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Adherence mechanism analysis: the role of *prsA* gene in *Lactobacillus acidophilus* and other infectious microorganisms

Introduction

Lactobacillus acidophilus (*acidophilus*) is a gram-positive bacterium that is abundant in the mouth, vagina, and intestine. Its cell wall consists of thick layers of peptidoglycan that give the cell a rigid structure. A gram stain must be performed in order to identify and view the bacteria under a microscope. The cells turn purple due to the peptidoglycan capturing the gram stain in its bilayer. *Lactobacillus acidophilus* plays a substantial role in sustaining human health. It can be used as a probiotic to promote the population of beneficial microbes. The bacterium produces lactic acid to prevent harmful bacterium from colonizing the mouth, vagina, and intestine. *L. acidophilus* produces an enzyme called lactamase that works to break down lactose, a disaccharide found in milk, and produces lactic acid in the process, which protects the body from other infectious microorganisms (Akolkar, Sajgure, & Lele, 2005). The probiotic may come in capsules, powders, and creams to treat a broad range of conditions. For example, *acidophilus* is highly effective in treating bacterial vaginosis, lung infections, acne, diarrhea, eczema, and many other conditions (Robertson, 2017). During vaginal birth, the mother inoculates her newborn with *L. acidophilus* as the baby passes through the vaginal canal (Boris, Suárez, Vázquez, & Barbés, 1998). In a previous study conducted by Carlsson and Gotherfors, the Lactobacilli flora was found in the “vagina of the mother and in the mouth of the child at the time of delivery in 6 out of 13 cases” (Carlsson & Gotherfora, 1974).

The purpose of this research study was to examine the mechanism of transmission of *Lactobacillus acidophilus* between mother and progeny. Upon investigation of scholarly articles and previous studies of *L. acidophilus*, glycoproteins can account for the adherence of *L. acidophilus* in the vaginal canal and the skin of the newborn baby. The specific mechanism of adherence has not been found yet. However, glycoproteins have been thought to assist the cells to adhere to surfaces of hosts. The *prsA* gene was also found in *L. acidophilus* (strain FS14) through studies including Kontinen and Sarvas' experiment on *Bacillus subtilis* (Kontinen & Sarvas, 1993). This gene plays a major role in the process of protein secretion by directing proteins that must be secreted out of the cell to fold. IMG/M and NCBI was used to investigate how the *prsA* gene may play a role in adherence.

In order to study the possible mechanism, the *prsA* gene was searched through genomic databases. The following organisms also had this particular gene: *Streptococcus suis* (strain 05HAS68), *Neisseria meningitidis* (strain 331401), *Klebsiella pneumoniae* (strain 11), and *Providencia rettgeri* (strain RB151). *S. suis* is a gram positive organism responsible for transmitting various invading diseases and syndromes to humans from pigs by adhering to endothelial cells (Benga, Friedl, Valentin, 2005). *N. meningitidis* is a gram negative microbe that causes meningitis by attaching to the epithelial cells in the nasopharynx. It can be spread by respiratory or throat secretion in humans (Chen & Seifert, 2011). In addition, *K. pneumoniae* is a gram positive bacteria capable of causing pneumoniae, meningitis, ear infections, and many other serious illnesses. In humans, this organism adheres itself to the epithelial cell of the bronchitis (Podlogar & Verspohl, 2011). *P. rettgeri* is responsible for causing urinary tract infections, eye infections, and traveller's diarrhea by joining to the epithelial cells (Charbek,

2017). Finally, *L. acidophilus* is a gram positive healthy microbe that attaches to the epithelial cells in the intestine, vagina, and the mouth (Martin, Sanchez, Suarez, & Urdaci, 2012). All of these organisms have the *prsA* gene, which is suspected to account for the adherence mechanism in their host.

Methods

In order to examine *Lactobacillus acidophilus*' mode of transmission between mothers and their infants, genomic analyses were utilized to determine a common gene that may account for the process in *L. acidophilus*, *Streptococcus suis*, *Neisseria meningitidis*, *Klebsiella pneumoniae*, and *Providencia rettgeri*. The GenBank on the National Center of Biotechnology Institute (NCBI) and the Integrated Microbial Genomes & Microbiomes (IMG/M) were used to study the *prsA* gene. This gene was first entered in the GenBank tool on NCBI to determine which microbes were composed of the *prsA* gene. Four organisms were randomly chosen to further investigate the relationship between *L. acidophilus*, *S. suis*, *N. meningitidis*, *K. pneumoniae*, and *P. rettgeri*. A complete genomic sequence of each organism was obtained through NCBI's genome sequence database (table 1). In order to compare genomes between the microbes, a phylogenetic tree was created using IMG/M's distance tree tool by entering the microorganism in the tool box (figure 1).

Results

Organism with Strain	Accession Number	Reference
<i>Lactobacillus acidophilus</i> FSI4	CP010432	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4392141/
<i>Streptococcus suis</i> 05HAS68	CP006930	https://www.ncbi.nlm.nih.gov/nucleore/821177616
<i>Neisseria meningitidis</i> 331401	CP012694	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5442631/
<i>Klebsiella pneumoniae</i> 11	CP003200	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3302456/
<i>Providencia rettgeri</i> RB151	CP017671	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5255920/

Table 1 Complete genome sequences of studied microbes

L. acidophilus, *S. suis*, *N. meningitidis*, *K. pneumoniae*, and *P. rettgeri* were shown to have a common gene, *prsA*, that serves as a virulence factor to adhere to their specific host. Table 1 displays each microbe's complete genome sequences, accession number, and previously conducted research studies (National Center for Biotechnology Information). *L. acidophilus* is most closely related to *S. suis*, based on the proximity between the two species on the tree. *N. meningitidis*, *K. pneumoniae*, and *P. rettgeri* share a common ancestor depicted by the .0655 node (Fig. 1), which forms a monophyletic group. An unknown speciation event can account for *K. pneumoniae* and *P. rettgeri* being the most closely related microbes shown by the .0555 node. Based off of figure 1, all five organisms do not have a common ancestor, but the *prsA* gene is included in their genome found through NCBI.

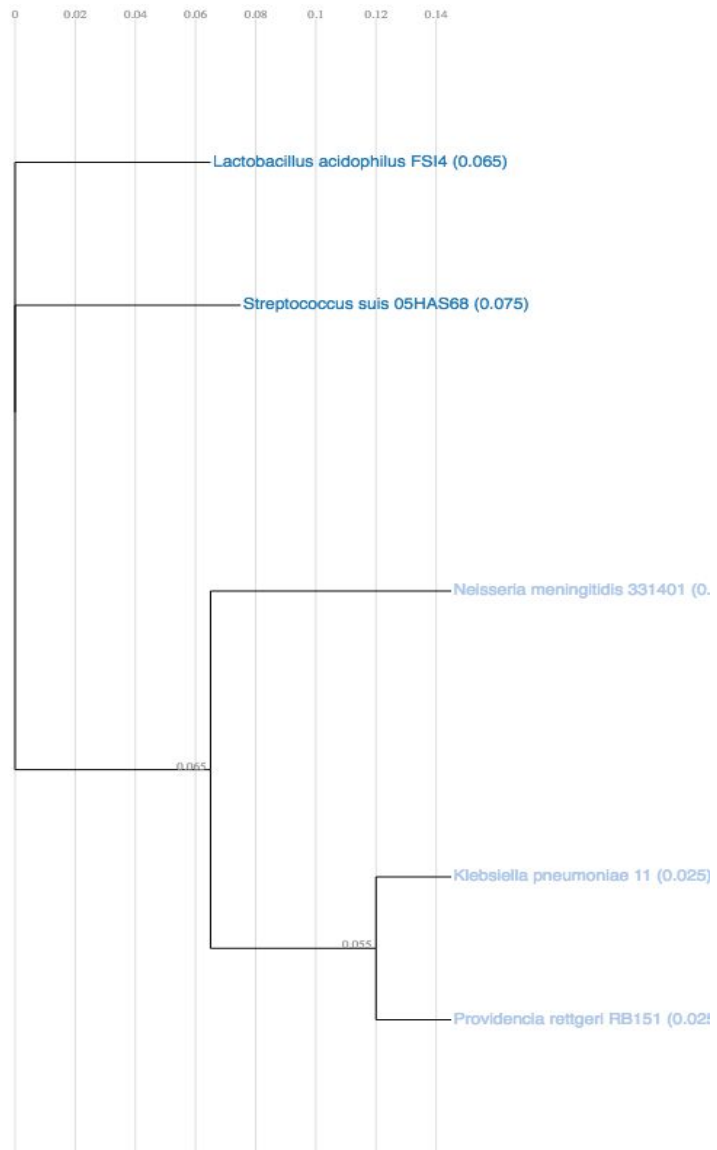


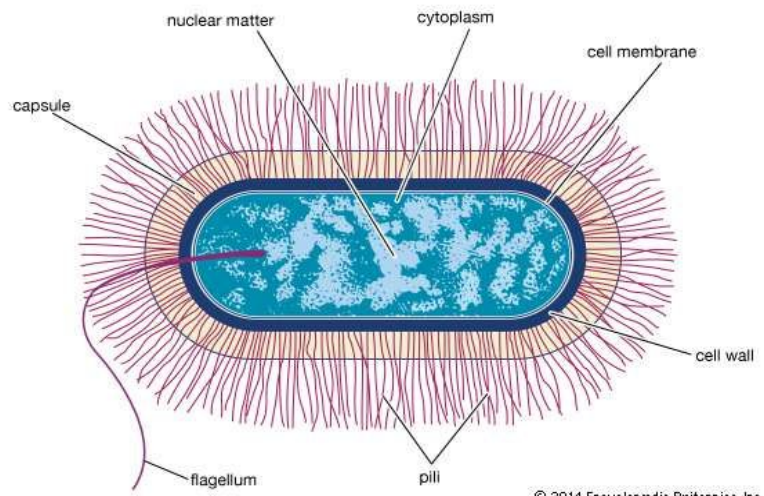
Figure 1 Phylogenetic tree

Delivery no.	No. of isolates								
	<i>L. acidophilus</i>			<i>L. jensenii</i>			Other lactobacilli ^a		
	Infant	Mother		Infant	Mother		Infant	Mother	
	Mouth	Vagina	Rectum	Mouth	Vagina	Rectum	Mouth	Vagina	Rectum
1	4	5	2						4
2				5					
3					1	1			3
4	5	5	5						
5	2	3		1	2	5			
6				5	3	5			
7				4	5	5	1		
8	5	5	4						1
9					3				5
10									5
11			1			1			1
12									2
13									

^a In rectums of the mothers *L. casei* was found in five deliveries, *L. salivarius* and *L. plantarum* in one delivery each, and heterofermentative lactobacilli in three. The lactobacillus species found in one infant's mouth was heterofermentative.

Table 2 Lactobacilli found in mothers and infants at the time of delivery (Carlsson & Gothers, 1974).

Lactobacilli flourish in the human body by adhering to the host through the use of their capsule and pili (Figure 2). *Lactobacilli* colonize by attaching themselves to the various open crevices of the body. Table 2 demonstrates that *Lactobacilli* can establish themselves in the mouth of the newborn by transmission from the mother due to their adherence capabilities.



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Figure 2 Bacteria labeled (Britannica 2016)

Discussion

The *prsA* gene may account for the mechanism of adherence in *L. acidophilus*. The gene is translated into a protein that is helpful in binding itself to epithelial cells of the host. *PrsA* aids in the adhesion of *L. acidophilus* to the vaginal canal and to the skin microbiota of newborns by secreting extracellular adhesion proteins. NCBI's GenBank tool was utilized to ascertain the presence of the *prsA* gene in *Lactobacillus acidophilus*, *Streptococcus suis*, *Neisseria meningitidis*, *Klebsiella pneumoniae*, and *Providencia rettgeri*'s genome. All of these organisms have similar modes of adherence.

Streptococcus suis can cause invasive diseases in pigs, which can be passed to humans through pork consumption. The bacterial infection can reach the blood, leading to organ failure, known as sepsis. Meningitis, which is characterized by the inflammation of the meninges in the brain and spinal cord, can also occur with severe bacterial infection (Benga, Friedl, Valentin, 2005). *S. suis* adheres to the endothelial cells in the body, aiding microbial invasion and causing harmful health effects.

Neisseria meningitidis can cause meningitis. It uses its pili and capsule to transmit itself into the epithelial cells of hosts. The pathogenic microbe first colonizes the mucous covered nasopharyngeal, the upper part of the throat and behind the nose, through the glycosylated type IV pili (Chen & Seifert, 2011). The bacterium then invades the blood vessels and travels to the brain and spinal cord to begin the process of infection. *N. meningitidis* can be transmitted to humans through the secretion of bodily fluids spreading by coughing and sneezing. Viruses can also cause meningitis through a similar mechanism, but "bacterial infections are much more serious with approximately 5% of cases resulting in death" (Nature, 2009).

Klebsiella pneumoniae causes a range of diseases, depending on where it infection takes place in the body. However, the most common sickness the microbe can cause is pneumonia in the respiratory tract. The microorganism has type I and III pili that facilitate adherence and biofilm formation on epithelial cells of its hosts. Normal numbers of *Klebsiella* reside in the body. If the pathogenic bacterium exceeds the normal abundance, the microbe will typically form in the bronchitis of the lungs. The bacterium can be spread through host-to-host interactions.

Providencia rettgeri can trigger a wide range of infections, including complicated urinary tract infections, traveler's diarrhea, septicemia, and ocular infections (Charbek, 2017). This microbe is prevalent in immunocompromised patients, such as elderly residents and hospitalized patients. *P. rettgeri* begin infecting their hosts by attaching to the epithelial cells in specific areas of the body, which include the uroepithelial cells and corneal epithelial cells. Respiratory secretions or contaminated water have been the cause of *P. rettgeri* infections.

Unlike the other harmful pathogens, *Lactobacillus acidophilus* is a healthy probiotic that is beneficial for the human body to fight off potentially harmful infections and enhance immunity. In order to defend the body from pathogens, *L. acidophilus* produces lactic acid and other organic acids which “inhibit the adherence and multiplication of pathogenic microbes” (*Lactobacillus*, 2011). They colonize the small intestine, vaginal canal, mouth, and other open crevices by attaching to specific endothelial cells in their host (Peter, K. et al., 2004).

Lactobacillus acidophilus, *Streptococcus suis*, *Neisseria meningitidis*, *Klebsiella pneumoniae*, and *Providencia rettgeri* are complex microorganisms that vary in several ways. Despite the different health effects they may impose on humans, they adhere to their host

through a similar process. The *prsA* gene is found in *L. acidophilus*, which may explain its mechanism of adherence. *S. suis*, *N. meningitidis*, *K. pneumoniae*, and *P. rettgeri* also have the same gene that is responsible for the secretion of glycoproteins, which are thought to be the targets of attachment by microbes (Saurez & Vazquez, 1998).

Conclusion

The specific mechanism of adherence in *Lactobacilli* is unknown and researchers are still studying their method of transmission. Through gene sequencing, the *prsA* gene was found in *L. acidophilus*, *S. suis*, *N. meningitidis*, *K. pneumoniae*, and *P. rettgeri*. Despite the fact that *Lactobacilli* are beneficial organisms, and *S. suis*, *N. meningitidis*, *K. pneumoniae*, and *P. rettgeri* are harmful pathogens, all of these organisms adhere to specific parts of the body to protect or infect the host. This study concludes that the *prsA* gene, important for the folding of glycoproteins, may be responsible for the transmission of *Lactobacillus acidophilus* between mothers and their newborns at the time of birth.

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