DIVISION OF BIOCHEMICAL TECHNOLOGY OF THE AMERICAN CHEMICAL SOCIETY

BIOT

The Best of BIOT Awards: November 7, 2018

Area	Date	Time	Presenter	Institution
End-to-End Bioprocessing	**Wednesday**, November 7th	12:00-12:30 PM	**Varnika Roy**	GlaxoSmithKline
		Developing an end to end bio-manufacturing platform for the new paradigm of SAM (Self Amplifying mRNA vaccines)		
		12.30 -1:00 PM	**Camille Bilodeau**	Rensselaer Polytechnic
		Effects of protein and ligand structure on protein-multimodal ligand interactions in antibody systems		
Moderated by Dr. Shahid Rameez, Merck & Co.				

Webinar registration can be made at [ACS BIOT WebEx Webinars]

Developing an end to end bio-manufacturing platform for the new paradigm of SAM (Self Amplifying mRNA vaccines)

Varnika Roy, Mandy Xie, Sonia Gregory, Kelly Forney-Stevens, Marcin Bugno, Diana Chinchilla-Olszar, Kunal Aggarwal, Derek O'Hagan and Jeffrey Ulmer

Vaccines Technical Research and Development, GlaxoSmithKline

The SAM (Self Amplifying) platform aims to revolutionize the way we prevent and treat infectious diseases by developing the next generation of best-in-class mRNA vaccines. The SAM platform represents a fully synthetic RNA vaccine technology combining a self-amplifying RNA backbone and a non-viral delivery system. While naked mRNA by itself is immunogenic, facilitated delivery is required to attain full potency. The delivery system is a cationic nanoemulsion (CNE), which binds to the SAM RNA, enables its delivery intra-cellularly and prevents degradation and thereby substantially increases the potency of the vaccine. The product is a two vial presentation one for the RNA drug product DP and the second for the CNE DP mixed at the patient's bedside to yield the reconstituted vaccine. Unique challenges such as RNAase contamination, control strategy for novel raw-materials in an in-vitro transcription reaction to yield RNA and various others are encountered from a manufacturing and analytical control strategy perspective when advancing this novel platform. The challenges and mitigation strategies implemented to overcome them will be discussed. The end to end bio-manufacturing platform developed with this SAM platform presents a disruptive innovation to simplify vaccine discovery and development by providing an optimized CMC model for producing mRNA vaccines rather than specific antigen development which hinders a platform CMC approach.

The Effects of Protein and Ligand Structure on Protein-Multimodal Ligand Interactions

Camille Bilodeau, Ed Lau, Shekhar Garde, Steve Cramer

Rensselaer Polytechnic Institute

Multimodal chromatography uses multiple modes of interaction including charge, hydrophobic, aromatic, and hydrogen bonding interactions to achieve challenging separations and unique selectivities. These modes of interactions when included on a single ligand can affect each other in unintuitive ways making overall chromatographic behavior difficult to understand and predict. The lack of fundamental understanding of these systems poses a significant barrier to multimodal process development and multimodal ligand design. In this work, we use molecular dynamics simulations to investigate the role that ligand chemistry and architecture play in governing multimodal ligand-protein interactions. In particular, we examine interactions between a set of multimodal cation exchange ligands and a set of chemically diverse antibody fragments. We first characterize the conformational and hydration preferences of each ligand in the absence of any protein. We find that minor changes in ligand structure can significantly affect ligand solvation. We then perform simulations with each ligand in free solution around each protein and investigate how these preferences effect protein-ligand binding dynamics. We find that differences in individual ligand solvation can lead to differences in desolvation dynamics upon protein-ligand binding. Finally, we analyze the effect of ligand structure on the overall strength of protein-ligand interactions on different regions of the protein surface. We find that differences in ligand desolvation upon binding drive differences in the overall binding strength of ligands to hydrophobic regions of the protein surface. This work provides a basis for characterizing the relationship between ligand structure and the overall strength of ligand-protein interactions. This fundamental understanding will serve to guide design of new multimodal ligands as well as resin selection for multimodal polishing steps.