Ingenuity® Science Spotlight:

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Aquaporin-4 is increased in the sclerotic hippocampus in human temporal lobe epilepsy.

Tih Shih Lee, Tore Eid, Shrikant Mane, Jung H. Kim, Dennis D. Spencer, Ole Petter Ottersen, and Nihal C. de Lanerolle. Acta Neuropathol (Berl). 2004 Dec;108(6):493-502.

http://www.ncbi.nlm.nih.gov/pubmed/15517312?dopt=Abstract

Mesial temporal lobe epilepsy (MTLE) is a disorder characterized by chronic seizures. The hippocampus of patients with MTLE is typically fibrotic and shrunken by patterned loss of neurons and astroglial proliferation. The molecular basis of hippocampal sclerosis is still obscure.

The authors investigated whether aquaporin-4 (AQP4), a water channel transporter protein in the brain, plays a role in hippocampal sclerosis. AQP4 couples water transport to K+ clearance. This study characterized the spatial distribution of AQP4, its expression profiles, and the regulation of genes in its functional pathways.

Hippocampal specimens obtained from patients were processed for analysis by immunohistochemistry, quantitative real time PCR, and the Affymetrix7 GeneChip7 U133A array. Data generated from both light and electron microscopy combined with immunohistochemistry showed that the AQP4 protein was localized in the CA1 area of the mesial temporal lobe. In addition, AQP4 was localized to the membranes of astrocytic end-feet, next to endothelial cells. Increased AQP4 expression was detected by quantitative real time PCR as well as microarray analysis. As one of the reporter sequences on the U133A array, expression of AQP4 was also detected in the CA1 region of the hippocampus.

IPA was used to investigate the molecular pathways and gene networks associated with AQP4 function in the hippocampal specimens from patients. As shown in the network in Figure 4 of this paper, the expression of six genes increased and five genes decreased. The elevation of AQP4 expression is correlated with increased GFAP (astrocyte marker glial fibrillary acidic protein) expression. Conversely, increased AQP4 is associated with decreased expression of dystrophin, a protein implicated in the anchoring of AQP4 to perivascular endfeet. IPA also revealed that along with increased AQP4 expression in the sclerotic region of the hippocampus, expression levels of several genes related to dystrophin-associated protein complex were also altered. This complex anchors AQP4 protein to cellular membranes and regulates its function in the brain.