AGE-DEPENDENT CHANGE IN THE GENE EXPRESSION PROFILE OF AN ANIMAL MODEL OF ALZHEIMER'S DISEASE

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In this study, using a microarray approach, we investigated the gene expression profile in the hippocampus of young and old AD transgenic and control mice.

A global gene expression profile in the hippocampi obtained from 3xTgAD (expressing mutant human APP, PS1, and tau), PS1KI (expressing human mutant PS1), and WT mice at 3 and 12 months of age was studied by employing a Mouse OneArray Whole Genome DNA microarray. Hierarchical clustering analysis was performed by using Cluster 3.0 and treeview software. Data were also analyzed with the Ingenuity Pathways Analysis (IPA) in order to achieve a classification of the results on the basis of their biological functions and disclose functional networks and/or pathways.

When comparing 3xTg-AD and PS1KI mice to WT mice, clustering revealed the selective presence of hundreds of up-regulated and down-regulated transcripts. IPA analysis of the upregulated genes identified their involvement in cell to cell signaling interaction, nervous system development and function, as well as in cell death and pathways linked to GABA neurotransmission and mitochondrial dysfunction. The analysis of the down-regulated genes indicates areas related to cellular growth and proliferation, gene expression, and lipid metabolism, these genes appear to participate in pathways associated with calcium and CREB signaling.

We find that over-expression of AD-related genes such as mutant APP, PS1, and tau modulates the expression of genes that are critical for inhibitory neurotransmission, energy production and homeostasis of calcium. These results may help to unravel the role of gene expression in both AD progression and/or neuroprotection.