Integrative analysis reveals metabolic switch in aging astrocytes

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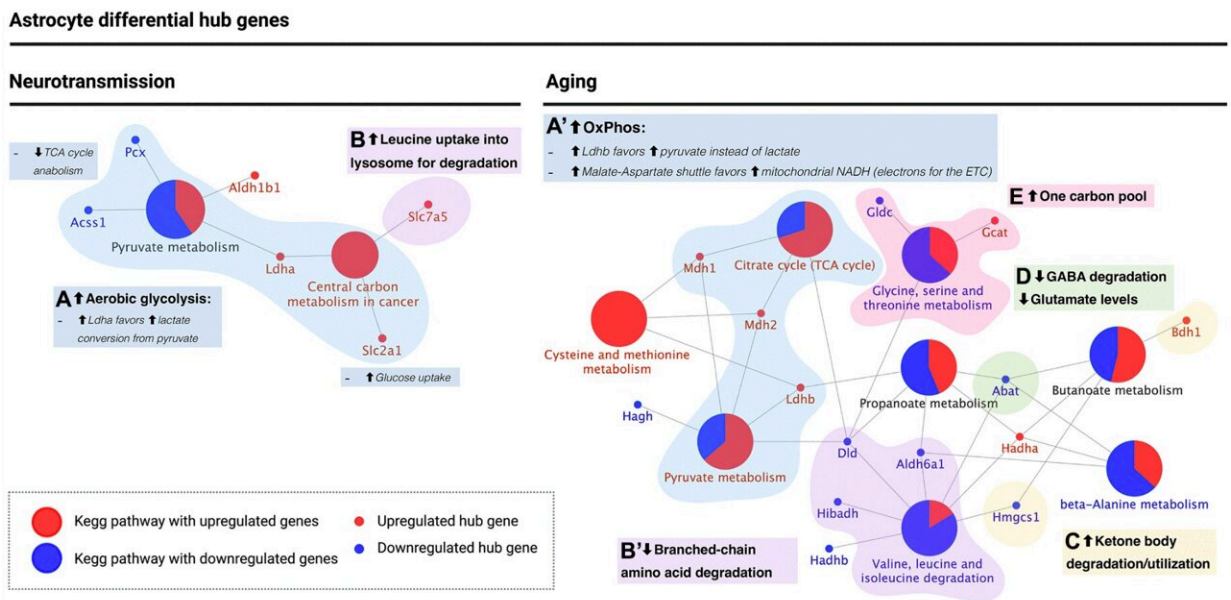

KEGG pathway enrichment analysis of astrocyte differential hub genes suggests a metabolic switch from aerobic glycolysis to oxidative phosphorylation during aging. Credit: *Aging* (2023). DOI: 10.18632/aging.204663

A new research paper titled "Metabolic switch in the aging astrocyte supported via integrative approach comprising network and transcriptome analyses" has been published in *Aging*.

Dysregulated central-energy metabolism is a hallmark of brain aging. Supplying enough energy for neurotransmission relies on the neuron-astrocyte metabolic network. In their new study, researchers Alejandro Acevedo, Felipe Torres, Miguel Kiwi, Felipe Baeza-Lehnert, L. Felipe Barros, Dasfne Lee-Liu, and Christian González-Billault from Universidad de Chile, Cedenna, University of California, San Diego, Centro de Estudios Científicos (CECs), Geroscience Center for Brain Health and Metabolism (GERO), Universidad San Sebastián, and the Buck Institute for Research on Aging aimed to identify genes contributing to age-associated brain functional decline.

The researchers write, "[...] we formulated an approach to analyze the metabolic network by integrating flux, network structure and transcriptomic databases of neurotransmission and aging."

Their findings support that during brain aging:

- The astrocyte undergoes a metabolic switch from aerobic glycolysis to oxidative phosphorylation, decreasing lactate supply to the neuron, while the neuron suffers intrinsic energetic deficit by downregulation of Krebs cycle genes, including mdh1 and mdh2 (Malate-Aspartate Shuttle);
- Branched-chain amino acid degradation genes are downregulated, identifying dld as a central regulator;
- Ketone body synthesis increases in the neuron, while the astrocyte increases their utilization, in line with neuronal energy deficit in favor of astrocytes.

"The genes identified here are valuable candidates for future studies to understand the molecular mechanisms of healthy brain aging and prevent brain age-associated failure using energy metabolism as a target," the researchers conclude.

More information: Alejandro Acevedo et al, Metabolic switch in the aging astrocyte supported via integrative approach comprising network and transcriptome analyses, *Aging* (2023). DOI: 10.18632/aging.204663