Patients with LRRK2 mutations reveal α-synuclein and tangle pathology and neuronal loss at autopsy. This suggests that LRRK2 may play a central role in the etiology of sporadic Parkinson Disease (sPD). To better understand the relationship between LRRK2 and protein inclusions in PD, we investigated the distribution and cellular localization of LRRK2 in regions affected in the prodromal and motor stage of sPD.

We immunostained sections from incidental Lewy Body Disease (iLBD), sPD and control cases throughout the olfactory bulb, medulla oblongata, locus coeruleus and the substantia nigra using antibodies specific for LRRK2 (NB 300-268) and pathological α-synuclein (Novocastra). LRRK2-immunoreactivity (IR) in the olfactory bulb was predominantly localized in the anterior olfactory nucleus, mitral cell layer and granular cell layer. iLBD and PD cases showed markedly more granular LRRK2-IR in of the dorsal motor nucleus, substantia nigra and locus coeruleus, whereas control cases reveal diffuse cellular staining in these brainstem regions. Double immunofluorescence showed that LRRK2-IR did not overlap with punctate α-synuclein but did in larger accumulations of pathological α-synuclein and Lewy Bodies and Lewy Neurites. Both iLBD and sPD cases also showed cells with distinct LRRK2-IR spherical granules whereas controls did not. These cells did not reveal α-synuclein pathology. Our results show that LRRK2 co-localizes with pathological α-synuclein in larger aggregates but does not in punctate α-synuclein pathology. LRRK2 also accumulates in distinct spherical granules in cells absent of α-synuclein pathology suggesting that LRRK2 may also pathologically accumulate separately from α-synuclein.