CHEMICAL ENGINEERING

DISTINGUISHED YOUNG SCHOLARS SERIES

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Engineering and applying next-generation antibody and TCR therapeutics for infectious diseases

ABSTRACT: Antibodies have been engaging with infectious diseases since the evolution of cartilaginous fish, though it is only in very recent history that humans have been able to harness this expertise. The concept of using antibodies as therapeutics was first put into practice in the late 1890's and was called serum therapy. Although this remedy was revolutionary for the treatment of virulent infections, significant side effects as well as the introduction of modern antibiotics caused a rapid decline of the practice in the 1930s. It is now 80 years later and antibodies for infectious indications are experiencing a renaissance. In particular, the evolution of antibiotic-resistant bacteria, the emergence of new pathogens, a growing population of immunocompromised individuals, and the continual search for the next cure has caused many to take a second look at antibodies. The exceptional specificity and biocompatibility of antibodies makes them agreeable therapeutics, and the invention and maturation of protein engineering has given us a toy box of new strategies for their design.

"Next-generation" protein formats, such as antibody mixtures, bispecific antibodies, and T-cell-receptor driven approaches, may be key for the treatment of infectious diseases. These new formats are able to provide broad coverage against mutable pathogens and open new therapeutic avenues by redirecting the immune system. In this talk I will first discuss our work developing antibodies for whooping cough, with emphasis on the increased efficacy of an antibody mixture and bispecific antibody and the concomitant mechanistic insights. Whooping cough continues to cause significant morbidity and mortality in children worldwide, and we hope that our therapeutic, currently in baboon trials, could be used to prevent infection in high-risk

populations. Secondly, I will discuss our efforts to expand the therapeutic repertoire of engineered proteins by utilizing T-cell receptor (TCR) moieties. TCRs are membrane-bound receptors which recognize peptide-MHC (pMHC) complexes on host cells, and are particularly relevant for targeting viral diseases. A soluble TCR is therefore an interesting therapeutic molecule, but is not often pursued due to poor stability and expression and a prohibitively low wild-type affinity. We have developed a system to display functional TCR on the surface of CHO cells, and have successfully used this system for affinity maturation of a human TCR. We are currently working to optimize soluble expression of this TCR from CHO cells, and hope to eventually test this format in a model disease system.

BIOGRAPHY: Ellen Wagner is a research fellow at The University of Texas at Austin, where she recently completed her Ph. D. in chemical engineering under the guidance of Dr. Jennifer Maynard. Ellen is particularly interested in engineering novel antibody formats, and investigating how these formats can induce alternative therapeutic mechanisms in the treatment of infectious diseases. Ellen is a co-inventor on a patent for humanized pertussis antibodies, one of which is now in non-human primate testing for the prevention of whooping cough. Ellen is a NSF graduate fellow, and as part of this program spent 6 months at the University of Oslo in Norway, where she worked with Dr. Inger Sandlie on antibodies for the detection of celiac disease. Ellen received her B. S. in chemical and biological engineering from the University of Colorado at Boulder.

LECTURE 4:00 – 5:00 (PAA) A110
Happy Hour in Benson Hall Lobby Following

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