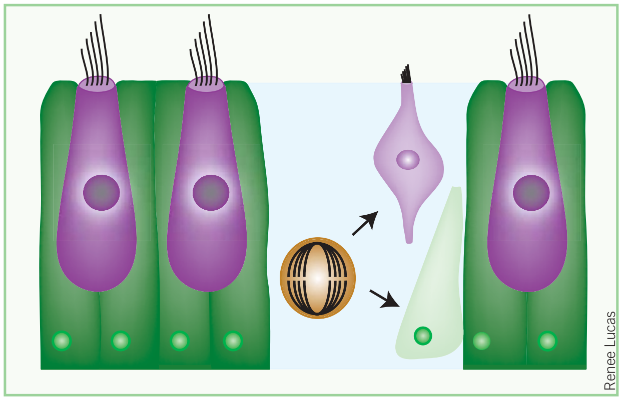


Figure 1 Potential role of stem cells in the mammalian utricle. The sensory epithelia of the inner ear are composed primarily of hair cells (purple) and supporting cells (green). Li *et al.* provide evidence that a small number of stem or progenitor cells (orange) may also be present in the epithelia. In response to the loss of hair cells, these cells may enter the cell cycle and give rise to progenitor cells that can develop as either hair cells or supporting cells.

opment, an individual generates a specific number of hair cells. These are slowly lost with aging, leading to progressive and permanent hearing loss. Ototoxic drugs or loud noises accelerate this process.

Before 1980, similar levels of hair-cell loss were assumed to occur in the ears of all vertebrates. However, a series of studies, culminating in 1988 with two papers in *Science*, showed that most nonmammalian vertebrates retain the ability to generate new hair cells throughout their lives[2,3,6–8]. In these species, the loss of existing hair cells triggers a proliferative response that results in the production of new hair-cell precursors. In contrast, consistent with the lack of recovery in function, similar hair-cell loss in the mammalian inner ear results in limited or no cellular proliferation[9–12]. Based on these results, it seemed plausible that the stem or progenitor cells that give rise to hair-cell precursors in other vertebrates might either be lost or in deep quiescence in the adult mammalian ear.

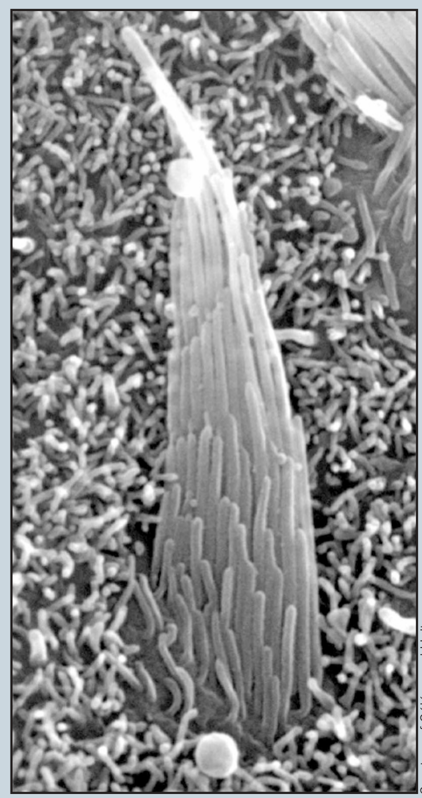
Li *et al.* show that, when isolated and maintained in serum-free medium, spheres develop from 0.25% of the cells within the mouse utricular macula, a patch of mechanosensory hair cells and associated supporting cells within the ear's vestibular region, which is responsible for the sensations of balance and acceleration. In addition, the number of spheres increased in the presence of epidermal growth factor and insulin-like growth factor-1, both previously implicated in the induction of proliferation in the utricle.

After sphere formation, a subset of these cells expressed several different markers characteristic of mechanosensory hair cells or their associated supporting cells. And when transplanted into the otocyst or amniotic cavity of an embryonic chick, cells derived from these spheres developed into multiple cell types, including muscle cells and, most importantly, mechanosensory hair cells.

These results show for the first time that stem cells capable of giving rise to new hair cells are present in the adult mammalian utricle (**Fig. 1**). A number of issues still needs to be addressed, however. Considering the limited amount of proliferation that occurs in the adult utricle *in vivo*, is it possible that these stem cells are normally quiescent and only become activated when isolated *in vitro*, as has been reported for neural stem cells[13]? If this is the case, will it be possible to induce the activation of these cells *in vivo*? Once activated, what will be the nature of these cells *in vivo*, and will they behave as stem cells or as hair-cell progenitors?

Depending on the answers to these questions, it may be possible to make significant progress toward the induction of hair-cell regeneration in mammals. In the more immediate future, however, the identification of utricular stem cells should lead to advances in our understanding of the molecular and biochemical nature of mechanosensory hair cells. The limited availability of hair cells has impeded their study and made it logistically difficult to carry out many biochemical and molecular biological assays. The ability to isolate and expand hair-cell progenitors *in vitro* should better equip researchers to identify the

In your ear



All the essential elements of the hair cells in the inner ear assemble at a lightning-quick pace, at least by the standards of mouse developmental biology, report Gwénaëlle Géléoc and Jeffrey Holt in the 1 October *Nature Neuroscience*. Between embryonic days 15 and 17, hair cell morphology snaps into place and the hairs appear fully functional.

Shown is a scanning electron micrograph of a hair cell excised from a region of the inner ear. Numerous microvilli extend from the hair cell, which are linked at their tips by tiny molecular bridges, dubbed 'tip-links'. When the extensions are deflected—by movement of the head or by sound, for instance—the tip-links convey a rise in tension. The tip-links are linked to mechanosensory ion channels that increase the conductance of cations such as calcium in response to increased tension: the greater the tension, the greater the flow of ions.

Focusing on the vestibular region, which mediates balance, Géléoc and Holt examined various indicators of hair cell development, and by all criteria observed quick assembly. The molecular motor myosin Ic might provide the basis for speed, speculate the authors. Myosin Ic, the only identified component of the tension-transducing apparatus, might head toward the tips of the microvilli, bringing components of the tip-link and associated molecules with it. The investigators are eager to find the molecular trigger that sets these events in motion.

Charlotte Schubert