Life Science

Robust Gene Dys-Regulation in Alzheimer's Brains

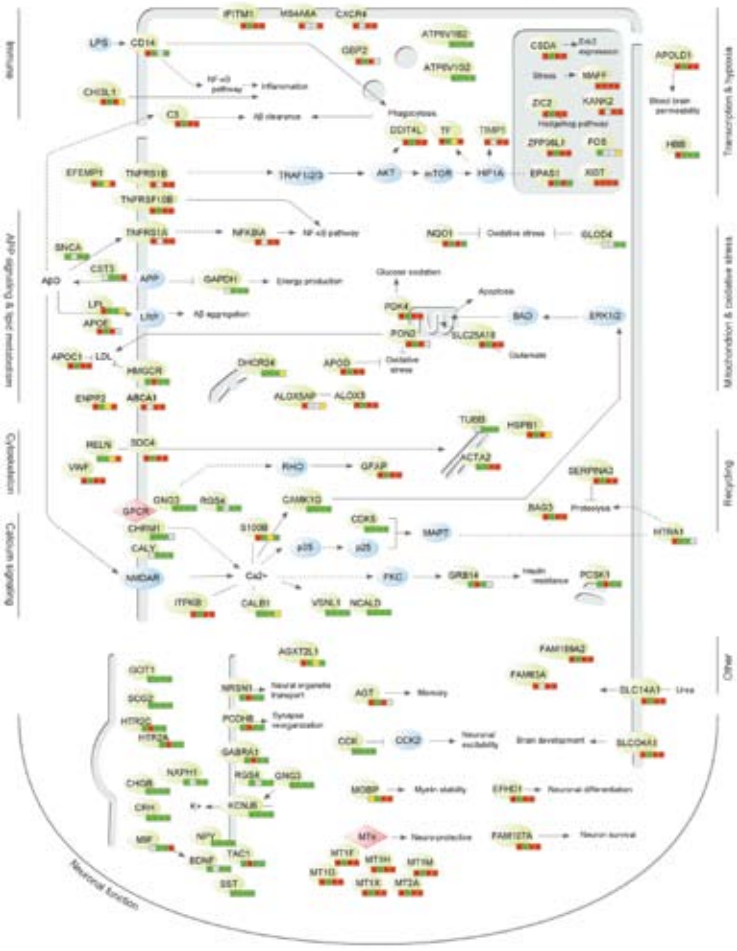
Recently, a team of researchers led by Prof. LEI Hongxing at the Beijing Institute of Genomics (BIG), CAS achieved a new breakthrough in their exploration into the pathogenic mechanism of the Alzheimer's disease, a progressive neurodegenerative disorder occurring in old age.

Treating and preventing Alzheimer's disease (AD) requires better understanding of the disease's pathogenic mechanism, for which the brain transcriptome of AD offers some clues at the gene expression level. So far, thousands of genes have been reported to be dys-regulated in the brains of patients suffering from AD. However, the consistency or discrepancy among these studies has not been thoroughly examined.

Towards this end, Prof. LEI Hongxing's lab at BIG conducted a comprehensive survey of the brain transcriptome datasets for AD and other neurological diseases. The researchers first demonstrated that the frequency of observed dys-regulation in AD was highly correlated with the reproducibility of the dys-regulation. Based on this observation, they selected 100 genes with the highest frequency of dys-regulation to illustrate the core perturbation in AD brains, and the dys-regulation of these genes was validated in several independent datasets for AD.

Further, they identified 12 genes whose gene expression has strong correlation with disease progression. The relevance of these genes to disease progression was also validated in an independent dataset.

Also, the researchers found an intriguing transcriptional "cushion" for these 100 selected genes in the visual cortex region of the brain, which is less vulnerable to AD. This "cushion" may be a critical component of the protection mechanism for less vulnerable brain regions. In addition, they proposed the critical roles of several transcription regulators, especially ZFP36L1.



The top 100 genes selected based on AD brain transcriptome. The dys-regulation of each gene at the four major datasets is indicated by colored banner below the gene ID (red for up-regulation, green for down-regulation, yellow for mixed perturbation, and gray for non-perturbation). The selected 100 genes are indicated by light green color. Other important genes have been added to the map to enhance the functional connections. (Image by LEI's group)

To facilitate the research in this field, Prof. LEI and his team have developed a publicly accessible web server "AlzBIG" (http://alz.big.ac.cn) to make the relevant information available to the research community.