Neuropath: Multi-Computational Framework for Developing a Receptor-Based Transcytosis Approach to Facilitate BDNF Transmission for Alzheimer’s Progression Prevention

Ramani, Arpit (School: Wheeler High School)

Affecting 60-70% of the 55 million dementia patients in the world, Alzheimer's Disease (AD) has established itself as one of the most profound neurodegenerative diseases in today's society. Research has revealed a major reduction in neurochemicals like Brain-Derived Neurotrophic Factor (BDNF) in AD patients, leading to efforts to synthesize and reintroduce it for AD treatment. However, due to BDNF's properties and Blood-Brain-Barrier's (BBB) semi-permeability, there is no accurate and safe BDNF delivery technique today. By targeting the Transferrin Receptor 1 (TFR1) protein on the BBB's surface, a nanoparticle containing BDNF can undergo receptor-mediated transcytosis and enter into the CNS. To develop this, TFR1 and Transferrin were evaluated for their energies using protein-docking algorithms. Clusters with highest energies were then anchored into CHARMM-GUI nanoparticles using glycerophospholipid surface modifications. Prior to drug encapsulation, two novel components were created to increase efficiency of the drug: i) BDNF-TRKB pathway detachable competitive inhibitor to prevent tumorigenesis tested through RMSD fluctuation via GROMACs, ii) Novel magnetic nanoparticles with docking mechanisms to apply heating onto a-synuclein to increase TRKB proliferation tested through temperature influx via GROMACS. After encapsulation, alteration of Newton's Law of Viscosity to simplify blood-stream flow was used to apply a force onto the nanoparticle to evaluate stability. Ultimately, the nanoparticle radius of gyration shows a direct effect of the bloodstream on the nanoparticle, and described stabilization throughout triangular force application. Results also showcased release of the drug at optimal positions, showcasing efficacy in high-stress artery and CNS environments.