Exploration and analysis of the PD map

Integrating pathways of Parkinson's disease in a molecular interaction map

Molecular Neurobiology

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Exploring the PD map

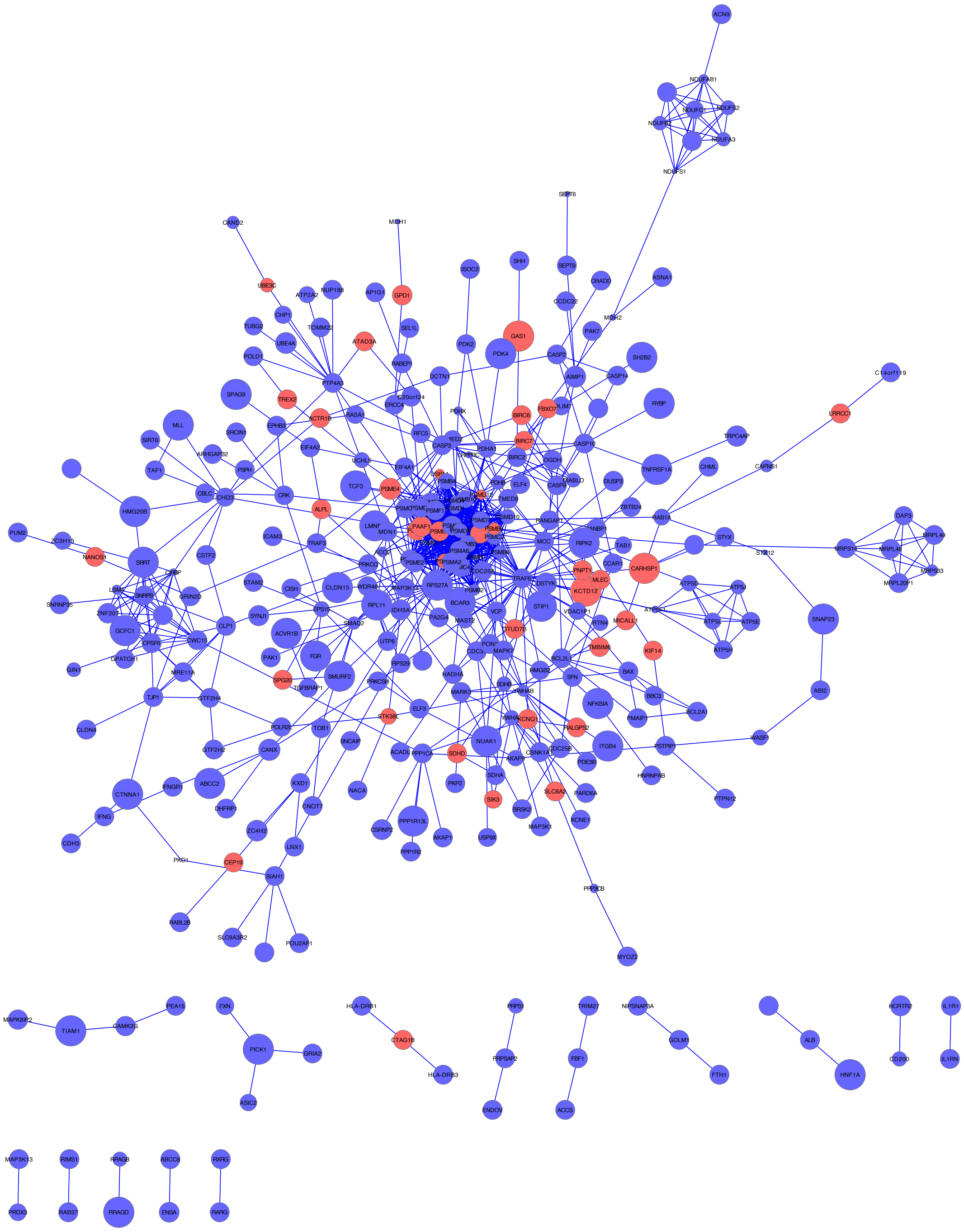
Online and browsable version of the map can be found under the address: http://minerva.uni.lu/MapViewer/map?id=pdmap. This version allows browsing the map, search for elements (box in the upper left corner) and checking the bioinformatics annotation and evidence behind interactions. Left click displays the annotation in the panel on the left. Please, note that all the annotations are hyperlinks, leading directly to the original resource. Right click on an element or interaction shows “What it is?” option, similarly displaying the annotation, and “Send feedback” option, allowing the user to send a request or information to curators of the map.

The visualization of differential gene regulation for two FDR values (0.01 and 0.05) are available via the buttons in the upper right corner. These results base on the analysis of 8 transcriptome studies in PD (see Manuscript).

Our database annotation service annotates map elements with information found in a number of publicly available databases, like UniProtKB, HGNC, EMBL, Ensembl, UCSC genome browser database, RefSeq, EntrezGene, UniGene, GeneCards, PDB, Gene Ontology(GO), KEGG, PANTHER, Reactome, Pfam, InterPro or PharmGKB.

The full contents of PD map (see PD_map.xml file) are provided in the .xml format in Online resource 2. This file should be opened in CellDesigner 4.3 software that can be downloaded using the following link: http://celldesigner.org/download.html.

Network enrichment and analysis



Supplementary Fig 1 Enrichment of the PD map using gene expression and protein-protein interaction datasets

The figure depicts network of elements present in the PD map (in blue) and new elements suggested to be included in the PD map (in red). The size of the nodes corresponds to the expression levels of the genes in the network. Please, note that the enrichment process changed the layout of the original PD map and that a proper magnification is required to notice all the details.

The map provided in Online resource 2 can be transformed into a graph, which in turn can be processed using different network analysis methodologies outlined in the Manuscript. This way insights into the structure of PD pathways can be gained.

In the current PD map nodes with high centrality correspond to proteins involved in neuronal plasticity and regulators of calcium or cAMP signalling pathways. Subsequently, analysis of inter-modular communication indicates the importance of interactions between synaptic functions: elements of protein degradation system and dopamine transport. Both approaches indicate that the proteins of apoptosome, various reactive oxygen species as well as components of energy production pathway, including metabolites of citric acid cycle and glycolysis, are important. For the detailed list see Online resource 3, Supplementary Tables 1 and 2.

Simple path analysis is such a method which, for instance, indicates that proteins involved in electron transport chain, proteolysis, mitochondrion organisation, regulation of protein modification and synaptic transmission are influencing mitochondrial dysfunction. For the detailed list see Online resource 3, Supplementary Table 3.