



CDB SEMINAR

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16:00~17:00 C1F CDB Auditorium

Mechanosensory Tip-link is an Asymmetric Filament with Cadherin 23 and Protocadherin 15 at Opposite Ends

Summary

Hair cells of the inner ear are mechanosensors that transduce mechanical forces arising from sound waves and head movement into electrochemical signals to provide our sense of hearing and balance. Each hair cell contains at the apical surface a bundle of stereocilia. Mechanoelectrical transduction (MET) takes place close to the tips of stereocilia in proximity to extracellular tip-link filaments that connect the stereocilia and are thought to gate the MET channel. Recent reports on the composition, properties and function of tip links are conflicting. Here we demonstrate that two cadherins that are linked to inherited forms of deafness in humans interact to form tip links. Immunohistochemical studies show that cadherin 23 (CDH23) and protocadherin 15 (PCDH15) localize to the upper and lower part of tip links, respectively. The N-termini of the two cadherins co-localize on tip-link filaments. Biochemical experiments show that CDH23 homodimers interact in trans with PCDH15 homodimers to form a filament with structural similarity to tip links. Ion that affects tip-link integrity and a mutation in PCDH15 that causes a recessive form of deafness disrupt interactions between CDH23 and PCDH15. Our studies define the molecular composition of tip links and provide a conceptual base for exploring the mechanism of sensory impairment associated with mutations in CDH23 and PCDH15.

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