Parkinson’s disease (PD) is a progressive neurodegenerative disorder defined clinically by the combination of tremor, rigidity, bradykinesia, and postural instability. The pathological hallmark of PD, Lewy body, is a hyaline cytoplasmic inclusion found in the neuronal perikarya. Similar inclusions found in neuronal cell processes are called Lewy neurites.1-3 Alpha (α)-synuclein is the most prominent protein in Lewy bodies and Lewy neurites.1-3

The mechanisms whereby α-synuclein deposition leads to neurodegeneration are not fully elucidated.4 However, accumulating evidence suggests that α-synuclein deposition occurs early in the course of PD and may antedate the appearance of the clinical features of the disease.5 This provides the rationale for in vivo assessment of α-synuclein deposition in body fluids and tissues as a biomarker for PD.5 A suitable biomarker could identify patients early in the clinical course of the disease, improve diagnostic accuracy, and provide a surrogate endpoint for neuroprotective and disease-modifying therapies.7-9 This goal has not been fully realized.

At present, the diagnosis of PD is made by a clinician with expertise in the diagnosis of neurodegenerative disorders. Although a number of criteria exist to support a clinical diagnosis of PD, the International Parkinson and Movement Disorder Society’s 2015 clinical diagnosis of PD statement provides a clear path to ‘Clinically Established PD’ and ‘Clinically Probable PD’.10 The criteria are based on the inclusion of certain items (response to levodopa, levodopa-induced dyskinesias, rest tremor of a limb, olfactory loss, or cardiac sympathetic denervation) combined with exclusionary criteria (including alternative diagnoses that may be more likely) with other items that increase or decrease the probability of a diagnosis of PD.10 Despite the inclusion of clinical criteria for diagnosis of PD, these tools do not provide an effective means for early diagnosis and still suffer from incorrect diagnosis rates as high as 25%, particularly in early disease.11

At present, dopamine transporter imaging (DaTscan) is available to aid in the diagnosis of PD. DaTscan has limited utility because it is only available in academic or large regional medical centers, is expensive, and may have <50% accuracy for early diagnosis.12-16 In addition, DaTscan cannot distinguish PD from non-synucleinopathy degenerative disorders such as progressive supranuclear palsy (PSP).17

With the identification of phosphorylated α-synuclein as the pathological hallmark of synucleinopathy, interest in in vivo tissue diagnosis of PD has grown.1 Based on the evidence of peripheral autonomic denervation in PD, a number of laboratories have sought evidence of peripheral α-synuclein deposition within peripheral nerves. Skin biopsies have been an attractive source of tissue for investigation. We and others have detected the presence of phosphorylated α-synuclein from punch skin biopsies of patients with PD.15-26 To date, in academic laboratories a total of 241 patients with PD and 238 healthy controls have been studied by skin biopsy for detection of phosphorylated α-synuclein.20,22,23,25,27-33 This data reveals that phosphorylated α-synuclein is detected in 88% of patients with PD, whereas it has not been detected in any of the 238 healthy control samples.

The robust data from multiple academic laboratories has established skin biopsy as an effective tool to detect phosphorylated α-synuclein in patients with suspected PD. CND Life Sciences is proud to be the first commercial lab to bring this technology into the hands of physicians. We hope you will find this significant advance in the field to be a boon to patients who have struggled to confirm a diagnosis.
REFERENCES


REFERENCES (CONTINUED)