"LRRK2 neurobiology and Parkinson's disease pathogenesis"
Presented by Wanli W. Smith, MD, PhD

Abstract

Mutations in the leucine-rich repeat kinase-2 (LRRK2) gene cause autosomal-dominant Parkinson's disease (PD) and contribute to sporadic PD. My presentation covers the research findings from our group on LRRK2 neurobiology and its pathological roles in PD pathogenesis. Previously we identified that LRRK2 kinase and GTP binding activities play critical roles in neurodegeneration and protein inclusion formation. We generated LRRK2-based PD models including LRRK2 transgenic drosophila and mice. Recently we have identified a series of LRRK2 GTP binding inhibitors which can inhibit LRRK2 kinase activity and provide a useful tool for further studying LRRK2 functions and for developing potential therapeutics for LRRK2-linked PD intervention. We found that LRRK2 GTP binding inhibitors protected against PD-linked mutant LRRK2-induced neuronal degeneration and partially attenuated other cellular abnormalities. Our findings not only provide insight into molecular mechanisms underlying PD pathogenesis but also identify lead-compounds for further drug discovery.