

LRRK2 – novel target for Parkinson's Disease and Parkinson-related Syndroms

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Challenge

Parkinson's disease (PD) is a severe, progressive, age-associated, neurodegenerative disorder. Current therapies are symptomatic and not effective at halting or significantly slowing the disease progress. The search for etiologic-based therapies has focused largely on genetic findings made in familial forms of this disease. Mutations of five genes have been unequivocally linked to PD; two of these, LRRK2 and PINK1, encode kinases and as such are attractive tools to understand the disease process. Furthermore, preliminary functional data suggest that these proteins, or the pathways in which they are involved, are viable therapeutic targets.

Technology

In a joint effort of the Helmholtz Zentrum München, the Mayo Foundation for Medical Education, the University Clinic Tübingen and the University of British Columbia, Vancouver, the leucine-rich repeat kinase 2 (LRRK2) was identified in families with late-onset autosomal dominant PD. Several mutations were described. LRRK2 is a key player in the patho-genesis of PD. Mutations in the LRRK2 gene account for up to 10% of all autosomal dominant forms of familial and for approximately 1-3% of sporadic PD patients. Clinical and pathological studies have demonstrated that in the majority of cases LRRK2 mutations lead to PD with classical clinical and pathological features. However, in some patients the pathological features can be distinct and/or more extensive than typically seen in PD. Collectively, these findings provide important clues into the mechanisms by which LRRK2 mutations can lead to demise of dopaminergic neurons.

Commercial Opportunity

LRRK2 is a promising point of therapeutic intervention for PD and its genetic diagnosis. Offered are

- a license covering the diagnostic use of the LRRK2 gene and its mutations
- monoclonal antibodies against LRRK2 and GST-tagged protein domains
- expression vectors for LRRK2 domains
- co-operation for further elucidation of LRRK2 functions

Patent Situation

Patent applications covering the LRRK2 mutations R793M, Q930R, S1096C, L1114L, I1122V, S1228T, R1441C, Y1699C and/or I2020T have been filed in the US, Canada, Europe and Australia. A further patent application (W006068492) covering the G2019S mutation was filed by the Mayo Clinic and would also be available for in-licensing.

Further Reading

Zimprich et al., Neuron. 2004 Nov 18; 44(4): 601-7; West et al., PNAS, 2005, Nov. 15; 102(46): 16842-7; Gloeckner et al., Hum Mol Genet. 2006 Jan 15; 15(2): 223-32; Taylor et al., Trends Mol Med. 2006 Jan 7 (Review); Ozelius et al., N Engl J Med 2006; 354(4): 424-5; Lesage et al., N Engl J Med 2006; 354(4): 422-3.