DIVISION OF BIOCHEMICAL TECHNOLOGY OF THE AMERICAN CHEMICAL SOCIETY

BIOT

The Best of BIOT Awards

Area	Date	Time	Presenter	Institution
Biomolecular and Biophysical Processes	Tuesday, December 11th	12:00-12:30 PM	**Hadley Sikes**	Massachusetts Institute of Technology
		Engineered binding proteins as replacements for antibodies in immunoassays		
		12.30 -1:00 PM	**Philipp Vormittag**	Karlsruhe Institute of Technology
		Predicting the solubility of VLPs: Qualitative structure property relationship (QSPR) modeling applied to HBcAg VLPs		
Moderated by Steve Raso, Epizyme				

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

Engineered binding proteins as replacements for antibodies in immunoassays

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Antibodies are unrivaled as molecular recognition agents in the context of the immune system of an organism. However, in the context of an*in vitro* device, certain opportunities for improvement can be readily identified. Engineering strategies and accomplishments towards replacing antibodies in medical diagnostic tests with engineered binders produced from the reduced charge Sso7d protein scaffold (rcSso7d) will be presented. Differences of these engineered binders from antibodies include twenty-fold smaller size, one-hundred-fold better thermal stability, and the potential to engineer universal compatibility of each clone with the *in vitro* test format while avoiding the cross-reactivity that is often observed with antibodies. Each of these differences comes with both challenges and opportunities that will be discussed in terms of how to modify the binding molecule so that it functions when i.) coupled to a solid support and ii.) coupled to a label that signifies capture of an analyte molecule.

“Predicting the solubility of VLPs: Qualitative structure property relationship (QSPR) modeling applied to HBcAg VLPs

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Engineered chimeric virus-like particles (VLPs) have shown great potential as cancer immunotherapeutic. Chimeric VLPs incorporate antigenic epitopes that can alter the assembly competence, solubility and stability of the virus proteins. To reduce those effects, the epitope inserts are fused to linkers. However, integration of a linker often does not lead to the desired effect of creating an assembly competent, soluble and stable VLP, suggesting there is a dependence of these properties on the VLP platform and the structure of the inserted epitope and linker. In this paper, we propose an in silico approach to predict VLP solubility in clarified harvest based on a chimeric Hepatitis B virus core antigen (HBcAg) VLP platform and reveal critical insert properties.

Recent computational advances have rendered molecular dynamics (MD) simulations applicable to more complex protein structures. From X-Ray diffraction structures of the native HBcAg dimer we generated by homology modeling and MD simulations 3D models of 27 virus protein dimers associated with chimeric HBcAg VLPs, varying in the sequence of the insert. These 27 VLPs were characterized by their solubility in clarified E. coli harvest. We created in silico models to predict VLP solubility applying QSPR modeling.

Based on the protein 3D structure and amino acid sequence, molecular descriptors related to geometry, charge and hydrophobicity were calculated. Besides well-established descriptors, we implemented descriptors that were specifically designed for this study, assuming that a rational design of the QSPR model potentially decreases the probability of including unnecessary or erratic descriptors. With principal component analysis (PCA) data dimension was reduced and solubility class membership was predicted by classification of the constructs into clusters. The model assigned more than 95% of the constructs correctly in cross-validation. Analysis of the model uncovered critical insert properties that may aid the design of novel inserts or be the basis for the modification of insoluble constructs.

In conclusion, we developed a rational QSPR approach to predict VLP solubility. We established a tool to reduce screening efforts in early VLP drug development, cutting down the number of required experiments including DNA synthesis, plasmid transformation and expression of potential candidates by the ability of identifying insoluble VLP species thus potentially decreasing time-to-market and R&D costs.