Myosin-15a is essential not only for proper elongation but also for thickening of mechanosensory stereocilia in the mammalian auditory hair cells

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Myosin-15a is essential for the normal elongation of stereocilia, the hair-like projections of the mechanosensory hair cells of the inner ear. There are two isoforms of myosin-15a with different functions and expression profiles. The short isoform of myosin-15a is expressed early in postnatal development and responsible for normal elongation of stereocilia, while the long isoform with an N-terminus extension is expressed later and is responsible for the maintenance of transducing, shorter row stereocilia in the hair bundle (Fang et al., 2015). However, the role of Myosin-15a in formation of other features of the hair bundle such as the number and diameter of stereocilia has not been investigated. Therefore, we are exploring the role of myosin-15a in the hair bundle development using two mice strains: (i) shaker2 mice where both isoforms are affected, and (ii) isoform-specific "deltaN" mice lacking the long isoform.

We used scanning electron microscopy to image stereocilia bundles of inner (IHC) and outer (OHC) hair cells at mid-cochlear location at postnatal days: 0, 1, 3, 6, 10,16, and 20 (P0 through P20). We found that the number of stereocilia per bundle decreases between P0 and P6 in both control heterozygous and mutant homozygous shaker2 mice, in both IHCs and OHCs. This decrease followed the normal developmental program, in which nascent hair bundles are formed by supernumerary stereocilia and are shaped later by retraction of redundant stereocilia. We did not observe a difference in the total number of stereocilia per bundle between controls and shaker2 homozygous animals.

We did not observe differences in the developmental changes of stereocilia diameter between control and shaker2 OHCs. Stereocilia in different rows of OHCs have similar diameters, with redundant stereocilia showing minimal decrease at P1 - P6. In contrast, stereocilia diameters of IHCs undergo dramatic re-shaping in postnatal development. In control IHCs, diameters of the first and second row stereocilia increase gradually between P0 and P20, while the third and fourth row stereocilia become thinner. Although thickening of the first and second row stereocilia is still present in shaker2 IHCs, the third row and the rest of the stereocilia do not thin and keep the same diameter as seen at P1.

We conclude that myosin-15a does not affect the developmental program establishing the total number of stereocilia per hair bundle. However, it is essential for the formation of stereocilia diameter differences in the IHC but not OHC bundles. We are currently exploring the hypothesis that these differences between IHCs and OHCs may be related to the different expression of long isoform of myosin-15a in IHCs and OHCs. This isoform was observed in all stereocilia rows in OHCs but only in the shorter row stereocilia in IHCs (Fang et.al, 2015).