Whole genome methylomic profiling in Parkinson’s: An integrated genetic-epigenetic approach

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Whole genome methylomic profiling in Parkinson's: An integrated genetic-epigenetic approach

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Parkinson's UK

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2

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Research Abstract

Our understanding of idiopathic Parkinson’s has recently been enhanced by large genome-wide association (GWA) studies which have collectively identified susceptibility variants at over 18 loci that increase risk for Parkinson’s. However, the biological basis for Parkinson’s associations identified through GWA studies remain unsolved. In this project we propose to look beyond the traditional aetiology of genetic mutations in Parkinson’s by examining the role of epigenetic mechanisms in the idiopathic form of this disorder.

We propose that epigenetic mechanisms can mediate an increased risk to Parkinson’s, and in particularly, genotype-DNA methylation interactions can facilitate the increased risk carried by genetic susceptibility variants implicated by GWA studies.
This proposal will address the paucity of epigenetic studies in Parkinson’s by conducting a series of molecularly robust and statistically well powered analyses to establish whether DNA methylation (DNAm) is correlated with Parkinson’s susceptibility loci. We will also investigate whether previously implicated biological pathways are enriched for changes in DNAm, directly following-up our previous observation that variants implicated by Parkinson’s-GWA studies implicate genes of shared biological function. Finally, we will also perform the largest genome wide investigation of differentially methylated regions that either increase risk to Parkinson’s or are correlated with Parkinson’s progression.
This work has the potential to impact greatly upon the clinical diagnosis, prognosis and future treatment of Parkinson’s. Moreover, given the potential reversibility of epigenetic mechanisms it is possible that our analyses will highlight novel targets for the development of therapeutic interventions for Parkinson’s.

Further information available at:

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