OVERLAPPING MOLECULAR SIGNATURES IN PARKINSON'S PATIENT LEUKOCYTES BEFORE AND AFTER TREATMENT AND IN MOUSE MODEL BRAIN REGIONS.

By elsc_admin
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Abstract:

Parkinson's disease (PD) is a chronic and progressive neurodegenerative disease with worldwide increasing incidence. PD is the second most prevalent neurodegenerative disease and the first that involves motor symptoms. The great majority of cases, defined as sporadic with non-familial disease, show a highly variable risk of disease due to environmental and genetic factors that remain largely unknown. Furthermore, the neurodegenerative process typically initiates decades prior to the appearance of hallmark motor symptoms; therefore, clinical diagnosis is enabled only when most of the relevant neurons have died and current treatment is palliative at best. Here, we review the application of genomic scale microarray based research aimed to enable early diagnosis and identify novel targets for therapeutic intervention. We demonstrate that blood leukocytes can serve as a feasible and reliable tissue source to test for disease-induced and treatment-related transcript changes. We cover our reports of transcription and alternative splicing modifications in PD patient's leukocytes based on 3' and exon microarray analyses and the identified inflammatory modulations. We further describe the effects of deep brain stimulation (DBS) neurosurgery on the leukocyte transcripts as reflecting the patient's neurological status. A focus is gained on common genes identified both in the molecular signature of human PD leukocytes and in brain RNA from engineered PD mouse models subjected to risk and protection manipulations. Finally, we discuss potential future directions of high-throughput RNA research as facilitators of the PD knowledge base through next generation sequencing technologies of both short and long RNA transcripts including microRNAs.

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