G-protein signaling in sensory neuron development

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The nematode *Caenorhabditis elegans* senses chemical cues from its environment using 11 pairs of chemosensory neurons. The dendrite endings of these neurons have specialized cilia, embedded in glia-like cells, the sheath cells. Most of the sensory cilia are exposed directly to the environment and will take up fluorescent dyes such as DiO (dye filling). In the past, mutant *C. elegans* strains were isolated that showed no dye filling (*dyf*, dye filling defective). These mutants identified genes important for the proper development of the sensory cilia, including components of the transport system known as "intraflagellar transport" (IFT), and genes important for the functioning of the sheath cells.
The G-alpha subunit GPA-3 is specifically expressed in many sensory neurons and overexpression of a dominant active mutant of this G-alpha subunit (GPA-3QL) leads to a dye filling defective phenotype. This suggests that G protein signaling regulates the development of the sensory cilia. Visualization of the structure of the sensory neurons using antibodies and sensory neuron and sheath cell specific GFP-fusion constructs showed altered morphology of the sensory cilia in *gpa-3QL* animals, but identified no defects of the dendrites and axons of the sensory cells or the sheath cells. We also observed accumulation of cilia-specific proteins in the dendrites. Similar defects were observed in animals with defects in IFT, suggesting a role for GPA-3 in the regulation of intracellular transport.
We performed a genetic screen for suppressors of the *gpa-3QL dyf* phenotype. Nine independent suppressor mutants where isolated and mapping suggested mutations in five loci. We have mapped three loci to regions of 70-150 kB. We are currently sequencing genes from these regions and performing rescue experiments to identify the genes involved. We expect that this approach will identify the signaling pathway in which GPA-3 participates and how G proteins regulate cilia development.

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