

The white spot of inner ear research

A new technique based on labelled sugar molecules is providing previously unknown insights into the inner ear. A study by the University of Konstanz and Charité-Universitätsmedizin Berlin shows that the cupula in the inner ear of zebrafish completely regenerates within approximately two months. These findings open up a new avenue for research into sudden hearing loss and acute disorders of the sense of balance.

In a way, the inner ear with the hearing and the vestibular organ remains a terra incognita – an unexplored territory. Despite medical advances, surprisingly little is known about the causes of abruptly occurring conditions such as sudden hearing loss or disorders of the vestibular system. Unlike the eye, we cannot see the inner ear, resulting in very limited knowledge of this area. It is safely embedded within the hardest bone of the human body, the petrous bone. Although we generally understand the anatomy of the inner ear well, it has so far been scarcely possible to observe its physiological and pathophysiological processes.

A new experimental technique developed by the University of Konstanz and Charité-Universitätsmedizin Berlin has now made it possible to visualize physiological processes in the inner ear of zebrafish – an animal species whose inner ear closely resembles that of humans. The researchers led by Valentin Wittmann (University of Konstanz) and Hans Scherer (Charité Berlin) introduced labelled sugar molecules into the body of the fish. The investigation focused on the cupula, the sensory structure responsible for detecting angular acceleration. The results show that the cupula of zebrafish is not a static structure, but is continuously renewed within around 60 days. The research results have now been published as the cover article of the scientific journal "Angewandte Chemie".

The trail of sugar molecules

The cupula is a membrane-like structure that lies within a bulge within the semicircular canals of the vestibular system. Each ear contains three such canals, oriented along the three spatial axes, enabling the detection of accelerations in all planes. When rotational acceleration occurs, the fluids within these canals shift, causing slight movement of the cupula. Hair cells beneath the cupula convert this rotational mechanical energy into electrical signals, which are transmitted to the central nervous system. These sensors serve to maintain balance during head movements and rotations. Previous studies suggested that damage to the cupula can lead to balance disorders. Until now, however, it has not been possible to observe the physiological processes of the cupula.

Chemist Valentin Wittmann and Hans Scherer, a physician, have now developed a process to do just that. They applied a chemical method known as "metabolic glycoengineering": Put simply, tiny sugar molecules are chemically labelled and administered to the zebrafish. When these molecules are incorporated, this also happens in the cupula of the inner ear. Using fluorescence techniques, these labelled molecules can then be made visible histologically. Tracing the path of the sugar molecules, it becomes possible for the researchers to observe the physiological processes in the otherwise inaccessible inner ear.

The regeneration of the cupula

Until now, it had remained unclear whether the cupula is a permanent structure or whether it is constantly renewing itself. The study from Konstanz and Berlin has resolved this question: "Our investigations show for the first time that the renewal of the cupula is a continuous process", says Wittmann. "Long-term observations over several weeks suggest that the cupula of the zebrafish is completely renewed within eight to ten weeks."

"The vestibular organs in fish are very similar to those in humans", adds Scherer. "This means that findings obtained in fish can largely be transferred to humans". The new method therefore provides a promising starting point for further investigating inner ear disorders that have so far remained poorly understood. The regeneration of the cupula could explain, for example, why the sense of balance recovers after a few days in some cases following sudden disturbances. The same applies to sudden hearing loss, whose cause is likewise unknown and which can also resolve spontaneously after a few days.

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