Charles Jones Abstract:

Genetic vaccines offer a treatment opportunity based upon successful gene delivery to specific immune cell modulators. Driving the process is the vector chosen for gene cargo packaging and subsequent delivery to antigen presenting cells (APCs) capable of triggering an immune cascade. As such, the delivery process must successfully navigate a series of requirements and obstacles associated with the chosen vector and target cell. In this work, we present the development and assessment of a hybrid gene delivery vector containing biological and biomaterial components. Each component was chosen to separately design and engineer gene delivery in a complimentary and fundamentally distinct fashion. A bacterial (*Escherichia coli*) inner core and a biomaterial (poly(beta-amino ester))-coated outer surface allowed the simultaneous application of molecular biology and polymer chemistry to address barriers associated with APC gene delivery which include cellular uptake and internalization, phagosomal escape, and intracellular cargo concentration. The approach combined and synergized normally disparate vector properties and tools, resulting in increased *in vitro* gene delivery beyond individual vector components or commercially-available transfection agents. Furthermore, the hybrid device demonstrated a strong, efficient, and safe *in vivo* humoral immune response when compared to traditional forms of antigen delivery. In summary, the flexibility, diversity, and potential of the hybrid design were developed and featured in this work as a platform for multivariate engineering at the vector and cellular scales for new applications in gene delivery immunotherapy.