#105 Joe Thomas Advisor(s): Jin Montclare

Role of protein secondary structure in protein-lipid hybrid vehicle for non-viral gene delivery

Gene therapy has the potential to treat various diseases, but a vehicle capable of safely delivering nucleic acids does not currently exist for widespread clinical use. We have recently developed a lipoproteoplex (LPP) consisting of a super-charged coiled-coil protein (CSP) and a cationic liposomal carrier, that has the ability to condense nucleic acids and deliver them in vivo. The LPP is distinct from other liposomal gene delivery systems in that it utilizes a modular protein component to drive transfection activity as opposed to relying on the passive effects of the cationic lipids. A CSP library has been rationally designed to improve the efficacy of the LPP compared to the parent protein via increased nucleic acid binding and endosomal escape through the use of extended histidine tags and increased positive charge. The secondary structure and nucleic acid binding ability of each library member was assessed using circular dichroism and electrophoretic mobility shift assay, then compared to functional transfection data. Structural and functional data suggests that increasing alpha-helicity of the protein component of the LPP improves nucleic acid binding affinity and drives successful transfection with a favorable safety profile.