580d The Design of Potent Nanoscale Anthrax Toxin Inhibitors

Kunal Gujraty, Amit Joshi, Saleem Basha, Jeremy Mogridge, and Ravi S. Kane

Polyvalency – the simultaneous binding of multiple ligands on one biological entity to multiple receptors on another – is a phenomenon that is ubiquitous in nature. We are using a biomimetic approach, inspired by polyvalency, to design potent inhibitors of anthrax toxin. Inhibitors based on polyvalency are orders of magnitude more potent than their corresponding monovalent inhibitors. Since the major symptoms and death from anthrax are due primarily to the action of anthrax toxin, the toxin is a prime target for therapeutic intervention. We have screened a phage display library to yield peptides that bind to anthrax toxin and through a series of truncations/mutations, have identified a minimal peptide sequence required for activity. We have also identified the binding site for the peptide on the target protein. We will also describe the design, characterization, and testing of novel inhibitors that prevent the assembly of anthrax toxin and inhibitors directed towards the cellular receptor for the toxin. The inhibitors developed during this work may enable the successful treatment of anthrax during the later stages of the disease when antibiotic treatment is ineffective.