Parkinson's disease map facilitated gene expression analysis reveals new insights in PD pathogenesis

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Recent developments in 'omics' technologies allow studying molecular pathogenesis/mechanisms of diseases in great detail. However, comprehensive interpretation of such data requires their integration with the existing body of knowledge on a given disease. The Parkinson's disease (PD) map, developed by the Luxembourg Centre of Systems Biomedicine (LCSB) together with the Systems Biology Institute, Tokyo, Japan, makes the information from more than 1500 research articles and public databases available for interpretation in a molecular interaction map.

The MINERVA platform, developed at LCSB, which is tailored for visualization and management of disease maps, allows for overlay of experimental data from 'omics' studies, thereby enabling an interpretation of the data in the context of disease related cellular compartments and molecular processes.

PD map platform was successfully applied in the past for the interpretation of transcriptomic data from animal models of PD. The objective of the study was to identify early disease marker for PD, which is essential, since the disease is already in an advanced state when motor symptoms become obvious. The transgenic mouse model used shows a moderate overexpression of mutated human alpha-synuclein. This protein can form aggregates and fibers, resembling contents of Lewy bodies that are supposed to be involved in human PD pathology. Consequently, the mouse line shows mild PD-like pathology starting at 9 months of age.

Transcriptomic data were generated from ventral midbrain tissue samples, of 3, 9 and 13 months-old mice, to identify perturbations in relevant molecular pathways before neurodegenerative or behavioral changes appear. Analysis of differential gene expression using the PD map reveals early molecular changes in PD-related processes such as dopamine metabolism and calcium signaling. In addition, the system provides hypotheses on perturbations of regulatory elements, such as transcription factors, that may trigger the disease progression. Furthermore, PD map tools enable translation of the results to human by direct comparisons with data from human studies. Finally, by overlaying gene variants data from NGS studies in humans and linkage out to drug databases PD map will support patient stratification in precision medicine and the identification of potential drug targets.