Structural Mechanisms of Ciliary Assembly

by

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Abstract:

Cilia are hair-like organelles that protrude from the surface of most eukaryotic cells where they serve various functions in motility, sensory reception and signalling. They consist of a microtubule-based axoneme and are surrounded by the flagellar membrane. Cilia are built by intraflagellar transport (IFT), the bi-directional movement of proteinaceous material underneath the flagellar membrane, a process that is powered by kinesin and dynein motors and relies on a 20-subunit 1.6MDa complex known as the IFT complex. Our lab is studying the IFT complex with the goal of elucidating its structure as well as the molecular mechanisms of ciliary cargo and motor recognition. To this end we have reconstituted a number of IFT complexes including a complete nonameric IFT core complex from the green algae Chlamydomonas reinhardtii. The interactions holding the IFT complex together have been mapped biochemically and we have determined crystal structures of a number of sub-complexes at high resolution. Additionally, we have started to map interactions with ciliary cargo and have identified a highly conserved tubulin-binding module in the IFT74/81 sub-complex and find that this module is required for ciliogenesis in human cells. Collectively, the data are providing us with an emerging picture of the molecular mechanisms underlying cilium formation via IFT.

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