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Ion channels: Hearing aid

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Mechanically controlled ion channels — transduction channels — are a key feature of the cells that detect sound, touch and movement. In fruitfly ears, the channels belong to a very familiar group of proteins.

Sensory information, such as that carried by light, odours and sound, continuously washes over us, revealing the nature of the outside world. Because organisms place a premium on detecting such signals with high specificity and sensitivity, specialized cells have evolved to capture each type of stimulus. Mechanical stimuli are no exception, and most organisms use mechanoreceptor cells to detect sound, touch and movement. Central to mechanoreception are ion channels located in the outer membranes of mechanoreceptor cells; these 'transduction' channels detect mechanical stimuli and, by modulating ion entry, control the cells' electrical excitability in proportion to the size of the stimulus. That excitation in turn enables appropriate electrical signals to be sent to the brain. The precise channels involved in mechanoreception have, for the most part, evaded identification, because the cells are exceedingly scarce. However, in an exciting report on page 81 of this issue, Kim and colleagues[1] show that Nanchung — a newly discovered member of the TRP protein family — is the transduction channel needed for fruitflies to hear.

A fly detects courtship songs with its ear, Johnston's organ[2]. The molecular details of this feat are largely unknown, however. One reason for wanting to find out is that many molecular systems in *Drosophila* are closely related evolutionarily to those in higher organisms — and so identifying the molecules that transduce mechanical stimuli in flies should have broader significance. Advantages to studying mechanotransduction in flies rather than more complex organisms include the ability to carry out genetic screens.

Although several such screens have been conducted, progress in finding the molecules responsible for touch perception and hearing has been slow[3]. A notable success was the discovery that flies rely on NompC, another TRP channel, to detect movement of their sensory bristles — small hairs that decorate their bodies[4]. NompC could not, however, be the only fly transduction channel; fruitflies that lack this protein still retain a small residual electrical response when their bristles are deflected[4]. Moreover, these flies enjoy nearly normal hearing[2]. Additional transduction channels clearly awaited discovery.

Nanchung ('Nan' for short) is one such channel: Kim *et al*.[1] present compelling evidence that this TRP-family member is essential for *Drosophila* hearing. In the absence of the *nan* gene, flies do not hear. Moreover, *nan* is expressed by mechanoreceptor cells in Johnston's organ, particularly in the outer dendritic segment (Fig. 1), where transduction is thought to take place. Finally, expression of *nan* in tissue-culture cells leads to the appearance of a channel that is activated by one type of mechanical stimulus, osmotic challenge. Although Nan might be working by activating another channel in these cells, it is more likely that Kim *et al*. have described some of the conductance properties of the transduction channel that is directly responsible for sound detection. TRP channels — named after *transient receptor potential*, a fly gene essential for phototransduction — have been found to mediate sensory transduction in a wide variety of cell types[5]. Nan belongs to the TRPV subfamily, which has been implicated in sensing pain, temperature, odours, osmotic pressure and touch[6]. With Kim and colleagues' findings, we can now add sound to this list.

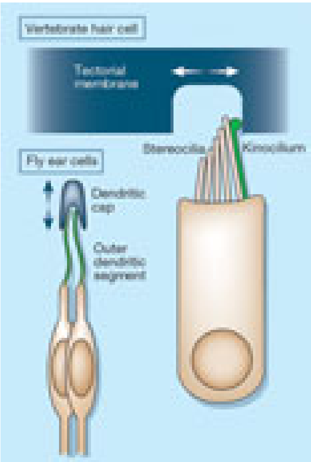

Figure 1 Fly and vertebrate auditory mechanoreceptors. Full legend

High resolution image and legend (73k)

Fly hearing may be a valuable model system for understanding other mechanoreceptors, not least the vertebrate inner ear's hair cell. This hypothesis has not been accepted by all, perhaps in part because of differences in appearance between the two cell types (Fig. 1). For instance, fly mechanoreceptors such as those in Johnston's organ rely on a single long, thin protrusion, or 'sensory process', to perceive mechanical stimuli[7]. By contrast, a vertebrate hair cell carries out transduction with its hair bundle, which is composed of some 100 clustered processes called stereocilia[8]. Beyond sheer numbers, these processes differ fundamentally in their structural proteins: hair-cell stereocilia are filled with actin, whereas the fly sensory process derives from a cilium constructed of tubulin.

Despite these anatomical differences, there are some remarkable similarities. Both types of sensory process are bathed in an unusual fluid, endolymph, which is distinguished by a high K^+ concentration and a substantial extracellular potential[7, 8]. Moreover, the responses of *Drosophila* and vertebrate mechanoreceptors to mechanical stimuli show striking resemblances in their speed, sensitivity and adaptation[4]. Finally, vertebrate and invertebrate ears have conserved the molecules that control development of mechanoreceptor cells[8]. These cells may well be derived from a common, ancient precursor — supporting that idea, although vertebrate hair cells rely on stereocilia for transduction, they too have a tubulin-based cilium (the kinocilium; Fig. 1).

If these cells are evolutionarily linked, additional molecular similarities should emerge — and indeed they have. In one example, NompA, a component of the structure that caps the fly's sensory process[9], resembles the tectorins — proteins that contribute to a similar structure in vertebrate ears (Fig. 1). In another, NompC (found in *Drosophila* bristles) underlies transduction in zebrafish hair cells[10]. Although mammalian genomes conspicuously lack a close relative of the *nompC* gene, its presence in zebrafish nevertheless dramatically reinforces the hypothesis that the molecules responsible for *Drosophila* mechanotransduction have relatives in vertebrate systems.

Could the transduction channel in mammalian hair cells — like that in fruitfly ears[1] — belong to the TRPV subfamily? Of the six known vertebrate TRPV proteins, a tempting candidate is TRPV4, which is found in one class of hair cells (auditory hair cells) and can be activated osmotically when expressed in tissue-culture cells[11]. To complicate the story, however, the hair-cell transduction channel may not be made up of a single type of protein; for example, multiple TRP-channel subunits interact to achieve correct targeting and function of sensory channels in the worm *Caenorhabditis elegans*[12]. Although the demonstration of the role of Nan in fly hearing does not pinpoint the identity of the hair-cell transduction channel, it does direct our gaze firmly at the TRPV subfamily.

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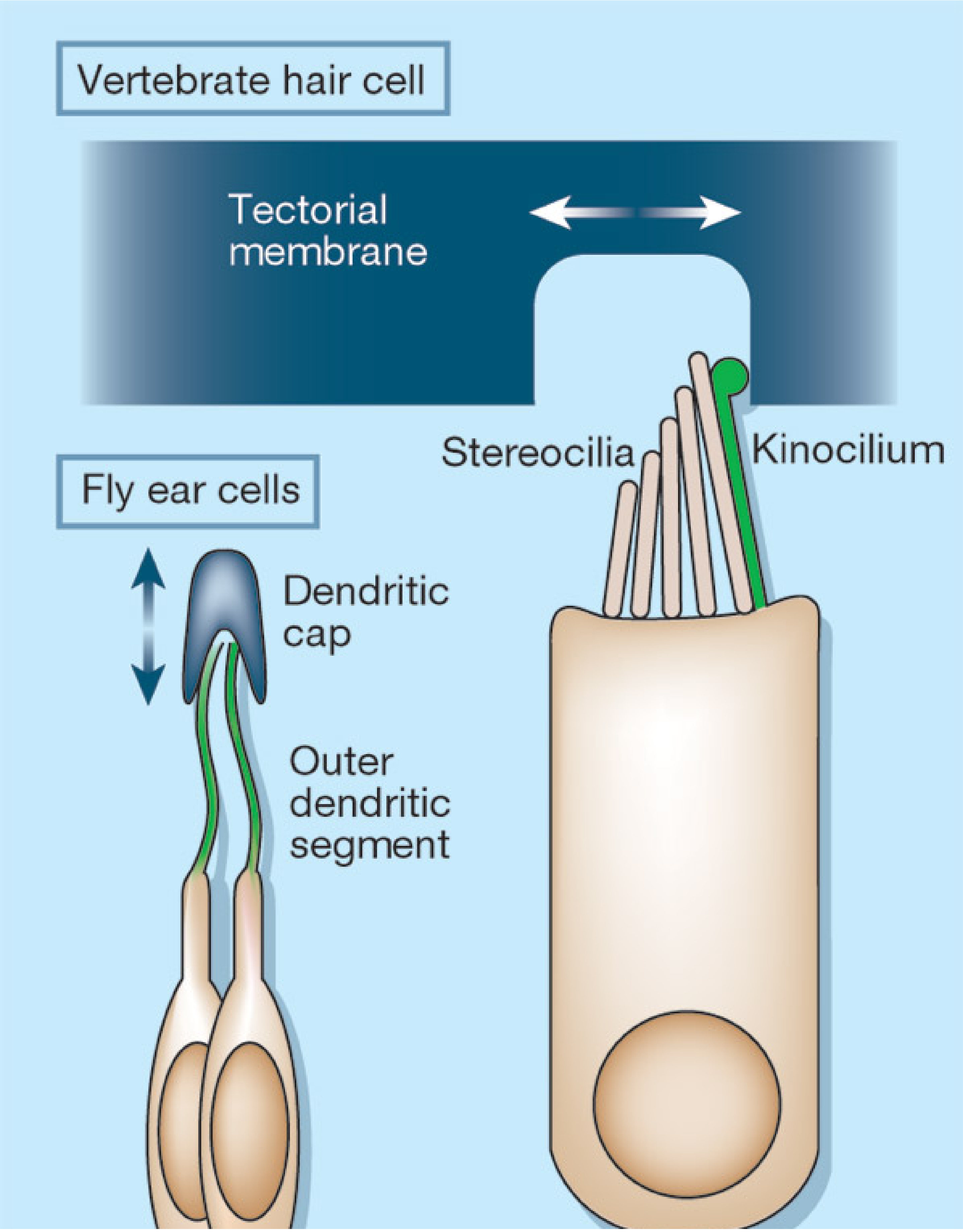

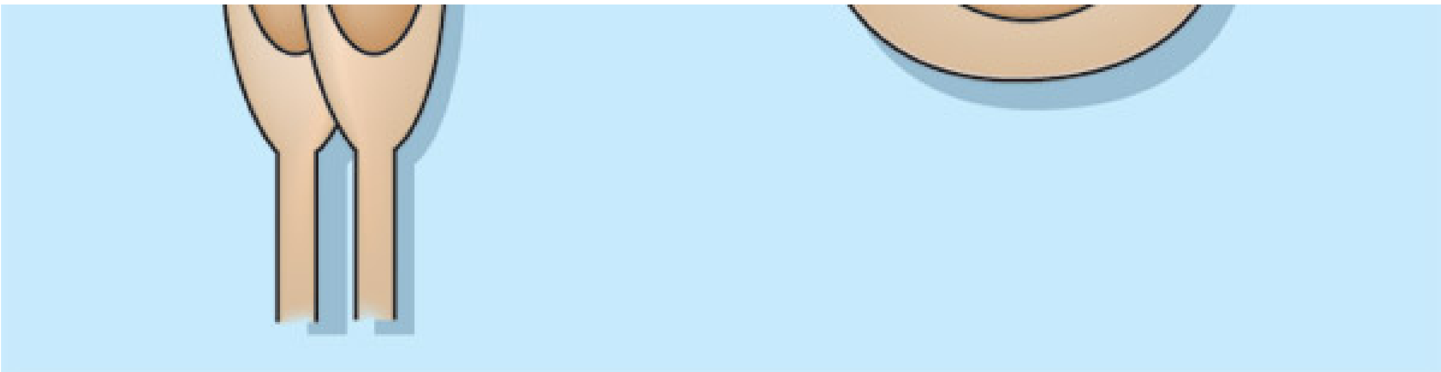

Figure 1 Fly and vertebrate auditory mechanoreceptors. In the fly ear, pairs of mechanoreceptor cells are stimulated when the overlying dendritic cap, in response to sound waves, moves relative to the cells (arrow). Kim *et al.*[1] have found that the Nan ion channel is located in the outer dendritic segment, where transduction the detection of sound stimuli and their conversion into the electrical response of the cell is thought to take place. In a vertebrate hair cell, the movement of the overlying tectorial membrane relative to the cell deflects stereocilia, triggering transduction; the kinocilium helps to couple these processes. The kinocilium is present in hair cells in all vertebrates, at least during development. Structures that are anatomically and molecularly similar between fly ear cells and vertebrate hair cells include the dendritic cap and tectorial membrane (blue), and the outer dendritic segment and kinocilium (green).

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