Wbp2 is a novel deafness gene

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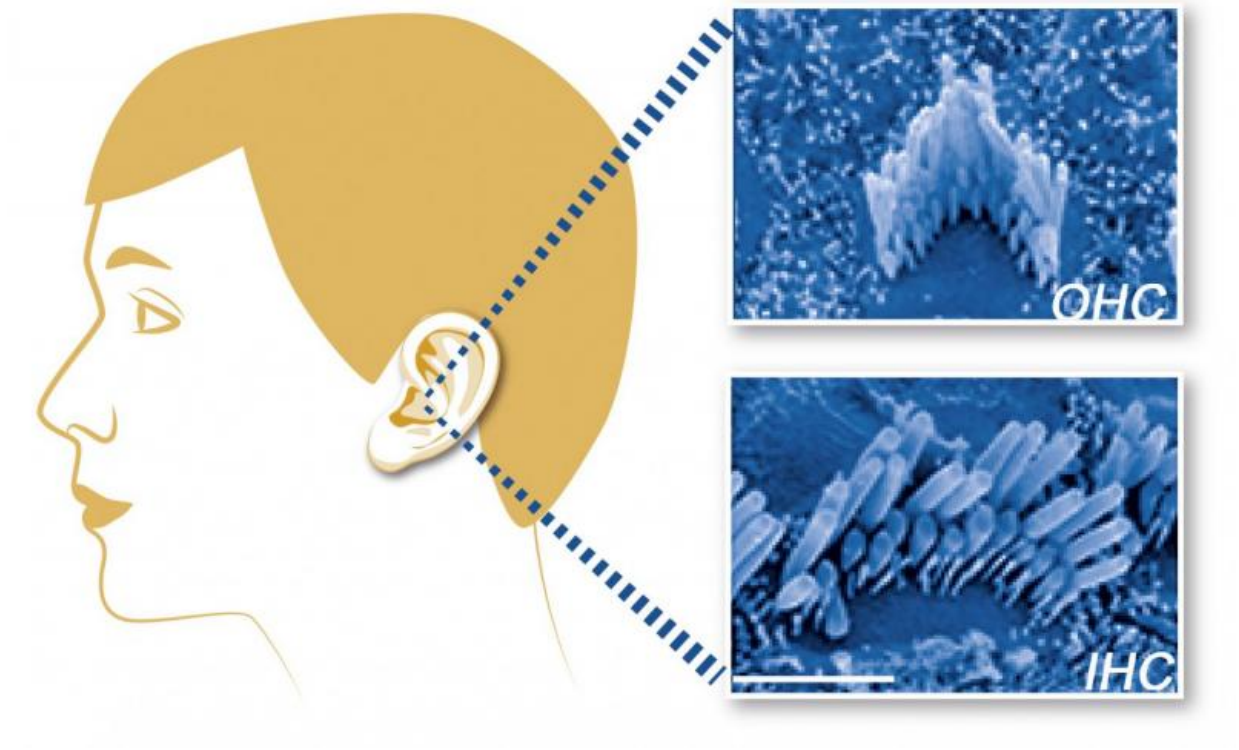

Scanning electron microscopy images of outer (OHC) and inner (IHC) hair cells of the ear of a Wbp2-deficient mouse. Credit: EMBO

Researchers at King's College London and the Wellcome Trust Sanger Institute in the United Kingdom have for the first time demonstrated a direct link between the Wbp2 gene and progressive hearing loss. The scientists report that the loss of Wbp2 expression leads to progressive high-frequency hearing loss in mouse as well as in two clinical cases of

children with deafness with no other obvious features. The results are published in *EMBO Molecular Medicine*.

The scientists have shown that hearing impairment is linked to hormonal signalling rather than to hair cell degeneration. Wbp2 is known as a transcriptional co-activator for estrogen receptor Esr1 and progesterone receptor Pgr. The loss of Wbp2 causes not only progressive high frequency hearing loss, but also results in reduced expression of Esr1, Esr2 and Pgr in the cochlea – a part of the inner ear. Understanding the estrogen-sensitive molecular networks specific to hearing offers an unprecedented putative new target for the control of the estrogen signalling pathway in the auditory system that could prevent or reverse progressive hearing loss.

"Our study demonstrates that hearing thresholds are normal in young Wbp2 mutant mice, but are raised at high frequencies by four weeks of age," says EMBO Member Karen Steel of King's College London, the senior author of the study. "More importantly, we also demonstrate that Wbp2 is crucial for hearing in humans. We found two children affected by severe to profound deafness, each carrying two variants of the WBP2 gene."

Progressive hearing loss is a very common disease. However, very little is known about its molecular mechanisms. As a result, targets for medical therapies have been lacking. It has been known that estrogen signalling protects against noise-induced hearing loss. However, estrogen-based therapies have not been generally considered for hearing impairment due to their widespread effects. This study opens up the Wbp2 pathway as a new route to therapeutic approaches that more specifically target the inner ear.

Wbp2 was found to be involved in progressive hearing loss during a large-scale screen for hearing defects in newly-generated targeted mouse

mutants. The finding of a new gene involved in human deafness following the initial discovery of its role in the mouse also emphasizes the value of mouse genetics research for better understanding human disease.

More information: "Wbp2 is required for normal glutamatergic synapses in the cochlea and is crucial for hearing." DOI: 10.15252/emmm.201505523

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