Dcc Mediates Functional Assembly of Peripheral Auditory Circuits

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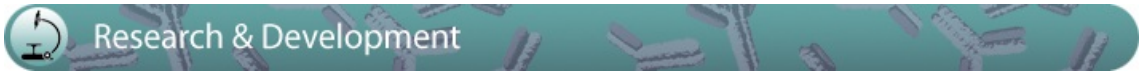

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Proper structural organization of spiral ganglion (SG) innervation is crucial for normal hearing function. However, molecular mechanisms underlying the developmental formation of this precise organization remain not well understood. Here, we report in the developing mouse cochlea that deleted in colorectal cancer (Dcc) contributes to the proper organization of spiral ganglion neurons (SGNs) within the Rosenthal's canal and of SGN projections toward both the peripheral and central auditory targets. In Dcc mutant embryos, mispositioning of SGNs occurred along the peripheral auditory pathway with misrouted afferent fibers and reduced synaptic contacts with hair cells. The central auditory pathway simultaneously exhibited similar defective phenotypes as in the periphery with abnormal exit of SGNs from the Rosenthal's canal towards central nuclei. Furthermore, the axons of SGNs ascending into the cochlear nucleus had disrupted bifurcation patterns. Thus, Dcc is necessary for establishing the proper spatial organization of SGNs and their fibers in both peripheral and central auditory pathways, through controlling axon targeting and cell migration. Our results suggest that Dcc plays an important role in the developmental formation of peripheral and central auditory circuits, and its mutation may contribute to sensorineural hearing loss.

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