LRRK2 Inhibitors

Leucine-rich repeat kinase 2 (LRRK2) is a protein that can be found in the cytoplasm and the mitochondrial outer membrane. LRRK2 gain-of-function mutants are associated with increased risk for Crohn's disease as well as Parkinson's disease. Models of Parkinson's disease show that LRRK2 mutations affect vesicular trafficking, autophagy, protein synthesis, and cytoskeletal function[1].

LRRK2 interacts with Parkin, a ligase involved in protein degradation; mutant forms of Parkin are associated with the development of a juvenille familial form of Parkinson's disease[2]. Expression of LRRK2 mutants results in shortening of dendrites in neurons in vitro[3]. Other mutations induce calcium imbalance, autophagic clearance of mitochondria, and neuro-degeneration and inflammation, all signs of Parkinson's disease[4-5].

Currently, few options are available to slow or prevent the progression of this disease. Although some compounds show activity in research models, the field is still growing. However, inhibition of LRRK2 suppresses its kinase activity, lessening pathologies associated with Parkinson's disease in cellular and animal models.

LKT Laboratories carries several LRRK2 inhibitors that are currently under investigation for their neuroprotective applications in various research models.

PF-06447475 (P2100) suppresses neurodegeneration and inflammation induced by α-synuclein in animal models[5]. In vitro, **CZC-54252 (C9808)** limits mutant LRRK2-induced injury of rodent and human neurons[6]. **GNE-7915 (G5216)** inhibits LRRK2 with high potency across several species[7].

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