AI/ML-Driven Systems-Level Analysis Identifies CEACAM1 as a Neuroinflammatory-Metabolic Signaling Vulnerability in Parkinson's Disease

Aggarwal, Arnav (School: Loveless Academic Magnet Program High School)

Parkinson disease (PD) remains a progressive neurodegenerative disorder that is characterized by dopaminergic neuronal loss, immune metabolic dysregulation, and chronic neuroinflammation. The current therapies primarily target neuronal pathways, although emerging evidence shows that immune checkpoint signaling also plays a role in the progression of PD. We employed an AI/ML integrated system biology approach that uses multi-omics datasets, pathway enrichment analysis, and regulatory network modeling to identify key unexplored therapeutic targets. Our findings revealed CEACAM1 is one of the key immunomodulatory receptors linked to metabolic homeostasis, inflammatory signaling, and cell-cell communication. However, the exact role in the PD pathogenesis remains unclear. In-silico pipeline also revealed a strong association of CEACAM1 with the NF-KB signaling that is implicated in neurodegeneration. The implementation of structure-based virtual drug screening of 11000 natural compounds and 6000 FDA-approved drugs showed eriocitrin and glyburide as the potential modulators of CEACAM1. Further molecular docking and MD simulation studies demonstrated stable binding of CEACAM1 with both eriocirtrin and glyburide, with minimal root-mean-square deviations (RMSD) and favorable binding energies. In order to experimentally validate these findings, in vitro studies were conducted using the SH-SY5Y cell model. The model, when treated with rotenone, exhibited an increased intracellular reactive oxygen species (ROS) production, thereby mimicking the PD-associated oxidative stress. Treatment with glyburide reduced ROS levels, suggesting potential neuroprotective effects. Overall, these findings predict CEACAM1 is a key modulatory target in PD and demonstrates the translational potential.

Awards Won: