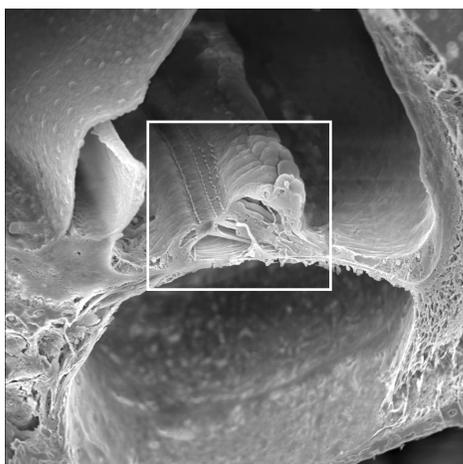


Pump up the volume

Vivienne Baillie Gerritsen

There is not much we would hear without our cochlea. Our what? The cochlea is a part of our inner ear and looks remarkably like a snail's shell. This minute masterpiece of mammal physiology - only a few millimetres large - acts as a sound amplifier and without it the noises which surround us would be mere fuzz. And how does it amplify sound? Amongst the many controversial theories, there is one which is based on the behaviour of quite a singular protein: prestin. Why singular? Because prestin is the only cellular motor to date which does not require biological energy – such as ATP – to function.



Cross section of the cochlea and, towards its centre, the organ of Corti.

Courtesy of B. Kachar, NIDCD, NIH

Understanding the biophysics of hearing stretches back to the 6th century. Pythagorus reasoned that sound was a vibration in the air. His followers showed that the membrane in our outer ear – the eardrum – vibrated in response to sound and this was how it was transmitted further inside. Not much more progress was made until the 16th century when the existence of three ossicles were described in the middle ear: the hammer, the anvil and the stirrup. And in 1561, the snail-shaped cochlea was discovered. Two hundred years later, the Italian anatomist Alfonso Corti (1822-1876) had a closer look at the cochlea. A cross section revealed a complicated structure which nests within three 'tubes', is bathed in fluid and follows the length of the cochlea; he named the structure the organ of Corti.

The organ of Corti is characterised by rows of both inner and outer hair cells which coat a membrane known as the basilar membrane. A second membrane – the tectorial membrane – caps the rows of outer hair cells. Thanks to two eminent scientists – the German scientist Herman Helmholtz (1821-1894) and the Hungarian physicist Georg von Békésy (1899-1972) – it became clear that the organ of Corti is the playing field for sound. And recently, prestin was shown to have a fundamental role in its transmission to the brain.

What did Helmholtz and von Békésy discover? Helmholtz was one of the first to propound that sensations of any kind were of a physico-chemical nature. He suggested that the basilar membrane in the organ of Corti vibrates in response to sound entering the ear. And von Békésy proved it. Von Békésy worked in the research laboratory of the Hungarian Post Office where his task was to improve communication. To do so, he studied the tissues of a number of corpses' ears in the hope of unravelling the mechanics of the inner ear. Following Helmholtz's discovery, he was aware that the basilar membrane was of great importance, and he made a number of measurements which proved what the German scientist had assumed: the existence of travelling waves along the basilar membrane. And not only did the basilar membrane vibrate in response to sound but it also amplified the sound which was then transmitted to the brain.

Sound hits the eardrum causing it to beat. The beats are passed on to the three ossicles, the last of which stirs the basilar membrane. The stereocilia on the outer hair cells – which coat the basilar membrane – then push against the

tectorial membrane above. This causes the stereocilia to bend to one side, a bit like a sea current brushing the tentacles of a sea anemone in the direction of the current. The brushing movement opens pores in the stereocilia letting potassium ions seep in, which create an electric current. There is where prestin steps in. Prestin is a transmembrane protein found at the base of every outer hair cell and acts as an anion transporter when it senses a change in transmembrane potential.

Anion transporters are nothing new. Prestin, however, does not transport the anions but plays ping pong with them. It catches those floating around the cytoplasm and swings them to the other side of the membrane, in response to hyperpolarization. At this stage, instead of letting them go, prestin flings the anions back into the cytoplasm in response to depolarization. This ping-pong movement is extremely rapid and creates conformational changes in the protein which lengthens and shortens depending on the presence or absence of anions, respectively. As one could expect, the net result is a lengthening and shortening of the outer hair cells *per se* in response to sound. Hence, prestin is a semi-transporter, or cellular motor, which does not involve any enzymatic process – such as ATP/GTP hydrolysis – as all other cellular motors known to date do.

It is believed by some that the pumping movement caused by the lengthening and shortening of prestin within the cells' membranes may be a means of amplifying sounds which otherwise would be too

weak to be transmitted to the brain. The pumping of the outer hair cells, caused by the conformational changes of prestin in response to the initial sound vibration, would be fed back to the basilar membrane. This feedback oscillation, or amplification, would then be fed into the inner hair cells which would transmit electric signals to nerves and ultimately to the brain. In effect, without any amplification our perception of sound would be 100 times less effective! For this reason, it is thought that mutations occurring in prestin could be at the heart of congenital loss of hearing since the cochlear amplification would not take place.

Besides the probable implications of prestin in helping those who are hard of hearing, it is of great interest in the field of nanotechnology. Indeed, here is a minute cellular motor which converts electricity into a mechanical force...and very fast. In fact, it is the fastest cellular motor protein known to date – hence its name borrowed from the musical notation '*presto*'. And what is more, it requires no extra biological energy such as ATP since it functions by way of the conversion of electricity flow into a mechanical force. Such a feature makes it a precious molecule and already there are hopes of developing a pump for specific drugs, or a sensor of mechanical stress or even a condenser in electrical nanocircuits. A great destiny for such a minute molecule.

Cross-references to Swiss-Prot

Prestin, *Rattus norvegicus* (Rat) : Q9EPH0
Prestin, *Homo sapiens* (Human) : P58743
Prestin, *Mus musculus* (Mouse) : Q99NH7
Prestin, *Meriones unguiculatus* (Mongolian gerbil): Q9JKQ2

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