EXPLORING LRRK2-TAU INTERPLAY IN PARKINSON'S DISEASE

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Parkinson's disease (PD) is a chronic and progressive movement disorder characterized by neuron loss in the substantia nigra and in other brain area. The neuropathological hallmark of PD is the appearance of intraneuronal protein aggregates known as Lewy bodies (LBs) and neurites consistent with filamentous inclusions mainly composed of α-synuclein (α-Syn). Accumulating evidence highlights also the implication of the microtubule-associated protein tau in the pathogenesis of PD, as component of LBs and of neurofibrillary tangles in different brain regions. Of interest, tau pathology has been predominantly found in Leucine-rich repeat kinase 2 (LRRK2) G2019S carriers. The presence of hyperphosphorylated and aggregated tau in the brains of PD patients suggest an interesting cross-talk between LRRK2 and tau to be explored. Intriguingly, the kinase LRRK2 has been revealed as a crucial mediator of the neuroinflammatory response, and neuroinflammation has been reported to play a direct role in the formation of tau inclusions.

Based on these observations, in this study we explore if and how LRRK2-mediated neuroinflammation impacts neuronal tau-related pathways leading to pathological aggregates by using *in vitro* and *in vivo* models. Our preliminary results showed that aged LRRK2-G2019S knock-in (KI) mouse brains exhibited increased levels of phosphorylated tau and an enhanced neuroinflammatory response compared to WT mice.