrimidin-4-ol	YES
9	I18	indol-3-ylmethoxy-2-thienylmethane	YES
9	J18	4,6-dimethyl-5-nitro-2-oxohydropyridine-3-carbonitrile	No
9	K18	3-[(4-fluorophenyl)methylthio]-1,2,4-thiadiazole-5-ylamine	No
9	L18	3-quinazolin-4-ylthiopropanoic acid	No
9	M18	pyrrolidinyl 2-sulfanylbenzothiazol-5-yl ketone	No
9	N18	N-butyl-N'-(3-imidazolylpropyl)ethane-1,2-diamide	No
9	O18	6-(6-bromo(2H-benzo[d]1,3-dioxolan-5-yl))-5-nitropiperidin-2-one	No
9	P18	ethyl 2-(1H-1,2,3,4-tetraazol-5-yl)acetate	No
9	A19	2-(2,5-dimethoxyphenyl)-3-hydroxychromen-4-one	No
9	B19	(phenylsulfonyl)(2,2,6,6-tetramethyl(4-piperidyl))amine	No
9	C19	5-acetyl-1-hydroxy-4-methyl-2-(2-thienyl)imidazole	No
9	D19	N'-(methylethyl)-N-(2,2,6,6-tetramethyl(4-piperidyl))ethane-1,2-diamide	No
9	E19	1-[(3,4-dimethoxyphenyl)methyl]-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline	No

9	F19	6-chloro-3-hydroxy-2-(2-thienyl)chromen-4-one	No
9	G19	4-hydroxy-3-[(4-methylpiperidyl)methyl]chromen-2-one	No
9	H19	3-[(2-chlorophenyl)methylthio]-1,2,4-thiadiazole-5-ylamine	YES
9	I19	5-amino-1,2-dimethylimidazole-4-carboxamide	No
9	J19	1-acetyl-3-(4-pyridyl)-4-oxa-1,2-diazaspiro[4.6]undec-2-ene	No
9	K19	6,7-dimethoxy-4-methylchromen-2-one	No
9	L19	1,2,3,4,6,11-hexahydrobenzimidazolo[2,1-b]quinazolin-12-one	No
9	M19	3-oxo-2H,4H-benzo[e]1,4-oxazaperhydroine-6-carboxylic acid	No
9	N19	2-(5,7-dichloro-2-methylindol-3-yl)ethylamine	No
9	O19	(1R,6R)-5-azabicyclo[4.4.0]decan-2-one	No
9	P19	2-(adamantanylamino)ethan-1-ol	No
9	A20	1H-1,2,4-triazol-3-yl-N-(2-morpholin-4-ylethyl)carboxamide	No
9	B20	2-(4-hydroxy-5,7-dimethylpyridino[2,3-d]pyrimidin-2-ylthio)acetic acid	No
9	C20	2H-benzo[3,4-d]1,3-dioxolan-5-yl[(4-methoxynaphthyl)sulfonyl]amine	No
9	D20	[(2,5-dimethoxyphenyl)sulfonyl]ethylamine	No
9	E20	[2-(1-methyl(1,2,3,4-tetraazol-5-ylthio))ethyl][(4-methylphenyl)sulfonyl]amine	No
9	F20	methoxy-N-[5-(morpholin-4-ylmethyl)(1,3-thiazol-2-yl)]carboxamide	No
9	G20	4-indol-3-yl-N-(2-phenylthioethyl)butanamide	No
9	H20	5-[(6-chloro(2H,4H-benzo[e]1,3-dioxin-8-yl))methylthio]-1-phenyl-1,2,3,4-tetra azole	No
9	I20	6-(6-chloro(2H-benzo[d]1,3-dioxolan-5-yl))-5-nitropiperidin-2-one	No
9	J20	[(4-aminophenyl)sulfonyl]phenylamine	No
9	K20	ethyl 2-cyano-3,3-disulfanylprop-2-enoate	No
9	L20	(2R)-2-amino-3-indol-3-ylpropanoic acid	No
9	M20	5-(1,2-dihydroxyethyl)-3,4-dihydroxy-5-hydrofuran-2-one	No
9	N20	N-[(4-aminophenyl)sulfonyl]acetamide, oxamethane, sodium salt	No
9	O20	N-(1,3-dioxobenzo[c]azolin-2-yl)methoxycarboxamide	No
9	P20	(3,4-dimethoxyphenyl)(1-methylimidazol-2-yl)methan-1-ol	No
9	A21	hydrazino(phenylamino)methane-1-thione	No
9	B21	1-[(4S,2R,5R)-4-hydroxy-5-(hydroxymethyl)oxolan-2-yl]-5-iodo-1,3-dihydropyrimi dine-2,4-dione	No
9	C21	5-((4R)-2,2-dimethyl(1,3-dioxolan-4-yl))(5S)-3,4-dihydroxy-5-hydrofuran-2-one	No
9	D21	2,4-dichloro-5-sulfamoylbenzoic acid	No
9	E21	2,4,6-triphenoxy-1,3,5-triazine	No
9	F21	3-(3-oxohydroisobenzofuranyl)-3-hydroisobenzofuran-1-one	YES
9	G21	9-methoxyfurano[3,2-g]chromen-2-one	No
9	H21	5-bromo-2,4-dimethoxybenzaldehyde	YES
9	I21	5-((1E)-2-(1H-indazol-5-yl)-2-azavinyl)-2H-benzo[d]1,3-dioxolane	No

9	J21	2H-benzo[3,4-d]1,3-dioxolan-5-yl-N-[4-(2H-benzo[3,4-d]1,3-dioxolan-5-ylcarbony lamino)(1,2,5-oxadiazol-3-yl)]carboxamide	No
9	K21	5-{(1E)-2-[4-(dimethylamino)-3-nitrophenyl]-1-azavinyl}-3-hydrobenzimidazol-2- one	No
9	L21	2-bromo-2-nitropropane-1,3-diol	No
9	M21	2-(phenylmethylthio)-1,2,3-trihydroquinazolin-4-one	No
9	N21	methyl 2-(4-oxo-3-prop-2-enyl-3-hydroquinazolin-2-ylthio)acetate	No
9	O21	aminobenzoxazol-2-ylcarboxamidine	No
9	P21	8-ethoxy-2-(4-methoxyphenyl)-4,4-dimethyl-2,4,5-trihydroisothiazolo[5,4-c]quin oline-1-thione	No
9	A22	(4,6-dimethylpyrimidin-2-yl){imino[(2-propoxyphenyl)amino]methyl}amine	No
9	B22	2-(2,3-dihydroperimidin-2-yl)-1,4-dimethoxybenzene	No
9	C22	3-(1,2,3,4-tetraazolyl)propanoic acid	No
9	D22	5-bromo-1-(2-naphthylsulfonyl)indoline	No
9	E22	7-(phenylcarbonyl)-2H,4H,5H-benzo[f]1,4-oxazepin-3-one	No
9	F22	3-aminohydropyridin-2-one	No
9	G22	3-(2-cyclohexylthiobenzimidazolyl)propan-1-ol	No
9	H22	8-quinazolin-4-ylthiopurine-6-ylamine	No
9	I22	2-(3-cyanoindolyl)-N-(2-indol-3-ylethyl)acetamide	No
9	J22	4-(2-benzimidazol-2-ylthioethoxy)-1-(methylpropoxy)benzene	No
9	K22	1-cyclohexyl-2-(phenylmethylthio)benzimidazole	No
9	L22	1-chloro-4-[2-(1-cyclohexylbenzimidazol-2-ylthio)ethoxy]benzene	No
9	M22	1,3-bis(morpholin-4-ylmethyl)-3-hydrobenzimidazol-2-one	No
9	N22	1-{[4-(4,6-dipiperidyl(1,3,5-triazin-2-yl))piperazinyl]sulfonyl}-4-chlorobenze ne	No
9	O22	4-{4-[(2,4-dimethoxyphenyl)amino]quinazolin-2-yl}-1-(phenylsulfonyl)piperazine	No
9	P22	{2-[(4-chloro-2-nitrophenyl)amino]ethyl}(methylsulfonyl)amine	No
Plate	**Well**	**IUPAC NAME**	**Inhibitor Y/N**
10	A03	8-{[2-(4-chlorophenoxy)ethyl]amino}-1,3,7-trimethyl-1,3,7-trihydropurine-2,6-d ione	No
10	B03	2-cyclohexylthio-1-benzylbenzimidazole	No
10	C03	2-[(1,2,5-trimethylpyrrol-3-yl)methylene]-1,3-thiazolidino[3,2-a]benzimidazol- 3-one	No
10	D03	4-naphthyl-3,4,5,3a,9b-pentahydrocyclopenta[1,2-c]quinoline-8-carboxylic acid	No
10	E03	[(4-methylphenyl)sulfonyl]-1,2,4-triazol-4-ylamine	No
10	F03	cyclopentyl[(4-methylphenyl)sulfonyl]amine	No
10	G03	(phenylsulfonyl)pyrimidin-2-ylamine	No
10	H03	(phenylsulfonyl)-1,2,4-triazol-4-ylamine	No
10	I03	benzothiazol-2-yl(phenylsulfonyl)amine	No

10	J03	(phenylsulfonyl)indoline	No
10	K03	2-methylpiperidyl 2-thienyl ketone	No
10	L03	1-(2-hydroxyethyl)-4-(phenylsulfonyl)piperazine	No
10	M03	[(4-methoxyphenyl)sulfonyl]dimethylamine	No
10	N03	1-(2-hydroxyethyl)-4-[(4-methoxyphenyl)sulfonyl]piperazine	No
10	O03	[(4-fluorophenyl)sulfonyl]phenylamine	No
10	P03	bisbenzyl(methylsulfonyl)amine	No
10	A04	N-cyclohexyl-N-ethyl-2-thienylcarboxamide	No
10	B04	ethyl 4-(2-thienylcarbonyl)piperazinecarboxylate	No
10	C04	N-[3-(diethylamino)propyl]-2-thienylcarboxamide	No
10	D04	3,5-dimethylpiperidyl 2-thienyl ketone	No
10	E04	N-cycloheptyl-2-thienylcarboxamide	No
10	F04	(2-methoxyethyl)(phenylsulfonyl)amine	No
10	G04	2-[(cyanomethyl)(phenylsulfonyl)amino]ethanenitrile	No
10	H04	2-[(phenylsulfonyl)amino]ethanenitrile	No
10	I04	(2-methylpropyl)(phenylsulfonyl)amine	No
10	J04	(phenylsulfonyl)(2-pyridylmethyl)amine	No
10	K04	benzyl(phenylsulfonyl)-2-pyridylamine	No
10	L04	(oxolan-2-ylmethyl)(phenylsulfonyl)amine	No
10	M04	[3-(diethylamino)propyl][(4-chlorophenyl)sulfonyl]amine	No
10	N04	2-{[(4-chlorophenyl)sulfonyl](cyanomethyl)amino}ethanenitrile	No
10	O04	(3-imidazolylpropyl)[(4-methylphenyl)sulfonyl]amine	No
10	P04	cyclohexyl(2-hydroxyethyl)[(4-methoxyphenyl)sulfonyl]amine	No
10	A05	[(4-methoxyphenyl)sulfonyl]diprop-2-enylamine	No
10	B05	[(4-methoxyphenyl)sulfonyl](2-pyridylmethyl)amine	No
10	C05	cyclohexylethyl[(2,4,6-trimethylphenyl)sulfonyl]amine	No
10	D05	pentyl[(2,4,6-trimethylphenyl)sulfonyl]amine	No
10	E05	2-{(cyanomethyl)[(2,4,6-trimethylphenyl)sulfonyl]amino}ethanenitrile	No
10	F05	2-{[(2,4,6-trimethylphenyl)sulfonyl]amino}ethanenitrile	No
10	G05	(2-methylpropyl)[(2,4,6-trimethylphenyl)sulfonyl]amine	No
10	H05	(methylpropyl)[(2,4,6-trimethylphenyl)sulfonyl]amine	No
10	I05	[(4-fluorophenyl)sulfonyl]methylphenylamine	No
10	J05	cyclohexylethyl[(4-fluorophenyl)sulfonyl]amine	No
10	K05	[(4-fluorophenyl)sulfonyl](3-methoxypropyl)amine	No
10	L05	dibutyl[(4-fluorophenyl)sulfonyl]amine	No
10	M05	[(4-fluorophenyl)sulfonyl]diprop-2-enylamine	No
10	N05	2-{(cyanomethyl)[(4-fluorophenyl)sulfonyl]amino}ethanenitrile	No
10	O05	[(4-fluorophenyl)sulfonyl]benzyl-2-pyridylamine	No
10	P05	cycloheptyl[(4-fluorophenyl)sulfonyl]amine	No
10	A06	[(2,5-dichlorophenyl)sulfonyl](3-methoxypropyl)amine	No
10	B06	[(2,5-dichlorophenyl)sulfonyl]diprop-2-enylamine	No

10	C06	2-{[(2,5-dichlorophenyl)sulfonyl](cyanomethyl)amino} ethanenitrile	No
10	D06	2-{[(2,5-dichlorophenyl)sulfonyl]amino}ethanenitrile	No
10	E06	[(2,5-dichlorophenyl)sulfonyl]propylamine	No
10	F06	[(2,5-dichlorophenyl)sulfonyl](methylpropyl)amine	No
10	G06	[(2,5-dichlorophenyl)sulfonyl](3-imidazolylpropyl)amine	No
10	H06	[2-chloro-5-(trifluoromethyl)phenyl](methylsulfonyl)amine	No
10	I06	(2,5-dichlorophenyl)(methylsulfonyl)amine	No
10	J06	(2,3-dichlorophenyl)(methylsulfonyl)amine	No
10	K06	(2,4-dichlorophenyl)(methylsulfonyl)amine	No
10	L06	(5-chloro-2-methoxyphenyl)(methylsulfonyl)amine	No
10	M06	(2,4-dimethoxyphenyl)(methylsulfonyl)amine	No
10	N06	(4-chloro-2,5-dimethoxyphenyl)(methylsulfonyl)amine	No
10	O06	1-(4-fluorophenyl)-4-(methylsulfonyl)piperazine	No
10	P06	dibutyl(methylsulfonyl)amine	No
10	A07	2-(methylsulfonyl)-1,2,3,4-tetrahydroisoquinoline	No
10	B07	(tert-butyl)[(4-methoxyphenyl)sulfonyl]amine	No
10	C07	[(4-methoxyphenyl)sulfonyl](methylethyl)amine	No
10	D07		No
10	E07	butyl[(4-fluorophenyl)sulfonyl]amine	No
10	F07	[(4-fluorophenyl)sulfonyl]hexylamine	No
10	G07	4-chloro-1-[(2-ethylpiperidyl)sulfonyl]benzene	No
10	H07	1-[(4-methoxyphenyl)sulfonyl]-1,2,3,4-tetrahydroquinoline	No
10	I07	[(4-methoxyphenyl)sulfonyl]indoline	No
10	J07	(4-pyridylmethyl)[(2,4,6-trimethylphenyl)sulfonyl]amine	No
10	K07	1-[(2,4,6-trimethylphenyl)sulfonyl]-1,2,3,4-tetrahydroquinoline	YES
10	L07	[(2,4,6-trimethylphenyl)sulfonyl]indoline	No
10	M07	1-[(2-ethylpiperidyl)sulfonyl]-4-fluorobenzene	No
10	N07	1,4-dichloro-2-[(2-ethylpiperidyl)sulfonyl]benzene	No
10	O07	1-(methylsulfonyl)-1,2,3,4-tetrahydroquinoline	No
10	P07	ethyl 1-(methylsulfonyl)piperidine-4-carboxylate	No
10	A08	methyl(methylsulfonyl)benzylamine	No
10	B08	N-[3-(dimethylamino)propyl]-2-thienylcarboxamide	No
10	C08	[3-(dimethylamino)propyl][(4-chlorophenyl)sulfonyl]amine	No
10	D08	[3-(dimethylamino)propyl][(2,4,6-trimethylphenyl)sulfonyl]amine	No
10	E08	(3-fluorophenyl)[(4-fluorophenyl)sulfonyl]amine	No
10	F08	benzothiazol-2-yl[(4-fluorophenyl)sulfonyl]amine	No
10	G08	[(4-fluorophenyl)sulfonyl]pyrimidin-2-ylamine	No
10	H08	[(2,5-dichlorophenyl)sulfonyl](6-methyl(2-pyridyl))amine	No
10	I08	[(2,5-dichlorophenyl)sulfonyl][3-(dimethylamino)propyl]amine	No
10	J08	[(2,5-dichlorophenyl)sulfonyl]-3-pyridylamine	No

10	K08	[(2,5-dichlorophenyl)sulfonyl]-2-pyridylamine	No
10	L08	(2,4-difluorophenyl)(methylsulfonyl)amine	No
10	M08	N-cyclohexyl-N-ethyl-2-methylpropanamide	No
10	N08	N-[3-(diethylamino)propyl]-2-methylpropanamide	No
10	O08	1-azaperhydroepinyl-2-methylpropan-1-one	YES
10	P08	N-cyclohexyl-2-methyl-N-methylpropanamide	No
10	A09	1-(2,6-dimethylmorpholin-4-yl)-2-methylpropan-1-one	No
10	B09		No
10	C09	[benzylsulfonyl]diprop-2-enylamine	No
10	D09	4-benzyl-1-[benzylsulfonyl]piperidine	No
10	E09	cyclohexylmethyl[benzylsulfonyl]amine	No
10	F09	benzothiazol-2-yl[benzylsulfonyl]amine	No
10	G09	[benzylsulfonyl]-1,2,4-triazol-4-ylamine	No
10	H09	2-{[(4-bromophenyl)sulfonyl](cyanomethyl)amino}ethanenitrile	No
10	I09	2-{[(4-bromophenyl)sulfonyl]amino}ethanenitrile	No
10	J09	[(4-bromophenyl)sulfonyl]-4-pyridylamine	No
10	K09	[(4-bromophenyl)sulfonyl]-3-pyridylamine	No
10	L09	2-furyl-N-(4-iodophenyl)carboxamide	No
10	M09	N,N-bis(cyanomethyl)-2-furylcarboxamide	No
10	N09	3,5-dimethylpiperidyl 2-furyl ketone	No
10	O09	2-furyl-N-heptylcarboxamide	No
10	P09	2,6-dimethylmorpholin-4-yl 2-furyl ketone	No
10	A10	2H-benzo[3,4-d]1,3-dioxolen-5-yl-N-cyclopentylcarboxamide	No
10	B10	2H-benzo[3,4-d]1,3-dioxolen-5-yl-N-[3-(dimethylamino)propyl]carboxamide	No
10	C10	1,3-dimethyl-7-{2-oxo-2-[4-benzylpiperidyl]ethyl}-1,3,7-trihydropurine-2,6-dio ne	No
10	D10	N,N-bis(cyanomethyl)xanthen-9-ylcarboxamide	No
10	E10	N-cyclopentylxanthen-9-ylcarboxamide	No
10	F10	N-methylxanthen-9-ylcarboxamide	No
10	G10	4-methylpiperazinyl xanthen-9-yl ketone	No
10	H10	ethyl 4-(morpholin-4-ylcarbonyl)piperazinecarboxylate	No
10	I10	N-(3-methoxypropyl)morpholin-4-ylcarboxamide	No
10	J10	3,5-dimethylpiperidyl morpholin-4-yl ketone	No
10	K10	N-cycloheptylmorpholin-4-ylcarboxamide	No
10	L10	azaperhydroepinyl morpholin-4-yl ketone	No
10	M10	N,N-diethylmorpholin-4-ylcarboxamide	No
10	N10	indolinyl morpholin-4-yl ketone	No
10	O10	ethyl 1-(morpholin-4-ylcarbonyl)piperidine-4-carboxylate	No
10	P10	2-methylpiperidyl morpholin-4-yl ketone	No
10	A11	2,6-dimethylmorpholin-4-yl morpholin-4-yl ketone	No
10	B11	ethyl 2-(3,5-dimethylpiperidyl)-2-oxoacetate	No

10	C11	ethyl 2-(2,6-dimethylmorpholin-4-yl)-2-oxoacetate	No
10	D11	ethyl (N-(1,2,4-triazol-4-yl)carbamoyl)formate	No
10	E11	2-ethyl-N,N-diprop-2-enylhexanamide	No
10	F11	N,N-bis(cyanomethyl)-2-ethylhexanamide	No
10	G11	2-ethyl-N-(oxolan-2-ylmethyl)hexanamide	No
10	H11	N-(tert-butyl)-2-ethylhexanamide	No
10	I11	1-(2,6-dimethylmorpholin-4-yl)-2-ethylhexan-1-one	No
10	J11	N-(2-morpholin-4-ylethyl)-N'-(2-morpholin-4-ylethyl)ethane-1,2-diamide	No
10	K11	N,N-dipropyl-N',N'-dipropylethane-1,2-diamide	No
10	L11	1,2-diindolinylethane-1,2-dione	No
10	M11	ethyl 1-{2-[4-(ethoxycarbonyl)piperidyl]-2-oxoacetyl}piperidine-4-carboxylate	No
10	N11	[(4-bromophenyl)sulfonyl](5-chloro(2-pyridyl))amine	No
10	O11	N-(5-chloro(2-pyridyl))xanthen-9-ylcarboxamide	No
10	P11	N-[4-(dimethylamino)phenyl]morpholin-4-ylcarboxamide	No
10	A12	4-({[(4-chlorophenyl)sulfonyl]amino}methyl)benzenesulfonamide	No
10	B12	[(4-chlorophenyl)sulfonyl](methylbutyl)amine	No
10	C12	(methylbutyl)[(2,4,6-trimethylphenyl)sulfonyl]amine	No
10	D12	[(4-bromophenyl)sulfonyl](methylbutyl)amine	No
10	E12	N-(methylbutyl)morpholin-4-ylcarboxamide	No
10	F12	5,6-dimethylbenzimidazolyl morpholin-4-yl ketone	No
10	G12	[(4-fluorophenyl)sulfonyl](3-methylbutyl)amine	No
10	H12	[(2,5-dichlorophenyl)sulfonyl](3-methylbutyl)amine	No
10	I12	(3-methylbutyl)(methylsulfonyl)amine	No
10	J12	[(4-bromophenyl)sulfonyl](3-methylbutyl)amine	No
10	K12	dimethyl[(4-phenylpiperazinyl)sulfonyl]amine	No
10	L12	N-[3-(dimethylamino)propyl]-2-(2-thienyl)acetamide	No
10	M12	[(dimethylamino)sulfonyl](oxolan-2-ylmethyl)amine	No
10	N12	2-methyl-N-(oxolan-2-ylmethyl)butanamide	No
10	O12	2-methyl-N-(oxolan-2-ylmethyl)pentanamide	No
10	P12	[(dimethylamino)sulfonyl](methylethyl)benzylamine	No
10	A13	(3,4-dichlorophenyl)[(dimethylamino)sulfonyl]amine	No
10	B13	N-hexyl-2-(2-thienyl)acetamide	No
10	C13	[(hexylamino)sulfonyl]dimethylamine	No
10	D13	N-cyclopentyl-2-(2-thienyl)acetamide	No
10	E13	2-methyl-N-(1,3-thiazol-2-yl)butanamide	No
10	F13	dimethyl{[4-benzylpiperidyl]sulfonyl}amine	No
10	G13	[(dimethylamino)sulfonyl](4-bromophenyl)amine	No
10	H13	N,N-diprop-2-enyl-2-(2-thienyl)acetamide	No
10	I13	[(dimethylamino)sulfonyl](phenylethyl)amine	No
10	J13	3-methyl-N-pentylbutanamide	No

10	K13	[(dimethylamino)sulfonyl](4-ethoxyphenyl)amine	No
10	L13	[(dimethylamino)sulfonyl]methylphenylamine	No
10	M13	N,N-diethyl-2-(2-thienyl)acetamide	No
10	N13	N-cycloheptyl-2-(2-thienyl)acetamide	No
10	O13	N-cycloheptyl-3-methylbutanamide	No
10	P13	N-cycloheptyl-2-methylpentanamide	No
10	A14	[(dimethylamino)sulfonyl](5-chloro-2-methoxyphenyl)amine	No
10	B14	ethyl 1-[(dimethylamino)sulfonyl]piperidine-4-carboxylate	No
10	C14	ethyl 1-(3-methylbutanoyl)piperidine-4-carboxylate	No
10	D14	[(dimethylamino)sulfonyl][(4-methoxyphenyl)methyl]amine	No
10	E14	[(dimethylamino)sulfonyl]benzylamine	No
10	F14	[(dimethylamino)sulfonyl][(4-methylphenyl)methyl]amine	No
10	G14	1-azaperhydroepinyl-2-methylbutan-1-one	No
10	H14	N-(3-imidazolylpropyl)-2-(2-thienyl)acetamide	No
10	I14	1-(2,6-dimethylmorpholin-4-yl)-2-(2-thienyl)ethan-1-one	No
10	J14		No
10	K14	N,N-dibutyl-2-(2-thienyl)acetamide	No
10	L14	[(dimethylamino)sulfonyl]ethylphenylamine	No
10	M14	dimethyl{[(methylpropyl)amino]sulfonyl}amine	No
10	N14	dimethyl(piperidylsulfonyl)amine	No
10	O14	[(dimethylamino)sulfonyl][4-(methylethyl)phenyl]amine	No
10	P14	ethyl 2-(2-methylpentanoylamino)acetate	No
10	A15	N-(2-methoxy-isopropyl)-2-thienylcarboxamide	No
10	B15	(6-methoxybenzothiazol-2-yl)(phenylsulfonyl)amine	No
10	C15	4-{[4-(2H-benzo[d]1,3-dioxolen-5-ylmethyl)piperazinyl]sulfonyl}-1-chlorobenzen e	No
10	D15	(4,6-dimethylpyrimidin-2-yl)[(4-methylphenyl)sulfonyl]amine	No
10	E15	(2H-benzo[3,4-d]1,3-dioxolan-5-ylmethyl)[(4-methylphenyl)sulfonyl]amine	No
10	F15	1-(2H-benzo[d]1,3-dioxolen-5-ylmethyl)-4-[(2,4,6-trimethylphenyl)sulfonyl]pipe razine	No
10	G15	[(2,5-dichlorophenyl)sulfonyl](2-methoxy-isopropyl)amine	No
10	H15	2-{[4-(2H-benzo[d]1,3-dioxolen-5-ylmethyl)piperazinyl]sulfonyl}-1,4-dichlorobe nzene	No
10	I15	ethyl 1-(methylsulfonyl)piperidine-3-carboxylate	No
10	J15	[(4-bromophenyl)sulfonyl](5-methylisoxazol-3-yl)amine	No
10	K15	4-{[4-(2H-benzo[d]1,3-dioxolen-5-ylmethyl)piperazinyl]sulfonyl}-1-bromobenzene	No
10	L15	methyl 1-(2-furylcarbonyl)piperidine-4-carboxylate	No
10	M15	ethyl 1-[2-(1,3-dimethyl-2,6-dioxo-1,3,7-trihydropurin-7-yl)acetyl]piperidine- 3-carboxylate	No
10	N15	ethyl 1-(morpholin-4-ylcarbonyl)piperidine-3-carboxylate	No

10	O15	ethyl [N-(5-methyl-1,3,4-thiadiazol-2-yl)carbamoyl]formate	No
10	P15	ethyl [N-(5-methylisoxazol-3-yl)carbamoyl]formate	No
10	A16	ethyl 2-[3-(ethoxycarbonyl)piperidyl]-2-oxoacetate	No
10	B16	2-ethyl-N-(2-methoxy-isopropyl)hexanamide	No
10	C16	N-(2-methoxy-isopropyl)-2-(2-thienyl)acetamide	No
10	D16	N-(ethylpropyl)-2-(2-thienyl)acetamide	No
10	E16	ethyl 2-[2-(3,3-dimethylbutanoylamino)-1,3-thiazol-4-yl]acetate	No
10	F16	ethyl 1-(3,3-dimethylbutanoyl)piperidine-3-carboxylate	No
10	G16	methyl 1-(3,3-dimethylbutanoyl)piperidine-4-carboxylate	No
10	H16	ethyl 1-(2,2-dimethylbutanoyl)piperidine-3-carboxylate	No
10	I16	(2H-benzo[3,4-d]1,3-dioxolen-5-ylmethyl)[(dimethylamino)sulfonyl]amine	YES
10	J16	2-{[(dimethylamino)sulfonyl]amino}-6-(methylsulfonyl)benzothiazole	No
10	K16	{[4-(2H-benzo[d]1,3-dioxolen-5-ylmethyl)piperazinyl]sulfonyl}dimethylamine	No
10	L16	methyl 1-(2-methylbutanoyl)piperidine-4-carboxylate	No
10	M16	2-methyl-N-(5-methylisoxazol-3-yl)pentanamide	No
10	N16	(7S,11S,13S,17S,18S,12R,14R,15R,16R)-2,15,17,27,29-pentahydroxy-11-methoxy-3,7 ,12,14,16,18,22-heptamethyl-6,23-dioxo-8,30-dioxa-24-azatetracyclo[23.3.1.1<4, 7>.0<5,28>]triaconta-1(28),2,4,9,19,21,25(29),26-octaen-13-yl acetate	No
10	O16	4-chloro-1-methylpyrazole-3-carboxylic acid	No
10	P16	4-chloro-1-methylpyrazole-5-carboxylic acid	No
10	A17	1-methyl-3-(trifluoromethyl)pyrazole-5-carboxylic acid	No
10	B17	5-methyl-7-(trifluoromethyl)-8-hydropyrazolo[1,5-a]pyrimidine-3-carboxylic aci d	No
10	C17	8-hydropyrazolo[1,5-a]pyrimidine-2-carboxylic acid	No
10	D17	N,N-diprop-2-enylxanthen-9-ylcarboxamide	No
10	E17	N-(2-morpholin-4-ylethyl)-2-(2-thienyl)acetamide	No
10	F17	(4-iodophenyl)(2-naphthylsulfonyl)amine	No
10	G17	7-nitrobenzo[c]1,2,5-oxadiazole-4-ylamine	No
10	H17	ethyl 5-(aminomethyl)furan-2-carboxylate	No
10	I17	methyl 2-{3-[(3-oxo-1,3-thiazolidino[3,2-a]benzimidazol-2-ylidene)methyl]indol yl}acetate	No
10	J17	4-morpholin-4-yl-1-nitro-2-(2-pyridylthio)benzene	No
10	K17	6-[(4-fluoronaphthyl)methylthio]purine	No
10	L17	4-(1,3-dithiolan-2-yl)-6-methoxy-2-nitrophenol	No
10	M17	2-[(2H-benzo[3,4-d]1,3-dioxolan-5-ylamino)methyl]-4-bromophenol	No
10	N17	(5S,2R,3R,4R)-3,5-diacetyloxy-6-bromo-2-(methoxycarbonyl)-2H-3,4,5,6-tetrahydr opyran-4-yl acetate	No
10	O17	3,5-dibromopyridine	No
10	P17	2,4,6-trimethoxybenzaldehyde	No
10	A18	5-bromothiophene-2-carbaldehyde	No

10	B18	diethyl 2-(2-cyanoethyl)propane-1,3-dioate	No
10	C18	2-[(carboxymethylthio)thioxomethylthio]acetic acid	No
10	D18	((4S,5S)-2-methyl-5-phenyl(1,3-oxazolin-4-yl))methoxymethane	No
10	E18	diethyl (2E)-2,3-dicyanobut-2-ene-1,4-dioate	No
10	F18	4-chloro-2,6-dinitrophenylamine	No
10	G18	chloro[(4-methylphenyl)sulfonyl]methane	No
10	H18	methyl 4,6-dimethoxyindole-2-carboxylate	No
10	I18	(2S,3R,6R)-2-(acetyloxymethyl)-6-ethoxy-2H-3,6-dihydropyran-3-yl acetate	No
10	J18	(2Z)-3-[(ethoxycarbonyl)methoxy]-2-pyrazol-3-yl-3-azaprop-2-enoic acid	No
10	K18	5-bromo-3-nitro-4H-1,2,4-triazole	No
10	L18	spiro[4-imidazolino[4,5-b]pyridine-2,1'-cyclohexane]	No
10	M18	5-bromo-6-methyl-1,3-dihydropyrimidine-2,4-dione	No
10	N18	1,1-diethoxy-2-piperidylethane	No
10	O18	(dimethylamino){[(dimethylamino)thioxomethyl]disulfanyl}methane-1-thione	No
10	P18		No
10	A19	6-methoxybenzothiazole-2-carbonitrile	No
10	B19	1-ethyl-4-oxohydro-7H-1,3-dioxoleno[4,5-g]cinnoline-3-carboxylic acid	No
10	C19	(3-methylbut-2-enyl)purin-6-ylamine	No
10	D19	1-ethyl-6-fluoro-4-oxo-7-piperazinylhydropyridino[2,3-b]pyridine-3-carboxylic acid	No
10	E19	(4E)-6-(4-hydroxy-6-methoxy-7-methyl-3-oxohydroisobenzofuran-5-yl)-4-methylhex -4-enoic acid	No
10	F19	(2S,3S,4S,6S,5R)-3,4,5-trihydroxy-6-(4-methyl-2-oxochromen-7-yloxy)-2H-3,4,5,6 -tetrahydropyran-2-carboxylic acid	No
10	G19	1-(2,3,4,5,6-pentafluorophenyl)azoline-2,5-dione	YES
10	H19	2-(2-thienyl)-2H,3H-benzo[e]1,3-oxazin-4-one	No
10	I19	7-chloro-3-phenyl-1,3-thiazolino[4,5-d]pyrimidine-2-thione	No
10	J19	3-phenyl-2-thioxo-1,3-thiazolino[4,5-d]pyrimidin-7-ol	No
10	K19	5-butyl-2,3-diphenyl-1,2,3,4-tetraazole, bromide	No
10	L19	3-(4-nitrophenyl)-2,5-diphenyl-1,2,3,4-tetraazole, bromide	No
10	M19	(prop-2-enylamino)(xanthen-9-ylamino)methane-1-thione	No
10	N19		No
10	O19	1,3-dimethyl-5-(3-thienylmethyl)-1,3,5-trihydropyrimidine-2,4,6-trione	No
10	P19	1-(tert-butyl)-5-(indol-2-ylmethylene)-1,3-dihydropyrimidine-2,4,6-trione	No
10	A20	{[(5-chloro-2-pyridyl)amino]methylene}methane-1,1-dicarbonitrile	No
10	B20	2-hydroxy-2-(6-hydroxy-2-oxocyclohex-1(6)-enyl)-2-hydrocyclopenta[1,2-a]benzen e-1,3-dione	No

10	C20	4-[(5-chloro-2,4-dimethoxyphenyl)azamethylene]-2-hydroxynaphthalen-1-one	No
10	D20	5-(hydroxyimino)indeno[3,2-b]pyridine	No
10	E20	2-piperidyl-5-(2-pyridylmethylene)-1,3-thiazolin-4-one	No
10	F20	1-[(2,5-dichlorophenyl)sulfonyl]pyrrolidine-2-carboxylic acid	No
10	G20	N-{5-[(4-methylpiperidyl)methyl]-1,3-thiazol-2-yl}acetamide	No
10	H20	3-methyl-2-[(5-methyl(3-furyl))carbonylamino]butanoic acid, sodium salt	No
10	I20	5-({[(dipropylamino)thioxomethyl]amino}azamethylene)-1,3-dihydropyrimidine-2,4 ,6-trione	No
10	J20	methylthio(3,4,5-trimethoxyphenyl)methanimine, iodide	No
10	K20	5-(indol-3-ylmethyl)-1,3,4-thiadiazole-2-ylamine	No
10	L20	3-(nonylsulfonyl)-1H-1,2,4-triazole-5-ylamine	No
10	M20	5-(4-methyl-5-nitro-1,2,4-triazol-3-ylthio)-4H-1,2,4-triazole-3-ylamine	No
10	N20	1,5-dimethyl-3-(2-oxo-2-piperidylethyl)-1,3,5-triazaperhydroine-2,4,6-trione	No
10	O20	[(1E)-2-(4-bromo-3-methylphenyl)-2-azavinyl](4-bromo-3-methylphenyl)amine	No
10	P20	5-naphthyl-4-(2-thienyl)-1,3-thiazole-2-ylamine	No
10	A21	2-((2E)-3-phenylprop-2-enylthio)-5-(phenylmethylthio)-1,3,4-thiadiazole	No
10	B21	5-[(4-fluorophenyl)methylthio]-2-(phenylmethylthio)-1,3,4-thiadiazole	No
10	C21	2,5-bis[(4-fluorophenyl)methylthio]-1,3,4-thiadiazole	No
10	D21	N-((1Z)-2-(2-thienyl)-1-azaprop-1-enyl)(2-methyl(3-furyl))carboxamide	No
10	E21	N-[(2-oxo(1H-benzo[d]azolin-3-ylidene))azamethyl]-2-pyridylcarboxamide	No
10	F21	2,2-dimethyl-6-hydro-2H-pyrano[5,6-c]quinolin-5-one	No
10	G21	4-(chlorodifluoromethoxy)phenylamine	No
10	H21	(4R)-2-(6-methyl-4-oxochromen-3-yl)-1,3-thiazolidine-4-carboxylic acid	No
10	I21	3-(2,3-dimethyl-5-oxo-1-phenyl(3-pyrazolin-4-yl))-5-methylspiro[1,3-thiazolidi ne-2,3'-indoline]-4,7-dione	No
10	J21	3-[(5-ethyl-1,3,4-thiadiazol-2-yl)amino]benzo[d]1,2-thiazole-1,1-dione	YES
10	K21	2-(1,6-dimethylpyrrolo[2,1-c]piperazin-2-yl)-4-(4-bromophenyl)-1,3-thiazole	No
10	L21	6-chloro-3-hydroxy-2-(3-pyridyl)chromen-4-one	No
10	M21	2,8-diazaspiro[5.5]undecane-1,7-dione	No
10	N21	2-((2E)-3-phenylprop-2-enylthio)-4,6-di(2-thienyl)pyridine-3-carbonitrile	No
10	O21	(2,4-dinitrophenyl)-1,3-thiazol-2-ylamine	No
10	P21	2-[(5-nitro-2-furyl)methylene]cyclopenta[1,2-a]benzene-1,3-dione	No
10	A22	2,5-bis(4-methylphenyl)-8-hydropyrazolo[1,5-a]pyrimidine-7-ylamine	No
10	B22	2-fluoren-9-ylthiobenzothiazole	No

10	C22	2-[(4-phenylphenyl)methylthio]benzoxazole	No
10	D22	2-[5-(3-bromophenyl)(1,3,4-oxadiazol-2-ylthio)]-1,3-dinitro-5-(trifluoromethyl)benzene	No
10	E22	8-benzimidazol-2-ylthio-1,3,7-trimethyl-1,3,7-trihydropurine-2,6-dione	No
10	F22	2-[(4-fluoronaphthyl)methylthio]benzoxazole	No
10	G22	6,7-bis(4-chlorophenyl)-7,8,12-trihydro-6H-chromeno[4,3-d]1,2,4-triazolo[1,5-a]pyrimidine	No
10	H22	2-methyl-5-({2,4,6-trimethyl-3-[(5-methyl(1,3,4-thiadiazol-2-ylthio))methyl]ph enyl}methylthio)-1,3,4-thiadiazole	No
10	I22	4-methyl-3-(phenoxymethyl)-1-xanthen-9-yl-1,2,4-triazoline-5-thione	No
10	J22	N-(1,3,4-thiadiazol-2-yl)-2-thienylcarboxamide	No
10	K22		No
10	L22	2-(1-methylbenzimidazol-2-ylthio)-5-nitropyridine	No
10	M22	4-[(4-methylthiophenyl)methylene]-3-phenylisoxazol-5-one	No
10	N22	3-nitro-5H-benzimidazolo[2,1-b]benzo[d]1,3-thiazine	No
10	O22	5-methyl-5-nitrospiro[1,3-dioxane-2,3'-indoline]-8-one	No
10	P22	3-acetyl-1-(2-cyclohex-1-enylethyl)-5-hydroxy-2-methylindole	No

Plate	**Well**	**IUPAC NAME**	**Inhibitor Y/N**
11	A03	2-methylpyrano[3,2-c]chromene-4,5-dione	No
11	B03	N-cyclopropyl(4-oxo(3-hydrophthalazinyl))carboxamide	No
11	C03	methyl 5-(methoxycarbonyl)-1-[3-(2-oxopyrrolidinyl)propyl]-4-(2-thienyl)-1,4-d ihydropyridine-3-carboxylate	No
11	D03	N-(2H,3H-benzo[3,4-e]1,4-dioxin-6-yl)-2-(5-(2-furyl)-4-prop-2-enyl(1,2,4-triaz ol-3-ylthio))acetamide	No
11	E03	7-[2-(3-nitro-1,2,4-triazolyl)ethoxy]chromen-2-one	No
11	F03	(2S)-2-amino-3-(5-hydroxyindol-3-yl)propanoic acid	No
11	G03	5-[(3-bromo-4-prop-2-ynyloxyphenyl)methylene]-1,3-diazolidine-2,4-dione	No
11	H03		YES
11	I03	2-thioxo-5-({5-[3-(trifluoromethyl)phenyl](2-furyl)}methylene)-1,3-thiazolidin -4-one	No
11	J03	5-[(3,5-dimethoxyphenyl)methylene]-2-thioxo-1,3-thiazolidin-4-one	No
11	K03	5-(3-thienylmethylene)-2-thioxo-1,3-thiazolidin-4-one	No
11	L03	3-{[(4,6-dipiperidyl-1,3,5-triazin-2-yl)amino]azamethylene}-1H-benzo[d]azolin- 2-one	No
11	M03		No
11	N03	3-({[4,6-bis(phenylamino)-1,3,5-triazin-2-yl]amino}azamethylene)-1H-benzo[d]az olin-2-one	No
11	O03	10-(???methyl)-10-hydroacridin-9-one	No
11	P03	N-[(1,1-dioxobenzo[d]1,2-thiazolin-3-yl)methylamino]-2-phenoxyacetamide	No
11	A04	N'-[2-(1,1-dioxobenzo[d]1,2-thiazolin-3-yloxy)ethyl]-N-phenylethane-1,2-diamid e	No

11	B04	3-[2-(1,1-dioxobenzo[d]1,2-thiazolin-3-yl)hydrazino]propanenitrile	No
11	C04	1-(4-nitrophenyl)pyrrole-2-carbaldehyde	No
11	D04	2-[(4,6-dipiperidyl-1,3,5-triazin-2-yl)amino]ethan-1-ol	No
11	E04	3-[(4-butylthiophenyl)amino]benzo[d]1,2-thiazoline-1,1-dione	No
11	F04	3-({2-[(4-chlorophenyl)methoxy]ethyl}amino)benzo[d]1,2-thiazoline-1,1-dione	No
11	G04	1-(2,4-dinitrophenyl)-3,5-dimethylpyrazole	No
11	H04	1,3-bis(hydroxymethyl)-5-methoxy-3-hydrobenzimidazol-2-one	YES
11	I04	4-[4-((1E)-2-(2-furyl)-1-azavinyl)phenyl]morpholine	No
11	J04	4-{4-[(1E)-2-(1,2-dimethylindol-3-yl)-1-azavinyl]phenyl}morpholine	No
11	K04	5-{[(2H-benzo[3,4-d]1,3-dioxolen-5-ylmethyl)amino]methylene}-1-(2-furylmethyl) -1,3-dihydropyrimidine-2,4,6-trione	No
11	L04	1-(2-furylmethyl)-5-{[(2-thienylmethyl)amino]methylene}-1,3-dihydropyrimidine- 2,4,6-trione	No
11	M04	1-(2-furylmethyl)-5-(1,2,3,4-tetrahydroquinolylmethylene)-1,3-dihydropyrimidin e-2,4,6-trione	No
11	N04	2-({[1-(2-furylmethyl)-2,4,6-trioxo-1,3-dihydropyrimidin-5-ylidene]methyl}amin o)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carbonitrile	No
11	O04	1-(4-bromophenyl)-5-{[(2-furylmethyl)amino]methylene}-2-thioxo-1,3-dihydropyri midine-4,6-dione	No
11	P04	1-cyclohexyl-5-(indolinylmethylene)-1,3-dihydropyrimidine-2,4,6-trione	No
11	A05	5-{[(2H-benzo[3,4-d]1,3-dioxolen-5-ylmethyl)amino]methylene}-1,3-dimethyl-2-th ioxo-1,3-dihydropyrimidine-4,6-dione	No
11	B05	5-{[(2-furylmethyl)amino]methylene}-1,3-dimethyl-2-thioxo-1,3-dihydropyrimidin e-4,6-dione	No
11	C05	5-{[(4-fluorophenyl)amino]methylene}-1,3-dimethyl-2-thioxo-1,3-dihydropyrimidi ne-4,6-dione	No
11	D05	3-[(2-furylmethyl)(methylsulfonyl)amino]propanenitrile	No
11	E05	2-{3-[(2,4,6-trioxo-1,3-dihydropyrimidin-5-ylidene)methyl]indolyl}acetic acid	No
11	F05	2-furylmorpholin-4-ylmethane-1-thione	No
11	G05	2-[(1Z)-2-(3,4-dimethoxyphenyl)-1-cyanovinyl]-4,6-diaminopyridine-3,5-dicarbon itrile	No
11	H05	2-(2-methylthiobenzimidazolyl)acetamide	No
11	I05	pyrrolidinyl-2-thienylmethane-1-thione	No
11	J05	2-[2-(phenylmethylthio)quinazolin-4-ylthio]acetic acid	YES
11	K05	(hydroxyimino)(4-morpholin-4-ylphenyl)methane	No
11	L05	2-quinazolin-4-ylthiopropanoic acid	No
11	M05	4-(1-ethylbenzimidazol-2-ylthio)quinazoline	No
11	N05	6-{5-[(4-oxo-2-thioxo-1,3-thiazolidin-5-ylidene)methyl]-2-furyl}-4a,9a-dihydro anthracene-9,10-dione	No

11	O05	2-[3-((1E)-2-cyano-3-oxo-3-pyrrolidinylprop-1-enyl)indolyl]-N-(oxolan-2-ylmeth yl)acetamide	No
11	P05	5-{[3-(4-methylphenyl)-1,2,4-oxadiazol-5-yl]methoxy}-2H-benzo[d]1,3-dioxolene	No
11	A06	5-[(2-chloro-6-fluorophenyl)methylene]-2-thioxo-1,3-diazolidin-4-one	No
11	B06	5-{[1-(2-methoxyethyl)-2,5-dimethylpyrrol-3-yl]methylene}-2-thioxo-1,3-dihydro pyrimidine-4,6-dione	No
11	C06	2-(2,5-dimethylpyrrolyl)-4-methyl-5-propylthiophene-3-carbonitrile	No
11	D06	8-[(2-chlorophenyl)methylthio]purine-6-ylamine	No
11	E06	2-(6-aminopurin-8-ylthio)-N-(4-methoxyphenyl)acetamide	No
11	F06	2-(2-cyclohexylthiobenzimidazolyl)acetamide	No
11	G06	1-(tert-butyl)-4-[2-(2-methylquinazolin-4-ylthio)ethoxy]benzene	No
11	H06	morpholin-4-yl(4-nitrophenyl)methane-1-thione	No
11	I06	(4-iodophenyl)[(3-nitrophenyl)sulfonyl]amine	No
11	J06	(phenylsulfonyl)-3-pyridylamine	No
11	K06	(2,4-dinitrophenyl)benzotriazole	No
11	L06	1-naphthylbenzotriazole-5,6-dicarbonitrile	No
11	M06	(7S,11S,13S,17S,18S,12R,14R,15R,16R)-26-formyl-2,15,17,27,29-pentahydroxy-11-m ethoxy-3,7,12,14,16,18,22-heptamethyl-6,23-dioxo-8,30-dioxa-24-azatetracyclo[2 3.3.1.1<4,7>.0<5,28>]triaconta-1(28),2,4,9,19,21,25(29),26-octaen-13-yl acetat e	No
11	N06	2-amino-4-(3,4-dimethylphenyl)-5-methylthiophene-3-carbonitrile	No
11	O06	2-amino-4-[4-(2-methylpropyl)phenyl]thiophene-3-carbonitrile	No
11	P06	2-amino-5-methyl-4-[4-(methylethyl)phenyl]thiophene-3-carbonitrile	No
11	A07	2-amino-4-(2,4-dichlorophenyl)thiophene-3-carbonitrile	No
11	B07	2-amino-5-methyl-4-(4-propylphenyl)thiophene-3-carbonitrile	No
11	C07	2-amino-4-(2,5-dimethylphenyl)thiophene-3-carbonitrile	No
11	D07	2-amino-4-(4-phenylphenyl)thiophene-3-carbonitrile	No
11	E07	2-amino-4-(4-butylphenyl)thiophene-3-carbonitrile	No
11	F07	[(1-ethylpyrazol-4-yl)methyl]methylamine	No
11	G07	4-[4-nitro-2-(trifluoromethyl)phenyl]morpholine	No
11	H07	5-iodo-1,3-dihydropyrimidine-2,4-dione	No
11	I07	1-benzyl-5-{[1-benzylindol-3-yl]methylene}-1,3-dihydropyrimidine-2,4,6-trione	No
11	J07	5-({6-methyl-5-nitro-4-[(2-oxo(3-hydrobenzimidazol-5-yl))amino]pyrimidin-2-yl} amino)-3-hydrobenzimidazol-2-one	No
11	K07	2-(2-pyridylthio)-1-[4-(2-(2-pyridylthio)acetyl)piperazinyl]ethan-1-one	No
11	L07	2-furyl-N-(5-methyl(1,3,4-thiadiazol-2-yl))carboxamide	No
11	M07	3-[amino(2-(2-pyridyl)ethyl)amino]benzo[d]1,2-thiazole-1,1-dione	No
11	N07	3-[amino(3-oxo-3-piperidylpropyl)amino]benzo[d]1,2-thiazole-1,1-dione	No

11	O07	ethyl 4-(2-furylcarbonyl)piperazinecarboxylate	No
11	P07	2-{4-[4-nitro-2-(trifluoromethyl)phenyl]piperazinyl}ethan-1-ol	No
11	A08	6-[(5-methyl(1,3,4-thiadiazol-2-ylthio))methyl]-4-morpholin-4-yl-1,3,5-triazin e-2-ylamine	No
11	B08	1-[4-nitro-2-(trifluoromethyl)phenyl]piperidin-3-ol	No
11	C08	1-acetyl-3-{[5-(4-chlorophenyl)(1,3,4-oxadiazol-2-ylthio)]methyl}-2,4,6-trimet hylbenzene	No
11	D08	4-[2,6-dinitro-4-(trifluoromethyl)phenyl]-1-(methylsulfonyl)piperazine	No
11	E08	1-[2-(1-cyclohexylbenzimidazol-2-ylthio)ethyl]-3-methyl-3-hydrobenzimidazole-2 -thione	No
11	F08	3-(carboxymethyl)indole-2-carboxylic acid	No
11	G08	4-benzotriazolyl-5-(4-fluorophenoxy)benzene-1,2-dicarbonitrile	No
11	H08	1-(2-hydroxypropyl)-4,6-dimethyl-2-oxohydropyridine-3-carbonitrile	No
11	I08	5-[(prop-2-enylamino)sulfonyl]-3-hydrobenzimidazol-2-one	No
11	J08	benzo[3,4-b]benzo[d]furan-3-yl{[4-(4-bromophenoxy)phenyl]sulfonyl}amine	No
11	K08	(2R,6R)-2,6-diaminoheptanedioic acid	No
11	L08	3-nitrodibenzo[b,f]oxepinylamine	No
11	M08	2-{[4-(2-fluorophenyl)piperazinyl]methyl}-6-hydroxy-2-hydropyridazin-3-one	No
11	N08	3-(4-fluorophenyl)-5-{[4-(4-fluorophenyl)piperazinyl]methylene}-2-thioxo-1,3-t hiazolidin-4-one	No
11	O08	({5-[(2-{[(1E)-1-(methylamino)-2-nitrovinyl]amino}ethylthio)methyl](2-furyl)}m ethyl)dimethylamine	No
11	P08	1-(methylethyl)-5-oxopyrrolidine-3-carboxylic acid	No
11	A09	2-methyl-4-hydro-2H,3H-1,3-thiazolidino[2,3-b]quinazolin-5-one	No
11	B09	2-[1-(4-fluorophenyl)-1,2,3,4-tetraazol-5-ylthio]acetamide	No
11	C09	1-acetyl-3-[(5-(2-furyl)(1,3,4-oxadiazol-2-ylthio))methyl]-2,4,6-trimethylbenz ene	No
11	D09	{1-[(2-fluorophenyl)methyl]benzimidazol-2-yl}phenylmethan-1-ol	No
11	E09	N-(tert-butyl)-2-(3-nitro(1,2,4-triazolyl))acetamide	No
11	F09	(3-aminophenyl)[(dimethylamino)sulfonyl]amine	No
11	G09	N-(2-methyl-5-oxochromeno[3,4-c]pyridin-4-yl)propanamide	No
11	H09	1-((2E)-3-(2-furyl)prop-2-enoyl)pyrrolidine-2-carboxylic acid	No
11	I09	(1S,9S,13R)-13-acetyl-9-methyl-11-thioxo-8-oxa-10,12-diazatricyclo[7.3.1.0<2,7 >]trideca-2,4,6-triene	No
11	J09	4,6-dimethyl-2-oxopyran-5-carboxylic acid	No
11	K09	4-((1Z)-2-nitrovinyl)-1,2,3-tris(phenylmethoxy)benzene	No
11	L09	spiro[7,6a-dihydro-14aH-chromano[4',3'-2,3]pyrano[5,6-c]chromene-7,3'-indoline]-6,8,24-trione	No
11	M09	2-oxo-3-(6-oxo(7H-chromeno[3,2-c]chromen-7-yl))chromen-4-yl acetate	No

11	N09	5-bromo-1-[2-(4-chlorophenoxy)ethyl]-1,3-dihydropyrimidine-2,4-dione	No
11	O09	1-{[2-(4-chlorophenoxy)ethoxy]methyl}-6-methyl-1,3-dihydropyrimidine-2,4-dione	No
11	P09	1-(diphenylmethyl)-1,3-dihydropyrimidine-2,4-dione	No
11	A10	1-(diphenylmethyl)-5-bromo-1,3-dihydropyrimidine-2,4-dione	No
11	B10		No
11	C10		No
11	D10	methyl 5-(methoxycarbonyl)-1,2,6-trimethyl-4-(2-thienyl)-1,4-dihydropyridine-3 -carboxylate	No
11	E10	methyl 5-(methoxycarbonyl)-1,2,6-trimethyl-4-(3-thienyl)-1,4-dihydropyridine-3 -carboxylate	No
11	F10	3,3,7,8-tetramethyl-11-[4-(trifluoromethoxy)phenyl]-2,3,4-trihydro-5H,10H,11H- benzo[b]benzo[2,1-f]1,4-diazepin-1-one	No
11	G10	11-(9-ethylcarbazol-3-yl)-3,3,7,8-tetramethyl-2,3,4-trihydro-5H,10H,11H-benzo[b]benzo[2,1-f]1,4-diazepin-1-one	No
11	H10	11-(3-bromo-4,5-dimethoxyphenyl)-3,3,7,8-tetramethyl-2,3,4-trihydro-5H,10H,11H -benzo[b]benzo[2,1-f]1,4-diazepin-1-one	No
11	I10	6-bromo-4-(6-chloro(2H-benzo[d]1,3-dioxolan-5-yl))-1,3,4-trihydrobenzo[h]quino lin-2-one	YES
11	J10	6-methyl-3-(3,3,7,8-tetramethyl-1-oxo(2,3,4-trihydro-5H,10H,11H-benzo[b]benzo[2,1-f]1,4-diazepin-11-yl))chromen-4-one	No
11	K10	11-(2,6-difluorophenyl)-3,3,7,8-tetramethyl-2,3,4-trihydro-5H,10H,11H-benzo[b] benzo[2,1-f]1,4-diazepin-1-one	No
11	L10	11-(5-bromo-2-fluorophenyl)-3,3,7,8-tetramethyl-2,3,4-trihydro-5H,10H,11H-benz o[b]benzo[2,1-f]1,4-diazepin-1-one	YES
11	M10	11-(3,4-difluorophenyl)-3-phenyl-2,3,4-trihydro-5H,10H,11H-benzo[b]benzo[2,1-f]1,4-diazepin-1-one	No
11	N10	oxolan-2-ylmethyl 4-(5-bromo-2-methoxyphenyl)-2-methyl-5-oxo-1,4,6,7,8-pentahy droquinoline-3-carboxylate	No
11	O10	methyl 5-(methoxycarbonyl)-4-(2,4,5-trimethoxyphenyl)-1,4-dihydropyridine-3-ca rboxylate	No
11	P10	3-phenyl-11-[4-(trifluoromethoxy)phenyl]-2,3,4-trihydro-5H,10H,11H-benzo[b]ben zo[2,1-f]1,4-diazepin-1-one	No
11	A11	cyclohexyl 2-methyl-4-(5-methyl(2-furyl))-5-oxo-1,4,6,7,8-pentahydroquinoline- 3-carboxylate	No
11	B11	oxolan-2-ylmethyl 2,7,7-trimethyl-4-(5-methyl(2-furyl))-5-oxo-1,4,6,7,8-pentah ydroquinoline-3-carboxylate	No
11	C11	11-naphthyl-3-phenyl-2,3,4-trihydro-5H,10H,11H-benzo[b]benzo[2,1-f]1,4-diazepi n-1-one	No
11	D11	2-ethylthioethyl 2-methyl-5-oxo-4-(3-thienyl)-1,4,6,7,8-pentahydroquinoline-3- carboxylate	No
11	E11	cyclopentyl 2-methyl-4-(5-methyl(2-thienyl))-5-oxo-1,4,6,7,8-pentahydroquinoli ne-3-carboxylate	No

11	F11	11-(3-bromo-4-fluorophenyl)-3-phenyl-2,3,4-trihydro-5H,10H,11H-benzo[b]benzo[2 ,1-f]1,4-diazepin-1-one	No
11	G11	3-phenyl-11-(4-phenylphenyl)-2,3,4-trihydro-5H,10H,11H-benzo[b]benzo[2,1-f]1,4 -diazepin-1-one	No
11	H11	11-(4-bromo-2,5-dimethoxyphenyl)-3,3,7,8-tetramethyl-2,3,4-trihydro-5H,10H,11H -benzo[b]benzo[2,1-f]1,4-diazepin-1-one	No
11	I11	methyl 2-methyl-5-oxo-4,7-di(2-thienyl)-1,4,6,7,8-pentahydroquinoline-3-carbox ylate	YES
11	J11	methyl 2-methyl-4-(5-methyl(2-thienyl))-5-oxo-7-(2-thienyl)-1,4,6,7,8-pentahyd roquinoline-3-carboxylate	No
11	K11	11-(2,5-difluorophenyl)-3-phenyl-2,3,4-trihydro-5H,10H,11H-benzo[b]benzo[2,1-f]1,4-diazepin-1-one	No
11	L11	methoxy(2-methylindol-3-yl)-2-thienylmethane	No
11	M11	5-nitro-6-(3,4,5-trimethoxyphenyl)piperidin-2-one	No
11	N11	3-(2-chlorophenyl)-11-[3-(trifluoromethyl)phenyl]-2,3,4-trihydro-5H,10H,11H-be nzo[b]benzo[2,1-f]1,4-diazepin-1-one	No
11	O11	6-(2-bromo-3,4,5-trimethoxyphenyl)-5-nitropiperidin-2-one	No
11	P11	methylethyl 4-methyl-2-oxo-6-[4-(trifluoromethyl)phenyl]-1,3,6-trihydropyrimid ine-5-carboxylate	No
11	A12	ethyl 5-(ethoxycarbonyl)-1,2,6-trimethyl-4-(3-thienyl)-1,4-dihydropyridine-3-c arboxylate	No
11	B12	ethyl 6-acetyl-2-amino-4,5,6,7-tetrahydrothiopheno[2,3-c]pyridine-3-carboxylat e	No
11	C12	2-ethylthioethyl 2-methyl-5-oxo-4-(4-oxochromen-3-yl)-1,4,6,7,8-pentahydroquin oline-3-carboxylate	No
11	D12	2-ethoxyethyl 2-methyl-5-oxo-4-(4-oxochromen-3-yl)-1,4,6,7,8-pentahydroquinoli ne-3-carboxylate	No
11	E12	propyl 2,7,7-trimethyl-4-(5-methyl(2-furyl))-5-oxo-1,4,6,7,8-pentahydroquinoli ne-3-carboxylate	No
11	F12	methylethyl 2,7,7-trimethyl-4-(6-methyl-4-oxochromen-3-yl)-5-oxo-1,4,6,7,8-pen tahydroquinoline-3-carboxylate	No
11	G12	oxolan-2-ylmethyl 2-methyl-4-(5-methyl(2-furyl))-5-oxo-1,4,6,7,8-pentahydroqui noline-3-carboxylate	No
11	H12	2-ethoxyethyl 2-methyl-5-oxo-4-(2-thienyl)-1,4,6,7,8-pentahydroquinoline-3-car boxylate	No
11	I12	2-methylpropyl 2-methyl-5-oxo-4-(3-thienyl)-1,4,6,7,8-pentahydroquinoline-3-ca rboxylate	No
11	J12	methyl 5-(methoxycarbonyl)-1-methyl-4-(2-thienyl)-1,4-dihydropyridine-3-carbox ylate	No
11	K12	2-ethylthioethyl 2-methyl-4-(5-methyl(2-furyl))-5-oxo-1,4,6,7,8-pentahydroquin oline-3-carboxylate	No
11	L12	2-propoxyethyl 4-(6-bromo(2H-benzo[d]1,3-dioxolan-5-yl))-2,7,7-trimethyl-5-oxo -1,4,6,7,8-pentahydroquinoline-3-carboxylate	YES

11	M12	oxolan-2-ylmethyl 2,7,7-trimethyl-5-oxo-4-[4-(trifluoromethyl)phenyl]-1,4,6,7, 8-pentahydroquinoline-3-carboxylate	No
11	N12	3-[3-(2-chlorophenyl)-1-oxo-2,3,4-trihydro-5H,10H,11H-benzo[b]benzo[2,1-f]1,4- diazepin-11-yl]chromen-4-one	No
11	O12	methyl 4-(6-bromo(2H-benzo[d]1,3-dioxolan-5-yl))-5-(methoxycarbonyl)-1-methyl- 1,4-dihydropyridine-3-carboxylate	No
11	P12	methyl 4-(6-chloro(2H-benzo[d]1,3-dioxolan-5-yl))-5-(methoxycarbonyl)-1-methyl -1,4-dihydropyridine-3-carboxylate	No
11	A13	methyl 4-(6-chloro-4-oxochromen-3-yl)-2-methyl-5-oxo-1,4,6,7,8-pentahydroquino line-3-carboxylate	No
11	B13	N-(4-fluorophenyl)-2-pyrimidin-2-ylthioacetamide	No
11	C13	((4S,1R,2R)bicyclo[2.2.1]hept-2-yl)[(4-chlorophenyl)sulfonyl]amine	No
11	D13	N-cyclopropyl-3-phenylthiopropanamide	No
11	E13	4-({1-[4-(dimethylamino)phenyl]-2,5-dimethylpyrrol-3-yl}methylene)-3-methyl-1- phenyl-1,2-diazolin-5-one	No
11	F13	2-{3-[(2,4-dioxo(1,3-thiazolidin-5-ylidene))methyl]indolyl}-N-phenylacetamide	No
11	G13	5-{[1-(4-fluorophenyl)-2,5-dimethylpyrrol-3-yl]methylene}-2-thioxo-1,3-thiazol idin-4-one	No
11	H13	5-({1-[4-(dimethylamino)phenyl]-2,5-dimethylpyrrol-3-yl}methylene)-2-thioxo-1, 3-thiazolidin-4-one	No
11	I13	3-[(1E)-2-(4-iodophenyl)-2-azavinyl]-1-(3,5-dimethylphenyl)-2,5-dimethylpyrrol e	No
11	J13	5-[(2,5-dimethyl-1-(3-pyridyl)pyrrol-3-yl)methylene]-2-thioxo-1,3-thiazolidin- 4-one	No
11	K13	5-{[1-(4-chlorophenyl)-2,5-dimethylpyrrol-3-yl]methylene}-1,3-diazolidine-2,4- dione	No
11	L13	5-{[5-(diethylamino)(2-furyl)]methylene}-1,3-dimethyl-1,3-dihydropyrimidine-2, 4,6-trione	YES
11	M13	5-{[5-(4-chlorophenylthio)(2-furyl)]methylene}-2-[(4-fluorophenyl)azamethylene]-1,3-thiazolidin-4-one	No
11	N13	[1-(3-chlorophenyl)-2,5-dimethylpyrrol-3-yl](hydroxyimino)methane	No
11	O13	2-{3-[(3-oxo-1,3-thiazolidino[3,2-a]benzimidazol-2-ylidene)methyl]indolyl}acet ic acid	No
11	P13	2-[(1-phenylpyrrol-2-yl)methylene]-1,3-thiazolidino[3,2-a]benzimidazol-3-one	No
11	A14	2-(azapropylidene)-3-ethyl-5-{[4-methoxy-2-methyl-5-(methylethyl)phenyl]methyl ene}-1,3-thiazolidin-4-one	No
11	B14	1,3-dimethyl-5-[(4-methylthiophenyl)methylene]-2-thioxo-1,3-dihydropyrimidine- 4,6-dione	No
11	C14	(2E)-3-(1,3-dimethyl-2-oxo(3-hydrobenzimidazol-5-yl))-2-cyano-N-(oxolan-2-ylme thyl)prop-2-enamide	No
11	D14	(2E)-2-cyano-N-(oxolan-2-ylmethyl)-3-(5-phenylthio(2-furyl))prop-2-enamide	No

11	E14	1-(4-bromophenyl)-5-[(1-methylindol-3-yl)methylene]-2-thioxo-1,3-dihydropyrimi dine-4,6-dione	No
11	F14	5-(2H-benzo[3,4-d]1,3-dioxolen-5-ylmethylene)-1,3-dimethyl-1,3-dihydropyrimidi ne-2,4,6-trione	No
11	G14	1-(2H-benzo[3,4-d]1,3-dioxolan-5-yl)-5-[(5-pyrrolidinyl(2-furyl))methylene]-1, 3-dihydropyrimidine-2,4,6-trione	No
11	H14	5-({5-bromo-2-[(4-fluorophenyl)methoxy]phenyl}methylene)-1,3-diazolidine-2,4-d ione	No
11	I14	ethyl 2-{2,4-dioxo-5-[(5-pyrrolidinyl(2-furyl))methylene]-1,3-thiazolidin-3-yl }acetate	No
11	J14	methyl 4-[(2,4-dioxo-3-prop-2-ynyl-1,3-thiazolidin-5-ylidene)methyl]benzoate	No
11	K14	5-[(5-morpholin-4-yl(2-furyl))methylene]-3-prop-2-ynyl-1,3-thiazolidine-2,4-di one	No
11	L14	1-(4-fluorophenyl)-5-(3-furylmethylene)-2-thioxo-1,3-dihydropyrimidine-4,6-dio ne	No
11	M14	5-{[5-(4-bromo-3-chlorophenyl)(2-furyl)]methylene}-1-methyl-2-thioxo-1,3-dihyd ropyrimidine-4,6-dione	No
11	N14	1-acetyl-4-{5-[(1-methyl-4,6-dioxo-2-thioxo(1,3-dihydropyrimidin-5-ylidene))me thyl](2-furyl)}benzene	No
11	O14	2-[(1E)-2-(5-bromo(2-thienyl))-1-azavinyl]-4,5,6,7-tetrahydrobenzo[b]thiophene -3-carbonitrile	No
11	P14	(2E)-3-(5-azaperhydroepinyl(2-furyl))-2-cyano-N,N-dimethylprop-2-enamide	No
11	A15	5-({4-[(2,4-dichlorophenyl)methoxy]-3-methoxy-5-prop-2-enylphenyl}methylene)-1 ,3-diazolidine-2,4-dione	No
11	B15	2-({3-[(2,5-dioxo-1,3-diazolidin-4-ylidene)methyl]indolyl}methyl)benzenecarbon itrile	No
11	C15	5-{[5-(4-bromo-3-chlorophenyl)-2-furyl]methylene}-1,3-diazolidine-2,4-dione	No
11	D15	5-{[4-ethoxy-2-methyl-5-(methylethyl)phenyl]methylene}-3-prop-2-ynyl-1,3-thiaz olidine-2,4-dione	No
11	E15	5-[(3-bromo-4-methoxyphenyl)methylene]-3-prop-2-ynyl-1,3-thiazolidine-2,4-dion e	No
11	F15	2-[(1-cyclopentyl-2,5-dimethylpyrrol-3-yl)methylene]-1,3-thiazolidino[3,2-a]be nzimidazol-3-one	No
11	G15	(2E)-2-benzimidazol-2-yl-3-(5-chloro(2-thienyl))prop-2-enenitrile	No
11	H15	5-[(4-pyrrolidinylphenyl)methylene]-2-thioxo-1,3-diazolidin-4-one	No
11	I15	2-[(4-fluorophenyl)azamethylene]-5-(2-thienylmethylene)-1,3-thiazolidin-4-one	No
11	J15	2-[(4-fluorophenyl)azamethylene]-5-{[1-(4-nitrophenyl)pyrrol-2-yl]methylene}-1 ,3-thiazolidin-4-one	No
11	K15	2-[(4-fluorophenyl)azamethylene]-5-[(5-pyrrolidinyl(2-furyl))methylene]-1,3-th iazolidin-4-one	No
11	L15	(3-nitrophenyl)pyrrole	No

11	M15	[1-(3,4-dichlorophenyl)-2,5-dimethylpyrrol-3-yl]morpholin-4-ylmethane-1-thione	No
11	N15	N-pyrimidin-2-yl-2-thienylcarboxamide	No
11	O15	2-(4-bromophenoxy)-N-(oxolan-2-ylmethyl)acetamide	No
11	P15	2-(2,4-dichlorophenoxy)-N-(oxolan-2-ylmethyl)acetamide	No
11	A16	ethyl 2-[2-(2-furylcarbonylamino)-1,3-thiazol-4-yl]acetate	No
11	B16	adamantanyl-N-(2-morpholin-4-ylethyl)carboxamide	No
11	C16	[(4-chlorophenyl)sulfonyl]-4-pyridylamine	No
11	D16	1-indolinyl-2-naphthyloxyethan-1-one	No
11	E16	1-(2H,3H-benzo[3,4-e]1,4-dioxan-6-ylsulfonyl)piperidine-4-carboxamide	No
11	F16	N-cycloheptyl-2-furylcarboxamide	No
11	G16	(2H,3H-benzo[3,4-e]1,4-dioxan-6-ylsulfonyl)(4-{[(2-chlorophenyl)amino]sulfonyl }phenyl)amine	No
11	H16	N-(2-fluorophenyl)-2-(1,1,3-trioxo(2-hydrobenzo[d]isothiazol-2-yl))acetamide	No
11	I16	methyl 3-{[1-(4-fluorophenyl)-2,5-dimethylpyrrol-3-yl]methylene}-5-methyl-2-ox o-1-(oxolan-2-ylmethyl)azoline-4-carboxylate	No
11	J16	2-amino-4,6-dimethyl-5-(2-thienylmethylene)cyclopenta[2,1-b]pyridine-3,7-dicar bonitrile	No
11	K16	5-{[4-bromo-5-(4-chlorophenylthio)(2-furyl)]methylene}-2-thioxo-1,3-diazolidin -4-one	No
11	L16	2-(azaethylidene)-3-methyl-5-[(1-prop-2-ynylindol-3-yl)methylene]-1,3-thiazoli din-4-one	No
11	M16	2-(azaethylidene)-5-({1-[(4-fluorophenyl)methyl]indol-3-yl}methylene)-3-methyl -1,3-thiazolidin-4-one	No
11	N16	2-(azaethylidene)-5-({1-[4-(dimethylamino)phenyl]pyrrol-2-yl}methylene)-3-meth yl-1,3-thiazolidin-4-one	No
11	O16	2-(azaethylidene)-3-methyl-5-[(5-methyl(2-furyl))methylene]-1,3-thiazolidin-4- one	No
11	P16	5-[(1-(2H-benzo[3,4-d]1,3-dioxolan-5-yl)-2,5-dimethylpyrrol-3-yl)methylene]-2- (2-oxo-1-azapropylidene)-1,3-thiazolidin-4-one	No
11	A17	(2E)-3-(4,5-dibromo(2-furyl))-2-phenylprop-2-enenitrile	No
11	B17	2-(2,5-dimethylpyrrolyl)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylic acid	No
11	C17	2-(4-chlorophenylthio)-N-(oxolan-2-ylmethyl)propanamide	No
11	D17	2-(4-chlorophenylthio)-N-[2-(2-furylmethylthio)ethyl]acetamide	No
11	E17	[(3,4-dimethoxyphenyl)sulfonyl](2-phenylthioethyl)amine	No
11	F17	[2-(4-chlorophenylthio)ethyl](phenylsulfonyl)amine	No
11	G17	2H-benzo[3,4-d]1,3-dioxolan-5-yl[(3-bromo-4-methoxyphenyl)sulfonyl]amine	No
11	H17	[(4-fluorophenyl)sulfonyl](2-pyridylmethyl)amine	No
11	I17	{2-[(4-methylphenyl)methylthio]ethyl}(methylsulfonyl)amine	No

11	J17	(2H,3H-benzo[3,4-e]1,4-dioxin-6-ylsulfonyl)[2-(4-chlorophenylthio)ethyl]amine	No
11	K17	6-(azaperhydroepinylsulfonyl)-2H,3H-benzo[e]1,4-dioxin	No
11	L17	2-bromo-4-chloro-1-[(3-(3-pyridyl)(1,2,4-oxadiazol-5-yl))methoxy]benzene	No
11	M17	methyl 4-((3aS,4R,9bR)-6,9-dichloro-3,4,5,3a,9b-pentahydrocyclopenta[1,2-c]qui nolin-4-yl)benzoate	No
11	N17	(3aS,4R,9bR)-9-chloro-6-methoxy-4-naphthyl-3,4,5,3a,9b-pentahydrocyclopenta[1, 2-c]quinoline	No
11	O17	(3aS,4R,9bR)-6,9-dichloro-4-(3-pyridyl)-3,4,5,3a,9b-pentahydrocyclopenta[1,2-c]quinoline	No
11	P17	1-((3aS,4R,9bR)-6,8-dichloro(3,4,5,3a,9b-pentahydrocyclopenta[1,2-c]quinolin-4 -yl))-2-methoxybenzene	No
11	A18	(3aS,4R,9bR)-8-bromo-4-(4-pyridyl)-3,4,5,3a,9b-pentahydrocyclopenta[1,2-c]quin oline	No
11	B18	ethyl (3aS,4R,9bR)-8-bromo-3,4,5,3a,9b-pentahydrocyclopenta[1,2-c]quinoline-4- carboxylate	No
11	C18	(3aS,4R,9bR)-6-fluoro-4-(4-fluorophenyl)-3,4,5,3a,9b-pentahydrocyclopenta[1,2- c]quinoline	No
11	D18	(3aS,4R,9bR)-6-fluoro-4-(4-nitrophenyl)-3,4,5,3a,9b-pentahydrocyclopenta[1,2-c]quinoline	No
11	E18	(3aS,4R,9bR)-4-(9-anthryl)-6-fluoro-3,4,5,3a,9b-pentahydrocyclopenta[1,2-c]qui noline	No
11	F18	(3aS,4R,9bR)-8-fluoro-4-(3-pyridyl)-3,4,5,3a,9b-pentahydrocyclopenta[1,2-c]qui noline	No
11	G18	(3aS,4R,9bR)-4-(2-chlorophenyl)-8-fluoro-3,4,5,3a,9b-pentahydrocyclopenta[1,2- c]quinoline	No
11	H18	10-phenyl-9-azatetracyclo[10.2.1.0<2,11>.0<3,8>]pentadeca-3,5,7-triene-5-carbo xylic acid	No
11	I18	methyl 2-(acetylamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate	No
11	J18	2-(1-cyclohexyl-1,2,3,4-tetraazol-5-ylthio)propanoic acid	No
11	K18	N-(2-furylmethyl)-N'-(3-hydroxypropyl)ethane-1,2-diamide	No
11	L18	(4-amino(1,2,5-oxadiazol-3-yl))-N-{2-[(2-chloro-4,5-difluorophenyl)carbonylami no]ethyl}carboxamide	No
11	M18	5-(3-oxohydroisobenzofuran-5-yl)furan-2-carbaldehyde	No
11	N18	1-acetyl-4-[2-(6-aminopurin-8-ylthio)ethoxy]benzene	No
11	O18	2-(phenylmethylthio)pyrimidine-4,6-diamine	No
11	P18	5-[2-(methylethyl)-1,3-dioxobenzo[c]azolidin-5-yl]furan-2-carbaldehyde	No
11	A19	1-nitro-4-piperidyl-2-(2-pyridylthio)benzene	No
11	B19	4-(4-methylpiperazinyl)-1-nitro-2-(1-phenyl(1,2,3,4-tetraazol-5-ylthio))benzen e	No
11	C19	1-nitro-4-piperazinyl-2-(2-pyridylthio)benzene	No
11	D19	4-methyl-5-(2-phenylethyl)-1,2,4-triazole-3-thiol	No

11	E19	2-[2-(phenylmethylthio)benzimidazolyl]ethan-1-ol	No
11	F19	4-(2-nitro-5-piperidylphenyl)morpholine	No
11	G19	(8-nitro-5-quinolyl)piperazine	No
11	H19	cyclopropyl(2-nitro-5-piperazinylphenyl)amine	No
11	I19	2-(4-methyl(1,2,4-triazol-3-ylthio))-1-nitro-4-pyrrolidinylbenzene	No
11	J19	cyclopropyl[5-(4-methylpiperazinyl)-2-nitrophenyl]amine	No
11	K19	4-[3-(cyclopropylamino)-4-nitrophenyl]piperazinyl 2-furyl ketone	No
11	L19	2-methyl-4-nitro-5-pyrrolidinylphenylamine	No
11	M19	(5-chloro-2-nitrophenyl)(2-furylmethyl)amine	No
11	N19	(2-furylmethyl)(2-nitro-5-pyrrolidinylphenyl)amine	No
11	O19	(2-furylmethyl)(5-morpholin-4-yl-2-nitrophenyl)amine	No
11	P19	2-ethoxy-1-nitro-4-pyrrolidinylbenzene	No
11	A20	[5-(2,6-dimethylmorpholin-4-yl)-2-nitrophenyl]cyclopropylamine	No
11	B20	[3-(3,5-dimethylpyrazolyl)-4-nitrophenyl]piperazine	No
11	C20	1-[3-(3,5-dimethylpyrazolyl)-4-nitrophenyl]-4-methylpiperazine	No
11	D20		No
11	E20	(4-amino(1,2,5-oxadiazol-3-yl))-N-{2-[(4-nitrophenyl)amino]ethyl}carboxamide	No
11	F20	4-methyl-3-{2-[4-(4-nitrophenyl)piperazinyl]ethoxy}-1,2,5-oxadiazole	No
11	G20	(2-chloro-4-nitrophenyl)[2-(4-methoxy(1,2,5-oxadiazol-3-yloxy))ethyl]amine	No
11	H20	4-[5-(3-methylpiperazinyl)-2-nitrophenyl]morpholine	No
11	I20	2-{[5-(3-methylpiperazinyl)-2-nitrophenyl]amino}ethan-1-ol	No
11	J20	[4-nitro-2-(trifluoromethyl)phenyl]pyrrolidine	YES
11	K20	[2-nitro-4-(trifluoromethyl)phenyl]pyrrolidine	YES
11	L20	(3-morpholin-4-ylpropyl)(5-nitro(8-quinolyl))amine	No
11	M20	(5-chloro-2-nitrophenyl)(3-morpholin-4-ylpropyl)amine	No
11	N20	(3-morpholin-4-ylpropyl)(8-nitro(5-quinolyl))amine	No
11	O20	(3-morpholin-4-ylpropyl)(2-nitro-5-pyrrolidinylphenyl)amine	No
11	P20	(5-morpholin-4-yl-2-nitrophenyl)(3-morpholin-4-ylpropyl)amine	No
11	A21	(adamantanylethyl)(2-nitro-5-piperazinylphenyl)amine	No
11	B21	[2-nitro-4-(trifluoromethyl)phenyl]piperazine	No
11	C21	[2-(4-fluorophenoxy)ethyl](5-morpholin-4-yl-2-nitrophenyl)amine	No
11	D21	[2-(ethylamino)ethyl](5-nitro(8-quinolyl))amine	No
11	E21	4-methyl-1-[5-(4-methylpiperazinyl)-2-nitrophenyl]piperazine	No
11	F21	4-(2-furyl)-2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxamide	No
11	G21	1-[2-(2-methoxyphenoxy)ethyl]indole-3-carbaldehyde	No
11	H21	1-[2-(2-fluorophenoxy)ethyl]indole-3-carbaldehyde	No
11	I21	1-[2-(2-chlorophenoxy)ethyl]indole-3-carbaldehyde	No
11	J21	3-bromo-4-morpholin-4-ylphenylamine	No

11	K21	1-[4-(cyclopentylamino)-3-nitrophenyl]-2,5-dimethylpyrrole-3-carbaldehyde	YES
11	L21	[4-(2,5-dimethylpyrrolyl)-2-nitrophenyl]cyclopentylamine	No
11	M21	8-[2-(2-fluorophenoxy)ethylthio]purine-6-ylamine	No
11	N21	8-[2-(2-methylphenoxy)ethylthio]purine-6-ylamine	No
11	O21	8-[2-(4-methylphenoxy)ethylthio]purine-6-ylamine	No
11	P21	2-(6-aminopurin-8-ylthio)ethan-1-ol	No
11	A22	3-{2-[2-(4-chlorophenoxy)ethylthio]benzimidazolyl}propane-1,2-diol	No
11	B22	1-methyl-2-[(6-nitrobenzimidazol-2-yl)methylthio]benzimidazole	No
11	C22	2-(benzimidazol-2-ylmethylthio)-1-methylbenzimidazole	No
11	D22	2-{[1-benzylbenzimidazol-2-yl]methylthio}-1-propylbenzimidazole	No
11	E22	3-(4,6-dimethylpyrimidin-2-ylthio)propanoic acid	No
11	F22	2-(2-benzoxazol-2-ylthioethoxy)-1-methoxybenzene	No
11	G22	2-(2-benzoxazol-2-ylthioethoxy)-1-fluorobenzene	No
11	H22	4-(2-benzoxazol-2-ylthioethoxy)-1-chlorobenzene	No
11	I22	4-(2-benzoxazol-2-ylthioethoxy)-1-methoxybenzene	No
11	J22	2-{[1-benzylbenzimidazol-2-yl]methylthio}benzoxazole	No
11	K22	3-(2-methylquinazolin-4-ylthio)propanoic acid	No
11	L22	1,2-dimethyl-4-(2-purin-6-ylthioethoxy)benzene	No
11	M22	1-chloro-4-[2-(1-cyclohexyl(1,2,3,4-tetraazol-5-ylthio))ethoxy]benzene	No
11	N22	2-(1-cyclohexyl-1,2,3,4-tetraazol-5-ylthio)acetamide	No
11	O22	2-[(6-nitrobenzimidazol-2-yl)methylthio]benzothiazole	No
11	P22	4-[2-(6-bromobenzimidazol-2-ylthio)ethoxy]-1-chlorobenzene	No
Plate	**Well**	**IUPAC NAME**	**Inhibitor Y/N**
12	A03	2-[2-(6-bromobenzimidazol-2-ylthio)ethoxy]-1-fluorobenzene	No
12	B03	2-[2-(trifluoromethyl)benzimidazolyl]acetic acid	No
12	C03	cyclopropyl(2-nitro-5-pyrrolidinylphenyl)amine	No
12	D03	3-(3-bromophenyl)-5,7-dimethyl-8-hydropyrazolo[1,5-a]pyrimidine	No
12	E03	1,2-dimethoxy-4-(2-morpholin-4-yl(1,3-thiazol-4-yl))benzene	No
12	F03	5-(hydroxymethyl)quinolin-8-ol	No
12	G03	methyl 2-amino-5-methylthiophene-3-carboxylate	No
12	H03	1,2-dihydroxyanthracene-9,10-dione	No
12	I03	1,2,4-trihydroxyanthracene-9,10-dione	No
12	J03	3,4-dihydroxy-9,10-dioxoanthracene-2-sulfonic acid, sodium salt	No
12	K03	2-phenylbenzo[h]chromen-4-one	YES
12	L03	5-hydroxy-2-(3-hydroxyphenyl)chromen-4-one	No
12	M03	7-hydroxy-2-(3-hydroxyphenyl)chromen-4-one	No
12	N03	7-hydroxy-2-(4-methoxyphenyl)chromen-4-one	No
12	O03	adamantanyl-N-[3-(dimethylamino)propyl]carboxamide	No

12	P03	adamantanyl piperidyl ketone	No
12	A04	[(5-bromo(2-thienyl))sulfonyl][4-chloro-3-(trifluoromethyl)phenyl]amine	No
12	B04	1-[(4-methoxyphenyl)sulfonyl]-4-methylpiperazine	No
12	C04	[(4-fluorophenyl)sulfonyl]-3-pyridylamine	No
12	D04	2H-benzo[3,4-d]1,3-dioxolan-5-yl[(4-chlorophenyl)sulfonyl]amine	No
12	E04	(3,5-dichlorophenyl)(2-thienylsulfonyl)amine	No
12	F04	6-(piperidylsulfonyl)-2H,3H-benzo[e]1,4-dioxin	No
12	G04	(2H,3H-benzo[3,4-e]1,4-dioxin-6-ylsulfonyl)(4-{[(4-chlorophenyl)amino]sulfonyl }phenyl)amine	No
12	H04	4-methylpiperidyl 5-nitro(2-furyl) ketone	No
12	I04	5-[(1E)-2-(4-methylphenyl)vinyl]-2-(2-methylphenyl)-1,3,4-oxadiazole	No
12	J04	5-[(1E)-2-(2-chlorophenyl)vinyl]-2-(2-chlorophenyl)-1,3,4-oxadiazole	No
12	K04	5-((1E)-2-naphthylvinyl)-2-(2-chlorophenyl)-1,3,4-oxadiazole	No
12	L04	5-(5-bromo(2-furyl))-2-(2-chlorophenyl)-1,3,4-oxadiazole	No
12	M04	5-[(1E)-2-(4-fluorophenyl)vinyl]-2-(2-chlorophenyl)-1,3,4-oxadiazole	No
12	N04	5-(diphenylmethyl)-2-(2-bromophenyl)-1,3,4-oxadiazole	No
12	O04	5-(5-bromo(2-furyl))-2-phenyl-1,3,4-oxadiazole	No
12	P04	5-[(1E)-2-(4-fluorophenyl)vinyl]-2-phenyl-1,3,4-oxadiazole	No
12	A05	5-(2,4-dichlorophenyl)-2-(4-fluorophenyl)-1,3,4-oxadiazole	No
12	B05	5-(2,4-dichlorophenyl)-2-(3,5-dinitrophenyl)-1,3,4-oxadiazole	No
12	C05	5-((1E)-2-naphthylvinyl)-2-(2,4-dichlorophenyl)-1,3,4-oxadiazole	No
12	D05	5-((1E)-2-(2-furyl)vinyl)-2-(2,4-dichlorophenyl)-1,3,4-oxadiazole	No
12	E05	5-(2,4-dichlorophenyl)-2-[4-(tert-butyl)phenyl]-1,3,4-oxadiazole	No
12	F05	4-{(1E)-2-[5-(2,4-dichlorophenyl)(1,3,4-oxadiazol-2-yl)]vinyl}-1-methoxybenzen e	No
12	G05	5-[(1E)-2-(4-fluorophenyl)vinyl]-2-(2,4-dichlorophenyl)-1,3,4-oxadiazole	No
12	H05	2-(2,4-dichlorophenyl)-5-(2-methyl(3-furyl))-1,3,4-oxadiazole	No
12	I05	(7R,7aR)-3-(acetyloxymethyl)-7-amino-6-oxo-2H,7H-azetidino[2,1-b]1,3-thiazine- 4-carboxylic acid	No
12	J05	(2S,5R,6R)-6-amino-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carb oxylic acid	YES
12	K05		No
12	L05	6-methyl-4-(3-thienyl)-2-thioxo-1,5,6,7,8-pentahydropyridino[3,2-c]pyridine-3- carbonitrile	No
12	M05	2-(5-(2-furyl)(1,3,4-oxadiazol-2-ylthio))-1-(5-methyl(2-furyl))ethan-1-one	No
12	N05	2-(acetylamino)-5-(amidinoamino)pentanoic acid	No
12	O05		No

12	P05	(2S)-5,7-dihydroxy-2-(3-hydroxy-4-methoxyphenyl)chroman-4-one	No
12	A06	2-(hydroxymethyl)-5-(6-imino-1-methylhydropurin-9-yl)oxolane-3,4-diol	No
12	B06	(2R)-2-[(4-{[(2-amino-4-oxo(8-hydropteridin-6-yl))methyl]amino}phenyl)carbonyl amino]pentanedioic acid, hydrate	No
12	C06	5-(amidinoamino)-2-(aminocarbonylamino)pentanoic acid	No
12	D06	4-hydroxy-2-methoxy-5-(phenylcarbonyl)benzenesulfonic acid	No
12	E06	2-hydroxy-3-indol-3-ylpropanoic acid	No
12	F06	N-[5-(chlorosulfonyl)-4-methyl-1,3-thiazol-2-yl]acetamide	No
12	G06	{[((2S,4S,1R)-2-hydroxy-7,7-dimethylbicyclo[2.2.1]heptyl)methyl]sulfonyl}dicyc lohexylamine	No
12	H06	(2S)-2-amino-3-(1-methylindol-3-yl)propanoic acid	No
12	I06	di2,4-dihydroxyphenyl ketone	No
12	J06	5-(6-aminopurin-9-yl)-2-(hydroxymethyl)oxolan-3-ol, hydrate	No
12	K06	((4S,1R)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptyl)methanesulfonic acid, N	No
12	L06	((4S,1R)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptyl)methanesulfonamide	No
12	M06	4-indol-3-ylbutanoic acid, potassium salt	No
12	N06	(5,7-dimethyl(8-hydro-1,2,4-triazolo[1,5-a]pyrimidin-2-yl))chlorosulfone	No
12	O06	methyl 4-amino-1,2,5-oxadiazole-3-carboxylate	No
12	P06	3-(3-methoxypropyl)-5-(2-thienylmethylene)-2-thioxo-1,3-thiazolidin-4-one	No
12	A07	5-[(4-chlorophenyl)methylene]-2-pyrrolidinyl-1,3-thiazolin-4-one	No
12	B07	5-[(5-methyl(2-furyl))methylene]-2-(4-methylpiperidyl)-1,3-thiazolin-4-one	No
12	C07		No
12	D07	6-(2-furylmethylene)-3-phenyl-1,3-thiazolidino[2,3-c]1,2,4-triazol-5-one	No
12	E07	2-[(4-bromophenyl)(methylsulfonyl)amino]-N-(oxolan-2-ylmethyl)acetamide	No
12	F07	(3R)-3-((5R)-4-methoxy-6-methyl(5,6,7,8-tetrahydro-2H-1,3-dioxoleno[4,5-g]isoq uinolin-5-yl))-6,7-dimethoxy-3-hydroisobenzofuran-1-one	No
12	G07	1-methyl-3-(2-methylpropyl)-1,3,7-trihydropurine-2,6-dione	No
12	H07	9,10-dimethoxy-5,6-dihydro-2H-1,3-dioxolano[4,5-g]isoquinolino[3,2-a]isoquinol ine, chloride	No
12	I07	3-((5R)-6-methyl(5,6,7,8-tetrahydro-2H-1,3-dioxoleno[4,5-g]isoquinolin-5-yl))(3S)-6,7-dimethoxy-3-hydroisobenzofuran-1-one	No
12	J07	biotin	YES
12	K07		No
12	L07	8-(3,4,5-trimethoxyphenyl)-5,7,8-trihydro-2H-1,3-dioxolano[4,5-g]quinolin-6-on e	No

12	M07	[(2,4-difluorophenyl)amino][(5-bromo-3-methyl(2-pyridyl))amino]methane-1-thion e	No
12	N07	1-[(1E)-2-(1-hexyl(2-pyridyl))vinyl]-2,4-dimethoxybenzene, iodide	No
12	O07	5-[(1E)-2-(1-hexyl(2-pyridyl))vinyl]-2H-benzo[d]1,3-dioxolane, iodide	No
12	P07	methyl 2-[(2,5-dichlorophenyl)sulfonyloxy]-5-iodobenzoate	No
12	A08	2-[(2-hydroxyethyl)amino]-N-(4-iodophenyl)acetamide	No
12	B08	3,6-dichloro-2-methylbenzo[b]thiole-1,1-dione	No
12	C08	5-[4-(benzotriazolylmethyl)piperazinyl]-2H-benzo[d]1,3-dioxolene	No
12	D08	4,6-bis(4-chlorophenyl)-1,3,6-trihydropyrimidin-2-one	No
12	E08	4-ethyl-5-(4-fluorophenyl)-1,2,4-triazole-3-thiol	No
12	F08	4-phenyl-5-(2-thienyl)-1,2,4-triazole-3-thiol	No
12	G08	4-butyl-5-[(4-chlorophenoxy)methyl]-1,2,4-triazole-3-thiol	No
12	H08	2-(4-methyl(1,2,4-triazol-3-ylthio))-N-(2,4,5-trifluorophenyl)acetamide	No
12	I08	2-[4-(4-fluorophenyl)piperazinyl]-N-(2,4,5-trifluorophenyl)acetamide	No
12	J08	2,4,6-tri(2-pyridyl)-1,3,5-triazine	No
12	K08	3,3-bis(3-chloro-4-hydroxyphenyl)benzo[c]1,2-oxathiolene-1,1-dione	No
12	L08	2,5-dioxoazolidinyl (2,5-dioxoazolidinyloxy)formate	No
12	M08	2,5-dioxoazolidinyl (phenylmethoxy)formate	No
12	N08	2,5-dioxoazolidinyl (fluoren-9-ylmethoxy)formate	No
12	O08	2,5-dioxoazolidinyl [2-(methylsulfonyl)ethoxy]formate	No
12	P08		No
12	A09		No
12	B09	1-{6-[(2S,4S,5S,3R,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)(2H-3,4,5,6-tetrahydr opyran-2-yloxy)]-2,4-dihydroxyphenyl}-3-(4-hydroxyphenyl)propan-1-one	No
12	C09	2-methyl-4-(4-methylthiophenyl)(1,4,5-trihydropyrimidino[1,2-a]benzimidazol-3- yl) phenyl ketone	No
12	D09	5-(1,2,3,4-tetraazolyl)-3-hydroisobenzofuran-1-one	No
12	E09	(1-cyclohexylbenzimidazol-5-yl)[(4-fluorophenyl)sulfonyl]amine	No
12	F09	{4-amino-6-[(3,4-dimethylphenoxy)methyl](1,3,5-triazin-2-yl)}dimethylamine	No
12	G09	{[4-amino-6-(dimethylamino)(1,3,5-triazin-2-yl)]methyl}methyl(phenylsulfonyl)a mine	No
12	H09	{[1-(methylsulfonyl)indolin-5-yl]sulfonyl}[4-(4-pyridylmethyl)phenyl]amine	No
12	I09	2-[(1,3-dimethyl-2-oxo-3-hydrobenzimidazol-5-yl)methyl]benzo[c]azolidine-1,3-d ione	No
12	J09	1,2-dimethoxy-4-(5-methylthio-4-prop-2-enyl(1,2,4-triazol-3-yl))benzene	No
12	K09	1-(2-naphthylsulfonyl)-4-(4-nitrophenyl)piperazine	No

12	L09	N,N-diethyl-2-(1,1,3-trioxo(2-hydrobenzo[d]isothiazol-2-yl))acetamide	No
12	M09	1-[3-(2-chlorophenoxy)propyl]indole-3-carbonitrile	No
12	N09	1-acetyl-3-[4-(tert-butyl)phenyl]-4-oxa-1,2-diazaspiro[4.4]non-2-ene	No
12	O09	N-(2H-benzo[3,4-d]1,3-dioxolan-5-yl)-N'-(2H-benzo[3,4-d]1,3-dioxolen-5-yl)etha ne-1,2-diamide	No
12	P09	2H-1,3-thiazolidino[3,2-a]benzimidazol-3-one	No
12	A10	5-[(3,5-dichloro-4-hydroxyphenyl)methylene]-1,3-dimethyl-2-thioxo-1,3-dihydrop yrimidine-4,6-dione	No
12	B10	5-[(5-chloro-2-thienyl)methylene]-1,3-thiazolidine-2,4-dione	No
12	C10	2-(azaethylidene)-3-methyl-5-[(5-methyl(2-thienyl))methylene]-1,3-thiazolidin- 4-one	No
12	D10	[4-bromo-5-(4-chlorophenylthio)(2-furyl)](hydroxyimino)methane	No
12	E10	3-(3-bromophenyl)-4-ethyl-1,2,4-triazoline-5-thione	No
12	F10	3-(3-bromophenyl)-1,2,4-triazoline-5-thione	No
12	G10	2-(2,4-dihydroxyphenyl)chromen-4-one	No
12	H10	3,6-dimethoxy-2-phenylchromen-4-one	No
12	I10	3-hydroxy-2-(3-hydroxyphenyl)chromen-4-one	No
12	J10	3,6-dihydroxy-2-(4-hydroxyphenyl)chromen-4-one	YES
12	K10	7,8-dihydroxy-2-(2-hydroxyphenyl)chromen-4-one	No
12	L10	7,8-dihydroxy-2-(3-hydroxyphenyl)chromen-4-one	No
12	M10	2-(3,4-dihydroxyphenyl)-3-hydroxychromen-4-one	No
12	N10	2-naphthyl[(phenanthridin-6-ylmethylthio)methyl]amine	No
12	O10	4-{[4-(4-bromophenoxy)phenyl]sulfonyl}morpholine	No
12	P10	phenyl(xanthen-9-ylamino)methane-1-thione	No
12	A11	[(2,4-dichlorophenyl)methyl]thiocarboxamidine, chloride	No
12	B11	5-[(3,5-dibromo-2-hydroxyphenyl)methylene]-2-thioxo-1,3-diazolidin-4-one	No
12	C11	5-{5-[(1,3-dimethyl-2,4,6-trioxo-1,3-dihydropyrimidin-5-ylidene)methyl]-2-fury l}benzene-1,3-dicarboxylic acid	No
12	D11		No
12	E11	4-(1H-1,2,3,4-tetraazol-5-yl)-1,2,5-oxadiazole-3-ylamine	No
12	F11	1-(4-bromophenyl)-1,2-diazolidine-3,5-dione	No
12	G11	5-hydrazino-3-hydrobenzimidazol-2-one, chloride	No
12	H11	2-methyl-4-morpholin-4-yl-5-hydropyridino[1,2-a]benzimidazolecarbonitrile	No
12	I11	2-(4-methyl(1,2,4-triazol-3-ylthio))-1-nitro-4-piperidylbenzene	No
12	J11	2-[2-(3-methoxyphenoxy)ethylthio]hydroquinazolin-4-one	No
12	K11	2-[2-(2-fluorophenoxy)ethylthio]hydroquinazolin-4-one	No
12	L11		No
12	M11	1-methyl-4,5-diphenyl-4-imidazoline-2-thione	No
12	N11	(4-amino(1,2,5-oxadiazol-3-yl))-N-{2-[(methylsulfonyl)amino]ethyl}carboxamide	No

12	O11	4-nitro-5-[(oxolan-2-ylmethyl)amino]benzene-1,2-dicarbonitrile	No
12	P11	4,5-diaminobenzene-1,2-dicarbonitrile	No
12	A12	4-(4-quinoxalin-2-ylphenoxy)benzene-1,2-dicarbonitrile	No
12	B12	5-[(4-bromo-3-nitropyrazolyl)methyl]furan-2-carboxylic acid	No
12	C12	5-(2-furyl)-7-(trifluoromethyl)-8-hydropyrazolo[1,5-a]pyrimidine-2-carboxylic acid	No
12	D12	5-(1,3-dimethylpyrazol-4-yl)-7-(trifluoromethyl)-4H,5H,6H,7H-pyrazolo[1,5-a]1, 3-diazaperhydroine-2-carboxylic acid	No
12	E12	5,7-bis(difluoromethyl)-8-hydropyrazolo[1,5-a]pyrimidine-2-carboxylic acid	No
12	F12	1-adamantanyl-4-nitropyrazole-3-carboxylic acid	No
12	G12	2-[3-(4-chloro-5-methyl-3-nitropyrazolyl)adamantanyl]acetic acid	No
12	H12	5-(2-thienyl)-7-(trifluoromethyl)-4H,5H,6H,7H-pyrazolo[1,5-a]1,3-diazaperhydro ine-2-carboxylic acid	No
12	I12	5-methyl-7-(1,1,2,2,2-pentafluoroethyl)-4H,5H,6H,7H-pyrazolo[1,5-a]1,3-diazape rhydroine-2-carboxylic acid	No
12	J12	2-(3,5-dimethyl-1-phenylpyrazol-4-yl)-3-hydroxy-1,2,3-trihydroquinazolin-4-one	No
12	K12	2-[(3-methyl-4-nitropyrazol-5-yl)sulfinyl]acetic acid	No
12	L12	1-[(3-nitro-1,2,4-triazolyl)methyl]pyrazole-3-carboxylic acid	No
12	M12	2-amino-4-(3,4-diethoxyphenyl)-7,7-dimethyl-5-oxo-4H-6,7,8-trihydrochromene-3- carbonitrile	No
12	N12	(4S)-2-[1-((4S)-4-phenyl(1,3-oxazolin-2-yl))-isopropyl]-4-phenyl-1,3-oxazoline	No
12	O12	2,4,5-trichlorophenyl (tert-butoxy)formate	No
12	P12	6-[(6-hydroxy-2-naphthyl)disulfanyl]naphthalen-2-ol	No
12	A13	5-bromo-3-fluoro-2-methoxy-1-nitrobenzene	No
12	B13	2-methoxy-4-nitrophenol, potassium salt, hydrate	No
12	C13	2-[(3,4-dihydroxyphenyl)(3-hydroxy-4-oxocyclohexa-2,5-dienylidene)methyl]benze nesulfonic acid, sodium salt	No
12	D13	2-phenyl-2-(3,4,5-trihydroxy-6-{[3,4,5-trihydroxy-6-(hydroxymethyl)(2H-3,4,5,6 -tetrahydropyran-2-yloxy)]methyl}(2H-3,4,5,6-tetrahydropyran-2-yloxy))ethaneni trile	No
12	E13	(3Z)-4-{N-[(4-amino-2-methylpyrimidin-5-yl)methyl]carbonylamino}-3-(phenylcarb onylthio)pent-3-enyl dihydrogen phosphate	No
12	F13	(1S,12S,14R)-9-methoxy-4-methyl-11-oxa-4-azatetracyclo[8.6.1.0<1,12>.0<6,17>]h eptadeca-6,8,10(17),15-tetraen-14-ol	No
12	G13	4-[4-(3,4-dihydroxyphenyl)-2,3-dimethylbutyl]benzene-1,2-diol	No
12	H13	methyl 3-indol-3-yl-2-(methoxycarbonylamino)propanoate	No
12	I13		No
12	J13	2-amino-4-bromophenol	No
12	K13	2-benzimidazol-2-ylethylamine	No

12	L13	N-[1,3-bis(hydroxymethyl)-2,5-dioxo(1,3-diazolidin-4-yl)]-N-(hydroxymethyl)[(h ydroxymethyl)amino]carboxamide	No
12	M13	7,8-dihydroxy-2-(4-hydroxyphenyl)chromen-4-one	No
12	N13	(3S,4aS,5aS,4R,14aR)-3-hydroxy-1,2,3,4,5,11,14,14a,4a,5a-decahydrobenzo[1,2-g] indolo[2,3-a]quinolizine-4-carboxylic acid, oxamethane	No
12	O13	[(4aS,1R,10aR)-1,4a-dimethyl-7-(methylethyl)-1,2,3,4,9,10,10a,4a-octahydrophen anthryl]methylamine	No
12	P13	(1R)(6-methoxy(4-quinolyl))(5-vinylquinuclidin-2-yl)methan-1-ol	No
12	A14	(4bS,1R,10aR,4aR)-1,4a-dimethyl-7-(methylethyl)-1,2,3,4,5,6,10,10a,4a,4b-decah ydrophenanthrenecarboxylic acid	No
12	B14		No
12	C14	N-methyl(1,8,3a-trimethylpyrrolidino[2,3-b]indolin-5-yloxy)carboxamide	No
12	D14	2-((3S)-3-hydroxy-3-methylpent-4-enyl)(1S,6S,2R,3R)-1,3,7,7-tetramethylbicyclo [4.4.0]decan-3-ol	No
12	E14	(1S)(5-ethylquinuclidin-2-yl)(6-methoxy(4-quinolyl))methan-1-ol	No
12	F14		No
12	G14	(11S,18S,22S,1R,20R,21R)-4,5-dimethoxy-12-oxa-8,17-diazaheptacyclo[15.5.2.0<1, 18>.0<2,7>.0<8,22>.0<11,21>.0<15,20>]tetracosa-2,4,6,14-tetraen-9-one	No
12	H14	4-[5-((6S,2R,3R,4R,5R)-3,4,5-trihydroxy-6-methyl(2H-3,4,5,6-tetrahydropyran-2- yloxy))(1S,5S,7S,11S,2R,3R,10R,14R,15R,17R)-3,7,11,17-tetrahydroxy-2-(hydroxym ethyl)-15-methyltetracyclo[8.7.0.0<2,7>.0<11,15>]heptadec-14-yl]-5-hydrofuran- 2-one, hydrate	No
12	I14	(2S,3S,5S,8S,11S,12S,14S,4R,9R)-11-[(3S,6S,2R,4R)-4-(dimethylamino)-3-hydroxy- 6-methyl(2H-3,4,5,6-tetrahydropyran-2-yl)oxy]-9-((5S,6S,2R,4R)-5-hydroxy-4-met hoxy-4,6-dimethyl(2H-3,4,5,6-tetrahydropyran-2-yl)oxy)-5-ethyl-3,4,12-trihydro xy-2,4,8,10,12,14-hexamethyl-6-oxacyclotetradecane-1,7-dione, hydrate	No
12	J14	7-chloro-4,6,12-trimethoxy-14-methylspiro[2-hydrobenzo[b]furan-2,4'-cyclohexan e]-11-ene-3,10-dione	No
12	K14	(1S)-4-quinolyl(5-vinylquinuclidin-2-yl)methan-1-ol	No
12	L14	(3aS,2R,3R,9aR)-2-(hydroxymethyl)-6-imino-9-hydro-2H,3H-oxolano[2,3-d]pyrimidi no[2,1-b]1,3-oxazolidin-3-ol, chloride	No
12	M14	(2Z,4E)-5-(1-hydroxy-2,6,6-trimethyl-4-oxocyclohex-2-enyl)-3-methylpenta-2,4-d ienoic acid	No
12	N14	3-[(2E)-3-(3,4-dihydroxyphenyl)prop-2-enoyloxy](1S,3R,4R,5R)-1,4,5-trihydroxyc yclohexanecarboxylic acid	No
12	O14	7-hydroxy-6-[3,4,5-trihydroxy-6-(hydroxymethyl)(2H-3,4,5,6-tetrahydropyran-2-y loxy)]chromen-2-one	No
12	P14	(5S,8S,15S,18S,1R,2R,10R,14R,20R)-18-hydroxy-1,2,5,8,15,19,19-heptamethyl-13-o	No

		xopentacyclo[12.8.0.0<2,11>.0<5,10>.0<15,20>]docos-11-ene-8-carboxylic acid	
12	A15	(1S,3S,4S,7S,14S,2R,10R,11R)-7,14-dihydroxy-1-methyl-6-methylene-15-oxo-16-oxa pentacyclo[9.3.2.1<4,7>.0<2,11>.0<4,10>]heptadec-12-ene-3-carboxylic acid	No
12	B15		No
12	C15	10-[((1R)-6,7-dimethoxy(1,2,3,4-tetrahydroisoquinolyl))methyl](10S,11aS,9R)-9- ethyl-2,3-dimethoxy-5,6,7,11a-tetrahydropiperidino[2,1-a]isoquinoline	No
12	D15	(2S,5S,6S,9S)-5,9,13-trimethyl-3-oxatricyclo[7.4.0.0<2,6>]trideca-1(13),10-die ne-4,12-dione	No
12	E15	amino(iminomorpholin-4-ylmethyl)carboxamidine	No
12	F15		No
12	G15	2,3,3-trihydroxy-2-(2,3,3-trihydroxy-1-oxoindan-2-yl)indan-1-one	No
12	H15	(2E)-3-(3-bromo-4-fluorophenyl)prop-2-enoic acid	No
12	I15	5-nitropyrazole-3-carboxylic acid	No
12	J15	3-prop-2-ynyl-5-[(4-pyrrolidinylphenyl)methylene]-1,3-thiazolidine-2,4-dione	No
12	K15	3-indol-3-yl-2-oxopropanoic acid	No
12	L15	2-(methylethylidene)butanedioic acid	No
12	M15	(2-fluorophenyl){6-[(2-fluorophenyl)amino](1,2,5-oxadiazolo[3,4-e]pyrazin-5-yl)}amine	No
12	N15	3-(pyrrolidinylsulfonyl)phenylamine	No
12	O15	5-{[1-(2-(2H-benzo[3,4-d]1,3-dioxolen-5-yloxy)ethyl)indol-3-yl]methylene}-1,3- dihydropyrimidine-2,4,6-trione	No
12	P15	5-[(2,5-dimethyl-1-(3-pyridyl)pyrrol-3-yl)methylene]-1-(4-bromophenyl)-2-thiox o-1,3-dihydropyrimidine-4,6-dione	No
12	A16	2-{2-[(2,5-dioxo(1,3-diazolidin-4-ylidene))methyl]-4-bromophenoxy}acetic acid	No
12	B16	2-{2-methoxy-6-prop-2-enyl-4-[(2,4,6-trioxo(1,3-dihydropyrimidin-5-ylidene))me thyl]phenoxy}acetic acid	No
12	C16	5-[(1E)-2-(4-morpholin-4-ylphenyl)-2-azavinyl]-2-benzimidazol-2-ylthiofuran	No
12	D16	5-{(1E)-2-[1-(4-bromophenyl)pyrrol-2-yl]-1-azavinyl}-2-methoxypyridine	No
12	E16	N-(4-{[2-(N-cyclopropylcarbamoyl)pyrrolidinyl]sulfonyl}phenyl)acetamide	No
12	F16	4,5-bis(3,4-dimethoxyphenyl)-1,2,4-triazole-3-thiol	No
12	G16	[4-amino-6-(ethylthioethyl)(1,3,5-triazin-2-yl)](2-methoxyphenyl)amine	No
12	H16	2-{[4-(4-methoxyphenyl)piperazinyl]sulfonyl}dibenzo[b,d]furan	No
12	I16	1-(2-oxo-2-(2-1,2,3,4-tetrahydroisoquinolyl)ethyl)benzo[d]azolidine-2,3-dione	No

12	J16	3-cyclohexyl-2-sulfanyl-3,5,6,7,8-pentahydrobenzo[b]thiopheno[2,3-d]pyrimidin- 4-one	No
12	K16	2-chloro-N-(4-fluorophenyl)acetamide	No
12	L16	N-(2,6-dichlorophenyl)-2-chloroacetamide	No
12	M16	2-chloro-N-(2-chloro(3-pyridyl))acetamide	No
12	N16	N,N-diethyl(3-methyl-4-oxo(3-hydrophthalazinyl))carboxamide	No
12	O16	N-cyclohexyl(3-methyl-4-oxo(3-hydrophthalazinyl))carboxamide	No
12	P16	(3-methyl-4-oxo(3-hydrophthalazinyl))-N-prop-2-enylcarboxamide	No
12	A17	2H,3H-benzo[e]1,4-dioxin-6-yl(5-nitro(2-pyridyl))amine	No
12	B17	N-(tert-butyl)-2-(2-methylindol-3-yl)-2-oxoacetamide	No
12	C17	1-indol-3-yl-2-morpholin-4-ylethane-1,2-dione	No
12	D17	N,N-diethyl-2-(1-methylindol-3-yl)-2-oxoacetamide	No
12	E17	N-cyclopropyl-2-(2-methylindol-3-yl)-2-oxoacetamide	No
12	F17	1,3-dimethyl-6-(piperidylsulfonyl)-1,3-dihydroquinazoline-2,4-dione	No
12	G17	6-[(cyclopropylamino)sulfonyl]-1,3-dimethyl-1,3-dihydroquinazoline-2,4-dione	No
12	H17	4-(benzothiazol-2-ylthiomethyl)hydroquinolin-2-one	No
12	I17	4-[(5-amino-1,3,4-thiadiazol-2-ylthio)methyl]hydroquinolin-2-one	No
12	J17	4-[(5-(2-furyl)-4-phenyl-1,2,4-triazol-3-ylthio)methyl]hydroquinolin-2-one	No
12	K17	4-{[4-methyl-5-(phenoxymethyl)-1,2,4-triazol-3-ylthio]methyl}hydroquinolin-2-o ne	No
12	L17	2-methyl-4-[4-(methylethyl)phenyl](1,4,5-trihydropyrimidino[1,2-a]benzimidazol -3-yl) phenyl ketone	No
12	M17	5-phenyl-3-(3-pyridylmethylthio)-1,2,4-triazole-4-ylamine	No
12	N17	N-benzo[3,4-b]benzo[d]furan-3-yl-2-indol-3-yl-2-oxoacetamide	No
12	O17	methoxy-N-{5-[(4-methylpiperidyl)methyl](1,3-thiazol-2-yl)}carboxamide	No
12	P17	3-{[(4-fluorophenyl)sulfonyl]methylamino}thiolane-1,1-dione	No
12	A18	11-chloro-7,8,9,10,12-pentahydrobenzimidazolo[1,2-b]isoquinoline-6-carbonitril e	No
12	B18	5,8-dimethoxy-4-methylhydroquinolin-2-one	No
12	C18	2-chloro-5,8-dimethoxy-4-methylquinoline	No
12	D18	(2,6-dimethylphenyl)[(2,4,6-trimethyl-3-(1,2,3,4-tetraazolyl)phenyl)sulfonyl]a mine	No
12	E18	(4-oxo(3-hydrophthalazinyl))-N-prop-2-enylcarboxamide	No
12	F18	N-(5-methylisoxazol-3-yl)(4-oxo(3-hydrophthalazinyl))carboxamide	No
12	G18	6-({[3,5-bis(trifluoromethyl)phenyl]amino}sulfonyl)-2H,4H-benzo[e]1,4-oxazin-3 -one	No
12	H18	4-{[4-(4-(1,2,3,4-tetraazolyl)phenyl)phenyl]sulfonyl}morpholine	No
12	I18	5-chloro-2-[(4-phenylpiperazinyl)sulfonyl]thiophene	No
12	J18	5-chloro-2-{[4-(4-methoxyphenyl)piperazinyl]sulfonyl}thiophene	No

12	K18	oxolan-2-yl-N-{4-[(pyrimidin-2-ylamino)sulfonyl]phenyl}carboxamide	No
12	L18	difluoro-8-quinolyloxymethane	No
12	M18	6,7,8,9,11-pentahydrobenzo[b]thiopheno[2,3-d]pyrrolidino[1,2-a]pyrimidin-10-on e	No
12	N18	methyl 2-{1-[(methoxycarbonyl)methyl]-2,4-dioxo-1,3-dihydroquinazolin-3-yl}ace tate	No
12	O18	1,4-dimethyl-6-nitro-1,4-dihydroquinoxaline-2,3-dione	No
12	P18	5-(4-chlorophenyl)-2-[(3-phenyl(1,2,4-oxadiazol-5-yl))methylthio]-1,3,4-oxadia zole	No
12	A19	1-phenyl-5-[(3-phenyl(1,2,4-oxadiazol-5-yl))methylthio]-1,2,3,4-tetraazole	No
12	B19	2-(3,4-dimethoxyphenyl)-6,7-dimethoxynaphthol	No
12	C19	1-(methylsulfonyl)-6-{[benzylamino]sulfonyl}-1,2,3,4-tetrahydroquinoline	No
12	D19	2,4,6-trimethyl-3-(1,2,3,4-tetraazolyl)benzenesulfonamide	No
12	E19	7-methyl-3-oxo-2H,4H-benzo[e]1,4-oxazine-6-sulfonamide	No
12	F19	1-acetylindoline-5-sulfonamide	No
12	G19	1-(methylsulfonyl)indoline-5-carboxamide	No
12	H19	5-(2-furyl)-3-(morpholin-4-ylmethyl)-1,3,4-oxadiazoline-2-thione	No
12	I19	5-(2-furyl)-3-(piperidylmethyl)-1,3,4-oxadiazoline-2-thione	No
12	J19	6-(piperidylsulfonyl)-2H,4H-benzo[e]1,4-oxazin-3-one	No
12	K19	{[4-methoxy-2-methyl-5-(methylethyl)phenyl]sulfonyl}pyrrolidine	No
12	L19	2-[5-(2-hydroxypropyl)-4-methyl(1,2,4-triazol-3-ylthio)]-1-(1,2,3,4,5,6,7,8,9- nonahydro-4aH-carbazol-9-yl)ethan-1-one	No
12	M19	3,5,6-trimethyl-2-(2-(1,2,3,4,5,6,7,8,9-nonahydro-4aH-carbazol-9-yl)-2-oxoethy lthio)-3-hydrothiopheno[2,3-d]pyrimidin-4-one	No
12	N19	5-((1E)-2-nitroprop-1-enyl)-2H-benzo[d]1,3-dioxolene	No
12	O19	2-chloro-3-phenylquinoxaline	No
12	P19	2-(2-{[2-(1,3-dioxobenzo[c]azolin-2-yl)ethyl]amino}ethyl)benzo[c]azoline-1,3-d ione	No
12	A20	2-{[4-amino-6-(phenylamino)(1,3,5-triazin-2-yl)]methylthio}-3-methyl-3-hydroqu inazolin-4-one	No
12	B20	3-(diphenylmethyl)-4-methyl-1,2,4-triazoline-5-thione	No
12	C20	[2-(2-chlorophenoxy)ethyl](dibenzo[b,d]furan-2-ylsulfonyl)amine	No
12	D20	cyclohexyl({4-[(dibenzo[b,d]furan-2-ylsulfonyl)amino]phenyl}sulfonyl)methylami ne	No
12	E20	1-{4-[(6-ethoxybenzothiazol-2-ylthio)methyl]phenoxy}-1,1,2,2-tetrafluoroethane	No
12	F20	5-adamantanyl-4-prop-2-enyl-1,2,4-triazole-3-thiol	No
12	G20	benzo[b]naphtho[2,3-e]thiin-12-one	No
12	H20	5-{[4-(1,1,2,2-tetrafluoroethoxy)phenyl]methylthio}-1,3,4-thiadiazole-2-ylamin e	No
12	I20	3-(4-methyl-5-methylthio-1,2,4-triazol-3-yl)naphthalen-2-ol	No

12	J20	[5-(3-hydroxypropyl)-4-phenyl(1,2,4-triazol-3-yl)]thiocarboxylic acid	No
12	K20	(dibenzo[b,d]furan-2-ylsulfonyl)[(4-ethylphenyl)ethyl]amine	No
12	L20	[3,5-bis(trifluoromethyl)phenyl](dibenzo[b,d]furan-2-ylsulfonyl)amine	No
12	M20	5-methyl-2-(2-methyl(4-quinolylthio))-1,3,4-thiadiazole	No
12	N20	3-[(2-chloro-4,5-difluorophenyl)methylthio]-5-phenyl-4-benzyl-1,2,4-triazole	No
12	O20	1-{[2-((2E)but-2-enylthio)(1Z)-2-(4-chlorophenylthio)-1-azavinyl]sulfonyl}-4-n itrobenzene	No
12	P20	2-[(2-chloro-4,5-difluorophenyl)methylthio]-6-ethoxybenzothiazole	No
12	A21	2-[(2,6-dichlorophenyl)methylthio]-4-phenyl-1,3-thiazole	No
12	B21	10-(3-{4-[4-(4-fluorophenyl)(1,3-thiazol-2-yl)]piperazinyl}propyl)-2-(trifluor omethyl)phenothiazine	No
12	C21	4-(imidazolylmethyl)phenylamine	No
12	D21	2-[3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-4H-1,2,4-triazine-3,5-dione	No
12	E21	9-[(4S,2R,3R,5R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-2-amino-8-bromohy dropurin-6-one	No
12	F21	6-(hydroxymethyl)-2-[3,4,5-trihydroxy-6-(hydroxymethyl)(2H-3,4,5,6-tetrahydrop yran-2-yloxy)]-2H-3,4,5,6-tetrahydropyran-3,4,5-triol, hydrate	No
12	G21	2-[3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-3-thioxo-4H-1,2,4-triazin-5-one	No
12	H21	1-[(5S,2R)-5-(hydroxymethyl)oxolan-2-yl]-1,3-dihydropyrimidine-2,4-dione	No
12	I21	N-{1-[3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-2-oxohydropyrimidin-4-yl}ben zamide	No
12	J21	6-amino-3-[4-hydroxy-5-(hydroxymethyl)oxolan-2-yl]-3-hydropyrimidin-2-one, chl oride	No
12	K21	1-[3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-4-hydroxyhydropyridin-2-one	No
12	L21	9-[(3S,5S,4R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-3-hydropurin-6-one	No
12	M21	3-[3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-6-hydrazino-3-hydropyrimidin-2- one	No
12	N21	5-ethyl-1-[4-hydroxy-5-(hydroxymethyl)oxolan-2-yl]-1,3-dihydropyrimidine-2,4-d ione	No
12	O21	2-amino-9-[3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-8-thioxo-3,7-dihydropur in-6-one	No
12	P21	cytidine	No
12	A22	1-[(1R,2R,4R,5R)-4-(hydroxymethyl)-7,7-dimethyl-3,6,8-trioxabicyclo[3.3.0]oct- 2-yl]-1,3-dihydropyrimidine-2,4-dione	No
12	B22	1-[(4S,2R,5R)-4-hydroxy-5-(hydroxymethyl)oxolan-2-yl]-5-methyl-1,3-dihydropyri midine-2,4-dione	No

12	C22	1-[(4S,2R,5R)-4-hydroxy-5-(hydroxymethyl)oxolan-2-yl]-5-fluoro-1,3-dihydropyri midine-2,4-dione	No
12	D22	1-[(4S,2R,3R,5R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-5-fluoro-1,3-dihy dropyrimidine-2,4-dione	No
12	E22	1-[(3,4-dihydroxyphenyl)methyl]-1,2,3,4-tetrahydroisoquinoline-6,7-diol, bromi de	No
12	F22	5-[3-(2-pyridyl)-6-(5-sulfo(2-furyl))-1,2,4-triazin-5-yl]furan-2-sulfonic acid , sodium salt, sodium salt	No
12	G22	(2E)-2-benzimidazol-2-yl-3-(2-methylindol-3-yl)prop-2-enenitrile	No
12	H22	1-(2-nitro-5-piperazinylphenyl)-4-[2-nitro-4-(trifluoromethyl)phenyl]piperazin e	No
12	I22	4-(4-{[5-(1,3-dioxo(2H-benzo[c]azolin-5-yl))(2-furyl)]methylene}-5-oxo-3-(trif luoromethyl)-1,2-diazolinyl)benzoic acid	No
12	J22	2-(7-chloro-4-nitrobenzo[c]1,2,5-thiadiazol-5-ylthio)-3-hydroquinazolin-4-one	No
12	K22	N-cyclopentyl-2-(3-{[1-(2-methoxyethyl)-4,6-dioxo-2-thioxo(1,3-dihydropyrimidi n-5-ylidene)]methyl}indolyl)acetamide	No
12	L22	5-{5-[(1Z)-2-(2-oxo(3-hydrobenzimidazol-5-yl))-2-azavinyl]-2-furyl}benzene-1,3 -dicarboxylic acid	No
12	M22	2-{[(3-methyl-5-oxo-1-phenyl-1,2-diazolin-4-ylidene)azamethyl]amino}anthracene -9,10-dione	No
12	N22	5-[(5-hydroxy-3-methyl-1-phenylpyrazol-4-yl)diazenyl]-4H-1,2,4-triazole-3-carb oxylic acid	No
12	O22	1-ethyl-5-{[1-(2-oxo-2-pyrrolidinylethyl)indol-3-yl]methylene}-1,3-dihydropyri midine-2,4,6-trione	No
12	P22	5-{[(3-bromo-4-morpholin-4-ylphenyl)amino]methylene}-1-phenyl-2-thioxo-1,3-dih ydropyrimidine-4,6-dione	No

Plate	**Well**	**IUPAC NAME**	**Inhibitor Y/N**
13	A03	5-{[5-cyano-2-hydroxy-1-(2-hydroxyethyl)-4-methyl-6-oxo-3-hydropyridyl]diazeny l}-4H-1,2,4-triazole-3-carboxylic acid	No
13	B03	4-chloro-3-{[5-cyano-2-hydroxy-1-(2-hydroxyethyl)-4-methyl-6-oxo(3-hydropyridy l)]diazenyl}benzenesulfonic acid	No
13	C03	8-{2-[4-(tert-butyl)phenoxy]ethylthio}purine-6-ylamine	No
13	D03	2-(1-cyclohexyl(1,2,3,4-tetraazol-5-ylthio))-1-phenothiazin-10-ylethan-1-one	No
13	E03	2-{cyclohexyl[(4-fluorophenyl)sulfonyl]amino}-N-(oxolan-2-ylmethyl)acetamide	No
13	F03	1,2-dichloro-4-[(4-{3-[(2-morpholin-4-ylethyl)amino]-4-nitrophenyl}piperazinyl)sulfonyl]benzene	No
13	G03	N-((4S,1R,2R)bicyclo[2.2.1]hept-2-yl)-2-phenylthiopropanamide	No
13	H03	N-(2H-benzo[3,4-d]1,3-dioxolan-5-yl)-2-[5-(indol-3-ylmethylene)-2,4-dioxo(1,3- thiazolidin-3-yl)]acetamide	No
13	I03	2-oxoindoline-3-carbaldehyde	No
13	J03	6,8-dibromo-11,13,13-trimethylspiro[2H-chromene-2,2'-indoline]	YES

13	K03	3-(2-ethylisoxazol-5-yl)benzenesulfonic acid	No
13	L03	4-(2-aminoethyl)benzenesulfonamide	No
13	M03		No
13	N03	(2S)-2-(3-aminopropanoylamino)-3-imidazol-4-ylpropanoic acid	No
13	O03	[(1R,2R,4R,5R)-4-(6-aminopurin-9-yl)-7,7-dimethyl-3,6,8-trioxabicyclo[3.3.0]oc t-2-yl]methan-1-ol	No
13	P03	[(2R,3R,4R,5R)-3,4-diacetyloxy-5-(3,5-dioxo(4H-1,2,4-triazin-2-yl))oxolan-2-yl]methyl acetate	YES
13	A04	(4S,2R,3R,5R)-2-(6-amino-8-bromopurin-9-yl)-5-(hydroxymethyl)oxolane-3,4-diol	No
13	B04	[(3S,2R,4R,5R)-5-(6-aminopurin-9-yl)-3,4-dihydroxyoxolan-2-yl]methyl dihydroge n phosphate	No
13	C04	9-[(4S,2R,3R,5R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-1,3-dihydropurine -2,6-dione	No
13	D04	1-[(4S,2R,3R,5R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-5-bromo-1,3-dihyd ropyrimidine-2,4-dione	No
13	E04	[(3S,2R,4R,5R)-3,4-dihydroxy-5-(6-oxohydropurin-9-yl)oxolan-2-yl]methyl dihydr ogen phosphate, sodium salt, sodium salt	No
13	F04	[(3S,2R,5R)-5-(6-aminopurin-9-yl)-3-hydroxyoxolan-2-yl]methyl dihydrogen phosp hate	No
13	G04	[(3S,2R,5R)-5-(2-amino-6-oxohydropurin-9-yl)-3-hydroxyoxolan-2-yl]methyl dihyd rogen phosphate, sodium salt	No
13	H04	[(3S,2R,5R)-3-acetyloxy-5-(5-methyl-2,4-dioxo(1,3-dihydropyrimidinyl))oxolan-2 -yl]methyl acetate	YES
13	I04	(3S,2R,4R,5R)-5-(2-amino-6-chloropurin-9-yl)-2-(hydroxymethyl)oxolane-3,4-diol	No
13	J04	(4S,2R,3R,5R)-5-(hydroxymethyl)-2-{6-[benzylamino]purin-9-yl}oxolane-3,4-diol	YES
13	K04	(3S,2R,4R,5R)-5-(6-chloropurin-9-yl)-2-(hydroxymethyl)oxolane-3,4-diol	No
13	L04	(3S,2R,4R,5R)-5-{6-[(2-furylmethyl)amino]purin-9-yl}-2-(hydroxymethyl)oxolane- 3,4-diol	No
13	M04	[(3S,2R,4R,5R)-5-(2-amino-6-oxohydropurin-9-yl)-3,4-dihydroxyoxolan-2-yl]methy l dihydrogen phosphate, sodium salt, sodium salt	No
13	N04	1-[(4S,2R,5R)-4-hydroxy-5-(hydroxymethyl)oxolan-2-yl]-1,3-dihydropyrimidine-2, 4-dione	No
13	O04	1-[(4S,2R,5R)-4-hydroxy-5-(hydroxymethyl)oxolan-2-yl]-5-bromo-1,3-dihydropyrim idine-2,4-dione	No
13	P04	(3S,2R,4R,5R)-5-(4-amino-2-oxohydropyrimidinyl)-4-hydroxy-2-(hydroxymethyl)oxo lan-3-yl dihydrogen phosphate	No
13	A05	[(3S,2R,4R,5R)-5-(6-aminopurin-9-yl)-3,4-dihydroxyoxolan-2-yl]methyl dihydroge n phosphate	No
13	B05	9-[(4S,2R,3R,5R)-3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-2-aminohydropurin -6-one	No

13	C05	3-{2-[7-((2E)-1,4,5-trimethylhex-2-enyl)-6-methylbicyclo[4.3.0]non-2-ylidene]e thylidene}-4-methylenecyclohexan-1-ol	No
13	D05	(1S,9S,2R,6R)-1,6,10,10-tetramethyl-5-oxatricyclo[7.4.0.0<2,6>]tridecan-4-one	No
13	E05	(10S,13S,16S,1R,9R,14R,18R)-13-ethyl-8-methyl-8,15-diazahexacyclo[14.2.1.0<1,9 >.0<2,7>.0<10,15>.0<12,17>]nonadeca-2,4,6-triene-14,18-diol	No
13	F05	(5S)-1-methyl-5-(3-pyridyl)pyrrolidin-2-one	No
13	G05	(2S,5S,10S,18S,1R,14R,15R,20R)-18-hydroxy-1,2,8,8,15,19,19-heptamethylpentacyc lo[12.8.0.0<2,11>.0<5,10>.0<15,20>]docos-11-ene-5-carboxylic acid	YES
13	H05		No
13	I05	3-(4-hydroxyphenyl)-1-(2,4,6-trihydroxyphenyl)propan-1-one	No
13	J05	(1S,8S,14R)-2-oxa-9-azatetracyclo[6.6.1.0<1,5>.0<9,14>]pentadeca-4,6-dien-3-on e	No
13	K05	(4S,6S,12aS,4aS,5aS)-4-(dimethylamino)-3,6,10,12,12a-pentahydroxy-6-methyl-1,1 1-dioxo-4,5,6,12a,4a,5a-hexahydronaphthacene-2-carboxamide, chloride	No
13	L05		No
13	M05	3-{2-[7-(1,5-dimethylhexyl)-6-methylbicyclo[4.3.0]non-2-ylidene]ethylidene}-4- methylenecyclohexan-1-ol	No
13	N05	(3S,2R)-2-(3,4-dihydroxyphenyl)chromane-3,5,7-triol	No
13	O05	2-{[4-hydroxy-2-methyl-5-(methylethyl)phenyl][2-methyl-5-(methylethyl)-4-oxocy clohexa-2,5-dienylidene]methyl}benzenesulfonic acid	No
13	P05	5-[(2,6-dichloro-3-sulfophenyl)(3-carboxy-5-methyl-4-oxocyclohexa-2,5-dienylid ene)methyl]-2-hydroxy-3-methylbenzoic acid	No
13	A06	4-nitro-1,2,5-oxadiazole-3-ylamine	No
13	B06	2,6-bis(tert-butyl)-4-sulfanylphenol	No
13	C06	2-(3-chloro-2-hydroxypropyl)benzo[c]azoline-1,3-dione	No
13	D06		No
13	E06		No
13	F06	bis[4-(dimethylamino)phenyl]phenylmethan-1-ol	No
13	G06	5-[(3-carboxy-4-hydroxyphenyl)(3-carboxy-4-oxocyclohexa-2,5-dienylidene)methyl]-2-hydroxybenzoic acid, N	No
13	H06	3,4,10,6a-tetrahydroxy-7,6a-dihydroindeno[2,1-c]chroman-9-one	No
13	I06	2,5-dihydroxy-3-undecylcyclohexa-2,5-diene-1,4-dione	No
13	J06	2-[(3,4-dihydroxyphenyl)(3-hydroxy-4-oxocyclohexa-2,5-dienylidene)methyl]benze nesulfonic acid	No
13	K06		No
13	L06		No
13	M06	2-[(5-bromo-2,3-dihydroxy-4-oxocyclohexa-2,5-dienylidene)(5-bromo-2,3,4-trihyd roxyphenyl)methyl]benzenesulfonic acid	No

13	N06	5-[(3-carboxy-4-hydroxyphenyl)(3-carboxy-4-oxocyclohexa-2,5-dienylidene)methyl]-2-hydroxybenzoic acid	No
13	O06	(4-{bis[4-(dimethylamino)phenyl]methyl}phenyl)dimethylamine	No
13	P06	5-[(3-carboxy-5-methyl-4-oxocyclohexa-2,5-dienylidene)(2-sulfophenyl)methyl]-2 -hydroxy-3-methylbenzoic acid	No
13	A07	2-{[4-hydroxy-2-methyl-5-(methylethyl)phenyl][2-methyl-5-(methylethyl)-4-oxocy clohexa-2,5-dienylidene]methyl}benzenesulfonic acid	No
13	B07	N-((7S)-10-hydroxy-1,2,3-trimethoxy-9-oxo-5,6,7-trihydrobenzo[d]heptalen-7-yl) acetamide	No
13	C07	7-((2R)-2-amino-2-phenylacetylamino)(7R,7aR)-3-chloro-6-oxo-2H,7H-azetidino[2, 1-b]1,3-thiazine-4-carboxylic acid	No
13	D07	(2E,4E,6E,8E)-3,7-dimethyl-9-(2,6,6-trimethylcyclohex-1-enyl)nona-2,4,6,8-tetr aen-1-ol	No
13	E07		No
13	F07	5,7-dihydroxy-2-(4-hydroxyphenyl)chroman-4-one	No
13	G07	1-methyl-3,4-dihydrobeta-carbolin-7-ol	No
13	H07	1-methylbeta-carbolin-7-ol	No
13	I07		No
13	J07	1,7-bis(3-methylbut-2-enyl)-3,6,8-trihydroxy-2-methoxyxanthen-9-one	No
13	K07	(5S,8S,12S,14S,1R,3R,9R,13R)-1-hydroxy-14-(1-hydroxy-isopropyl)-13-methyl-4,7, 10-trioxapentacyclo[6.4.1.1<9,12>.0<3,5>.0<5,13>]tetradecane-6,11-dione	No
13	L07	(5S,8S,12S,1R,3R,9R,13R,14R)-1-hydroxy-13-methyl-14-(1-methylvinyl)-4,7,10-tri oxapentacyclo[6.4.1.1<9,12>.0<3,5>.0<5,13>]tetradecane-6,11-dione	No
13	M07		No
13	N07	3-{N-[bis(4-methoxyphenyl)methyl]carbamoyl}-2-[(2-fluoren-9-ylacetyloxy)amino] propanoic acid	No
13	O07	5-hydroxy-2-(3-hydroxy-4-methoxyphenyl)-7-{3,4,5-trihydroxy-6-[(3,4,5-trihydro xy-6-methyl(2H-3,4,5,6-tetrahydropyran-2-yloxy))methyl](2H-3,4,5,6-tetrahydrop yran-2-yloxy)}chroman-4-one	No
13	P07		No
13	A08	furano[3,2-g]chromen-2-one	No
13	B08		No
13	C08	(8S,11S,13S,14S,1R,3R,6R,10R,12R)-12,14-bis(methylamino)-3,11,13-trihydroxy-6- methyl-2,7,9-trioxatricyclo[8.4.0.0<3,8>]tetradecan-4-one, chloride	No
13	D08	(10S,1R,4R,6R)-4,12,12-trimethyl-9-methylene-5-oxatricyclo[8.2.0.0<4,6>]dodeca ne	No
13	E08	(1S,5S,4R,6R)-5,6-dihydroxy-4,5,6-trimethyl-2,8-dioxa-13-azatricyclo[8.5.1.0<1 3,16>]hexadec-10-ene-3,7-dione	No
13	F08	5-methoxyfurano[3,2-g]chromen-2-one	No

13	G08	(12aS,6aS,2R)-8,9-dimethoxy-2-(1-methylvinyl)-1,2-dihydrochromano[3,4-b]furano [2,3-h]chroman-6-one	No
13	H08	(2-furylmethyl)purin-6-ylamine	No
13	I08	(2S,5S,9S,10S,1R,8R,15R,17R,18R,19R,20R)-17,18-dihydroxy-19-(hydroxymethyl)-1, 2,8,9,15,19-hexamethylpentacyclo[12.8.0.0<2,11>.0<5,10>.0<15,20>]docos-11-ene- 5-carboxylic acid	No
13	J08	4,10-dioxatricyclo[5.2.1.0<2,6>]decane-3,5-dione	No
13	K08	1,2,3,4-tetrahydroisoquinolylmethylamine	No
13	L08	1H-indazol-6-yl[(4-aminophenyl)sulfonyl]amine	No
13	M08	4,5-dihydroxybenzene-1,3-disulfonic acid, sodium salt, sodium salt, hydrate	No
13	N08	1,3-bis(4-chlorophenyl)-1,2-dihydrobenzo[f]quinazoline	No
13	O08	3-[(3-chlorophenyl)azamethylene]-1-[(4-phenylpiperazinyl)methyl]benzo[d]azolin -2-one	No
13	P08	3-[(1E)-2-(4-nitrophenyl)-1-azavinyl]-4H-1,2,4-triazole	No
13	A09	3-benzo[3,4-b]benzo[d]furan-3-yl-3-hydroquinazolin-4-one	No
13	B09	N-(2-furylmethyl)-N'-(3-morpholin-4-ylpropyl)ethane-1,2-diamide	No
13	C09	8-chloro-1,3-dinitrodibenzo[b,f]oxepin	No
13	D09	amino-N-(1-phenylbenzimidazol-5-yl)amide	No
13	E09	2-(dimethoxymethyl)-2-methyl-1,2,3-trihydroquinazolin-4-one	No
13	F09	1-(methylsulfonyl)-6-(pyrrolidinylsulfonyl)-1,2,3,4-tetrahydroquinoline	No
13	G09	4,4-bis(4-methylphenyl)-2-(2-chlorophenyl)-1H,2H-benzo[d]1,3-oxazine	No
13	H09	4-{[(3-carboxy-5-methyl(2-furyl))methylthio]methyl}-5-methylfuran-2-carboxylic acid	No
13	I09	5-{[(3-carboxy-5-methyl(2-furyl))methylthio]methyl}-2-methylfuran-3-carboxylic acid	No
13	J09	3-(morpholin-4-ylsulfonyl)phenylamine	No
13	K09	4-(4-methyl-1,2,4-triazol-3-yl)phenylamine	No
13	L09	methyl 4-(aminomethyl)-5-ethylfuran-2-carboxylate	No
13	M09	4-(aminomethyl)-5-(hydroxymethyl)-2-methylpyridin-3-ol, chloride	No
13	N09	2-[2-((4S,8R)-8-vinylquinuclidin-2-yl)indol-3-yl]ethan-1-ol	No
13	O09		No
13	P09		No
13	A10	8-(3,4-dichlorophenoxy)-5-methoxy-2,4-dimethylquinoline	No
13	B10	5-methoxy-2-phenoxyphenylamine	No
13	C10	2-(3,4-dichlorophenoxy)-5-methoxyphenylamine	No
13	D10	1-(3,4-dichlorophenoxy)-4-methoxy-2-nitrobenzene	No
13	E10	amino[(6-bromo-3-hydroxy-4-methoxyphenyl)methyl][2-(4-hydroxyphenyl)ethyl]meth yl-1-ol	No
13	F10		No
13	G10	5,6-dimethoxy-11-methylspiro[indane-2,1'-isoindoline]	No

13	H10	2,3-dioxo-1H-benzo[d]azoline-5-sulfonic acid, sodium salt, hydrate	No
13	I10	(7-amino-8-methylphenothiazin-3-ylidene)dimethylamine, chloride	No
13	J10	7-(diethylylidene)-3,4-dihydroxyphenoxazinecarboxamide, chloride	No
13	K10	1-((1E)-2-nitrovinyl)-2-(trifluoromethyl)benzene	No
13	L10	[(4,5-dimethoxy-2-nitrophenyl)methyl]thiocarboxamidine, bromide	No
13	M10	2-(2,3-dimethoxyphenyl)-6-methoxychromen-4-one	No
13	N10	4-formylbenzene-1,3-disulfonic acid	No
13	O10	(7R,7aR)-3-(acetyloxymethyl)-6-oxo-7-(2-(4-pyridylthio)acetylamino)-2H,7H-azet idino[2,1-b]1,3-thiazine-4-carboxylic acid, sodium salt	No
13	P10	(1R)((5S)-5-ethylquinuclidin-2-yl)(6-ethoxy(4-quinolyl))methan-1-ol	No
13	A11	4-[3-(2-pyridyl)-5-(5-sulfo(2-furyl))-1,2,4-triazin-6-yl]furan-2-sulfonic acid	No
13	B11	1-(1-methylindol-3-yl)-2-pyrrolidinylethane-1,2-dione	No
13	C11	2-(phenoxymethyl)-4-[(5-{[2-(phenoxymethyl)morpholin-4-yl]sulfonyl}naphthyl)su lfonyl]morpholine	No
13	D11	4,6-dimethyl-2-[(3-methylquinoxalin-2-yl)methylthio]pyrimidine	No
13	E11	3-[4-(tert-butyl)phenyl]-4-phenyl-1-[(3-phenylpyrrolidinyl)methyl]-1,2,4-triaz oline-5-thione	No
13	F11	3-(4-methylphenyl)-4-phenyl-1-[(3-phenylpyrrolidinyl)methyl]-1,2,4-triazoline- 5-thione	No
13	G11	1-{[2,3,4-trimethoxy-5-(1,2,3,4-tetrahydroquinolylsulfonyl)phenyl]sulfonyl}-1, 2,3,4-tetrahydroquinoline	YES
13	H11	2-amino-4,5-dimethoxyphenyl 6,7-dimethoxyisoquinolyl ketone	No
13	I11	2,6-bis(1-phenyl(1,2,3,4-tetraazol-5-yl)thio)-9-thiabicyclo[3.3.1]nonane	No
13	J11	4-phenyl-3-benzyl-1-[(3-phenylpyrrolidinyl)methyl]-1,2,4-triazoline-5-thione	No
13	K11	2,2-dimethyl-N-(1,2,3,4-tetrahydrobenzo[3,4-d]benzo[2,1-b]furan-8-yl)-N'-(1,2, 3,4-tetrahydrobenzo[3,4-d]benzo[2,1-b]furan-8-yl)propane-1,3-diamide	No
13	L11	1-acetyl-6-{[(tert-butyl)amino]sulfonyl}-1,2,3,4-tetrahydroquinoline	No
13	M11	2-[(5-(2H,3H-benzo[e]1,4-dioxin-2-yl)-4-phenyl(1,2,4-triazol-3-ylthio))methyl] -3-(4-chlorophenyl)-3-hydroquinazolin-4-one	No
13	N11	9-chloro-5,6,7,8-tetrahydroacridine	No
13	O11	4-chloro-2-methylquinoline	No
13	P11	[2-(hydroxymethyl)-4-oxa-1-azaspiro[4.5]dec-2-yl]methan-1-ol	No
13	A12	2-(phenylmethylthio)benzimidazole	No
13	B12	adamantanyl-N-(1,3-thiazol-2-yl)carboxamide	No
13	C12	4-(4-nitrophenyl)morpholine	No
13	D12	1-(2-naphthylsulfonyl)pyrrolidine-2-carbohydrazide	No
13	E12	ethyl 2-(acetylamino)-5-{[5-(acetylamino)-4-(ethoxycarbonyl)-3-methyl(2-thieny l)]disulfanyl}-4-methylthiophene-3-carboxylate	No
13	F12	1-benzyl-4-pyridylamine, bromide	No

13	G12	2-amino-6-methyl-4,5,6,7-tetrahydrothiopheno[2,3-c]pyridine-3-carbonitrile	OFFSCALE
13	H12	ethyl 2-amino-6-methyl-4,5,6,7-tetrahydrothiopheno[2,3-c]pyridine-3-carboxylat e	No
13	I12	spiro[1,4,5,6,7,8-hexahydroquinazoline-4,1'-cyclohexane]-2-thiol	No
13	J12	spiro[1,4,5,6,7-pentahydrocyclopenta[1,2-d]pyrimidine-4,1'-cyclopentane]-2-thi ol	No
13	K12	8-(benzimidazol-2-ylmethoxy)quinoline	No
13	L12		No
13	M12	3-(hydroxymethyl)-5,5-dimethyl-1,3-diazolidine-2,4-dione	No
13	N12	3-(di???methyl)thiolane-1,1-dione	No
13	O12	ethyl 6-bromo-2-oxochromene-3-carboxylate	No
13	P12	ethyl 2-(2-chloroacetylamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylat e	No
13	A13	1-(3-ethyl-3-hydrobenzothiazol-2-ylidene)acetone	No
13	B13	((1Z)-1-morpholin-4-yl-2-phenyl-2-azavinyl)phenylamine	No
13	C13	[4-(hydroxymethyl)-2-(phenoxymethyl)-1,3-oxazolin-4-yl]methan-1-ol	No
13	D13	[4-methyl-2-(phenoxymethyl)-1,3-oxazolin-4-yl]methan-1-ol	No
13	E13	6-oxo-5,7,8,9,10,6a-hexahydrobenzimidazolo[1,2-b]isoquinoline-11-carbonitrile	No
13	F13	1-(4,5-dimethyl(1,2,4-triazol-3-ylthio))-2-chloro-4-nitrobenzene	No
13	G13	6-iodo-3-hydroquinazolin-4-one	No
13	H13	1-[3-(trifluoromethyl)phenyl]-1,2,3,4-tetraazole	No
13	I13	1-[(2-chlorophenyl)methyl]-2-methylthiobenzimidazole	No
13	J13	1-acetylpyrrolidine-2-carboxylic acid	No
13	K13	3-methyl-1,3-dihydroquinazoline-2,4-dione	No
13	L13	4-(2-chloro-4-nitrophenyl)morpholine	No
13	M13	5-[(dimethylamino)methylene]-6-imino-1,3-dimethyl-1,3-dihydropyrimidine-2,4-di one	No
13	N13	1,4-dimethyl-1,4-dihydroquinoxaline-2,3-dione	No
13	O13	4,5-bisbenzyl-1,2,4-triazole-3-thiol	No
13	P13	3,6-dibromo-1-nitrocarbazole	No
13	A14	3-nitroquinoline-2,4-diol	No
13	B14	2-(2-methylpyridyl)-1-phenylethan-1-one, chloride	No
13	C14	4-amino-3-chlorothiolane-1,1-dione	No
13	D14	4-hydroxy-3-{[(2-phenylethyl)amino]methyl}chromen-2-one	No
13	E14	4-chloro-5-phenyl-3-(trifluoromethyl)pyrazole	No
13	F14	1-(4-nitrophenyl)-5-(trifluoromethyl)pyrazole-4-carboxylic acid	No
13	G14	4-chloro-5-methyl-3-(trifluoromethyl)pyrazole	YES
13	H14	4-[3-(trifluoromethyl)pyrazolyl]phenylamine	No
13	I14	2-amino-3-pyrrolo[2,3-b]pyridin-3-ylpropanoic acid	No
13	J14	4-[(3-carboxy-4-oxonaphthylidene)phenylmethyl]-1-hydroxynaphthalene-2-carboxyl ic acid	No

13	K14	(2S)-6-hydroxy-2,5,7,8-tetramethylchromane-2-carboxylic acid	No
13	L14	7-methyl-1H-indazole-5-ylamine	No
13	M14	methyl 1-methyl-4-oxopiperidine-3-carboxylate	No
13	N14	4-[(2R)-2-((1S,3S,5S)-3,5-dimethyl-2-oxocyclohexyl)-2-hydroxyethyl]azaperhydro ine-2,6-dione	No
13	O14	1,3,7-trimethyl-1,3,7-trihydropurine-2,6-dione	No
13	P14	26-[(1E)-2-(4-methylpiperazinyl)-2-azavinyl](7S,11S,13S,17S,18S,12R,14R,15R,16 R)-2,15,17,27,29-pentahydroxy-11-methoxy-3,7,12,14,16,18,22-heptamethyl-6,23-dioxo-8,30-dioxa-24-azatetracyclo[23.3.1.1<4,7>.0<5,28>]triaconta-1(28),2,4,9,1 9,21,25(29),26-octaen-13-yl acetate	No
13	A15		No
13	B15	6-(2-chloroacetyl)-3-hydrobenzoxazol-2-one	No
13	C15	3-(2-bromoacetyl)chromen-2-one	No
13	D15		No
13	E15	6-methyl-2,3,4-trihydrobeta-carbolin-1-one	No
13	F15	3-amino-1-(3-methylpiperidyl)propan-2-ol	No
13	G15	2-(2,3-dioxobenzo[d]azolidinyl)acetic acid	No
13	H15	3-[(ethylpropyl)amino]benzo[d]1,2-thiazoline-1,1-dione	No
13	I15	3-[(3-morpholin-4-ylpropyl)amino]benzo[d]1,2-thiazoline-1,1-dione	No
13	J15	(6R)-6-((5S)-6-methyl(5,6,7,8-tetrahydro-2H-1,3-dioxolano[4,5-g]isoquinolin-5- yl))-6-hydro-2H-1,3-dioxoleno[4,5-e]isobenzofuran-8-one	No
13	K15	3-nitro-4-pyrrolidinylbenzaldehyde	No
13	L15	3-nitro-4-phenylthiobenzaldehyde	No
13	M15	5-prop-2-ynylthio-1,3,4-thiadiazole-2-ylamine	No
13	N15	2-(2-indol-3-ylacetylamino)butanedioic acid	No
13	O15	4-(6-hydroxy-3-oxoxanthen-9-yl)benzene-1,3-dicarboxylic acid	No
13	P15		No
13	A16	2-(aminocarbonylamino)-3-indol-3-ylpropanoic acid	No
13	B16	oxolane-2,3,4,5-tetracarboxylic acid	No
13	C16		No
13	D16	5,7-dihydroxy-3-(4-methoxyphenyl)chromen-4-one	No
13	E16	2-(4,6-dimethylpyrimidin-2-ylthio)acetic acid, hydrate	No
13	F16	(2S,1R)-2-(2-thienylcarbonyl)cyclohexanecarboxylic acid	No
13	G16	[3,5-bis(trifluoromethyl)phenyl]methylamine	No
13	H16	(1S,14R)-20,21,25-trimethoxy-15,30-dimethyl-7,23-dioxa-15,30-diazaheptacyclo[2 2.6.2.2<3,6>.1<8,12>.1<14,18>.0<22,36>.0<27,31>]hexatriaconta-3,5,8(35),9,11,1 8(36),19,21,24(32),25,27(31),33-dodecaen-9-ol, chloride, chloride	No
13	I16	(1S,14S)-9,20,21,25-tetramethoxy-15,30-dimethyl-7,23-dioxa-15,30-diazaheptacyc	No

		lo[22.6.2.2<3,6>.1<8,12>.1<14,18>.0<22,36>.0<27,31>]hexatriaconta-3(33),4,6(34),8(35),9,11,18(36),19,21,24,26,31-dodecaene	
13	J16		No
13	K16	amino[(4-aminophenyl)sulfonyl]carboxamidine	No
13	L16	2-(4-chlorophenyl)-1-(2,4,6-trihydroxyphenyl)ethan-1-one	No
13	M16	2-amino-7-methyl-4-hydro-1,3,4-thiadiazolino[3,2-a]pyrimidin-5-one	No
13	N16	5-bromo-7-methyl-1H-indazole	No
13	O16	3,5-dimethyladamantanylamine	No
13	P16	(5S,1R)-8-methyl-8-azabicyclo[3.2.1]octan-3-ol	No
13	A17		No
13	B17	3,3-bis(4-hydroxyphenyl)benzo[c]1,2-oxathiolene-1,1-dione	No
13	C17	ethyl (2E)-2-[(3-methylphenyl)carbonylamino]-3-(4-nitrocyclopenta-1,3-dienyl)p rop-2-enoate	No
13	D17	2-bromo-3-methoxypyridine	No
13	E17	[4-chloro-3-(trifluoromethyl)phenyl](methylsulfonyl)amine	No
13	F17	3-(4-chlorophenyl)-5-methyl-7-(trifluoromethyl)-8-hydropyrazolo[1,5-a]pyrimidi ne	No
13	G17		YES
13	H17	1-(4-fluorophenyl)-5-{[1-(4-fluorophenyl)-2,4,6-trioxo(1,3,5-trihydropyrimidin -5-yl)]-4-pyridylmethyl}-1,3,5-trihydropyrimidine-2,4,6-trione	No
13	I17	[2-(4-chlorophenylthio)ethyl](methylsulfonyl)amine	No
13	J17	benzotriazolylphenylmethan-1-ol	No
13	K17	5-bromo-3-[(1H-1,2,3,4-tetraazol-5-ylamino)azamethylene]-1H-benzo[d]azolidin-2 -one	No
13	L17	benzo[d]furan-2-yl-N-{[(1-propyl(1,2,3,4-tetraazol-5-yl))amino]thioxomethyl}ca rboxamide	No
13	M17	(9S,1R)-6-oxo-7,11-diazatricyclo[7.3.1.0<2,7>]trideca-2,4-diene-11-carbaldehyd e	No
13	N17	(9S,1R)-11-acetyl-6-oxo-7,11-diazatricyclo[7.3.1.0<2,7>]trideca-2,4-diene	No
13	O17		No
13	P17	(1R,7R,17R)-4-ethylidene-7-hydroxy-7-methyl-6-methylene-2,9-dioxa-14-azatricyc lo[9.5.1.0<14,17>]heptadec-11-ene-3,8-dione	No
13	A18	[(4-aminophenyl)sulfonyl]methylamine	No
13	B18	(2S)-1-((2S)-3-acetylthio-2-methylpropanoyl)pyrrolidine-2-carboxylic acid	No
13	C18	5-phenyl-4-prop-2-enyl-1,2,4-triazole-3-thiol	No
13	D18	[(4-methyl-5-methylthio-1,2,4-triazol-3-yl)methoxy]benzene	No
13	E18	5-(2-bromophenyl)-4-methyl-1,2,4-triazole-3-thiol	No
13	F18	3-(4-prop-2-enyl-5-sulfanyl-1,2,4-triazol-3-yl)naphthalen-2-ol	No
13	G18	2-(4-methyl-5-sulfanyl-1,2,4-triazol-3-yl)phenol	No

13	H18	1-{[4-(diphenylmethyl)piperazinyl]methyl}-4-methyl-3-phenyl-1,2,4-triazoline-5 -thione	No
13	I18	3-{2-[(2,4-dinitrophenyl)amino]ethyl}-1,3-oxazolidin-2-one	No
13	J18	7-chloro-4-methoxyquinoline	No
13	K18	6-nitro-1,4-dihydroquinoxaline-2,3-dione	No
13	L18	[2,6-dinitro-4-(trifluoromethyl)phenyl]imidazole	No
13	M18	5-(methylsulfonyl)-1-phenyl-1,2,3,4-tetraazole	No
13	N18	4-methyl-5-phenyl-1,2,4-triazole-3-thiol	No
13	O18	5-(3-chloro-4-methylphenyl)-4-methyl-1,2,4-triazole-3-thiol	No
13	P18	5-(4-methoxyphenyl)-4-methyl-1,2,4-triazole-3-thiol	No
13	A19	4-methyl-5-benzyl-1,2,4-triazole-3-thiol	No
13	B19	4-(2-morpholin-4-ylethyl)morpholine	No
13	C19	3-methyl-3,5,6,7,8-pentahydrobenzo[b]thiopheno[2,3-d]pyrimidin-4-one	No
13	D19	5-(2-chloro-4-methylphenyl)-4-prop-2-enyl-1,2,4-triazole-3-thiol	No
13	E19	2,6,7-trihydroxy-9-methylxanthen-3-one	No
13	F19	1-(4-chlorophenyl)-2-(6-methoxyquinolyl)ethan-1-one, bromide	No
13	G19	2-(2-chloro-4-nitroimidazolyl)acetamide	No
13	H19	2-chloro-1-[(2-chloro-4-nitroimidazolyl)methyl]-4-nitroimidazole	No
13	I19	2-chloro-4-nitro-1-[(4-nitrophenyl)methyl]imidazole	No
13	J19	1-(2-chloro-4-nitroimidazolyl)-3-phenoxypropan-2-ol	No
13	K19	5-{[2,5-dimethyl-1-(4-morpholin-4-ylphenyl)pyrrol-3-yl]methylene}-1,3-thiazoli dine-2,4-dione	No
13	L19	5-{[(2-bromophenyl)amino]methylene}-1,3-dihydropyrimidine-2,4,6-trione	No
13	M19	4-(5-methyl-1,2,4-oxadiazol-3-yl)-1,2,5-oxadiazole-3-ylamine	No
13	N19	5-nitro-3-hydrobenzimidazole-2-thione	No
13	O19	(2S)-2-[(tert-butoxy)carbonylamino]-3-imidazol-4-ylpropanoic acid	No
13	P19	(1R)(6-methoxy(4-quinolyl))[1-benzyl-5-vinylquinuclidin-2-yl]methan-1-ol, chlo ride	No
13	A20	5-phenyl-2-(4-pyridyl)-1,3-oxazole	No
13	B20	3,5-diamino-6-chloropyrazine-2-carboxamide	No
13	C20	4-amino-2,3,5,6-tetrafluorobenzamide	No
13	D20	8-methyl-8-azabicyclo[3.2.1]octan-3-one	No
13	E20	2-[(2H,3H-benzo[3,4-e]1,4-dioxin-6-ylsulfonyl)(4-fluorophenyl)amino]-1-pyrroli dinylethan-1-one	No
13	F20	N-(2H,3H-benzo[3,4-e]1,4-dioxin-6-yl)(phenylamino)carboxamide	No
13	G20	N-(2-naphthyl)-2-(1,1,3-trioxo(2-hydrobenzo[d]isothiazol-2-yl))acetamide	No
13	H20	N-(4-iodophenyl)-2-(1,1,3-trioxo(2-hydrobenzo[d]isothiazol-2-yl))acetamide	No
13	I20		No

13	J20	N-(2,4-difluorophenyl)-2-(1,1,3-trioxo(2-hydrobenzo[d]isothiazol-2-yl))acetami de	No
13	K20		No
13	L20	ethyl 2-hydrazino-4-methyl-1,3-thiazole-5-carboxylate	No
13	M20	adamantanyl 4-(2-pyridyl)piperazinyl ketone	No
13	N20	ethyl 2-(5-hydroxy-3-methylpyrazolyl)-4-methyl-1,3-thiazole-5-carboxylate	No
13	O20	ethyl 2-[4-(2-furylmethylene)-3-methyl-5-oxo(1,2-diazolinyl)]-4-methyl-1,3-thi azole-5-carboxylate	No
13	P20	ethyl 4-methyl-2-{3-methyl-4-[(5-methyl(2-furyl))methylene]-5-oxo(1,2-diazolin yl)}-1,3-thiazole-5-carboxylate	No
13	A21	ethyl 4-methyl-2-{3-methyl-4-[(5-methyl(2-thienyl))methylene]-5-oxo(1,2-diazol inyl)}-1,3-thiazole-5-carboxylate	No
13	B21	ethyl 2-{4-[(5-ethyl(2-thienyl))methylene]-3-methyl-5-oxo(1,2-diazolinyl)}-4-m ethyl-1,3-thiazole-5-carboxylate	No
13	C21	ethyl 4-methyl-2-[3-methyl-5-oxo-4-(2-thienylmethylene)(1,2-diazolinyl)]-1,3-t hiazole-5-carboxylate	No
13	D21	ethyl 2-{4-[(1-(2H-benzo[3,4-d]1,3-dioxolan-5-yl)-2,5-dimethylpyrrol-3-yl)meth ylene]-3-methyl-5-oxo(1,2-diazolinyl)}-4-methyl-1,3-thiazole-5-carboxylate	No
13	E21	2-(5-bromo-2,3-dioxobenzo[d]azolidinyl)acetic acid	No
13	F21	1-(chloromethyl)-4-nitropyrazole	No
13	G21	2-(2-chloro-4-nitroimidazolyl)acetic acid	No
13	H21	1-[(5-bromo-2-thienyl)sulfonyl]pyrrolidine-2-carboxylic acid	No
13	I21	2-(5-bromo-2,3-dioxobenzo[d]azolidinyl)propanoic acid	No
13	J21	2H,4H-benzo[e]1,3-dioxin-6-ylamine	No
13	K21	1-(chloromethyl)-3-nitropyrazole	No
13	L21	5-bromo-7-methyl-1H-benzo[d]azolidine-2,3-dione	No
13	M21	methyl 6-methoxybenzothiazole-2-carboxylate	No
13	N21	2-(2,3-dioxobenzo[d]azolidinyl)propanoic acid	No
13	O21	N-(2,6-dimethoxypyrimidin-4-yl)-3-(1,2,3,4-tetraazolyl)propanamide	No
13	P21	N-[3,5-bis(trifluoromethyl)phenyl]-3-(1,2,3,4-tetraazolyl)propanamide	No
13	A22	N-benzotriazolyl-3-(1,2,3,4-tetraazolyl)propanamide	No
13	B22	N-(5-adamantan-2-yl(1,3-thiazol-2-yl))-3-(1,2,3,4-tetraazolyl)propanamide	No
13	C22	3-(1,2,3,4-tetraazolyl)-N-[5-(trifluoromethoxy)benzothiazol-2-yl]propanamide	No
13	D22	N-(3-cyano(4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl))-3-(1,2,3,4-tetraazolyl)pr opanamide	No
13	E22	N-(3-cyano(4,5,6-trihydrocyclopenta[2,1-d]thiophen-2-yl))-3-(1,2,3,4-tetraazol yl)propanamide	No
13	F22	methylethyl 3-[N-(2,6-dimethoxypyrimidin-4-yl)carbamoyl]propanoate	No
13	G22	N-(4-methyl(1,3-thiazol-2-yl))(1-methylpyrazol-5-yl)carboxamide	No
13	H22	N-(2,4-dichlorophenyl)tricyclo[4.3.0.0<3,9>]non-7-ylcarboxamide	No

13	I22	methylethyl 6-[N-(3-cyano-4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl)carbamoyl]cy clohex-3-enecarboxylate	No
13	J22	N-cycloheptyl[6-(3,4,4-trichlorobut-3-enoyl)cyclohex-3-enyl]carboxamide	No
13	K22	3-(4-{[4-(2,3-dihydroxypropoxy)phenyl]methyl}phenoxy)propane-1,2-diol	No
13	L22		No
13	M22	4-(3,5-di(1,2,3-thiadiazol-4-yl)phenyl)-1,2,3-thiadiazole	No
13	N22	4-hydroxy-3-iodo-5-methoxybenzaldehyde	No
13	O22	5-methylbenzene-1,3-diol	No
13	P22	5-((2S)-1,2,3-trihydroxypropyl)(3S,4R,5R)-3,4-dihydroxy-3,4,5-trihydrofuran-2- one	No

Plate	**Well**	**IUPAC NAME**	**Inhibitor Y/N**
14	A03	3-(3,5-dimethoxyphenyl)-1H-1,2,4-triazole-5-ylamine	No
14	B03	6-bromo-4-oxochromene-2-carboxylic acid	No
14	C03	7-methoxy-2-oxochromene-3-carbonitrile	No
14	D03	6-methyl-2-(3-methylphenyl)chromen-4-one	No
14	E03	4-hydroxy-6-methoxychromen-2-one	No
14	F03	3-acetyl-2-oxo-3-hydrobenzoxazole	No
14	G03	3-acetyl-2-oxo-3-hydrobenzothiazole	No
14	H03	6-[(2-oxo-3-hydrobenzoxazol-6-yl)carbonyl]-3-hydrobenzoxazol-2-one	No
14	I03	methyl 4-hydroxy-1,1-dioxo-2H-benzo[e]1,2-thiazine-3-carboxylate	No
14	J03	methyl 4-hydroxy-2-methyl-1,1-dioxobenzo[e]1,2-thiazine-3-carboxylate	No
14	K03	methyl 4-methyl-6-(2-thienyl)-2-thioxo-1,3,6-trihydropyrimidine-5-carboxylate	No
14	L03	ethyl 4-methyl-6-(5-methyl(2-thienyl))-2-oxo-1,3,6-trihydropyrimidine-5-carbox ylate	YES
14	M03	ethyl 6-(2,5-dimethyl(3-thienyl))-4-methyl-2-oxo-1,3,6-trihydropyrimidine-5-ca rboxylate	No
14	N03	ethyl 6-(2,5-dimethyl(3-thienyl))-4-methyl-2-thioxo-1,3,6-trihydropyrimidine-5 -carboxylate	No
14	O03	6-amino-4-{4-[(4-chlorophenylthio)methyl](2-thienyl)}-3-methyl-4H-pyrano[2,3-c]pyrazole-5-carbonitrile	No
14	P03	5-{[4-(diphenylmethyl)piperazinyl]methyl}-3-phenyl-1,2,4-oxadiazole	No
14	A04	2-(6-aminopurin-8-ylthio)butanoic acid	No
14	B04	2-{2-[(4-iodophenyl)azamethylene]-3-methyl-4-oxo(1,3-thiazolidin-5-yl)}-N-phen ylacetamide	No
14	C04	2-{2-[(4-iodophenyl)azamethylene]-3-methyl-4-oxo(1,3-thiazolidin-5-yl)}-N-(2-n itrophenyl)acetamide	No
14	D04	3-(N-(1,3-thiazol-2-yl)carbamoyl)propanoic acid	No

14	E04	6-amino-2-{[3-(2,6-dimethoxyphenyl)(1,2,4-oxadiazol-5-yl)]methylthio}pyrimidin -4-ol	No
14	F04	2-[5-(benzoxazol-2-ylthiomethyl)(1,2,4-oxadiazol-3-yl)]-1,3-dimethoxybenzene	No
14	G04	1,3-dimethoxy-2-{5-[(5-methoxybenzimidazol-2-ylthio)methyl](1,2,4-oxadiazol-3- yl)}benzene	No
14	H04	1,3-dimethoxy-2-{5-[(4-methyl(1,2,4-triazol-3-ylthio))methyl](1,2,4-oxadiazol- 3-yl)}benzene	No
14	I04	(1-cyclohexyl-5-oxopyrrolidin-3-yl)-N-(4-iodophenyl)carboxamide	YES
14	J04	3-(4-chlorophenylthio)-1-pyrrolidinylpropan-1-one	No
14	K04	N-(4-bromophenyl)[1-(4-fluorophenyl)-5-oxopyrrolidin-3-yl]carboxamide	YES
14	L04	N-(4-fluorophenyl)[1-(4-fluorophenyl)-5-oxopyrrolidin-3-yl]carboxamide	No
14	M04	5-bromo-1-methylindolin-2-one	No
14	N04	3-(3,4-dichlorophenyl)pyrazole-4-carbaldehyde	No
14	O04	2-(5-bromo-2-oxoindolinyl)propanoic acid	No
14	P04	2-(5-(2-furyl)(1,3,4-oxadiazol-2-ylthio))-1-(2,4,6-trimethylphenyl)ethan-1-one	No
14	A05	6-(indolinylsulfonyl)-2-methylthiobenzothiazole	No
14	B05	4-quinoxalin-2-ylphenol	No
14	C05	(diphenylmethyl){[1-(methylsulfonyl)indolin-5-yl]sulfonyl}amine	No
14	D05	2H,3H-benzo[3,4-e]1,4-dioxan-6-yl[(7-nitrobenzo[3,4-d]benzo[b]furan-2-yl)sulfo nyl]amine	No
14	E05	2H,3H-benzo[3,4-e]1,4-dioxin-6-yl[(4-methoxyphenyl)sulfonyl]amine	No
14	F05	N-(2H,3H-benzo[3,4-e]1,4-dioxin-6-yl)(3-chlorobenzo[b]thiophen-2-yl)carboxamid e	No
14	G05	[4-(4-pyridylmethyl)phenyl](pyrrolidinylsulfonyl)amine	No
14	H05	5-[(2-thienylsulfonyl)amino]-3-hydroisobenzofuran-1-one	No
14	I05	methyl{2-[methyl(phenylsulfonyl)amino]phenyl}(phenylsulfonyl)amine	No
14	J05	3-{2-[4-(tert-butyl)phenyl]-2-oxoethyl}-3-hydroxy-5-methylindolin-2-one	No
14	K05	6-[(butylsulfonyl)amino]-3-methyl-3-hydroquinazolin-4-one	No
14	L05	5-{[(2-methylthiobenzothiazol-6-yl)sulfonyl]amino}-3-hydroisobenzofuran-1-one	YES
14	M05	3-(2-(2H-benzo[3,4-d]1,3-dioxolan-5-yl)-2-oxoethyl)-3-hydroxy-5-methylindolin- 2-one	No
14	N05	adamantanyl-N-(1-oxo(3-hydroisobenzofuran-5-yl))carboxamide	No
14	O05	2,3-dimethyl-1-phenyl-4-[(pyrrolidinylsulfonyl)amino]-3-pyrazolin-5-one	No
14	P05	4-pyridino[4,3-e]pyrazin-3-ylphenol	No
14	A06	6,7-dimethoxyisochroman-3-one	No

14	B06	1-(methylsulfonyl)-5-({[2-({[1-(methylsulfonyl)indolin-5-yl]sulfonyl}amino)eth yl]amino}sulfonyl)indoline	No
14	C06	6-(pyrrolidinylsulfonyl)-3-hydrobenzothiazol-2-one	No
14	D06	1-{2-[4-(2H-benzo[3,4-d]1,3-dioxolen-5-ylmethyl)piperazinyl](1,3-thiazol-4-yl) }-4-methoxybenzene	No
14	E06	2-[4-(2H-benzo[3,4-d]1,3-dioxolen-5-ylmethyl)piperazinyl]-4-phenyl-1,3-thiazol e	No
14	F06	3-(2-phenoxyethyl)spiro[1,2,3-trihydroquinazoline-2,3'-indoline]-4,12-dione	No
14	G06	1-[(3,4-dichlorophenyl)sulfonyl]pyrrolidin-2-yl piperidyl ketone	No
14	H06	1-adamantanyl-2-benzothiazol-2-ylthioethan-1-one	No
14	I06	3-(4-fluorophenyl)-2-sulfanyl-3-hydroquinazolin-4-one	No
14	J06	(4-amino-5-sulfanyl(1,2,4-triazol-3-yl))phenylmethan-1-ol	No
14	K06	5-[(cyclohexylamino)sulfonyl]-1,3-diethyl-3-hydrobenzimidazol-2-one	No
14	L06	2-[4-(2H-benzo[3,4-d]1,3-dioxolen-5-ylmethyl)piperazinyl]-4-(4-methylphenyl)-1 ,3-thiazole	No
14	M06	(2H,3H-benzo[3,4-e]1,4-dioxin-6-ylsulfonyl)cyclohexylamine	No
14	N06	3-hydroxy-3-[2-(4-methylthiophenyl)-2-oxoethyl]indolin-2-one	No
14	O06	4-(2H-benzo[3,4-d]1,3-dioxolen-5-ylmethyl)-1-{[1-(methylsulfonyl)indolin-5-yl] sulfonyl}piperazine	No
14	P06	1,3-diethyl-5-(indolinylsulfonyl)-3-hydrobenzimidazol-2-one	No
14	A07	[(2,5-dimethoxyphenyl)sulfonyl](2-methoxybenzo[3,4-b]benzo[d]furan-3-yl)amine	No
14	B07	1-(methylsulfonyl)-5-[(4-phenylpiperidyl)sulfonyl]indoline	No
14	C07	[(4-cyclohexylphenyl)sulfonyl][1-(methylsulfonyl)indolin-5-yl]amine	No
14	D07	4-ethyl-1-(morpholin-4-ylmethyl)-3-phenyl-1,2,4-triazoline-5-thione	No
14	E07	2-adamantanyl-N-(1,3,5-trimethylpyrazol-4-yl)acetamide	No
14	F07	4-(4-fluorophenyl)-2-[4-(4-phenyl(1,3-thiazol-2-yl))piperazinyl]-1,3-thiazole	No
14	G07	[(3,4-dimethoxyphenyl)sulfonyl](6-methoxy(3-pyridyl))amine	No
14	H07	5-(chloromethyl)-2-(4-methylphenyl)-1,3,4-oxadiazole	No
14	I07	adamantanyl-N-{3-[(N-naphthylcarbamoyl)amino]phenyl}carboxamide	No
14	J07	4-[(4-phenyl(1,3-thiazol-2-ylthio))methyl]-6-(1,2,3,4-tetrahydroquinolyl)-1,3, 5-triazine-2-ylamine	No
14	K07	4-[(4-methyl-5-phenyl(1,2,4-triazol-3-ylthio))methyl]-6-(1,2,3,4-tetrahydroqui nolyl)-1,3,5-triazine-2-ylamine	No
14	L07	4-fluoro-1-[(4-pyrimidin-2-ylpiperazinyl)sulfonyl]benzene	No
14	M07	(4-adamantanylphenyl)dimethylamine	No
14	N07	2-adamantanyl-N-(3-{[(dimethylamino)sulfonyl]amino}phenyl)acetamide	No
14	O07	2-chloro-5-{[4-(4-nitrophenyl)piperazinyl]sulfonyl}thiophene	No

14	P07	2-chloro-5-(piperidylsulfonyl)thiophene	No
14	A08	N-adamantanyl(4-phenylpiperazinyl)carboxamide	No
14	B08	methyl 5-(methoxycarbonyl)-2,6-dimethyl-4-(2-thienyl)pyridine-3-carboxylate	No
14	C08	5-(2-thienyl)-1,3,4-oxadiazole-2-thiol	No
14	D08	N-adamantanyl({3-[(2-furylmethyl)amino]-4-nitrophenyl}amino)carboxamide	No
14	E08	4-piperidyl-1-(2-thienylcarbonyl)piperidine-4-carboxamide	No
14	F08	4-amino-5-(2-thienyl)-1,2,4-triazole-3-thiol	No
14	G08	4-{[4-cyclohexyl-5-benzyl(1,2,4-triazol-3-ylthio)]ethyl}-6-(1,2,3,4-tetrahydro quinolyl)-1,3,5-triazine-2-ylamine	No
14	H08	(4-amino-6-{[5-(4-fluorophenyl)-4-methyl(1,2,4-triazol-3-ylthio)]methyl}(1,3,5 -triazin-2-yl))methylphenylamine	No
14	I08	6-(2-pyridylthioethyl)-4-(1,2,3,4-tetrahydroquinolyl)-1,3,5-triazine-2-ylamine	No
14	J08	(dibenzo[b,d]furan-2-ylsulfonyl)(6-methoxy(3-pyridyl))amine	No
14	K08	(fluoren-2-ylsulfonyl)(6-methoxy(3-pyridyl))amine	No
14	L08	2,2,5,5-tetramethyl-4-(7-quinolylmethylene)-2,5-dihydrofuran-3-one	No
14	M08	3-(2-chlorophenyl)-6-methyl-5H,6H-1,3-thiazolidino[2,3-c]1,2,4-triazole	No
14	N08	3-(3-chlorophenyl)-6-methyl-5H,6H-1,3-thiazolidino[2,3-c]1,2,4-triazole	No
14	O08		No
14	P08		No
14	A09	3-adamantanyl-6-methyl-5H,6H-1,3-thiazolidino[2,3-c]1,2,4-triazole	No
14	B09	3-(6-methyl-5H,6H-1,3-thiazolidino[3,2-d]1,2,4-triazol-3-yl)phenylamine	No
14	C09		No
14	D09	4-[(1-methyl-1,2,3,4-tetraazol-5-ylthio)methyl]hydroquinolin-2-one	No
14	E09	(3-(10H,11H-dibenzo[b,f]azepin-5-yl)propyl)[4-(4-fluorophenyl)(1,3-thiazol-2-y l)]methylamine	No
14	F09	2-(3-chlorophenyl)pyrazolidino[1,2-a]1,2,4-triazolidine-1,3-dione	No
14	G09	1-{4-[(1,2,3,4-tetrahydrobenzo[3,4-d]benzo[2,1-b]furan-8-ylamino)sulfonyl]phen yl}pyrrolidin-2-one	No
14	H09	4-[4-(pyrrolidinylsulfonyl)phenyl]pyrrolidin-2-one	No
14	I09	3-(methyl{[4-(2-oxopyrrolidinyl)phenyl]sulfonyl}amino)thiolane-1,1-dione	No
14	J09	cyclohexyl[(2-ethoxy-5-(1,2,3,4-tetraazolyl)phenyl)sulfonyl]amine	No
14	K09	2-({[4-(2-oxopyrrolidinyl)phenyl]sulfonyl}amino)pentanedioic acid	No
14	L09	{[1-(methylsulfonyl)indolin-5-yl]sulfonyl}-1,2,3,4-tetrahydrobenzo[3,4-d]benzo [2,1-b]furan-8-ylamine	No
14	M09	[3,5-bis(trifluoromethyl)phenyl][(5-chloro(2-thienyl))sulfonyl]amine	No
14	N09	7-{[(4-fluorophenyl)sulfonyl]amino}-1,3,4-trihydroquinolin-2-one	No

14	O09	7-{[(4-methylthiophenyl)sulfonyl]amino}-1,3,4-trihydroquinolin-2-one	No
14	P09	cyclopropyl-N-(2-oxo(7-1,3,4-trihydroquinolyl))carboxamide	No
14	A10	(1,3-dimethyl-2,6-dioxo(1,3-dihydropyrimidin-4-yl))-N-(2-oxo(7-1,3,4-trihydroq uinolyl))carboxamide	No
14	B10	2H-benzo[3,4-d]1,3-dioxolen-5-yl{[1-(methylsulfonyl)indolin-5-yl]sulfonyl}amin e	No
14	C10	5-chlorothiopheno[3,2-b]pyridine-3-carbaldehyde	No
14	D10	[(1-acetylindolin-5-yl)amino]-N-adamantanylcarboxamide	No
14	E10	1-acetyl-5-{[(tert-butyl)amino]sulfonyl}indoline	No
14	F10	1-acetyl-5-[(cyclopropylamino)sulfonyl]indoline	No
14	G10	1-acetyl-5-(indolinylsulfonyl)indoline	No
14	H10	1-acetyl-5-[(diethylamino)sulfonyl]indoline	No
14	I10	1-acetyl-5-(morpholin-4-ylsulfonyl)indoline	No
14	J10	6,7-dimethoxy-2-oxo-1,3,4-trihydroquinoline-4-carboxylic acid	No
14	K10	2-thienyl-N-(2-(2-thienyl)ethyl)carboxamide	No
14	L10	(2-naphthylsulfonyl)(2-(2-thienyl)ethyl)amine	No
14	M10	N-adamantanyl[(4-pyridylmethyl)amino]carboxamide	No
14	N10	N-cyclopropyl[1-(methylsulfonyl)indolin-5-yl]carboxamide	No
14	O10	1-(methylsulfonyl)indolin-5-yl morpholin-4-yl ketone	No
14	P10	N-(2H-benzo[3,4-d]1,3-dioxolan-5-ylmethyl)[1-(methylsulfonyl)indolin-5-yl]carb oxamide	No
14	A11	2-indol-3-yl-1-(3-oxo(1,2,4-trihydroquinoxalinyl))ethane-1,2-dione	No
14	B11	2-methyl-4-[(3-oxo(1,2,4-trihydroquinoxalinyl))carbonyl]-2-hydrophthalazin-1-o ne	No
14	C11	3-methylquinoxaline-2-carbaldehyde	No
14	D11	[4-(2-methyl(1,3-oxazol-5-yl))phenyl]{[1-(methylsulfonyl)indolin-5-yl]sulfonyl }amine	No
14	E11	cyclohexyl-N-(3-oxo(2H,4H-benzo[3,4-e]1,4-thiazaperhydroin-6-yl))carboxamide	No
14	F11	cyclopentyl-N-(3-oxo(2H,4H-benzo[3,4-e]1,4-thiazaperhydroin-6-yl))carboxamide	No
14	G11	4-cyclohexyl-3-sulfanyl-1,2,4-triazolin-5-one	No
14	H11	2,2-diphenyl-N-[2-(trifluoromethyl)(6,11,5a-trihydrobenzimidazolo[2,1-b]benzot hiazol-4-yl)]acetamide	No
14	I11	3-oxo-2H,4H-benzo[e]1,4-thiazaperhydroine-6-carboxylic acid	No
14	J11		No
14	K11		YES
14	L11		No
14	M11	N-acenaphthen-5-yl(1-methyl-5-oxopyrrolidin-3-yl)carboxamide	No
14	N11	3-(morpholin-4-ylmethyl)-5-(2-thienyl)-1,3,4-oxadiazoline-2-thione	No
14	O11	2-[(2H,3H-benzo[e]1,4-dioxan-6-ylsulfonyl)amino]-3-indol-3-ylpropanoic acid	No

14	P11	4-(2-{5-[1-(2-naphthylsulfonyl)pyrrolidin-2-yl]-4-phenyl-1,2,4-triazol-3-ylthi o}acetyl)-1,3,4-trihydroquinoxalin-2-one	No
14	A12	5-(8,9-dimethoxy(1,2,3,4,10b,4a-hexahydro-6H-benzo[c]chromen-6-yl))-1,2,3-trim ethoxybenzene	No
14	B12	5-aminoquinolin-8-ol	No
14	C12	2-amino-5,5-dimethyl-4,5,6-trihydrobenzothiazol-7-one	No
14	D12	2-methylbenzo[g]benzothiazole	No
14	E12	2-benzyl-1H,3H-naphtho[1,2-e]1,3-oxazine	No
14	F12		No
14	G12	methyl 2-amino-5-propylthiophene-3-carboxylate	No
14	H12	methyl 2-amino-5-(methylethyl)thiophene-3-carboxylate	No
14	I12	4-chloro-1-[(4-fluorophenoxy)methyl]pyrazole-3-carboxylic acid	No
14	J12	3-bromo-6-fluorochromen-4-one	No
14	K12	5-aminoindole-3-carboxamide	YES
14	L12	2-(2,7-bis{[bis(carboxymethyl)amino]methyl}-6-hydroxy-3-oxoxanthen-9-yl)benzoi c acid	No
14	M12	(2S,6R,9R)-9-phenyl-7-oxa-1-azabicyclo[4.3.0]nonane-2-carbonitrile	No
14	N12	4-amino-6-(tert-butyl)-1-methyl-1,3,5-triazin-2-one	No
14	O12	5-hydroxy-2-phenylchromen-4-one	No
14	P12	7-(dimethylamino)phenothiazin-3-one	No
14	A13	2-{(carboxymethyl)[(7-hydroxy-4-methyl-2-oxochromen-8-yl)methyl]amino}acetic a cid	No
14	B13	ethyl 4-methyl-6-(5-methyl(2-thienyl))-2-thioxo-1,3,6-trihydropyrimidine-5-car boxylate	No
14	C13	methyl 6-(2,4-dimethylphenyl)-2-oxo-4-{[3-(trifluoromethyl)pyrazolyl]methyl}-1 ,3,6-trihydropyrimidine-5-carboxylate	No
14	D13	methyl 4-[(2,5-dichlorophenylthio)methyl]-6-(2,4-dimethylphenyl)-2-oxo-1,3,6-t rihydropyrimidine-5-carboxylate	No
14	E13	methyl 6-(2,4-dimethylphenyl)-4-[(2-furylmethylthio)methyl]-2-oxo-1,3,6-trihyd ropyrimidine-5-carboxylate	No
14	F13	({4-[(1-methyl-1,2,3,4-tetraazol-5-ylthio)methyl]-2-thienyl}methylene)methane- 1,1-dicarbonitrile	No
14	G13	methyl (2E)-2-cyano-3-{4-[(1-methyl(1,2,3,4-tetraazol-5-ylthio))methyl](2-thie nyl)}prop-2-enoate	YES
14	H13	ethyl (2E)-2-cyano-3-{4-[(1-methyl(1,2,3,4-tetraazol-5-ylthio))methyl](2-thien yl)}prop-2-enoate	No
14	I13	(2E)-2-(aminothioxomethyl)-3-{4-[(1-methyl(1,2,3,4-tetraazol-5-ylthio))methyl] (2-thienyl)}prop-2-enenitrile	No
14	J13	(2E)-3-{4-[(5-amino(1,3,4-thiadiazol-2-ylthio))methyl](2-thienyl)}-2-(aminothi oxomethyl)prop-2-enenitrile	No
14	K13	methyl (2E)-3-{4-[(5-amino(1,3,4-thiadiazol-2-ylthio))methyl](2-thienyl)}-2-cy anoprop-2-enoate	No

14	L13	ethyl (2E)-3-{4-[(5-amino(1,3,4-thiadiazol-2-ylthio))methyl](2-thienyl)}-2-cya noprop-2-enoate	No
14	M13	({4-[(5-amino-1,3,4-thiadiazol-2-ylthio)methyl]-2-thienyl}methylene)methane-1, 1-dicarbonitrile	No
14	N13	4-[(5-amino-1,3,4-thiadiazol-2-ylthio)methyl]thiophene-2-carbaldehyde	No
14	O13	[1-(4-fluorophenyl)-5-oxopyrrolidin-3-yl]-N-(4-iodophenyl)carboxamide	No
14	P13	N-(2,5-dichlorophenyl)(1-cyclohexyl-5-oxopyrrolidin-3-yl)carboxamide	No
14	A14	ethyl 2-(2,2-dimethylpropanoylamino)-4-methyl-1,3-thiazole-5-carboxylate	No
14	B14	ethyl 4-methyl-2-(propanoylamino)-1,3-thiazole-5-carboxylate	No
14	C14	ethyl 2-(butanoylamino)-4-methyl-1,3-thiazole-5-carboxylate	No
14	D14	(1-cyclohexyl-5-oxopyrrolidin-3-yl)-N-(4,5,6,7-tetrahydrobenzothiazol-2-yl)car boxamide	No
14	E14	N-(2H,3H-benzo[3,4-e]1,4-dioxin-6-yl)(1-cyclohexyl-5-oxopyrrolidin-3-yl)carbox amide	No
14	F14	N-(2H-benzo[3,4-d]1,3-dioxolen-5-yl)(1-cyclohexyl-5-oxopyrrolidin-3-yl)carboxa mide	No
14	G14	(1-cyclohexyl-5-oxopyrrolidin-3-yl)-N-(4-{[(oxolan-2-ylmethyl)amino]sulfonyl}p henyl)carboxamide	YES
14	H14	N-(3,5-difluorophenyl)-2-(1,3-dioxobenzo[c]azolidin-2-yl)acetamide	No
14	I14	N-(3,5-difluorophenyl)(1-cyclohexyl-5-oxopyrrolidin-3-yl)carboxamide	No
14	J14	3-(phenylsulfonyl)-N-(4,5,6,7-tetrahydrobenzothiazol-2-yl)propanamide	No
14	K14	N-(5,5-dimethyl-7-oxo(4,5,6-trihydrobenzothiazol-2-yl))-3-(phenylsulfonyl)prop anamide	No
14	L14	N-(3-chloro-4-fluorophenyl)[1-(4-fluorophenyl)-5-oxopyrrolidin-3-yl]carboxamid e	No
14	M14	[1-(4-fluorophenyl)-5-oxopyrrolidin-3-yl]-N-(3-pyridyl)carboxamide	No
14	N14	N-(2-fluoro-5-nitrophenyl)[1-(4-fluorophenyl)-5-oxopyrrolidin-3-yl]carboxamide	No
14	O14	N-(2,4-difluorophenyl)[1-(4-fluorophenyl)-5-oxopyrrolidin-3-yl]carboxamide	No
14	P14	N-(4-fluoro-3-nitrophenyl)[1-(4-fluorophenyl)-5-oxopyrrolidin-3-yl]carboxamide	No
14	A15	[1-(4-fluorophenyl)-5-oxopyrrolidin-3-yl]-N-(4-sulfamoylphenyl)carboxamide	No
14	B15	[1-(4-fluorophenyl)-5-oxopyrrolidin-3-yl]-N-[4-(pyrrolidinylsulfonyl)phenyl]ca rboxamide	No
14	C15	[1-(4-fluorophenyl)-5-oxopyrrolidin-3-yl]-N-(4,5,6,7-tetrahydrobenzothiazol-2- yl)carboxamide	No

14	D15	N-(2H,3H-benzo[3,4-e]1,4-dioxin-6-yl)[1-(4-fluorophenyl)-5-oxopyrrolidin-3-yl] carboxamide	No
14	E15	N-(2H-benzo[3,4-d]1,3-dioxolen-5-yl)[1-(4-fluorophenyl)-5-oxopyrrolidin-3-yl]c arboxamide	No
14	F15	2-(4-formyl-3-phenylpyrazolyl)acetic acid	No
14	G15	N-(5,5-dimethyl-7-oxo(4,5,6-trihydrobenzothiazol-2-yl))-2-[(4-methylphenyl)sul fonyl]acetamide	No
14	H15	(6S,2R)-2,12-bis(hydroxymethyl)-12-(2-hydroxyethyl)-2,6,8-trimethylspiro[bicyc lo[4.4.0]decane-7,5'-oxolane]-3-ol	No
14	I15		No
14	J15		No
14	K15	9,10-dimethoxy-8-benzyl-5,6,7,8-tetrahydro-2H-1,3-dioxoleno[4,5-g]isoquinolino [3,2-a]isoquinoline	No
14	L15	9,10-dimethoxy-8-benzyl-5,6,7,8,13,13a-hexahydro-2H-1,3-dioxoleno[4,5-g]isoqui nolino[3,2-a]isoquinoline	No
14	M15		No
14	N15		No
14	O15	4-(2H-benzo[3,4-d]1,3-dioxolen-5-yl)-2-methyl-3a-nitro-1H,9bH-chromano[4,3-d]1 ,2-oxazolidine	No
14	P15	4-(4-chlorophenyl)-2-methyl-3a-nitro-1H,9bH-chromano[4,3-d]1,2-oxazolidine	No
14	A16	4-[(1Z)-1-ethyl-2-(4-hydroxyphenyl)but-1-enyl]phenol	No
14	B16	5-((1E)-4-amino-2-azabut-1-enyl)-3-iodo-2-methoxyphenol	No
14	C16	3-[N-(4,5-dimethyl-1,3-thiazol-2-yl)carbamoyl]propanoic acid	No
14	D16	2-methylpropyl 5-(N-(2H-benzo[3,4-d]1,3-dioxolen-5-yl)carbamoyl)-3-hydroxypyrr olidinecarboxylate	No
14	E16	2-methylpropyl 3-hydroxy-5-[N-(4-iodophenyl)carbamoyl]pyrrolidinecarboxylate	No
14	F16	2-methylpropyl 3-hydroxy-5-[N-(4-iodo-2,6-dimethylphenyl)carbamoyl]pyrrolidine carboxylate	No
14	G16	tert-butyl 2-[N-(4-iodo-2-methylphenyl)carbamoyl]pyrrolidinecarboxylate	No
14	H16	N-(4-iodophenyl)[1-(2-thienylcarbonyl)pyrrolidin-2-yl]carboxamide	No
14	I16	2-methylpropyl 2-[N-(4-chlorophenyl)carbamoyl]pyrrolidinecarboxylate	No
14	J16	2-methylpropyl 2-(N-(4,5,6,7-tetrahydrobenzothiazol-2-yl)carbamoyl)pyrrolidine carboxylate	No
14	K16	2-{[3-(2,6-dichlorophenyl)-1,2,4-oxadiazol-5-yl]methylthio}benzoxazole	No
14	L16	2-{[3-(2,6-dichlorophenyl)-1,2,4-oxadiazol-5-yl]methylthio}benzothiazole	No
14	M16	2-[5-(benzothiazol-2-ylthiomethyl)(1,2,4-oxadiazol-3-yl)]-1,3-dimethoxybenzene	No
14	N16	[2-(4-methyl-5-phenyl(1,2,4-triazol-3-ylthio))ethyl](phenylsulfonyl)amine	No

14	O16	3-chloro-4,6-diphenylpyridazine	No
14	P16	2-(5-amino(1,3,4-thiadiazol-2-ylthio))-1-pyrrolidinylethan-1-one	No
14	A17	4-(3-methylpyrazolyl)phenylamine	No
14	B17	(hydroxyimino)(4-methylphenyl)-2-thienylmethane	No
14	C17	(2-hydroxyphenyl)-N-[(2-oxo(1H-benzo[d]azolidin-3-ylidene))azamethyl]carboxami de	No
14	D17	N-[(2-oxo(1H-benzo[d]azolidin-3-ylidene))azamethyl]-2-phenoxyacetamide	No
14	E17	2-(3,5-dimethylphenoxy)-N-[(2-oxo(1H-benzo[d]azolidin-3-ylidene))azamethyl]ace tamide	No
14	F17	N-[(2-oxo(1H-benzo[d]azolidin-3-ylidene))azamethyl]-N'-[(2-oxo(1H-benzo[d]azol idin-3-ylidene))azamethyl]hexane-1,6-diamide	No
14	G17		No
14	H17	1-[4-(chlorosulfonyl)phenyl]pyrrolidin-2-one	YES
14	I17	methyl 1,5-dimethylpyrazole-3-carboxylate	No
14	J17	2-(2-bromoethyl)benzo[c]azoline-1,3-dione	No
14	K17	4,5-diphenyl-1,3-oxazole-2-thiol	No
14	L17	1,2,4-triazino[5,6-b]indole-3-thiol	No
14	M17	1,2,4-triazino[5,6-b]indole-3-ylhydrazine	No
14	N17	[(4-aminophenyl)sulfonyl](3,4-dimethylisoxazol-5-yl)amine	No
14	O17	[(4-aminophenyl)sulfonyl]pyrimidin-2-ylamine	No
14	P17	5-amino-3-nitrophenol	No
14	A18	4,6-dimethylpyrimidine-2-thiol, chloride	No
14	B18	4-chloro-2-phenyl-5,6,7-trihydrocyclopenta[1,2-d]pyrimidine	No
14	C18	{[(4-chlorophenyl)methyl]sulfonyl}-4,5,6,7-tetrahydrobenzothiazol-2-ylamine	No
14	D18	ethyl 4-methyl-2-[(methylsulfonyl)amino]-1,3-thiazole-5-carboxylate	No
14	E18	ethyl 2-(2-ethylbutanoylamino)-4-methyl-1,3-thiazole-5-carboxylate	No
14	F18	ethyl 4-methyl-2-(pentanoylamino)-1,3-thiazole-5-carboxylate	No
14	G18	(1-cyclohexyl-5-oxopyrrolidin-3-yl)-N-(4-fluorophenyl)carboxamide	YES
14	H18	N-(2,4-difluorophenyl)(1-cyclohexyl-5-oxopyrrolidin-3-yl)carboxamide	No
14	I18	[1-(4-methoxyphenyl)-5-oxopyrrolidin-3-yl]-N-(4-pyridyl)carboxamide	No
14	J18	N-(5-chloro(2-pyridyl))[1-(4-fluorophenyl)-5-oxopyrrolidin-3-yl]carboxamide	No
14	K18	[1-(4-fluorophenyl)-5-oxopyrrolidin-3-yl]-N-(2,4,5-trichlorophenyl)carboxamide	No
14	L18	[1-(4-fluorophenyl)-5-oxopyrrolidin-3-yl]-N-(4-{[(oxolan-2-ylmethyl)amino]sulf onyl}phenyl)carboxamide	No
14	M18	N-(3,5-difluorophenyl)[1-(4-fluorophenyl)-5-oxopyrrolidin-3-yl]carboxamide	No
14	N18	3-[(4-chlorophenyl)phenylmethylthio]-1,2,4-thiadiazole-5-ylamine	No

14	O18	2-(2-piperazinylethyl)benzo[c]azolidine-1,3-dione	No
14	P18	6,7-dichloroquinoline-5,8-dione	No
14	A19	2-[(tert-butoxy)carbonylamino]-1,2,3,4-tetrahydronaphthalene-2-carboxylic acid	No
14	B19	2-[(fluoren-9-ylmethoxy)carbonylamino]indane-2-carboxylic acid	No
14	C19	1-[(fluoren-9-ylmethoxy)carbonylamino]indanecarboxylic acid	No
14	D19	2-[(fluoren-9-ylmethoxy)carbonylamino]-1,2,3,4-tetrahydronaphthalene-2-carboxy lic acid	No
14	E19	(2S,3S)-2-[(fluoren-9-ylmethoxy)carbonylamino]-3-methylpentanoic acid	No
14	F19	7-hydroxyphenoxazin-3-one	No
14	G19	7-hydroxyphenoxazin-3-one	No
14	H19	(2S)azetidine-2-carboxylic acid	No
14	I19	(5R,6R)-4-chloro-5,6-dihydroxycyclohexa-1,3-dienecarboxylic acid	No
14	J19	3-chloro-1H-indazole	No
14	K19	histidine, chloride, hydrate	No
14	L19	3-hydroxy-5-(hydroxymethyl)-2-methylpyridine-4-carbaldehyde	No
14	M19	6-methyl-2-(methylethyl)pyrimidin-4-ol	No
14	N19	2-(5-hydroxyindol-3-yl)acetic acid	No
14	O19	2-(5-methylpyrazol-3-yl)acetic acid	No
14	P19	2,8-bis(2,4-dihydroxyphenyl)-7-hydroxyphenoxazin-3-one	No
14	A20	2-(3,4-dihydroxyphenyl)-3,5,7,8-tetrahydroxychromen-4-one	No
14	B20	4,6-bis(1-cyclohexyl(1,2,3,4-tetraazol-5-yl)thio)-5-nitropyrimidine	No
14	C20	cyclohexyl-N-(2-(2-furyl)ethyl)carboxamide	No
14	D20	6-({4-[(2-oxochromen-6-yl)sulfonyl]-1,4-diazaperhydroepinyl}sulfonyl)chromen-2 -one	No
14	E20	[(2,5-dimethoxy-3,4,6-trimethylphenyl)sulfonyl]piperidine	No
14	F20	2-(2,4-dihydroxyphenyl)-3,5,7-trihydroxychromen-4-one, hydrate, hydrate	No
14	G20	1-nitro-3-(trifluoromethyl)dibenzo[b,e]1,4-dioxin	No
14	H20	N-(2-adamantanyloxypropyl)cyclopropylcarboxamide	No
14	I20	1-acetyl-5-{[(2-oxo(3-3,4,5-trihydrothienyl))amino]sulfonyl}indoline	No
14	J20	2-chloro-4-nitro-1-(2-pyridylthio)benzene	No
14	K20	1-cyclohexyl-5-[(4-nitrophenyl)methylthio]-1,2,3,4-tetraazole	No
14	L20	5-methyl-4-prop-2-enyl-1,2,4-triazole-3-thiol	No
14	M20	5-(3,4-dimethoxyphenyl)-4-prop-2-enyl-1,2,4-triazole-3-thiol	No
14	N20	5-[4-(tert-butyl)phenyl]-4-prop-2-enyl-1,2,4-triazole-3-thiol	No
14	O20	5-(4-methoxyphenyl)-4-prop-2-enyl-1,2,4-triazole-3-thiol	No
14	P20	5-(2-phenylethyl)-4-prop-2-enyl-1,2,4-triazole-3-thiol	No
14	A21	5-(2,4-dichlorophenyl)-4-prop-2-enyl-1,2,4-triazole-3-thiol	No
14	B21	5-(2-chlorophenyl)-4-prop-2-enyl-1,2,4-triazole-3-thiol	No

14	C21	methyl[(4-phenyl-5-sulfanyl(1,2,4-triazol-3-yl))methyl](phenylsulfonyl)amine	No
14	D21	3-imino-3-indolinyl-2-azaprop-1-ene-1,1-diamine, chloride	No
14	E21	(2-nitrophenyl)imidazole	No
14	F21	3-methyl-1-(4-nitrophenyl)pyrazole	No
14	G21	2-(hydroxyimino)adamantane	No
14	H21	[(1-methylbenzimidazol-2-yl)methoxy]benzene	No
14	I21	6-nitroquinoxaline	No
14	J21	6-methyl-2,3,4,9-tetrahydro-4aH-carbazol-1-one	No
14	K21	4-ethyl-5-(4-methylphenyl)-1,2,4-triazole-3-thiol	No
14	L21	4-cyclohexyl-5-benzyl-1,2,4-triazole-3-thiol	No
14	M21	7,8-dimethoxy-4-methylchromen-2-one	No
14	N21	phenyl 5-chloro-2-oxo-3-hydrobenzoxazole-3-carboxylate	No
14	O21	7-methoxy-4-methylchromen-2-one	No
14	P21	4-(4-chloro-2-nitrophenyl)morpholine	No
14	A22	1-cyclohexyl-5-oxopyrrolidine-3-carboxylic acid	No
14	B22	5-({2-[(4-carboxy-5-methyl(2-furyl))methylthio]ethylthio}methyl)-2-methylfuran -3-carboxylic acid	No
14	C22	N-(1,3-thiazol-2-yl)-2-thienylcarboxamide	No
14	D22	5-(pyrrolidinylsulfonyl)-3-hydrobenzimidazol-2-one	No
14	E22	(methylethyl)[(2,4,6-trimethyl-3-(1,2,3,4-tetraazolyl)phenyl)sulfonyl]amine	No
14	F22	6-(indolinylsulfonyl)-2H,4H-benzo[e]1,4-oxazin-3-one	No
14	G22	3-(3-methyl-4-oxo-3-hydroquinazolin-2-ylthio)-3,4,5-trihydrofuran-2-one	No
14	H22	(2-naphthylsulfonyl)(2-pyrrolylethyl)amine	No
14	I22	2-methyl-4-(1,2,3,4-tetrahydroquinolylcarbonyl)-2-hydrophthalazin-1-one	No
14	J22	(adamantanylmethyl)(3-nitro(2-pyridyl))amine	No
14	K22	3-(2-furylmethylthio)-1-indolinylacetone	No
14	L22	adamantan-2-yl(3-nitro(2-pyridyl))amine	No
14	M22	6-[(cyclohexylamino)sulfonyl]-2H,4H-benzo[e]1,4-oxazin-3-one	No
14	N22	6-{[(2-cyclohex-1-enylethyl)amino]sulfonyl}-2H,4H-benzo[e]1,4-oxazin-3-one	No
14	O22	1,3-diethyl-5-{[(methylethyl)amino]sulfonyl}-3-hydrobenzimidazol-2-one	No
14	P22	5-[(diethylamino)sulfonyl]-1,3-diethyl-3-hydrobenzimidazol-2-one	No

Plate	**Well**	**IUPAC NAME**	**Inhibitor Y/N**
15	A03	N-adamantanyl(4-pyrimidin-2-ylpiperazinyl)carboxamide	No
15	B03	3-[(5-phenyl-1,3,4-oxadiazol-2-yl)methylthio]thiolane-1,1-dione	No
15	C03	(3-nitro(2-pyridyl))(2-(2-thienyl)ethyl)amine	No
15	D03	N-(1-oxo(3-hydroisobenzofuran-5-yl))-2-quinolylcarboxamide	No

15	E03	(tert-butyl)[(2-methyl-5-(1,2,3,4-tetraazolyl)phenyl)sulfonyl]amine	No
15	F03	1-{4-[(cyclopropylamino)sulfonyl]phenyl}-2,3-dimethyl-4-(methylethyl)-3-pyrazo lin-5-one	No
15	G03	5-bromo-3-hydroxy-3-(2-oxo-2-(2-thienyl)ethyl)indolin-2-one	No
15	H03	3-(2-(2-furyl)-2-oxoethyl)-3-hydroxy-1-methylindolin-2-one	No
15	I03	6-hydroxy-2-[(4-phenylpiperazinyl)methyl]-2-hydropyridazin-3-one	No
15	J03	3a,8b-dihydroxy-1-propylindano[2,1-d]imidazolidine-2,4-dione	No
15	K03	6-[(4-phenylpiperazinyl)methyl]spiro[1,3-dioxolane-2,3'-indoline]-7-one	No
15	L03	{[4-(2-fluorophenyl)piperazinyl]methyl}benzimidazole	No
15	M03	3-methylthio-1,2,4-thiadiazole-5-ylamine	No
15	N03	1-indolinyl-2-(4-methyl(1,2,4-triazol-3-ylthio))ethan-1-one	No
15	O03	1-(2-thienylsulfonyl)pyrrolidine-2-carboxylic acid	No
15	P03	4-fluoro-1-(piperidylsulfonyl)naphthalene	No
15	A04	2-(7,9-diazabicyclo[4.3.0]non-7-en-8-ylthio)-1-morpholin-4-ylethan-1-one	No
15	B04	1,3-bis[(4-chlorophenyl)methyl]-2-(4-pyridyl)imidazolidine	No
15	C04	3-hydroxyadamantanecarboxylic acid	No
15	D04	1,3-dimethyl-5-(piperidylsulfonyl)-3-hydrobenzimidazol-2-one	No
15	E04	(fluoren-2-ylsulfonyl)(2-phenoxyethyl)amine	No
15	F04	5-(7-quinolylmethylene)-1,3-thiazolidine-2,4-dione	No
15	G04	{4-amino-6-[(2,2-dimethyl(2,3-dihydrobenzo[2,3-b]furan-7-yloxy))methyl](1,3,5- triazin-2-yl)}dimethylamine	No
15	H04	2-benzimidazol-2-ylfuran	No
15	I04		No
15	J04	(2E)-3-(2H-benzo[3,4-d]1,3-dioxolen-5-yl)-2-(6-methylbenzimidazol-2-yl)prop-2- enenitrile	No
15	K04	2-methyl-5-(morpholin-4-ylmethyl)furan-3-carboxylic acid	No
15	L04	5-[(2-bromophenyl)methylthio]-1,3,4-thiadiazole-2-ylamine	No
15	M04	3-methyl-1-(morpholin-4-ylmethyl)-3-hydrobenzimidazole-2-thione	No
15	N04	N-cyclohexyl-2-(5-methyl(1,3,4-thiadiazol-2-ylthio))acetamide	No
15	O04	2-(benzimidazol-2-ylmethylthio)-4-phenylimidazole	No
15	P04	[(dimethylamino)sulfonyl]fluoren-2-ylamine	No
15	A05	5-adamantanyl-4-methyl-1,2,4-triazole-3-thiol	No
15	B05	6-amino-2-[(4-fluoronaphthyl)methylthio]pyrimidin-4-ol	No
15	C05	1-[(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)methyl]-4-methyl-3-(phenoxymethyl)-1,2,4 -triazoline-5-thione	No
15	D05	1-(morpholin-4-ylmethyl)-3-benzyl-4-imidazoline-2-thione	No
15	E05	2-[(dibenzo[b,d]furan-2-ylsulfonyl)methylamino]acetic acid	No
15	F05	5-(dimethylamino)benzothiazole-2-thiol	No
15	G05	1-cyclohexyl-4-(morpholin-4-ylmethyl)-1,2,3,4-tetraazoline-5-thione	No
15	H05	6-amino-2-[(2,4,6-trimethylphenyl)methylthio]pyrimidin-4-ol	No

15	I05	4-methyl-5-phenyl-3-{[3-(trifluoromethyl)phenyl]methylthio}-1,2,4-triazole	No
15	J05	2-(1,2,3,4-tetrahydroquinolylsulfonyl)dibenzo[b,d]furan	YES
15	K05	8-(1H-1,2,4-triazol-5-ylthio)-1,3,7-trimethyl-1,3,7-trihydropurine-2,6-dione	No
15	L05	2-(ethylsulfonyl)-1-(2-pyridylmethyl)benzimidazole	No
15	M05	3,6-dibromofluorene	No
15	N05	3-methyl-1-[(4-phenylpiperidyl)methyl]-3-hydrobenzimidazole-2-thione	No
15	O05	2-(5-methyl(1,3,4-thiadiazol-2-ylthio))-N-(1,3-thiazol-2-yl)acetamide	No
15	P05	4-morpholin-4-yl-3-(morpholin-4-ylsulfonyl)phenylamine	No
15	A06	5-bromo-1,4-dimethoxy-2-nitrobenzene	No
15	B06	4-fluoro-1-(pyrrolidinylsulfonyl)benzene	No
15	C06	2H,3H-benzo[e]1,4-dioxan-2-ylmethan-1-ol	No
15	D06	4-{[(4-carboxy-5-methyl(2-furyl))methylthio]methyl}-5-methylfuran-2-carboxylic acid	No
15	E06	9-[3,4-dihydroxy-5-(hydroxymethyl)oxolan-2-yl]-8-bromohydropurin-6-one	No
15	F06	5-(2-furyl)-4-phenyl-1,2,4-triazole-3-thiol	No
15	G06	4-methyl-1,3-thiazole-5-carboxylic acid	No
15	H06	5-chloro-2-morpholin-4-ylphenylamine	No
15	I06	[4-(hydroxymethyl)-2-phenyl-1,3-oxazolin-4-yl]methan-1-ol	No
15	J06	2-(5-amino(1,3,4-thiadiazol-2-ylthio))-N-(1,3-thiazol-2-yl)acetamide	No
15	K06	2-(methylsulfonyl)benzimidazole	No
15	L06	1-acetyl-3-[(4-hydroxy-6-methylpyrimidin-2-ylthio)methyl]-2,4,6-trimethylbenze ne	No
15	M06	4-(dibenzo[b,d]furan-2-ylsulfonyl)morpholine	No
15	N06	4-[(1,3,3-trimethyl-6-azabicyclo[3.2.1]oct-6-yl)sulfonyl]phenylamine	No
15	O06	[4-(methylamino)phenyl]thiocarbonitrile	No
15	P06	2-(4-chlorophenyl)-4-(4-nitrophenyl)-1,3-dioxolane	No
15	A07	4-(2,4-dichlorophenyl)-2-morpholin-4-yl-1,3-thiazole	No
15	B07	2-[4-(diphenylmethyl)piperazinyl]-4-phenyl-1,3-thiazole	No
15	C07	1-{[4-(diphenylmethyl)piperazinyl]methyl}-3-(4-methoxyphenyl)-4-methyl-1,2,4-t riazoline-5-thione	No
15	D07	3-(3,4-dimethoxyphenyl)-1-{[4-(diphenylmethyl)piperazinyl]methyl}-4-methyl-1,2 ,4-triazoline-5-thione	No
15	E07	(2-methoxydibenzo[b,d]furan-3-yl)(pyrrolidinylsulfonyl)amine	No
15	F07	naphthyl(pyrrolidinylsulfonyl)amine	No
15	G07	2H,3H-benzo[e]1,4-dioxin-6-yl[(4-methylthiophenyl)sulfonyl]amine	No

15	H07	7-nitro-2-(pyrrolidinylsulfonyl)dibenzo[b,d]furan	No
15	I07	5-(isoxazol-3-ylmethylthio)-3-methyl-4-phenyl-1,2,4-triazole	No
15	J07	1-indol-3-yl-2-pyrrolidinylethane-1,2-dione	No
15	K07	3-[methyl(4-phenyl(1,3-thiazol-2-yl))amino]thiolane-1,1-dione	No
15	L07	5-(3-pyridylmethylthio)-1,3,4-thiadiazole-2-ylamine	No
15	M07	7-[(4-fluorophenyl)methyl]-8-imidazolyl-1,3-dimethyl-1,3,7-trihydropurine-2,6- dione	No
15	N07	8-benzimidazol-2-ylthio-7-[(2,4-dichlorophenyl)methyl]-1,3-dimethyl-1,3,7-trih ydropurine-2,6-dione	No
15	O07	7-[8-formyl-1,6,7-trihydroxy-3-methyl-5-(methylethyl)(2-naphthyl)]-2,3,8-trihy droxy-6-methyl-4-(methylethyl)naphthalenecarbaldehyde	No
15	P07	N-(5-bromo(2-pyridyl))-2-thienylcarboxamide	No
15	A08	2-(4-ethyl-5-(2-furyl)(1,2,4-triazol-3-ylthio))-N-(2-furylmethyl)acetamide	No
15	B08	N-cyclohexyl-2-thienylcarboxamide	No
15	C08	(7-chloro-4-quinolyl)piperazine	No
15	D08	N-cyclopentyl[1-(4-fluorophenyl)-5-oxopyrrolidin-3-yl]carboxamide	No
15	E08	1-(4-fluorophenyl)-4-(pyrrolidinylcarbonyl)pyrrolidin-2-one	No
15	F08	(5-chloro(2-pyridyl))(ethylsulfonyl)amine	No
15	G08	(3-benzimidazolylpropyl)(5-nitro(2-pyridyl))amine	No
15	H08	3-{[(3-methylquinoxalin-2-yl)methylthio]methyl}-1,2,4-triazolin-5-one	No
15	I08	4-(dibenzo[b,d]furan-2-ylsulfonyl)-2,6-dimethylmorpholine	No
15	J08	(5-nitro(2-pyridyl))(2-(2-thienyl)ethyl)amine	No
15	K08	3-{[(2-phenyl-1,3-thiazol-4-yl)methylthio]methyl}-1,2,4-triazolin-5-one	No
15	L08	8-imidazolyl-1,3,7-trimethyl-1,3,7-trihydropurine-2,6-dione	No
15	M08	(1,4-dioxan-2-ylmethyl)methylamine	No
15	N08	4-phenyl-1,2,5-oxadiazole-3-ylamine	No
15	O08	2-amino-1-(3-hydroxyphenyl)ethan-1-ol	No
15	P08	N-(6-hydroxypurin-2-yl)acetamide	YES
15	A09	2-methylnaphthalene-1,4-dione	No
15	B09	(2S)-3-indol-3-yl-2-(methylamino)propanoic acid	No
15	C09	5,7-dihydroxy-2-(4-methoxyphenyl)chromen-4-one	No
15	D09	((2S,5S,12S,16S,1R,9R,13R)-6,7,13-trimethyl-7-azapentacyclo[10.8.0.0<2,9>.0<5, 9>.0<13,18>]icos-18-en-16-yl)dimethylamine	No
15	E09	2-(3,4-dimethoxyphenyl)-5-{[2-(3,4-dimethoxyphenyl)ethyl]methylamino}-2-(methy lethyl)pentanenitrile, chloride	No
15	F09		No

15	G09	(5R,9R,5aR,8aR)-9-hydroxy-5-(3,4,5-trimethoxyphenyl)-5,8,9,5a,8a-pentahydro-2H -isobenzofurano[5',6'-2,1]benzo[4,5-d]1,3-dioxolan-6-one	No
15	H09	2-(2-pyridylmethylthio)benzothiazole	YES
15	I09	(5-bromo(2-pyridyl))[benzylsulfonyl]amine	YES
15	J09	(5-bromo(2-pyridyl))(methylsulfonyl)amine	YES
15	K09	(3-chlorobenzo[b]thiophen-2-yl)-N-(2-quinolyl)carboxamide	No
15	L09	(4S,5S,6S,12aS,4aR,5aR)-4-(dimethylamino)-3,5,6,10,12,12a-hexahydroxy-6-methyl -1,11-dioxo-4,5,6,12a,4a,5a-hexahydronaphthacene-2-carboxamide, chloride	No
15	M09	ethyl 1-(2,4-difluorophenyl)-7-chloro-6-fluoro-4-oxohydropyridino[2,3-b]pyridi ne-3-carboxylate	No
15	N09	5-ethyl-8-oxo-5-hydro-2H-1,3-dioxoleno[4,5-g]quinoline-7-carboxylic acid	No
15	O09	2-[(2E)-3-(3,4-dihydroxyphenyl)prop-2-enoyloxy]-3-(3,4-dihydroxyphenyl)propano ic acid	No
15	P09	2-(2,5-dioxo-3-3,4-dihydrofuryl)acetic acid	No
15	A10	1-methyl-4-nitroimidazole	No
15	B10	3-(3-pyridyl)-1H-1,2,4-triazole-5-ylamine	No
15	C10	6-methoxycyclohexane-1,2,3,4,5-pentaol	No
15	D10	(1S,5S,2R)-5-methyl-2-(methylethyl)cyclohexan-1-ol	No
15	E10	(3R,5R)-1,3,4,5-tetrahydroxycyclohexanecarboxylic acid	No
15	F10	(1S,10S,11S,15S,17S,2R,14R)-14,17-dihydroxy-14-(2-hydroxyacetyl)-2,15-dimethyl tetracyclo[8.7.0.0<2,7>.0<11,15>]heptadec-6-en-5-one	No
15	G10	(2S,1R,5R)-5-methyl-2-(methylethyl)cyclohexyl (2R)-2-hydroxypropanoate	No
15	H10	3-((2R)-2-piperidyl)pyridine	No
15	I10	7-[8-formyl-6,7-dihydroxy-3-methyl-5-(methylethyl)-1,4-dioxo(2-naphthyl)]-2,3- dihydroxy-6-methyl-4-(methylethyl)-5,8-dioxonaphthalenecarbaldehyde	YES
15	J10	2,2'-Diamino-5,5'-diisopropyl-7,7'-dimethyl-2H,2'H-[8,8']bi[naphtho[1,8-bc]furanyl]-3,4,3',4'-tetraol	No
15	K10	6-[2,4-dihydroxy-6-methyl-1-(methylethyl)-3-oxoindan-5-yl]-2,7-dihydroxy-5-met hyl-3-(methylethyl)indan-1-one	NO
15	L10		YES
15	M10	(11S,14S,17S,1R)-12-ethylidene-14-methyl-8,14-diazapentacyclo[9.5.2.0<1,9>.0<2 ,7>.0<14,17>]octadeca-2,4,6,9-tetraene-10-carbaldehyde, chloride	No
15	N10	(11S,17S,1R)-12-ethylidene-8,14-diazapentacyclo[9.5.2.0<1,9>.0<2,7>.0<14,17>]o ctadeca-2,4,6,9-tetraene-10-carbaldehyde	No
15	O10	9-((2E)-3,7-dimethylocta-2,6-dienyloxy)furano[3,2-g]chromen-2-one	No

15	P10	6-bromo-2-(3-methylphenyl)chromen-4-one	No
15	A11	3-hydroxy-7-methoxy-2-(4-methoxyphenyl)chromen-4-one	No
15	B11		No
15	C11	14-((1S,4R)-4-ethyl-1,5-dimethylhexyl)(1S,5S,10S,11S,2R,14R,15R)-2,15-dimethyl tetracyclo[8.7.0.0<2,7>.0<11,15>]heptadec-7-en-5-ol	No
15	D11	14-((2E)(4S,1R)-4-ethyl-1,5-dimethylhex-2-enyl)(1S,5S,10S,11S,2R,14R,15R)-2,15 -dimethyltetracyclo[8.7.0.0<2,7>.0<11,15>]heptadec-7-en-5-ol	No
15	E11	4-{N-[(1R)-2-({(2R)-2-((4S)-4-amino-4-carboxybutanoylamino)-2-[N-(carboxymethy l)carbamoyl]ethyl}disulfanyl)-1-[N-(carboxymethyl)carbamoyl]ethyl]carbamoyl}(2 S)-2-aminobutanoic acid	No
15	F11	7-methoxy-1-methylbeta-carboline	No
15	G11	(4S,3R,5R)-3,4,5-trihydroxycyclohex-1-enecarboxylic acid	YES
15	H11	(2S)-2-amino-5-(aminocarbonylamino)pentanoic acid	YES
15	I11	2-methoxy-4-prop-2-enylphenol	No
15	J11	3-((2S)-1-methylpyrrolidin-2-yl)pyridine	YES
15	K11	(1S,5S)-4,6,6-trimethylbicyclo[3.1.1]hept-3-en-2-one	YES
15	L11	3,7,11,15-tetramethylhexadec-1-en-3-ol	YES
15	M11	5,7-dihydroxy-2-phenylchromen-4-one	No
15	N11	3,7-dimethyloct-6-en-1-ol	No
15	O11	3,7-dimethylocta-1,6-dien-3-ol	No
15	P11	(2S,4S,5S,3R,6R)-6-(hydroxymethyl)-2-[2-(hydroxymethyl)phenoxy]-2H-3,4,5,6-tet rahydropyran-3,4,5-triol	No
15	A12	(5S)-2-methyl-5-(1-methylvinyl)cyclohex-2-en-1-one	No
15	B12	(1S,10S,11S,14S,15S,2R)-14-acetyl-2,15-dimethyl-5-oxotetracyclo[8.7.0.0<2,7>.0 <11,15>]heptadec-6-ene	No
15	C12	2-amino-4-(methylsulfinyl)butanoic acid	No
15	D12	(4S,5S,2R,3R,6R)-6-{[(4S,5S,2R,3R,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)(2H-3, 4,5,6-tetrahydropyran-2-yloxy)]methyl}-2H-3,4,5,6-tetrahydropyran-2,3,4,5-tetr aol	No
15	E12	(1R,4R)-1,7,7-trimethylbicyclo[2.2.1]heptan-2-one	No
15	F12	4-((1S,2S,5S,11S,15S,7R,10R,14R,16R)-5-{5-[5-((2S,4S,5S,6R)-4,5-dihydroxy-6-me thyl(2H-3,4,5,6-tetrahydropyran-2-yloxy))(4S,5S,2R,6R)-4-hydroxy-6-methyl(2H-3 ,4,5,6-tetrahydropyran-2-yloxy)](4S,5S,2R,6R)-4-hydroxy-6-methyl(2H-3,4,5,6-te trahydropyran-2-yloxy)}-11,16-dihydroxy-2,15-dimethyltetracyclo[8.7.0.0<2,7>.0 <11,15>]heptadec-14-yl)-5-hydrofuran-2-one	No
15	G12	(4S)-4-((1S,2S,11S,5R,7R,10R,14R,15R)-5-hydroxy-2,15-dimethyltetracyclo[8.7.0. 0<2,7>.0<11,15>]heptadec-14-yl)pentanoic acid	No
15	H12	(4bS,9aR)indano[2,1-c]chroman-1,2,6,7,9a-pentaol	YES

15	I12	3,7-dimethyl-1,3,7-trihydropurine-2,6-dione	No
15	J12	arginine	No
15	K12	7-[(5S,2R,3R,4R,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)(2H-3,4,5,6-tetrahydropy ran-2-yl)]-3,5,6,8-tetrahydroxy-1-methyl-9,10-dioxoanthracene-2-carboxylic aci d	YES
15	L12	(2S)-5-oxopyrrolidine-2-carboxylic acid	YES
15	M12	isosafrole	No
15	N12	6-methyl-2-phenylchromen-4-one	No
15	O12	5-hydroxy-2-methylnaphthalene-1,4-dione	No
15	P12	(10S,1R,2R,9R)-7,15-diazatetracyclo[7.7.1.0<2,7>.0<10,15>]heptadecane	No
15	A13	5,8-dichloro-2,4-dimethylquinoline	No
15	B13	1-[3-(dimethylamino)propyl]-1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5-carb onitrile	No
15	C13	1,1-bis(4-fluorophenyl)-1,3-dihydroisobenzofuran-5-carbonitrile	No
15	D13	1-(4-fluorophenyl)-1,3-dihydroisobenzofuran-5-carbonitrile	No
15	E13	4-[(4-fluorophenyl)hydroxymethyl]-3-(hydroxymethyl)benzenecarbonitrile	No
15	F13	4-((2E)-3-phenylprop-2-enyl)-1-(diphenylmethyl)piperazine	No
15	G13	(4-hydroxy-2-methyl-1,1-dioxobenzo[e]1,2-thiazin-3-yl)-N-(2-pyridyl)carboxamid e	No
15	H13	(1S,5S,11S,15S,2R,10R)-5-hydroxy-2,15-dimethyltetracyclo[8.7.0.0<2,7>.0<11,15>]heptadec-7-en-14-one	YES
15	I13	2,7-dinitrofluorene	YES
15	J13	4-nitropyrazole-3-carboxamide	No
15	K13	2-(1-phenyl-1,2,3,4-tetraazol-5-yloxy)phenylamine	YES
15	L13	7-[(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)methyl]-5,5-dimethylspiro[1,3-dioxane-2, 3'-indoline]-8-one	YES
15	M13	8-[(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)methyl]spiro[1,3-dioxepane-2,3'-indoline]-9-one	No
15	N13	6-[(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)methyl]spiro[1,3-dioxolane-2,3'-indoline]-7-one	No
15	O13	4-(4-fluorophenyl)-6,7,8,9,5a,9a-hexahydro-4H-thiopheno[3,2-c]chromene	No
15	P13	(2H,3H-benzo[3,4-e]1,4-dioxin-6-ylsulfonyl)[(phenylcyclopropyl)methyl]amine	No
15	A14	(4-fluorophenyl)[(3-methylquinoxalin-2-yl)methyl](methylsulfonyl)amine	No
15	B14	1-(2H,3H-benzo[3,4-e]1,4-dioxin-6-yl)-2-[1-adamantanyl-4-(4-chlorophenyl)imida zol-2-ylthio]ethan-1-one	No
15	C14	4-methyl-6-(morpholin-4-ylsulfonyl)-2H-benzo[e]1,4-oxazaperhydroin-3-one	No
15	D14	4-methyl-6-[(3-oxo(1,2,4-trihydroquinoxalinyl))sulfonyl]-2H-benzo[e]1,4-oxazap erhydroin-3-one	No

15	E14	6-(2H,3H-benzo[e]1,4-oxazin-4-ylsulfonyl)-4-methyl-2H-benzo[e]1,4-oxazaperhydr oin-3-one	No
15	F14	6-[(6-bromo(1,2,3,4-tetrahydroquinolyl))sulfonyl]-4-methyl-2H-benzo[e]1,4-oxaz aperhydroin-3-one	No
15	G14	4-[(4-(2-pyridyl)piperazinyl)carbonyl]-2-hydrophthalazin-1-one	YES
15	H14	N-(1-oxo(3-hydroisobenzofuran-5-yl))(4-oxo(3-hydrophthalazinyl))carboxamide	No
15	I14	N-(1-methylbenzimidazol-2-yl)(4-oxo(3-hydrophthalazinyl))carboxamide	YES
15	J14	{[4-amino-6-(dimethylamino)(1,3,5-triazin-2-yl)]methyl}(4-fluorophenyl)(methyl sulfonyl)amine	No
15	K14	5-(2H,3H,4H,5H-benzo[f]azepinylsulfonyl)-3-methyl-3-hydrobenzoxazol-2-one	YES
15	L14	5-{[(1,3-dimethyl-2-oxo(3-hydrobenzimidazol-5-yl))amino]sulfonyl}-3-methyl-3-h ydrobenzoxazol-2-one	YES
15	M14	5-(2H,3H-benzo[e]1,4-oxazin-4-ylsulfonyl)-3-methyl-3-hydrobenzoxazol-2-one	No
15	N14	5-({[(1,3-dimethyl-2-oxo(3-hydrobenzimidazol-5-yl))methyl]amino}sulfonyl)-3-me thyl-3-hydrobenzoxazol-2-one	No
15	O14	3-methyl-5-({[3-(pyrrolidinylsulfonyl)phenyl]amino}sulfonyl)-3-hydrobenzoxazol -2-one	No
15	P14	3-methyl-5-({[1-(methylsulfonyl)indolin-5-yl]amino}sulfonyl)-3-hydrobenzoxazol -2-one	No
15	A15	3-methyl-5-[(3-oxo(1,2,4-trihydroquinoxalinyl))sulfonyl]-3-hydrobenzoxazol-2-o ne	No
15	B15	5-{[(2,2-dimethylbenzo[d]1,3-dioxolan-5-yl)amino]sulfonyl}-3-methyl-3-hydroben zoxazol-2-one	No
15	C15	3-methyl-5-[(1,2,3,4-tetrahydronaphthylamino)sulfonyl]-3-hydrobenzoxazol-2-one	No
15	D15	3-[2-oxo-2-(3-oxo(1,2,4-trihydroquinoxalinyl))ethyl]-3-hydrobenzoxazol-2-one	No
15	E15	4-{[4-amino-6-(dimethylamino)(1,3,5-triazin-2-yl)]methyl}-1-(2-chlorophenyl)-1 ,2,3,4-tetraazolin-5-one	No
15	F15	3-{[4-(tert-butyl)phenyl]methylthio}-4-methyl-5-(2-thienyl)-1,2,4-triazole	No
15	G15	1-(1,2,3,4-tetraazolyl)-4-[(4-(1,2,3,4-tetraazolyl)phenyl)sulfonyl]benzene	No
15	H15	4-(2-bromophenyl)-1,2,4-triazole	No
15	I15	3-{[(7-methoxy-2-oxochromen-4-yl)methyl]methylamino}propanenitrile	YES
15	J15	7-methoxy-4-(morpholin-4-ylmethyl)chromen-2-one	YES
15	K15	3-{4-[(2S,4S,5S,3R,6R)-3,4,5-trihydroxy-6-(hydroxymethyl)(2H-3,4,5,6-tetrahydr opyran-2-yloxy)]phenyl}-5,7-dihydroxychromen-4-one	YES

15	L15	spiro[2-hydrocyclopenta[1,2-a]benzene-2,6'-8,9,10,11,4a-pentahydro-4aH-benzo[1 ,2-d]pyridino[2,1-b]1,3-oxazine]-1,3,16-trione	YES
15	M15	2,2,5-trimethylpiperidin-3-one	No
15	N15		No
15	O15	5-(4,5-diphenylimidazol-2-yl)-2-[(3-fluorophenyl)methoxy]-1-iodo-3-methoxybenz ene	No
15	P15	6H,11H,5aH-benzo[b]chromeno[2,3-e]1,4-diazepin-13-one	No
15	A16	(4-methyl-5-sulfanyl(1,2,4-triazol-3-yl))phenylmethan-1-ol	No
15	B16	di7-chloro(4-quinolyl) disulfide	No
15	C16	1,3,6-trimethyl-5-nitro-1,3-dihydropyrimidine-2,4-dione	No
15	D16	morpholin-4-yl 3,4,5-trimethoxyphenyl ketone	No
15	E16	3-prop-2-enyl-2-sulfanyl-3-hydroquinazolin-4-one	No
15	F16	4-cyclohexyl-5-phenyl-1,2,4-triazole-3-thiol	No
15	G16	5,6-dimethylbenzimidazole-2-thiol	No
15	H16	ethyl (2Z)-2-cyano-3-(2-furyl)prop-2-enoate	YES
15	I16	1-(methylsulfonyl)-6,8-dinitro-1,2,3,4-tetrahydroquinoline	No
15	J16	5-chloro-1,3-dimethyl-6-nitro-3-hydrobenzimidazol-2-one	No
15	K16	phenazine-2,5,10-triol	No
15	L16	benzo[a]phenazine-7,12-diol	No
15	M16	5-phenyl-1H-1,2,4-triazole-3-thiol	No
15	N16	(2-naphthylsulfonyl)indoline	No
15	O16	5-chloro-2-{[4-(4-phenyl(1,3-thiazol-2-yl))piperazinyl]sulfonyl}thiophene	No
15	P16	3-[(3-methylquinoxalin-2-yl)methyl]-3-hydrobenzoxazol-2-one	No
15	A17	4-[9-(4-fluorophenyl)-2,3-dimethoxypyrazino[2,1-a]isoquinolin-11-yl]-1,2-dimet hoxybenzene	No
15	B17	4-[(6-bromo-1,2,3,4-tetrahydroquinolyl)carbonyl]-2-hydrophthalazin-1-one	No
15	C17	adamantanyl piperazinyl ketone	No
15	D17	5-{[(adamantanylmethyl)methylamino]sulfonyl}-3-hydrobenzothiazol-2-one	No
15	E17	(adamantanylmethyl)[(4-methoxy-3-(1,2,3,4-tetraazolyl)phenyl)sulfonyl]methylam ine	No
15	F17	(adamantanylmethyl)[(5-bromo(2-thienyl))sulfonyl]methylamine	No
15	G17	methyl 6-{[(adamantanylmethyl)methylamino]sulfonyl}-1,2,3,4-tetrahydroquinolin ecarboxylate	YES
15	H17	2-{[5-(5-methyl-2-furyl)-1,3,4-oxadiazol-2-yl]methoxy}dibenzo[b,d]furan	No
15	I17	cyclopentyl-N-(4,5,6,7,8-pentahydrocyclohepta[1,2-d]1,3-thiazol-2-yl)carboxami de	No
15	J17	(2-methyl(3-furyl))-N-(4,5,6,7,8-pentahydrocyclohepta[1,2-d]1,3-thiazol-2-yl)c arboxamide	YES

15	K17	(2,2-dichloro-1-methylcyclopropyl)-N-(4,5,6,7,8-pentahydrocyclohepta[1,2-d]1,3 -thiazol-2-yl)carboxamide	YES
15	L17	3-cyclohexyl-N-(4,5,6,7,8-pentahydrocyclohepta[1,2-d]1,3-thiazol-2-yl)propanam ide	No
15	M17	1,3-dimethyl-1,3,5-trihydrofurano[3,4-d]pyrimidine-2,4,7-trione	No
15	N17	2-(trifluoromethyl)benzimidazole-5-ylamine	No
15	O17	2H,3H-benzo[e]1,4-dioxan-2-ylmethylamine	No
15	P17	(4-(2H-benzo[3,4-d]1,3-dioxolen-5-yloxy)phenyl)[(dimethylamino)sulfonyl]amine	No
15	A18	[(4-fluoren-9-ylpiperazinyl)sulfonyl]dimethylamine	No
15	B18	(adamantanylmethyl)[(dimethylamino)sulfonyl]methylamine	No
15	C18	(2-methyl(3-furyl))-N-(5-propyl(1,3,4-thiadiazol-2-yl))carboxamide	No
15	D18	N-(1-carbamoyl-3-methylbutyl)cyclopentylcarboxamide	No
15	E18	benzo[b]thiophen-2-yl-N-(oxolan-2-ylmethyl)carboxamide	No
15	F18	2-bicyclo[2.2.1]hept-2-yl-1-(4-(2-pyridyl)piperazinyl)ethan-1-one	No
15	G18	2-methyl-6-{[(oxolan-2-ylmethyl)amino]sulfonyl}-2H,4H-benzo[e]1,4-oxazin-3-one	YES
15	H18	6-methoxy-2H-benzo[d]1,3-dioxolene-5-ylamine	No
15	I18	5-nitro-2,6-dioxo-1,3-dihydropyrimidine-4-carboxylic acid	No
15	J18	(2S)-7-[(2S,4S,5S,3R,6R)-3-((2S,6S,3R,4R,5R)-3,4,5-trihydroxy-6-methyl(2H-3,4, 5,6-tetrahydropyran-2-yloxy))-4,5-dihydroxy-6-(hydroxymethyl)(2H-3,4,5,6-tetra hydropyran-2-yloxy)]-5-hydroxy-2-(4-hydroxyphenyl)chroman-4-one	YES
15	K18	2-amino-3-(6-fluoroindol-3-yl)propanoic acid	No
15	L18	3-{6-[((6S,2R,3R,4R,5R)-3,4,5-trihydroxy-6-methyl(2H-3,4,5,6-tetrahydropyran-2 -yloxy))methyl](2S,4S,5S,3R,6R)-3,4,5-trihydroxy(2H-3,4,5,6-tetrahydropyran-2- yloxy)}-2-(2,3-dihydroxyphenyl)-5,7-dihydroxychromen-4-one	No
15	M18	(2E,6E)-3,7,11-trimethyldodeca-2,6,10-trien-1-ol	No
15	N18	(1S,2S,5S,7S,11S,15S,10R)-5-hydroxy-2,15-dimethyltetracyclo[8.7.0.0<2,7>.0<11, 15>]heptadecan-14-one	No
15	O18	(1S,9R)-6,10,10-trimethyl-2-methylenebicyclo[7.2.0]undec-5-ene	No
15	P18	3-(4-chlorophenyl)-4,6-dimethylchromen-2-one	YES
15	A19		No
15	B19	(2R)-2,4-dihydroxy-N-(3-hydroxypropyl)-3,3-dimethylbutanamide	No
15	C19	4-((1S,2S,5S,11S,7R,10R,14R,15R)-5-{5-[5-((2S,4S,5S,6R)-4,5-dihydroxy-6-methyl (2H-3,4,5,6-tetrahydropyran-2-yloxy))(4S,5S,2R,6R)-4-hydroxy-6-methyl(2H-3,4,5 ,6-tetrahydropyran-2-yloxy)](4S,5S,2R,6R)-4-hydroxy-6-methyl(2H-3,4,5,6-tetrah ydropyran-2-yloxy)}-11-hydroxy-2,15-dimethyltetracyclo[8.7.0.0<2,7>.0<11,15>]h eptadec-14-yl)-5-hydrofuran-2-one	No
15	D19	2-({4-[(7-chloro(4-quinolyl))amino]pentyl}ethylamino)ethan-1-ol	No

15	E19	1-[(1S,2R,3R,5R)-2-hydroxy-7-(trichloromethyl)-4,6,8-trioxabicyclo[3.3.0]oct-3 -yl]ethane-1,2-diol	No
15	F19	2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)chroman-6-yl acetate	No
15	G19	(9Z,12Z,15Z)octadeca-9,12,15-trienoic acid	No
15	H19	(2S)-3-[(tert-butyl)amino]-1-(4-morpholin-4-yl(1,2,5-thiadiazol-3-yl)oxy)propa n-2-ol	YES
15	I19	2-[(3S,4S,2R,5R)-2,5-bis(hydroxymethyl)-4,5-dihydroxyoxolan-3-yloxy](2S,4S,3R, 5R,6R)-6-(hydroxymethyl)-2H-3,4,5,6-tetrahydropyran-3,4,5-triol	No
15	J19	1-cyclopropyl-7-(4-ethylpiperazinyl)-6-fluoro-4-oxohydroquinoline-3-carboxylic acid	No
15	K19		No
15	L19	8-ethyl-5-oxo-2-piperazinyl-8-hydropyridino[2,3-d]pyrimidine-6-carboxylic acid	No
15	M19	1-ethyl-6,8-difluoro-7-(3-methylpiperazinyl)-4-oxohydroquinoline-3-carboxylic acid	No
15	N19	1-ethyl-6-fluoro-4-oxo-7-piperazinylhydroquinoline-3-carboxylic acid	No
15	O19	6-fluoro-4-oxochromene-3-carboxylic acid	No
15	P19	4-(indolinylcarbonyl)-1-methylpyrrolidin-2-one	No
15	A20	2-benzo[3,4-d]benzo[b]furan-2-yloxyethylamine	No
15	B20	2-(3,5-dimethyladamantanyl)-1-[4-(methylsulfonyl)piperazinyl]ethan-1-one	No
15	C20	4-{2-[4-(2-adamantanylacetyl)piperazinyl]ethyl}-4-azatricyclo[5.2.1.0<2,6>]dec ane-3,5-dione	No
15	D20	2-adamantanyl-N-[5-(tert-butyl)(1,3,4-thiadiazol-2-yl)]acetamide	No
15	E20	1-adamantanylbenzimidazole-2-thiol	No
15	F20	2-adamantanyl-4,5-dimethoxyphenylamine	No
15	G20	6-[(adamantan-2-ylamino)sulfonyl]-2-methyl-2H,4H-benzo[e]1,4-oxazaperhydroin-3 -one	No
15	H20	2-(1-cyclohexyl-2,5-dioxo(1,3-diazolidin-4-yl))-N-spiro[benzo[d]1,3-dioxolane- 2,1'-cyclohexane]-5-ylacetamide	No
15	I20	(6-oxo(3-hydropyridyl))-N-spiro[benzo[d]1,3-dioxolane-2,1'-cyclohexane]-5-ylca rboxamide	No
15	J20	6-{[(3-imidazolylpropyl)amino]sulfonyl}-2-methyl-2H,4H-benzo[e]1,4-oxazaperhyd roin-3-one	No
15	K20	1-[4-(4-methoxyphenyl)(1,3-thiazol-2-yl)]-4-(pyrrolidinylsulfonyl)piperazine	YES
15	L20	1,8-bis{[5-(4-methylphenyl)(1,3,4-oxadiazol-2-yl)]methylthio}octane	No
15	M20	2-[2-(2,3-dioxobenzo[d]azolinyl)ethyl]benzo[c]azolidine-1,3-dione	No
15	N20	3-(2-naphthyl)-6-[(3-phenylpyrrolidinyl)methyl]spiro[1,3-thiazolidine-2,3'-ind oline]-4,7-dione	No

15	O20	11-methylspiro[2-hydrocyclopenta[1,2-a]benzene-2,6'-8,9,10,11,4a-pentahydro-4a H-benzo[1,2-d]pyridino[2,1-b]1,3-oxazine]-1,3,16-trione	No
15	P20	1-[(3,5-dimethylphenyl)amino]ethene-1,2,2-tricarbonitrile	No
15	A21	2-fluoro-5H-dibenzo[c,f]azepine-6,11-dione	No
15	B21	2H-benzo[d]1,3-dioxolen-5-yl(methylsulfonyl)amine	No
15	C21	2-(1-phenylpyrazol-4-yl)ethylamine	No
15	D21	1-(3-(3-pyridyl)-1,2,4-oxadiazol-5-yl)ethylamine	No
15	E21	5-oxo-1-(oxolan-2-ylmethyl)pyrrolidine-3-carboxylic acid	No
15	F21	3-methyl-4-oxo-5,6,7-trihydroindole-2-carboxylic acid	YES
15	G21	3,3-bis(4-hydroxyphenyl)-3-hydroisobenzofuran-1-one	YES
15	H21	5,7-dihydroxy-4-propylchromen-2-one	YES
15	I21	2-phenyl-6-hydro-1,2,3-triazolo[4,5-d]pyrimidin-7-one	No
15	J21	4-pyrrolidinyl-3-(trifluoromethyl)phenylamine	YES
15	K21	1-[(5-chloro-2-thienyl)sulfonyl]pyrrolidine-2-carboxylic acid	YES
15	L21	1,2,3-trimethoxy-5-{5-[(5-phenyl(1,3,4-oxadiazol-2-ylthio))methyl](1,3,4-oxadi azol-2-yl)}benzene	No
15	M21	N-(10-cyano(9-1,2,3,4,5,6,7,8-octahydrophenanthryl))-2-(1-methylimidazol-2-ylt hio)acetamide	No
15	N21		No
15	O21	3-hydroxy-3-(2-oxocycloheptyl)indolin-2-one	No
15	P21	5-bromo-3-hydroxy-3-(2-oxocyclohexyl)indolin-2-one	No
15	A22	3-(2-naphthylazamethylene)-1-[(4-phenylpiperazinyl)methyl]benzo[d]azolin-2-one	No
15	B22	N-(3-cyano-4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl)acetamide	No
15	C22	2-benzimidazol-2-yl-3-methylbut-2-enenitrile	No
15	D22	1,2-dimethyl-5,6-dinitrobenzimidazole	No
15	E22	1H-1,2,4-triazol-5-yl(2H-benzo[3,4-d]1,3-dioxolen-5-ylmethyl)amine	No
15	F22	2H-1,2,3,4-tetraazol-5-yl[(2,6-dichlorophenyl)methyl]amine	No
15	G22	23-ethylspiro[dibenzo[a,h]xanthene-14,3'-indoline]-24-one	No
15	H22	6-(2H-benzo[d]1,3-dioxolan-5-yl)-4-(4-methylthiophenyl)-2-oxohydropyridine-3-c arbonitrile	No
15	I22	(phenylamino)-N-[4-(N-phenylcarbamoyl)-1-thia-3,4-diazaspiro[4.4]non-2-en-2-yl]carboxamide	No
15	J22	N-[8-(tert-butyl)-4-(N-phenylcarbamoyl)-1-thia-3,4-diazaspiro[4.5]dec-2-en-2-y l](phenylamino)carboxamide	No
15	K22	(9Z)octadec-9-enylamine	No
15	L22	(2S,4S,3R,5R,6R)-6-(hydroxymethyl)-2-(2-naphthyloxy)-2H-3,4,5,6-tetrahydropyra n-3,4,5-triol	No
15	M22	(2R)-2-((4R,8R)-4,8,12-trimethyltridecyl)-2,5,7,8-tetramethylchroman-6-ol	No
15	N22	5-(1,2-dithiolan-3-yl)pentanoic acid	No

15	O22	2-[(3,4,5-trihydroxy-2H-3,4,5,6-tetrahydropyran-2-yl)amino]-2H-3,4,5,6-tetrahy dropyran-3,4,5-triol	No
15	P22		No
Plate	**Well**	**IUPAC NAME**	**Inhibitor Y/N**
16	A03	14-((2E)(1R,4R)-1,4,5-trimethylhex-2-enyl)(1S,5S,2R,11R,14R,15R)-2,15-dimethyl tetracyclo[8.7.0.0<2,7>.0<11,15>]heptadeca-7,9-dien-5-ol	No
16	B03	3-methylisoxazole-5-carboxylic acid	No
16	C03	6-methylthiopurine	No
16	D03	5-methyl-5-azabicyclo[4.4.0]dec-2-ylamine	No
16	E03	5-(2-furylmethylene)-3-(3-methoxypropyl)-2-thioxo-1,3-thiazolidin-4-one	No
16	F03	3-(2-methoxyethyl)-5-(2-thienylmethylene)-2-thioxo-1,3-thiazolidin-4-one	No
16	G03	2-(2-oxo-2-(2-5,6,7,8-tetrahydronaphthyl)ethyl)-2,5,6,7,7a-pentahydro-2-azapyr rolizine-1,3-dione	No
16	H03	2-imidazol-5-ylethylamine	No
16	I03	3-indolinylpropylamine	No
16	J03	4-(4-methylpiperazinyl)butylamine	YES
16	K03	1-(piperidylmethyl)cyclohexylamine	No
16	L03	2-methyl-1-(4-methylpiperazinyl)prop-2-ylamine	No
16	M03	1-methyl-2,7-diazabicyclo[5.3.0]decan-8-one	No
16	N03	(3-propylisoxazol-5-yl)methylamine	No
16	O03	phenyl-3-pyridylmethylamine	No
16	P03	(5-chlorobenzimidazol-2-yl)methylamine	No
16	A04	2-[3-(aminomethyl)piperidyl]ethan-1-ol	No
16	B04	2-methyl-1-(2-(4-piperidyl)ethyl)imidazole	No
16	C04	4-imidazolylbutylamine	No
16	D04	4-[(methylamino)methyl]quinolin-2-ol	No
16	E04	2-(4-piperidylmethoxy)pyridine	No
16	F04	(isochromanylmethyl)methylamine	No
16	G04	2-(1-methylbenzimidazol-2-yl)ethylamine	No
16	H04	1-ethylbenzimidazole-2-ylamine	No
16	I04	4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylic acid	No
16	J04	1-methyl-6-oxo-1,4,5-trihydropyridazine-3-carboxylic acid	No
16	K04	1,1-dioxothiolane-3-carboxylic acid	No
16	L04	[(5-bromo(2-thienyl))sulfonyl](2-cyclohex-2-enylethyl)amine	No
16	M04	3,6-dihydroxy-2-(3-hydroxyphenyl)chromen-4-one	No
16	N04	(3-methyl-1H-1,2,4-triazol-5-yl)methylamine	No
16	O04	(3,5-dimethylphenyl)[(5-bromo(2-thienyl))sulfonyl]amine	No
16	P04	leucine	No
16	A05	(2R)-2-aminopentanedioic acid	No

16	B05	(2R)-2-amino-3-(carboxymethylthio)propanoic acid	No
16	C05	alpha-D-fructopyranose	No
16	D05	2-(2-butoxyethoxy)-1-[(6-propyl(2H-benzo[d]1,3-dioxolen-5-yl))methoxy]ethane	No
16	E05	2-{(2S,3S,14S,1R,4R,8R,15R)-2-[5-(4,5-dihydroxy-4,6-dimethyl(2H-3,4,5,6-tetrah ydropyran-2-yl)oxy)-4-(dimethylamino)-3-hydroxy-6-methyl(2H-3,4,5,6-tetrahydro pyran-2-yl)oxy]-14-[5-(dimethylamino)-6-methyl(2H-3,4,5,6-tetrahydropyran-2-yl)oxy]-4-hydroxy-3-methoxy-8,15-dimethyl-6-oxo-7-oxacyclohexadeca-10,12-dienyl} ethanal	No
16	F05	2-sulfanylpyrimidin-4-ol	No
16	G05	2-[N-(adamantanylmethyl)-2-thienylcarbonylamino]ethyl thiophene-2-carboxylate	No
16	H05	2-[N-(adamantanylmethyl)-2-furylcarbonylamino]ethyl furan-2-carboxylate	No
16	I05	3-benzo[d]benzo[3,4-b]furan-3-ylspiro[1,2,3-trihydroquinazoline-2,3'-indoline] -4,12-dione	No
16	J05	3-benzo[d]benzo[3,4-b]furan-3-yl-5-methyl-6-(morpholin-4-ylmethyl)spiro[1,3-th iazolidine-2,3'-indoline]-4,7-dione	No
16	K05	2-adamantanyl-5-(2-pyridylmethylthio)-1,3,4-oxadiazole	No
16	L05	3-(2-oxo-2-(2-pyridyl)ethylthio)-4-phenyl-1,2,4-triazolin-5-one	No
16	M05	(5-adamantanyl-2-methyl(3-furyl))-N-(oxolan-2-ylmethyl)carboxamide	No
16	N05	1-(benzo[c]1,2,5-thiadiazol-5-ylmethoxy)-5-methyl-2-(methylethyl)-4-(1,2,3,4-t etraazolyl)benzene	No
16	O05	2-(benzo[c]1,2,5-thiadiazol-5-ylmethylthio)pyrimidine	No
16	P05	1,2,3-trimethoxy-5-[5-(pyrimidin-2-ylthiomethyl)(1,3,4-oxadiazol-2-yl)]benzene	No
16	A06	N-(2-oxo(3-3,4,5-trihydrothienyl))-2-pyrimidin-2-ylthioacetamide	No
16	B06	N-(adamantanylmethyl)-2-(3,5-dimethyladamantanyl)acetamide	No
16	C06	3-[(benzo[3,4-c]1,2,5-thiadiazol-5-ylmethylthio)methyl]-1,2,4-triazolin-5-one	No
16	D06	4-(benzo[3,4-c]1,2,5-thiadiazol-5-ylmethylthio)quinazoline	No
16	E06	N-(4-{[(5-oxo-1,2,4-triazolin-3-yl)methylthio]methyl}-1,3-thiazol-2-yl)acetami de	No
16	F06	5-{[5-(1,5-dimethylpyrrol-2-yl)(1,3,4-oxadiazol-2-yl)]methylthio}-2-phenyl-1,3 ,4-oxadiazole	No
16	G06	5-adamantanyl-2-methylfuran-3-carboxylic acid	No
16	H06	N-(adamantanylmethyl)-2-(1-cyclohexyl-2,5-dioxo(1,3-diazolidin-4-yl))acetamide	No
16	I06	2-(isoxazol-3-ylmethylthio)-6-methylpyrimidin-4-ol	No
16	J06	2-(isoxazol-3-ylmethylthio)-3-(2-naphthyl)-3-hydroquinazolin-4-one	No
16	K06	6-ethoxy-2-(isoxazol-3-ylmethylthio)benzothiazole	No

16	L06	2-(isoxazol-3-ylmethylthio)-3-methyl-3,5,6,7-tetrahydrocyclopenta[1,2-b]pyrimi dino[5,4-d]thiophen-4-one	No
16	M06	2-(3-bromophenyl)-5-(isoxazol-3-ylmethylthio)-1,3,4-oxadiazole	No
16	N06	5,7-dichloro-2-(isoxazol-3-ylmethylthio)-6-methylbenzoxazole	No
16	O06	2-(isoxazol-3-ylmethylthio)-4,5-diphenylimidazole	No
16	P06	1-[5-(isoxazol-3-ylmethylthio)-4-methyl(1,2,4-triazol-3-yl)]-4-methoxybenzene	No
16	A07	5,8-dimethoxy-4-methyl-2-{[5-(4-methylphenyl)(1,3,4-oxadiazol-2-yl)]methylthio }quinoline	No
16	B07	adamantanyl 4-(2-thienylcarbonyl)piperazinyl ketone	No
16	C07	adamantanyl 4-(cyclopropylcarbonyl)piperazinyl ketone	No
16	D07	2-[1-cyclopropyl-5-(trifluoromethyl)benzimidazol-2-ylthio]-1-indan-5-ylpropan- 1-one	No
16	E07	N-(2-oxo(3-3,4,5-trihydrothienyl))-2-quinazolin-4-ylthioacetamide	No
16	F07	2-(5,7-dichloro-6-methylbenzoxazol-2-ylthio)-1-indan-5-ylpropan-1-one	No
16	G07	2-[(2-cyclohexyl(1,3-thiazol-4-yl))methylthio]-3-methyl-3,5,6,7,8-pentahydrobe nzo[b]thiopheno[2,3-d]pyrimidin-4-one	No
16	H07	6-(benzo[3,4-c]1,2,5-thiadiazol-5-ylmethoxy)-1,2,3,4-tetrahydronaphthalene	No
16	I07	adamantanyl 4-(methylsulfonyl)piperazinyl ketone	No
16	J07	adamantanyl 4-[(5-bromo(2-thienyl))sulfonyl]piperazinyl ketone	No
16	K07	N-(adamantanylmethyl)(5-oxopyrrolidin-2-yl)carboxamide	No
16	L07	2-(isoxazol-3-ylmethyl)-2-hydrophthalazin-1-one	No
16	M07	(5-adamantanyl-2-methyl(3-furyl))-N-(5,7,8-trimethyl-3-oxo(2H,4H-benzo[3,4-e]1 ,4-oxazin-6-yl))carboxamide	No
16	N07	1,2,3-trimethoxy-5-[5-(quinazolin-4-ylthiomethyl)(1,3,4-oxadiazol-2-yl)]benzen e	No
16	O07	3-(4-chlorophenoxy)propane-1,2-diol	No
16	P07	3-((2E)-3,7,11,15-tetramethylhexadec-2-enyl)-2-methylnaphthalene-1,4-dione	No
16	A08	(2S,4S,5S,3R)-2,5-bis(3-pyridylcarbonyloxymethyl)-2-hydroxy-4-(3-pyridylcarbon yloxy)oxolan-3-yl pyridine-3-carboxylate	No
16	B08	2-[(1E,3E)-5-(3-ethyl(3-hydrobenzothiazol-2-ylidene))penta-1,3-dienyl]-3-ethyl benzothiazole, iodide	No
16	C08	4-((1S,2S,7S,11S,10R,14R,15R)-2,15-dimethyl-5,9,16-trioxotetracyclo[8.7.0.0<2, 7>.0<11,15>]heptadec-14-yl)pentanoic acid	No
16	D08	2-propylpentanamide	No
16	E08	(2S,6R)-4,8-dioxabicyclo[3.3.0]octane-2,6-diol	No
16	F08	(4R)-1,3-thiazolidine-4-carboxylic acid	No
16	G08	3-pyridylmethan-1-ol	No

16	H08	(1S,6S,5R,7R)-7-hydroxy-6-(hydroxymethyl)-2-oxabicyclo[3.3.0]octan-3-one	No
16	I08	6-(2-{(4S,2R,3R,5R)-4-[(5S,6S,2R,3R,4R)-3-amino-6-(aminomethyl)-4,5-dihydroxy(2H-3,4,5,6-tetrahydropyran-2-yloxy)]-3-hydroxy-5-(hydroxymethyl)oxolan-2-yloxy }(3S,6S,1R,2R,4R)-4,6-diamino-3-hydroxycyclohexyloxy)(3S,2R,4R,5R,6R)-5-amino- 2-(aminomethyl)-2H-3,4,5,6-tetrahydropyran-3,4-diol	No
16	J08	(2S,10S,11S,13S,15S,17S,1R,14R)-1-fluoro-17-hydroxy-14-(2-hydroxyacetyl)-2,13, 15-trimethyl-5-oxotetracyclo[8.7.0.0<2,7>.0<11,15>]heptadeca-3,6-dien-14-yl pe ntanoate	No
16	K08	2-((1S,10S,11S,15S,2R,14R)-14-hydroxy-2,15-dimethyl-5,17-dioxotetracyclo[8.7.0 .0<2,7>.0<11,15>]heptadec-6-en-14-yl)-2-oxoethyl acetate	No
16	L08	(1S,2S,3S,12S,16S,5R,11R,15R)-15-acetyl-9-chloro-2,16-dimethyl-6-oxopentacyclo [9.7.0.0<2,8>.0<3,5>.0<12,16>]octadeca-7,9-dien-15-yl acetate	No
16	M08	(1S,11S,15S,2R,10R,14R)-14-acetyl-8-chloro-2,15-dimethyl-5-oxotetracyclo[8.7.0 .0<2,7>.0<11,15>]heptadeca-6,8-dien-14-yl acetate	No
16	N08	2-((2S,10S,11S,15S,17S,1R,13R,14R)-1-fluoro-14,17-dihydroxy-2,13,15-trimethyl- 5-oxotetracyclo[8.7.0.0<2,7>.0<11,15>]heptadeca-3,6-dien-14-yl)-2-oxoethyl ace tate	No
16	O08	3-(4-phenylpiperazinyl)propane-1,2-diol	No
16	P08	(2S,3S,4S,5S)-1,6-dibromohexane-2,3,4,5-tetraol	No
16	A09	2-((1S,10S,11S,14S,15S,2R)-2,15-dimethyl-5-oxotetracyclo[8.7.0.0<2,7>.0<11,15>]heptadec-6-en-14-yl)-2-oxoethyl acetate	No
16	B09	(1S,11S,14S,15S,10R)-5-hydroxy-15-methyltetracyclo[8.7.0.0<2,7>.0<11,15>]hepta deca-2,4,6-trien-14-yl pentanoate	No
16	C09	(1S,11S,14S,15S,10R)-5-hydroxy-15-methyltetracyclo[8.7.0.0<2,7>.0<11,15>]hepta deca-2,4,6-trien-14-yl 3-cyclopentylpropanoate	No
16	D09	4-(dimethylamino)-2-[9-ethyl-2,7,8-trihydroxy-13-(5-hydroxy-4-methoxy-4,6-dime thyl(2H-3,4,5,6-tetrahydropyran-2-yloxy))-2,4,6,8,12,14-hexamethyl-5,11-dioxo- 10-oxacyclotetradecyloxy]-6-methyl(2H-3,4,5,6-tetrahydropyran-3-yl) ethyl buta ne-1,4-dioate	No
16	E09	3-{[2-((1S,10S,11S,15S,17S,2R,14R)-14,17-dihydroxy-2,15-dimethyl-5-oxotetracyc lo[8.7.0.0<2,7>.0<11,15>]heptadec-6-en-14-yl)-2-oxoethyl]oxycarbonyl}propanoic acid	No
16	F09	(1S,10S,11S,15S,17S,2R,14R)-17-hydroxy-14-(2-hydroxyacetyl)-2,15-dimethyl-5-ox	No

		otetracyclo[8.7.0.0<2,7>.0<11,15>]heptadec-6-en-14-yl butanoate	
16	G09	(1S,10S,11S,15S,17S,2R,14R)-17-hydroxy-14-(2-hydroxyacetyl)-2,15-dimethyl-5-ox otetracyclo[8.7.0.0<2,7>.0<11,15>]heptadec-6-en-14-yl pentanoate	No
16	H09	(1S,11S,15S,2R,10R,14R)-14-acetyl-2,15-dimethyl-5-oxotetracyclo[8.7.0.0<2,7>.0 <11,15>]heptadec-6-en-14-yl hexanoate	No
16	I09	(1S,11S,15S,2R,10R,14R)-14-ethynyl-15-methyl-5-oxotetracyclo[8.7.0.0<2,7>.0<11 ,15>]heptadec-6-en-14-yl acetate	No
16	J09	1-{3-imidazol-5-yl-2-[(5-oxopyrrolidin-2-yl)carbonylamino]propanoyl}pyrrolidin e-2-carboxamide	No
16	K09		No
16	L09	2-((1S,10S,11S,15S,17S,2R,14R)-14,17-dihydroxy-2,15-dimethyl-5-oxotetracyclo[8 .7.0.0<2,7>.0<11,15>]heptadeca-3,6-dien-14-yl)-2-oxoethyl acetate	No
16	M09	[(4S,6S,12aS,4aS,5aS)-4-(dimethylamino)-3,6,10,12,12a-pentahydroxy-6-methyl-1, 11-dioxo(4,5,6,12a,4a,5a-hexahydronaphthacen-2-yl)]-N-(pyrrolidinylmethyl)carb oxamide	No
16	N09		No
16	O09	(2R)-2-amino-3-[4-(4-hydroxy-3,5-diiodophenoxy)-3,5-diiodophenyl]propanoic aci d	No
16	P09	4-(2-fluorophenyl)-1-(piperidylsulfonyl)piperazine	No
16	A10	naphthyl(piperidylsulfonyl)amine	No
16	B10	1-{4-[(piperidylsulfonyl)amino]phenyl}pyrrolidin-2-one	No
16	C10	N-methyl{4-oxo-3-[(2-oxo(4-hydroquinolyl))methyl](3-hydrophthalazinyl)}carboxa mide	No
16	D10	N-adamantanyl(1-methyl-5-oxopyrrolidin-3-yl)carboxamide	No
16	E10	3-[(2-oxo-4-hydroquinolyl)methyl]-3,5,6,7-tetrahydrocyclopenta[2,1-d]pyrimidin o[4,5-b]thiophen-4-one	No
16	F10	2-[(adamantanylmethyl)dimethylamino]-1-(4-bromophenyl)ethan-1-one	No
16	G10	3-{[5-(5-methyl-2-furyl)-1,3,4-oxadiazol-2-yl]methylthio}thiolane-1,1-dione	No
16	H10	3-[2-oxo-2-(3-oxo(1,2,4-trihydroquinoxalinyl))ethylthio]thiolane-1,1-dione	No
16	I10	[(6,7-dimethoxyisoquinolyl)(3,4-dimethoxyphenyl)methyl](methylsulfonyl)amine	No
16	J10	3-benzo[d]benzo[3,4-b]furan-3-yl-11-methylspiro[1,2,3-trihydroquinazoline-2,3' -indoline]-4,12-dione	No
16	K10	2-octylcyclopropanecarboxylic acid	No
16	L10	2-(2H-3,4,5,6-tetrahydropyran-2-yl)acetic acid	No
16	M10	6-aminohexanoic acid	No

16	N10	2-aminobutanedioic acid	No
16	O10	(2S)-2-amino-5-[(aminothioxomethyl)amino]pentanoic acid	No
16	P10	2-(trimethylamino)ethyl acetate, chloride	No
16	A11	[5-(6-aminopurin-9-yl)-3,4-dihydroxyoxolan-2-yl]methyl hydrogen (phosphonooxy) (hydroxyphosphoryl) phosphate	No
16	B11	3-{[(2R)-2-((4R,8R)-4,8,12-trimethyltridecyl)-2,5,7,8-tetramethylchroman-6-yl] oxycarbonyl}propanoic acid	No
16	C11	(4R)-2-oxo-1,3-thiazolidine-4-carboxylic acid	No
16	D11	(1,1-dimethyl-2-phenylethyl)methylamine	No
16	E11	1-[10-(4-amino-2-methylquinolyl)decyl]-2-methyl-4-quinolylamine	No
16	F11	4-(4-amino-6,7-dimethoxyquinazolin-2-yl)piperazinyl 2-furyl ketone	No
16	G11	5,5-dimethyl-3-[4-nitro-3-(trifluoromethyl)phenyl]-1,3-diazolidine-2,4-dione	No
16	H11	3-(5-fluorobenzimidazol-2-yl)propylamine	No
16	I11	3-cyclohexylisoxazole-5-carboxylic acid	No
16	J11	ethyl 5-(ethoxycarbonyl)-2,6-dimethyl-1,4-dihydropyridine-3-carboxylate	No
16	K11	hydroquinolin-2-one	No
16	L11	2,6-bis(tert-butyl)-4-{1-[3,5-bis(tert-butyl)-4-hydroxyphenylthio]-isopropylth io}phenol	No
16	M11	1,3,4-trimethylpyrazolo[5,4-d]pyrimidine	No
16	N11	4-(methoxymethyl)-6-methylpyrazolo[5,4-b]pyridine-3-ylamine	No
16	O11	5-propyl-1,3,4-thiadiazole-2-ylamine	No
16	P11	1-(4-{[(bicyclo[2.2.1]hept-2-ylmethyl)amino]sulfonyl}phenyl)pyrrolidin-2-one	No
16	A12	6-{[(bicyclo[2.2.1]hept-2-ylmethyl)amino]sulfonyl}-2H,4H-benzo[e]1,4-oxazaperh ydroin-3-one	No
16	B12	6-{[(bicyclo[2.2.1]hept-2-ylmethyl)amino]sulfonyl}-5-chloro-3-methyl-3-hydrobe nzoxazol-2-one	No
16	C12	6-{[(bicyclo[2.2.1]hept-2-ylmethyl)amino]sulfonyl}-7-methyl-2H,4H-benzo[e]1,4- oxazin-3-one	No
16	D12	methyl 5-bromobenzo[d]furan-2-carboxylate	No
16	E12	dibenzo[b,f]azepine-5-carboxamide	No
16	F12	fluoren-9-ylpiperazine	No
16	G12	2-(morpholin-4-ylsulfonyl)-7-nitrodibenzo[b,d]furan	No
16	H12	N-(3,4-dichlorophenyl)tricyclo[4.2.2.0<1,5>]dec-8-yloxycarboxamide	No
16	I12	5-methyl-2-(methylethyl)-1-(2-quinolylmethoxy)-4-(1,2,3,4-tetraazolyl)benzene	No
16	J12	5-chloro-6-{[(2-cyclohex-1-enylethyl)amino]sulfonyl}-3-methyl-3-hydrobenzoxazo l-2-one	No
16	K12	(adamantanylmethyl)methyl(piperidylsulfonyl)amine	No

16	L12	1-[(5-bromo-2-thienyl)sulfonyl]pyrrolidin-2-one	No
16	M12	(4-fluorophenyl)(isoxazol-3-ylmethyl)(methylsulfonyl)amine	No
16	N12	2,5-bis(3-pyridylmethylthio)-1,3,4-thiadiazole	No
16	O12	5-(1,2,3,4-tetraazolyl)-2H-benzo[d]1,3-dioxolene	No
16	P12	2,3-bis(isoxazol-3-ylmethylthio)quinoxaline	No
16	A13	[(1-methylbenzimidazol-2-yl)methylthio]phthalazine	No
16	B13		No
16	C13	2H-benzo[3,4-d]1,3-dioxolen-5-yl(isoxazol-3-ylmethyl)(methylsulfonyl)amine	No
16	D13	1,3-bis(isoxazol-3-ylmethyl)-3-hydrobenzimidazol-2-one	No
16	E13	2-(isoxazol-3-ylmethylthio)-5,6-dimethoxybenzimidazole	No
16	F13	4-[(1E)-2-(4-bromophenyl)vinyl]pyridine	YES
16	G13	5,6-dimethoxy-2-[(1-methylbenzimidazol-2-yl)methylthio]benzimidazole	No
16	H13	1,2-bis(isoxazol-3-ylmethyl)-4-phenyl-1,2,4-triazolidine-3,5-dione	No
16	I13	2-(4-aminopyrimidin-2-ylthio)-1-(2,4,6-trimethylphenyl)ethan-1-one	No
16	J13	6-[(2H-benzo[3,4-d]1,3-dioxolen-5-ylamino)sulfonyl]-1,4-dimethyl-1,4-dihydroqu inoxaline-2,3-dione	No
16	K13	2-{[2-(4-methylphenyl)-1,3-thiazol-4-yl]methylthio}pyrimidine-4-ylamine	No
16	L13	methyl 2-(1,3,7-trimethyl-2,6,8-trioxo-1,3,7-trihydropurin-9-yl)acetate	No
16	M13	2-[(adamantanylmethyl)dimethylamino]-1-(4-chlorophenyl)ethan-1-one	No
16	N13	N-(10-cyano(9-1,2,3,4,5,6,7,8-octahydrophenanthryl))-2-(5-(2-thienyl)(1,3,4-ox adiazol-2-ylthio))acetamide	No
16	O13	4-(4-bromophenyl)-6-(4-ethylphenyl)pyrimidine-2-ylamine	No
16	P13	7-amino-1,3,11-trimethyl-2,4,12-trioxospiro[1,3-dihydro-5H-pyrano[2,3-d]pyrimi dine-5,3'-indoline]-6-carbonitrile	No
16	A14	2-(4-methylphenyl)-4-[(2-(1,3-thiazol-4-yl)benzimidazolyl)methyl]-1,3-thiazole	YES
16	B14	(2S)pyrrolidine-2-carboxamide	No
16	C14	1-[(4-chlorophenyl)methyl]cyclopropylamine	No
16	D14	3-[4-(2-hydroxyethyl)piperazinyl]propanoic acid	No
16	E14	tert-butyl 2-(aminomethyl)piperidinecarboxylate	No
16	F14	tert-butyl 3-(aminomethyl)piperidinecarboxylate	No
16	G14	1-propylpyrazole-4-carboxylic acid	No
16	H14	5-oxotricyclo[2.2.1.0<2,6>]heptane-3-carboxylic acid	No
16	I14	3-benzimidazol-2-ylchromen-2-one	No
16	J14	3-(4-amino-5-oxo-3-thioxo-2H-1,2,4-triazin-6-yl)propanoic acid	No
16	K14	2-imino-5-(2-oxo(1H-benzo[d]azolidin-3-ylidene))-1,3-thiazolidin-4-one	No

16	L14	N-(4-chlorophenyl)[(oxolan-2-ylmethyl)amino]carboxamide	No
16	M14	(4,6-dimethylpyrimidin-2-yl)(4-morpholin-4-ylphenyl)amine	No
16	N14	2-(2-(2-furyl)-4-oxochromen-6-yloxy)ethanenitrile	No
16	O14	5-(3-phenoxypropylthio)-4H-1,2,4-triazole-3-ylamine	No
16	P14	2-(5-methyl-10-hydro-1,2,4-triazolo[4,3-a]quinolinylthio)ethanenitrile	No
16	A15	2-(2-furyl)-5,6,7,8-tetrahydrobenzo[b]thiopheno[2,3-d]1,3-oxazin-4-one	No
16	B15	2,8-dimethyl-3-[(2-methylpiperidyl)methyl]quinolin-4-ol	No
16	C15	1-(7-methyl-5,6,7,8-tetrahydrobenzo[b]thiopheno[3,2-e]pyrimidin-4-ylthio)aceto ne	No
16	D15	2-[3-(4-oxo-5,6,7,8-tetrahydrobenzo[b]thiopheno[2,3-d]1,2,3-triazin-3-yl)propy l]benzo[c]azoline-1,3-dione	No
16	E15	7-methyl-3-pentyl-3,5,6,7,8-pentahydrobenzo[b]thiopheno[2,3-d]pyrimidin-4-one	No
16	F15	2,6,8-trimethyl-3-(morpholin-4-ylmethyl)quinolin-4-ol	No
16	G15	3-[(diethylamino)methyl]-2,6-dimethylquinolin-4-ol	No
16	H15	5,9-dimethoxy-2-methylfurano[3,2-g]chromen-4-one	No
16	I15	6-amino-5-methyl-3-hydropyrimidin-2-one	No
16	J15	4-[(2S,1R)-1-ethyl-2-(4-hydroxyphenyl)butyl]phenol	No
16	K15	???-N-(1,3-thiazol-2-yl)carboxamide	No
16	L15	1-(4-bromophenyl)-4-methylpyrazol-3-ol	No
16	M15	[2-(3-butylisoquinolyloxy)ethyl]dimethylamine	No
16	N15	6-methyl-3-(3-methylphenyl)-5H,6H-1,3-thiazolidino[2,3-c]1,2,4-triazole	No
16	O15	(4-chlorophenyl)-2-furyl(hydroxyimino)methane	No
16	P15	2-(4-nitrophenyl)-1,3,4-oxadiazole	No
16	A16	2-{1,4-dimethyl-4-[2-(phenylmethoxy)ethyl]piperazinyl}-1-(phenylmethoxy)ethane	No
16	B16	1,2,7-trihydrobenzo[a]4aH-carbazole	No
16	C16	2-(4-fluorophenyl)quinoxaline	No
16	D16	(hydroxyimino)(1-methylimidazol-2-yl)(4-nitrophenyl)methane	No
16	E16	3-(2,5-dioxo-1,3-diazolidin-4-yl)propanoic acid	No
16	F16	3-(3,6-diazabicyclo[4.3.0]non-3-yl)-1-(2-chlorophenothiazin-10-yl)propan-1-one	No
16	G16	3,9-di(2-furyl)-2,4,8,10-tetraoxaspiro[5.5]undecane	No
16	H16	5,5-dimethyl-4-methylene-1,3-dioxolan-2-one	No
16	I16	adamantanyl-N-{[(methylamino)thioxomethyl]amino}carboxamide	No
16	J16	4,5-dimethyl-1,3-dioxolen-2-one	No
16	K16	2,3-dimethyl-1-phenyl-3-pyrazoline-5-thione	No
16	L16	2-(3,5-diiodo-4-oxohydropyridyl)acetic acid	No
16	M16	1,3-bis[(4-nitrophenyl)methyl]imidazole	No

16	N16	5-(3,4,5-trimethoxyphenyl)-1,3,4-oxadiazole-2-thiol	No
16	O16	4-(2H-benzo[3,4-d]1,3-dioxolan-5-yl)-5-(3,4,5-trimethoxyphenyl)-1,2,4-triazole -3-thiol	No
16	P16	1-methyl-3-[(5-methyl-2-oxo(1,3-dioxolen-4-yl))methyl]-1,3-dihydroquinazoline- 2,4-dione	No
16	A17	ethyl(2-thienylcyclohexyl)amine	No
16	B17	1-phenylimidazole-2-thiol	No
16	C17	isoquinolinethiol	No
16	D17	2-[(5,6,7-trimethoxy-3-oxohydroisobenzofuran-4-yl)methyl]-4,7,3a,7a-tetrahydro isoindole-1,3-dione	No
16	E17	1-(2H-benzo[3,4-d]1,3-dioxolen-5-yl)-4-imidazoline-2-thione	No
16	F17	4-(4-indol-3-ylbutanoyl)-1,3,4-trihydroquinoxalin-2-one	No
16	G17	(1,3-dimethyl-2,4-dioxo(1,3-dihydroquinazolin-6-yl))-N-(2-oxo(3-3,4,5-trihydro thienyl))carboxamide	No
16	H17	isoquinolyl(2-methyl-1-azaprop-1-enyl)amine	No
16	I17	4-methyl-5-({3-[(5-methyl-2-oxo(1,3-dioxolen-4-yl))methylthio]quinoxalin-2-ylt hio}methyl)-1,3-dioxolen-2-one	No
16	J17	4,5,6-triethoxy-7-(1,3-oxazolino[4,5-b]pyridin-2-ylthiomethyl)-3-hydroisobenzo furan-1-one	No
16	K17	5-[4-(2H-benzo[3,4-d]1,3-dioxolen-5-yl)-5-(isoxazol-3-ylmethylthio)(1,2,4-tria zol-3-yl)]-1,2,3-trimethoxybenzene	No
16	L17	5-[(5-adamantanyl(1,3,4-oxadiazol-2-ylthio))methyl]-1,2,3-trimethoxybenzene	No
16	M17	2-[(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)methyl]-4-hydroxy-2-hydrophthalazin-1-on e	No
16	N17	4-(2H-benzo[d]1,3-dioxolan-5-yl)-2-amino-6-(4-chlorophenyl)benzene-1,3-dicarbo nitrile	No
16	O17	2-[(1,4-dioxa-8-azaspiro[4.5]dec-8-yl)methyl]-4-bromophenol	No
16	P17	1-[4-(adamantanylcarbonyl)piperazinyl]-3-cyclohexylpropan-1-one	No

Table A2. Results from the secondary screen for concentration-dependent inhibition of Prp.

Plate	**Well**	**Inhibitor Y/N**	**Plate**	**Well**	**Inhibitor Y/N**	**Plate**	**Well**	**Inhibitor Y/N**
1	A08	YES	1	I07	NO	2	H14	NO
1	D06	YES	1	I13	NO	2	J20	NO
1	I04	NO	1	K12	NO	2	G11	NO
1	G16	NO	1	K16	NO	2	G16	NO
1	H07	NO	1	L04	NO	2	H11	NO
1	H10	NO	1	L10	NO	2	H12	NO
1	H11	NO	1	M13	NO	2	H13	NO
1	H16	NO	2	H19	NO	2	H17	NO

Plate	Well	Inhibitor Y/N	Plate	Well	Inhibitor Y/N	Plate	Well	Inhibitor Y/N
2	H18	NO	6	I14	NO	9	M16	NO
2	J11	NO	6	K04	NO	9	D14	NO
3	P05	NO	6	M14	NO	9	F21	NO
3	G08	NO	6	N08	NO	9	G17	NO
3	P08	NO	6	O13	NO	9	G18	NO
3	L12	NO	6	N10	NO	9	H14	NO
3	I09	NO	6	N11	NO	9	H17	NO
3	P11	NO	6	N12	NO	9	H18	NO
3	G18	NO	6	N13	NO	9	H19	NO
3	G12	NO	6	N14	NO	9	H21	NO
4	B10	YES	6	N15	NO	9	I15	NO
4	G10	NO	6	O10	NO	9	I17	NO
4	G14	NO	6	P14	NO	9	I18	NO
4	H07	NO	7	D14	NO	9	J11	NO
4	H10	NO	7	N06	NO	9	J17	NO
4	H18	NO	7	B17	YES	9	K12	NO
4	L10	NO	7	G04	NO	9	K16	NO
4	P09	NO	7	G07	YES	9	L13	NO
5	A07	YES	7	H04	NO	9	L14	NO
5	A12	YES	7	I07	NO	9	M08	NO
5	B07	NO	7	K12	NO	9	N07	NO
5	E07	YES	8	A10	YES	9	O07	NO
5	E12	NO	8	M09	NO	10	G19	NO
5	I14	NO	8	J03	NO	10	I16	NO
5	M18	NO	8	J04	NO	10	J21	NO
5	P11	NO	8	B17	NO	10	K07	NO
5	D07	NO	8	C05	NO	10	O08	NO
5	G05	NO	8	G13	NO	11	L13	NO
5	H06	NO	8	H16	NO	11	L12	NO
5	J04	NO	8	H19	NO	11	L10	NO
5	J10	NO	8	J12	NO	11	K21	NO
5	J12	NO	8	J17	NO	11	K20	NO
5	M15	NO	8	K10	NO	11	J20	NO
6	C19	YES	8	K18	NO	11	H04	NO
6	D16	NO	8	L13	NO	11	H03	NO
6	F04	NO	8	L15	NO	11	I10	NO
6	G10	NO	8	N3	NO	11	I11	NO
6	H10	NO	8	P09	YES	11	J05	NO

Plate	Well	Inhibitor Y/N	Plate	Well	Inhibitor Y/N
12	J05	NO	15	H19	NO
12	J07	NO	15	H21	NO
12	J10	NO	15	I09	NO
12	K03	NO	15	I10	YES
13	G12	NO	15	I13	NO
13	G05	NO	15	I14	NO
13	G11	NO	15	I15	NO
13	G14	NO	15	J05	NO
13	G17	NO	15	J09	NO
13	H04	NO	15	J11	NO
13	J03	NO	15	J15	NO
13	J04	NO	15	J17	NO
13	P03	NO	15	J18	NO
14	G13	NO	15	J21	NO
14	G14	NO	15	K11	NO
14	G18	NO	15	K12	NO
14	H17	NO	15	K13	NO
14	I04	NO	15	K14	NO
14	K04	NO	15	K15	NO
14	K11	NO	15	K17	NO
14	K12	NO	15	K20	NO
14	L03	NO	15	K21	NO
14	L05	NO	15	L10	NO
15	F21	NO	15	L11	NO
15	G11	NO	15	L12	NO
15	G14	NO	15	L13	NO
15	G17	NO	15	L14	NO
15	G18	NO	15	L15	NO
15	G21	NO	15	P08	NO
15	H09	NO	15	P18	NO
15	H11	NO	16	A14	NO
15	H12	NO	16	F13	YES
15	H13	NO	16	J03	NO
15	H16	NO			

Table A3. Third screen of compounds and interference assay. Compounds were tested in triplicate at concentrations (μM) 30, 25, 20, 15, 10, 8, 6, 4, 3, 2, 1, and 0.5. Most compounds were either eliminated because the initial inhibition could not be reproduced at these concentrations (marked NO). Others were eliminated for interfering with fluorescence from the cleaved peptide (marked INT). One compound (highlighted) appeared to inhibit Prp in a concentration-dependent manner.

Plate	**Well**	**Inhibitor Y/N**	**Interference Y/N**
1	A08	NO	NO
1	D06	NO	NO
4	B10	NO	NO
5	A07	NO	NO
5	A12	NO	NO
5	E07	NO	NO
6	C19	NO	NO
7	B17	NO	NO
7	G07	NO	NO
8	A10	NO	NO
8	P09	NO	NO
15	I10	YES	YES
16	F13	YES	NO