BMC Neuroscience

Poster presentation

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SCO-C3 upregulation is tied to kinocilia formation, and gene knockdown causes hydrocephalus in zebrafish

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from Annual Meeting of the Study Group Neurochemistry. International Conference of the Gesellschaft für Biochemie und Molekularbiologie 2006 (GBM 2006): Molecular pathways in health and disease of the nervous system
Witten, Germany. 28–30 September 2006

Published: 23 March 2007

BMC Neuroscience 2007, **8**(Suppl 1):P14 doi:10.1186/1471-2202-8-S1-P14

Ependymal cells form a mostly single-layered epithelium at the surfaces of the cerebral ventricles. In order to gain insight into their function, a subtractive cDNA library of ependyma minus brain was screened for novel ependyma-specific proteins. One of the identified candidates is a WD40 repeat protein provisionally designated SCO-C3. It is abundantly expressed in testis and cultured ependymal cells. Low levels are found in lung and brain, respectively, while it is absent from kinocilia-free tissues. In testis and ependymal primary cultures, SCO-C3 mRNA appears concomitantly with the messages for sperm-associated antigen 6, a kinocilia marker, and for hydin, a protein linked to ciliary function and hydrocephalus. In testis, ependyma and respiratory epithelium, the SCO-C3 protein is upregulated together with kinocilia formation. The sco-c3 gene is restricted to genera in possession of kinocilia, and it is strongly conserved during evolution. The human and zebrafish proteins are identical in 62% of their aligned amino acids. On the mRNA level, the zebrafish SCO-C3 ortholog was found only in kinocilia-bearing tissues by in situ hybridisation. Gene knockdown in zebrafish embryos by antisense MO injection resulted in severe hydrocephalus formation with unaltered ependymal morphology or ciliary beat. SCO-C3 can be considered a differentiation marker of kinocilia-bearing cells, where it may function in generation or maintenance of cell polarity.