

Abstract Submitted
for the MAR06 Meeting of
The American Physical Society

The Design of Potent Liposome-Based Inhibitors of Anthrax Toxin PRAKASH RAI, CHAKRADHAR PADALA, VINCENT POON, ARUNDHATI SARAPH, SALEEM BASHA, SANDESH KATE, KEVIN TAO, JEREMY MOGRIDGE, RAVI KANE — Several biological processes involve the recognition of a specific pattern of binding sites on a target surface. Theoreticians have predicted that endowing synthetic biomimetic structures with statistical pattern matching capabilities may impact the development of sensors and separation processes. We demonstrated for the first time that statistical pattern matching significantly enhances the potency of a polyvalent therapeutic – an anthrax toxin inhibitor. We functionalized liposomes with an inhibitory peptide at different densities and observed a transition in potency at an inter-peptide separation that matches the distance between ligand-binding sites on the heptameric subunit of anthrax toxin. Pattern-matched polyvalent liposomes neutralized anthrax toxin *in vitro* at concentrations four orders of magnitude lower than the corresponding monovalent peptide. We also showed that polyvalent liposome-based inhibitors can neutralize a microbial toxin *in vivo*. Statistical pattern matching represents a facile strategy to enhance the potency of therapeutics targeting toxins or pathogens. Our results also illuminate other fundamental aspects of polyvalent recognition –specifically we found that the efficiency of polyvalent inhibition is influenced by the competition between the rates of ligand dissociation and diffusion.

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Date submitted: 18 Nov 2005

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