A Tool for Diagnosing and Staging Synucleinopathies

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Synucleinopathies are neurodegenerative diseases characterized by the abnormal accumulation of α-synuclein protein aggregates in the brain. Parkinson's Disease, the leading movement disorder and synucleinopathy, encompasses roughly 9 million people worldwide and costs in the United States alone total $25 billion yearly (Parkinson's Disease Foundation, 2016). However, there are no standard diagnostic tests for a biological marker of Parkinson's, such as a blood test or imaging scan. Difficulty in designing an imaging agent stems from the challenges of crossing the blood brain barrier, binding selectively to authentic lesions, and maintaining a low risk for human patients. This study aims to create an imaging agent that can detect and stage α-synuclein dispersion in vivo via positron emission tomography (PET). PET scans are imaging tests that convey how tissues/organs are functioning by utilizing a radioactive tracer, which will collect in areas with a higher concentration of activity and show up as bright spots on scans. In this study, a radioactive tag will be added to a molecule designed to bind to α-synuclein, thus revealing concentrated lesions in diseased brains as bright spots on scans, Using immunohistochemical methods, human tissue was stained using a commercially available polyclonal anti-α-synuclein antibody and imaged using a con-focal microscope. Tissue stained with our small molecules tagged with a fluorescent ligand recapitulated the images of the positive control, validating that our molecule bound to the target. Preliminary data have provided promising results of the development of an imaging agent that binds authentically to α-synuclein and has the characteristics necessary to pass the blood brain barrier while remaining safe for oral consumption. To continue verification, further testing will be done against Tau and β-amyloid protein to ensure the molecule's selectivity for α-synuclein. Successful completion of this project will provide an objective diagnostic tool for physicians and patients. This tool will be critical in earlier diagnosis and staging of disease, such as Parkinson's and Alzheimer's disease and other dementias, aiding patients and healthcare providers towards better medical treatment and disease outcome.