Gene Expression Differences in Peripheral Blood of Parkinson's Disease Patients with Distinct Progression Profiles

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Abstract:

The prognosis of neurodegenerative disorders is clinically challenging due to the inexistence of established biomarkers for predicting disease progression. Here, we performed an exploratory cross-sectional, case-control study aimed at determining whether gene expression differences in peripheral blood may be used as a signature of Parkinson's disease (PD) progression, thereby shedding light into potential molecular mechanisms underlying disease development. We compared transcriptional profiles in the blood from 34 PD patients who developed postural instability within ten years with those of 33 patients who did not develop postural instability within this time frame. Our study identified >200 differentially expressed genes between the two groups. The expression of several of the genes identified was previously found deregulated in animal models of PD and in PD patients. Relevant genes were selected for validation by real-time PCR in a subset of patients. The genes validated were linked to nucleic acid metabolism, mitochondria, immune response and intracellular-transport. Interestingly, we also found deregulation of these genes in a dopaminergic cell model of PD, a simple paradigm that can now be used to further dissect the role of these molecular players on dopaminergic cell loss. Altogether, our study provides preliminary evidence that expression changes in specific groups of genes and pathways, detected in peripheral blood samples, may be correlated with differential PD progression. Our exploratory study suggests that peripheral gene expression profiling may prove valuable for assisting in prediction of PD prognosis, and identifies novel culprits possibly involved in dopaminergic cell death. Given the exploratory nature of our study, further investigations using independent, well-characterized cohorts will be essential in order to validate our candidates as predictors of PD prognosis and to definitively confirm the value of gene expression analysis in aiding patient stratification and therapeutic intervention.

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