THE PERRY & RUBY STEVENS
Parkinson's Disease
CENTER OF EXCELLENCE

"a-Synuclein (a-Syn) Imaging: A Tool for Parkinson's Disease Research and Clinical Management"

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Abstract

Development of a selective alpha-Synuclein (a-Syn) PET radiotracer for use in Parkinson's disease (PD) and related disorders. We set out to develop a focused compound library of selective compounds that has the potential to bind the a-Syn fibrils.

To identify the best candidates for in vitro and in vivo evaluation we adopted an in-silico structure-based computational docking screen using Autodock Vina. Our focused library consists of chemical entities under two distinct structural motifs (Core 1-2). Initially we have designed and evaluated many a-Syn compounds in in-silico. Based on the in-silico molecular docking screening, we identified 20 best ligands based on the binding affinity and these ligands will further undergo molecular mechanics approach. These compounds are chemically synthesized with their corresponding precursor for carbon-11 or fluorine-18 radiolabeling. In parallel, we evaluated a-Syn binding affinity of the non-radiolabeled a-Syn ligands using microscale thermophoresis (MST) assay and also selectivity and specificity of the radiolabeled ligands in human post mortem brain tissues (PD/AD). During this exercise we can able to identify more specific and selective a-Syn ligand(s) that will be advanced to pre-clinical rodent PET imaging for brain penetration and in addition to the evaluation in transgenic mouse models of PD.