Design and Characterization of Polyvalent Therapeutics

By

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Abstract

Polyvalent ligands, synthesized by the attachment of multiple copies of suitable ligands to a scaffold, represent a promising class of therapeutics. This thesis focuses on the design, characterization, and optimization of polyvalent therapeutics. In particular, we have optimized scaffolds used for polyvalent ligand presentation, characterized the interaction of a monovalent ligand with its target receptor, and used phage display to identify novel ligands for target proteins.

We will first discuss how to improve liposome stability while still maintaining efficacy, and also how to use the concept of lipid phase separation to make more efficient use of the peptide ligands. We will then discuss the use of Nuclear Magnetic Resonance Spectroscopy to characterize the interaction between a second peptide ligand, one that binds to the cellular receptor for anthrax toxin, and its protein receptor. This study enabled us to determine the binding location for the peptide on the receptor protein, and provides clues to the peptide's mechanism of toxin inhibition. Finally, we will also discuss the identification of novel peptide ligands for the protein Serum Amyloid A.