# “LRRK2 Genetic Variation in a Malay Parkinson's disease Cohort”

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Parkinson’s disease (PD) is a progressive neurodegenerative disorder that affects 6.3 million people worldwide and currently, around 20,000 are diagnosed with PD in Malaysia. Despite being the second most common neurodegenerative disease, the aetiology of Parkinson’s disease (PD) remains elusive and only symptomatic treatment exists. Genome-wide association studies in America and Europe have identified a number of loci that confer risk of developing late onset PD. Discovered in 2004, leucine-rich repeat kinase 2 (*LRRK2*) is the greatest known genetic contributor to Parkinson's disease (PD). *LRRK2* has been found to have multiple cellular roles in PD through involvement in the synaptogenesis, cytoskeletal, mitochondrial-related and stress-induced pathways. Previous work in our lab has indicated that there are a number of mutations in *LRRK2* that are associated with the Malaysian Chinese PD cases, but these mutations are absent/very rare in the Malaysian Malay PD cases. The Malay PD cohort, remains a largely under-reported group in PD genetics with limited literature. To fill this gap, we screened fifteen exons in key domains within *LRRK2* to uncover other mutations that may be more relevant to the Malays. We detected two non-synonymous variants (p.R1628P and p.S1647T), and four synonymous variants (p.G1624G, p.K1637K, p.G1819G, p.E2108E). As p.R1628P has already been reported in our population, we focused on the p.S1647T variant and performed a case-control association study. There was no significant difference between the 404 PD patients and 396 controls screened, however there remains an issue with deviation from the Hardy-Weinberg equilibrium in the controls for this variant which complicates the interpretation. In conclusion, coding regions within key *LRRK2* domains were screened in Malays for the first time, and represents an important first step in understanding more about the contribution of *LRRK2* in the Malay cohort.

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