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Short Communication

The Influence of the Wnt Signaling Pathway on Utricle Hair Cell Polarity Formation

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DESCRIPTION

The organ that detects balance is the utricle. The polarization of hair bundles that are situated on the HC surface is necessary for proper utricle function. Numerous epithelial cell types, including those in the lateral ventricles of the brain and the respiratory airway, exhibit this cellular polarization. At the subcellular, cellular, and tissue-wide levels, the utricle's planar polarity was described [1]. Only the vestibular organ of the inner ear has tissue polarity. The stereociliary bundles of HCs are orientated to face the LPR in the mammalian utricle. At E15, mouse embryos still had a full LPR [2]. In contrast to the medial extrastriolar areas, the HCs in the lateral extrastriolar region (E13.5) arise later (E11.5).

E13.5 is thus a crucial time for the development of polarity [3]. In this investigation, we either added inhibitors or activators to utricles *in vitro* or eliminated -catenin *in vivo* at or before E13.5. The findings demonstrated that the polarity development of the utricle was influenced by the canonical Wnt signalling pathway.

Wnt signalling serves a variety of purposes at various developmental time periods and is a hallmark of embryonic development. There are both canonical and noncanonical versions of the Wnt signalling pathway. Early cochlea development has been investigated in relation to the Wnt signalling system. At E14.5, the cochlea of mice exhibits the Wnt signalling receptors (Fzd 1, 2, 3, 4, 6, Ryk, Ror2, and Lgr5). At E15 and E17, the cochlea may be shown to express Wnt7a, Wnt5a, Wnt2, Wnt10b, Wnt4, Wnt7b, Wnt8, and Wnt11 [4], and studies revealed a possible alternation between canonical and noncanonical signalling pathways.

In the utricle throughout early development, our investigation also identified genes associated to the canonical and noncanonical Wnt pathways. The majority of these genes were also changed between the two time points of E13.5 and P1. These significantly changed genes might help with legitimate differentiation, proliferation, or innervation. The proliferative region of Sox2-positive cells in the cochlea (E12.5) was dramatically extended when LiCl was introduced to activate the Wnt pathway *in vitro*, demonstrating that the canonical Wnt pathway controls HC proliferation and differentiation during early cochlea development [5].

Additionally, the cochlear sensory epithelium's sensory precursor cells began to proliferate when -catenin was overexpressed [6]. We consequently proposed that the Wnt pathway might have a similar function during the early development of the utricle. When we conditionally knocked out -catenin, the quantity of utricle HCs in the mic was affected, which was validated *in vivo*. We also discovered alterations in the polarity of hair cells.

In fact, the Wnt pathway is crucial for controlling inner ear polarity. The cochlea's HCs are predominantly polarized as seen by their convergence and extension, uniform ciliary orientation throughout the board, and V-shaped stereociliary bundle. The positioning of the stereocilia and the movement of the kinocilium in the vestibular organs are determined by the subcellular polarity. Supporting cells surround HCs, and in this investigation, all HCs demonstrated directional coordination. Cilia bundles of HCs are found on either side of the LPR face or travel away from the LPR in relation to tissue polarity. Numerous studies have been conducted on the Wnt/PCP pathway, a noncanonical Wnt pathway, and its role in inner ear polarity.

Spina bifida aperta, caudal axis bending, and tail truncation are all seen in a mouse with conditional deletion of -catenin in the dorsal neural folds. Similar polarity alterations were seen in mouse kidneys that had -catenin conditionally knocked out. There are, however, not many research on the canonical Wnt pathway in relation to the development of polarity in the inner ear, particularly in the vestibule.

CONCLUSION

In this study, we looked at how the expression of genes connected to the Wnt pathway changed over the mouse utricle's early development. Our observations indicated that the main effect of conditional deletion of -catenin *in vivo* is on hair cell quantity and may reveal an impact on stereociliary bundle orientation. We think that the canonical Wnt pathway is crucial for regulating HC polarity throughout mammalian utricle

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formation when combined with the *in vitro* results. Future research on the development of vestibule polarity may be inspired by our findings.

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