Comprehensive approach for genomic characterization of individuals with Parkinson's disease

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The majority of available genetic tests for Parkinson's disease are focused on a limited number of genes. These tests may not be informative particularly with the increasingly recognized genetic heterogeneity of PD. As more than 40 candidate genes have been discovered through whole-exome sequencing (WES) oriented studies, in addition to a number of genes previously identified by linkage and candidate gene approaches. Therefore, implementing a genetic assessment workflow that can capture the genetic lesions typically found in PD (copy number variations (CNVs) and single nucleotide variants (SNVs)), is essential for a comprehensive molecular characterization. In this study, we devised an integrative genomic evaluation workflow that can capture both SNVs and CNVs. The multistage strategy that we have employed involves screening samples for CNVs in known PD genes, followed by WES and variant prioritization. By applying this approach we have successfully identified 125 novel rare variants in 85% of our cases including 22 high confidence ones. All the discovered variants were present in new candidates genes that have not been previously reported in PD except for two (EIF4G1 and ATP13A2). Our combined molecular approach provides a comprehensive strategy applicable for complex genetic disorders.

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