Effect of Biodegradable PEI in HEK-293 Cells for siRNA Delivery

High molecular weight (≥25-kDa) PEI is an efficient nucleic acid carrier, but exhibits a high toxicity. Cytotoxicity is not a major concern *in vitro* because of the PEI concentration used. If PEI is to be pursued further for gene therapy, a larger volume of PEI is needed for siRNA delivery via PEI-siRNA polyplexes. Low molecular weight (0.8-kDa) PEI exhibits lower toxicity, but is an inefficient vector for siRNA delivery. Therefore, we have synthesized a biodegradable PEI using the commercially available 800-Da branched PEI, formed by reacting PEI with diacrylates to generate polyester. This project investigates the use of our novel cationic polymer for the delivery of siRNA in human embryonic kidney (HEK293) cells.

siRNA polyplexes were characterized with regard to siRNA condensation and determined to be fully condensed at 2.0 μg PEI/μg siRNA by gel retardation and significant quenching of ethidium bromide was measured at 0.6 μg PEI/μg siRNA. Diameters of all the polyplexes measured by dynamic light scattering were of roughly 30 to 200 nm. The targeted gene is luciferase, which is not typically found in HEK293 cells. Therefore, this project involved a co-transfection of both the plasmid pGL3 and GL3 siRNA. Various biodegradable PEI concentrations (4 – 14 μg/mL) were tested at three different siRNA concentrations (5, 25, 50 nM). From our *in vitro* experiments, the delivery efficiency of siRNA is highly dependent on the amount of PEI applied to the cells. At ≥8 μg/mL of biodegradable PEI, a downregulation ≥60 % is achieved with as little as 5 nM of siRNA.