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Molecular mechanism in the regenerative biology of hearing

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The neurosensory cells of the organ of Corti have a limited life span that may be further reduced by environmental insults. One strategy was trying to understand regeneration in the avian ear, and to transfer this knowledge to mammals to substitute for what may be missing there. Another strategy was to apply growth factors and cytokines with the hope to find a molecule with a regenerative effect. Unfortunately, both strategies failed.
An emerging strategy is to investigate the cellular and molecular basis of hair cell proliferation and differentiation in the organ of Corti. The induction of terminal differentiation is regulated by a class of cell cycle proteins designated as Cip/Kip cyclin-dependent kinase inhibitors (CKIs). Among other functions, they have been implicated to induce cell cycle exit during development and to maintain cells in a terminally differentiated state. In the organ of Corti the expression of the Cip/Kip CKI-family protein (p27Kip1) proved to be conserved to supporting cells at embryonic and adult stages. Disruption of the p27Kip1 gene allows for continued cell divisions in the organ of Corti in mice. Assuming that the inability of supporting cell to proliferate is the primary limiting factor for the initiation of hair cell regeneration, then a crucial question in the regenerative process may be solved. This implicates, if proliferation of supporting cells in the organ of Corti can be turned on by the inhibition of the cell-cycle inhibitor p27Kip1, hearing may be restored in cases of sensorineural hearing impairment caused by hair cell loss