

**S012** Engineered Microbial Proteins for Vaccination Therapy  
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Exotoxin A secreted from *Pseudomonas aeruginosa* (PE) is a 65 kD protein with remarkable functions that allow its use as a unique antigen delivery tool following application at mucosal surfaces of the body. Through a series of studies, a non-toxic form of PE (termed ntPE) has been shown to rapidly and efficiently traverse intact polarized epithelial barriers and target local, underlying antigen presentation cells (APCs) as well as local, draining lymph nodes. Using a green fluorescent protein chimera of ntPE, rapid epithelial transcytosis and targeting of a functionally folded protein has been demonstrated, highlighting the privileged nature of the pathway used by ntPE to enter the body and target APCs and lymph nodes. Genetic integration of conformational antigenic epitopes into ntPE has allowed for the induction of both mucosal and systemic antibody responses directed to surface structures of pathogens that are involved in either epithelial cell binding and/or pathogenesis. A candidate vaccine, designed to incite an immune response that blocks piliated *P. aeruginosa* from binding to airway epithelial cells, has been evaluated in a Phase I clinical trial. Initial safety and efficacy aspects of this trial, along with molecular and cellular aspects of ntPE-mediated vaccination, will be described.