Profiling post-translational modifications of histone proteins as a determinant of Parkinson’s susceptibility

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Profiling post-translational modifications of histone proteins as a determinant of Parkinson's susceptibility

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Parkinson's UK

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2

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Research Abstract

Large genome-wide association studies have now collectively identified susceptibility variants at over 28 loci that increase risk for idiopathic Parkinson’s disease (PD). However, in order to better understand the pathobiology of PD and to ultimately progress to the development of improved therapies, it is now essential that we understand the biological consequences of these susceptibility alleles. Post-translational modifications of histone proteins (hPTM) are an

important class of epigenetic modification that control the extent to which chromatin is condensed (heterochromatin) or relaxed (euchromatin). Genotype-epigenetic interactions are relevant to a number of complex disorders, and in a Parkinson's UK funded grant (G-1309) our preliminary analysis of DNA methylation suggests that it is also relevant to PD. As DNA methylation and hPTM are largely independent biological mechanisms it is important that we now investigate hPTM in relationship to PD. In this project we will therefore conduct a well-powered study to determine whether hPTM are correlated with well-established PD susceptibility loci in pathologically relevant post mortem brain tissue. Moreover, we will also investigate whether previously implicated biological pathways are enriched for changes in hPTM. As hPTM are potentially reversible using drugs that cross the blood brain barrier they are particularly tractable to therapeutic interventions for PD. Identifying hPTMs correlated with disease in the degenerating regions of the brains of PD patients could facilitate the development of improved drugs that target disease relevant changes in hPTM. It is therefore possible that our analyses will highlight novel targets for therapeutic interventions for PD.

Further information available at:

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