

**ABSTRACT**

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 the United States alone total $25 billion yearly. 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 α-synuclein and remaining low risk for human patients. This study aims to create an imaging agent that can detect and stage α-synuclein distribution in vivo (live in the patient) via positron emission tomography. 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 synuclein. Successful completion of this project will provide an objective diagnostic tool for PD.

**RESULTS (continued)**

2. Tissue sections prepared from the substantia nigra region of authentic PD brain demonstrate Lewy bodies (Fig. 5AB).

3. A fluorescent candidate small-molecule successfully stained Lewy bodies (Fig. 5C).

4. A fluorescent candidate small-molecule did not stain tau lesions (Fig. 6D).

**DISCUSSION**

- α-synuclein aggregates are a tractable target for small-molecule radiotracer development
- Binds recombinant α-synuclein selectively over tau and Aβ
- Binds authentic Lewy bodies in PD tissue
- Appropriate clogP, tPSA, and PK values suggest the scaffold class may have utility in vivo
- FUTURE STUDIES
  - Structure activity relationship analysis to identify lead molecule
  - Preparation of radiolabeled compounds for advanced preclinical investigation
  - Direct binding experiments
  - Distribution, metabolism, and pharmacokinetics

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**REFERENCES**


