Novel Design of Polymeric Nanoparticles for Targeted Drug Delivery to Glial Cells

Team 11: **Simrita Dhulekar, Elizabeth Hanchar, Alexandra Piñeiro, Rosangel Ramos Espinoza**
Technical Advisor: **Timothy O'Shea**

As the population ages, central nervous system (CNS) disorders have become more prevalent, yet the challenges associated with treating them persist. Glial cells, which maintain a healthy CNS, are an important target for drug therapy. To address glial dysfunction, our team designed polymeric nanoparticles to preferentially target microglia and deliver small-molecule drugs. We developed an in silico pipeline to identify uniquely-expressed glial surface transporters. This pipeline mined published datasets with expression reads for glial cell transporter genes and computed z-scores to normalize the expressions across datasets. Using data dimensionality reduction, we identified uniquely and highly expressed genes for glial cell types. From this analysis, we selected a microglial gene, SLC2A5, which is the only fructose transporter in the CNS. We designed a polymer that includes a fructose ligand to permit preferential binding to this transporter. To enable polymer functionalization, we acrylated fructose by an enzymatic reaction, purified it by flash chromatography, and confirmed purity by NMR. Branched polymers were synthesized via Michael Addition polymerization using different multifunctional thiol and acrylate oligomers before end-capping with fructose monoacrylate. Comparisons of polymer composition were evaluated by FTIR. These polymers were nanoprecipitated to generate nanoparticles (NPs). Stability and size of NPs were characterized using DLS. Formulations with optimized fructose percentage, stable ~100 nm size were pursued further. Polymers applied to neural cell cultures were non-toxic. Additional cell uptake assays are scheduled to determine microglial cell selectivity and specificity. Nanoparticles designed to interact with a specific cell transporter show promise to target cells for therapy.