Neuronal Primary Cilia and their Functions: A Work in Progress

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Abstract

My topic is neuronal primary cilia and the role they play in neuro-degeneration. Even though cilia were discovered over 100 years ago, many scientists to this day do not know the function of primary cilia. My research question is: What role do neuronal primary cilia have in the neuro-degeneration in mutant mice? Through the use of immunohistochemistry, which will enable us to study the changes in the brain and spinal cord of mutant mice with neurodegenerative diseases, we will observe cilia’s role in cell processes. We will determine whether cilia loss precedes neuro-degeneration and if so, whether there is a causal relationship between cilia loss and neuron cell death. By observing cilia in mice with degenerative diseases, we can better understand the role of cilia in brain function and survival of neurons.

Bibliography


Proposed Experiments

Fig 1. In many neuronal cilia, SSTR3 (green) and AC3 (red) are colocalized (yellow in the merged image, R). DAPI stains nuclei (blue). Rat dentate gyrus (Fuchs, Schwark, and Hsieh 2008).

Fig 4. Tufts of cilia on ependymal cells lining the 4th ventricle as well as cilia on neurons in the central gray area, are stained with DAB-tagged antibody raised to Goα11(brown). Cell bodies are counterstained for Nissl substance. Scale bar, 10 μm (Fuchs and Schwark 2004).

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Fig 3. It seems that many if not most neurons have a primary cilium which they shove between adjacent cells and into narrow pools of extracellular fluid in the brain. The cilium is a nonmotile sensor which, depending on the receptors, ion channels and other signaling devices studding its membrane, can send signals into the cell as well as through its axon to synaptically linked neighbors. In other words, neurons may have a cilium → synapse mechanism as well as the conventional synapse → dendrite → synapse mechanism (Whitfield 2004).

Fig 2. Hypothesized relationships between manipulated (----) and assessed (** ) conditions in the proposed experiment.

SS3 Receptors

SS3 receptors are somatostatin 3 receptors. Some cilia functions are likely to be mediated by SS3 (Fuchs, Schwark, and Hsieh 2008). If this can be proven then we will know how to regulate functions of the cilium. The SS3 receptors are, in most brain regions, concentrated mainly in neuronal cilia (Fuchs, Schwark, and Hsieh 2008). Knowing that SS3 are present on cilia, we are able to test for SS3 receptors to find out where neuronal cilia are located. By locating them we can better compare a normal brain to a brain going through degeneration and see if there is a noticeable difference in the location or quantity of cilia. We will see this difference by comparing mouse models of neurodegeneration with the wild type control mice.