A PBPK model for clearance of PEGylated nanomedicines

Anne M. Talkington
UNC Chapel Hill, annemt@email.unc.edu

Samuel K. Lai
UNC Chapel Hill, lai@unc.edu

M. Gregory Forest
UNC Chapel Hill, forest@unc.edu

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Anne M. Talkington[1], Samuel K. Lai[1,2,3,4], M. Gregory Forest[1,5]

[1]Program in Bioinformatics and Computational Biology, University of North Carolina, Chapel Hill, NC, USA
[2]Division of Pharmacoengineering and Molecular Pharmaceutics, Eshelman School of Pharmacy, University of North Carolina, Chapel Hill, NC, USA
[3]UNC/NCSU Joint Department of Biomedical Engineering, University of North Carolina, Chapel Hill, NC, USA
[4]Department of Microbiology and Immunology, School of Medicine, University of North Carolina, Chapel Hill, NC, USA
[5]Department of Mathematics, University of North Carolina, Chapel Hill, NC, USA

Physiologically based pharmacokinetic (PBPK) models are a means of conducting virtual experiments on a large scale as an alternative to extensive trials that would be prohibitively time-consuming, unethical, or otherwise costly. PBPK can be used to compute and test optimal dosing strategies, among other features, of proposed treatments using known or learned kinetics of the system mimicking complex human physiology. In turn, PBPK modeling can enable more efficient design and optimization of *in vivo* experiments, and consequently accelerate pre-clinical screening and development. I will discuss the application of PBPK modeling to an important problem in the medical community – the accelerated clearance of PEGylated drugs in the presence of anti-PEG antibodies (APA). While this phenomenon renders an entire class of drugs (i.e., PEGylated drugs) ineffective in many patients, the medical community is largely unaware of how drastically this can alter prognosis or how to mitigate this effect. I will describe a multi-compartment PBPK model to accurately capture and ultimately predict clearance behavior, with the goal of validating results against drug biodistribution data obtained via PET/CT technology. Specifically, I will focus on the initial transient dynamics as nanomedicines are cleared from the circulation in patients with high APA titers. I will then discuss further applications for this model in the context of targeted therapeutics.