Probing Mechanosensory Ion Channels in Cochlear Hair Cells by AFM

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In mammals, hearing is mediated by inner and outer hair cells in the inner ear, whereby a mechanical input is transduced into an electrical output. The hair cells consist of rod-like stereocilia at their apical pole arranged in rows of different height essential for the so-called mechanoelectrical transduction. Mechanosensitive ion channels are located within the plasma membrane of individual stereocilia. All stereocilia of a single cell taken together form a hair bundle of specialized structure.

Compared to voltage-gated and ligand-gated ion channels the mechanosensitive ion channel in the mammalian cochlea reveals much faster gating up to 100 kHz and more. It transforms sound into an electrical receptor current with sensitivity to forces in the PicoNewton range. So far mechanoelectrical transduction was investigated stimulating the entire hair bundle of cochlear hair cells rather than single stereocilia. Up to now the only way to get access to single channel events in this configuration is to examine artificial insensitive hair cells induced by accident or experimentally.

Here we use AFM as a nanomanipulator displacing single stereocilia of living outer hair cells of postnatal rats while the current response is measured simultaneously by patch clamp. The AFM is used in constant height mode applying an increasing force with a superimposed 98 Hz sine to the tips of single stereocilia resulting in a displacement of individual stereocilia. Tip links connecting adjacent stereocilia are supposed to pull directly at the mechanosensitive ion channel in the apical cell membrane. This allows cations to flow from outside into the cell resulting in depolarization of the hair cell.

Combination of AFM and patch clamp is a promising technique for probing mechanical and electrical properties of single mechanosensitive molecules in living cells.