This Week in The Journal

Planar Polarity in Cochlea Guides Spiral Ganglion Axons

Satish R. Ghimire and Michael R. Deans

(see pages 8013–8023)

Planar cell polarity (PCP) is the polarized distribution of structures in each cell of two-dimensional tissues. PCP occurs, for example, in *Drosophila* wings, where a hair emerges from the distal side of each cell. PCP is maintained by a set of core proteins, including transmembrane proteins of the Vangl and Frizzled (Fzd) families. These proteins become polarized to opposite sides of each cell, and they interact with partners in adjacent cells. In fly wings, for example, Fzd homologs localize to the distal side of cells, where they interact with Vangl homologs localized to the proximal side of adjacent cells (Goodrich and Strutt, 2011, *Development* 138:1877).

PCP proteins also have roles in axon guidance. Ghimire et al. recently showed (Ghimire et al, 2018, *Development* 145:dev159012) that Vangl2 helps to dictate the unique axonal trajectory of type II spiral ganglion neurons (SGNs) that innervate cochlear outer hair cells. When Vangl2 or another PCP protein (Celsr1) was knocked out, 30–50% of SGN axons turned toward the cochlear apex instead of toward the base after growing past cochlear supporting cells. Notably, knocking out Vangl2 selectively in SGN axons did not disrupt axon trajectories, suggesting that expression of Vangl2 in supporting cells is required for axon guidance.

In that work, knocking out Fzd3 had only mild effects on SGN axons. The authors now demonstrate that this is because Fzd6 can compensate for Fzd3 loss. Although knocking out either protein alone did not significantly alter axon trajectories, ~50% of axons in Fzd3/Fzd6 double mutants turned toward the apex, suggesting that the turning direction was random. Incorrect turning also occurred when Fzd3 and Fzd6 were knocked out selectively in the cochlea (not in SGN neurons), indicating that like Vangl2, Fzd proteins act nonautonomously to guide SGN axons. Finally, like in other epithelia, Vangl2 and Fzd3 were localized to opposite sides of cochlear supporting cells.

These data suggest that planar polarization in cochlear supporting cells is necessary for type II SGN axons to make appropriate turns to innervate outer hair cells. Notably, this is unlike the role of Fzd in the spinal cord, where its expression in axons is required for proper turning. Future work should determine which proteins in SGN axons recognize the guidance cues produced by supporting cells.

SGN axons normally turn toward the base of the cochlea (top), but when Fzd3 and Fzd6 are deleted selectively in cochlear cells, many SGN axons turn toward the apex (arrowheads, bottom). See Ghimire and Deans for details.

Loss of X Chromosome Alters Receptive Fields in V1–3

Tamar Green, Hadi Hosseini, Aaron Piccirilli, Alexandra Ishak, Kalanit Grill-Spector, et al.

(see pages 8079–8088)

Turner syndrome is the only human condition in which loss of an entire chromosome—in this case, one of the X chromosomes in females—is compatible with life. Survival is possible because one of the X chromosomes is inactivated early in embryonic development. Nonetheless, people with Turner syndrome can exhibit a range of phenotypes, including short

stature, cardiovascular and kidney abnormalities, and cognitive impairments, particularly in visual-spatial functions such as mental rotation and spatial working memory, as well as in executive control and social cognition. The primary driver of these symptoms is thought to be haploinsufficiency of the small percentage of X-chromosome genes that escape X inactivation, with secondary effects stemming from hormonal imbalances (Ibarra-Ramírez and Martínez-de-Villarreal, 2016, *Medicina Universitaria* 18:42). In the CNS, these genetic and hormonal influences lead to reductions in gray matter volume in several brain areas, including parietal lobe components of the dorsal visual stream, and to alterations in structural and functional connections between the parietal lobe and frontal and occipital cortical areas.

Green et al. hypothesized that disruption of processing in primary visual cortex also contributes to deficits in visual-spatial processing in people with Turner syndrome. To test this, they used functional MRI to assess visual receptive fields of voxel-sized populations of neurons in V1, V2, and V3. Receptive field sizes, visual-field coverage, and overall topographic organization in these visual areas were similar in girls with Turner syndrome and control subjects. But the average eccentricity (center) of population receptive fields was closer to the center of gaze in girls with Turner syndrome than in control subjects, and there was sparser coverage of the peripheral field. In addition, the volume and surface area of primary visual cortical areas responding to the visual stimuli were smaller in people with Turner syndrome than in control subjects.

These results suggest that processing in early visual areas is altered in Turner syndrome. Because the magnitude of some changes was inversely correlated with performance on a visual task, however, the authors propose that the changes help to compensate for the reduced cortical surface area. Nonetheless, reduced coverage of the peripheral visual field might contribute to some impairments in spatial processing in people with Turner syndrome.

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