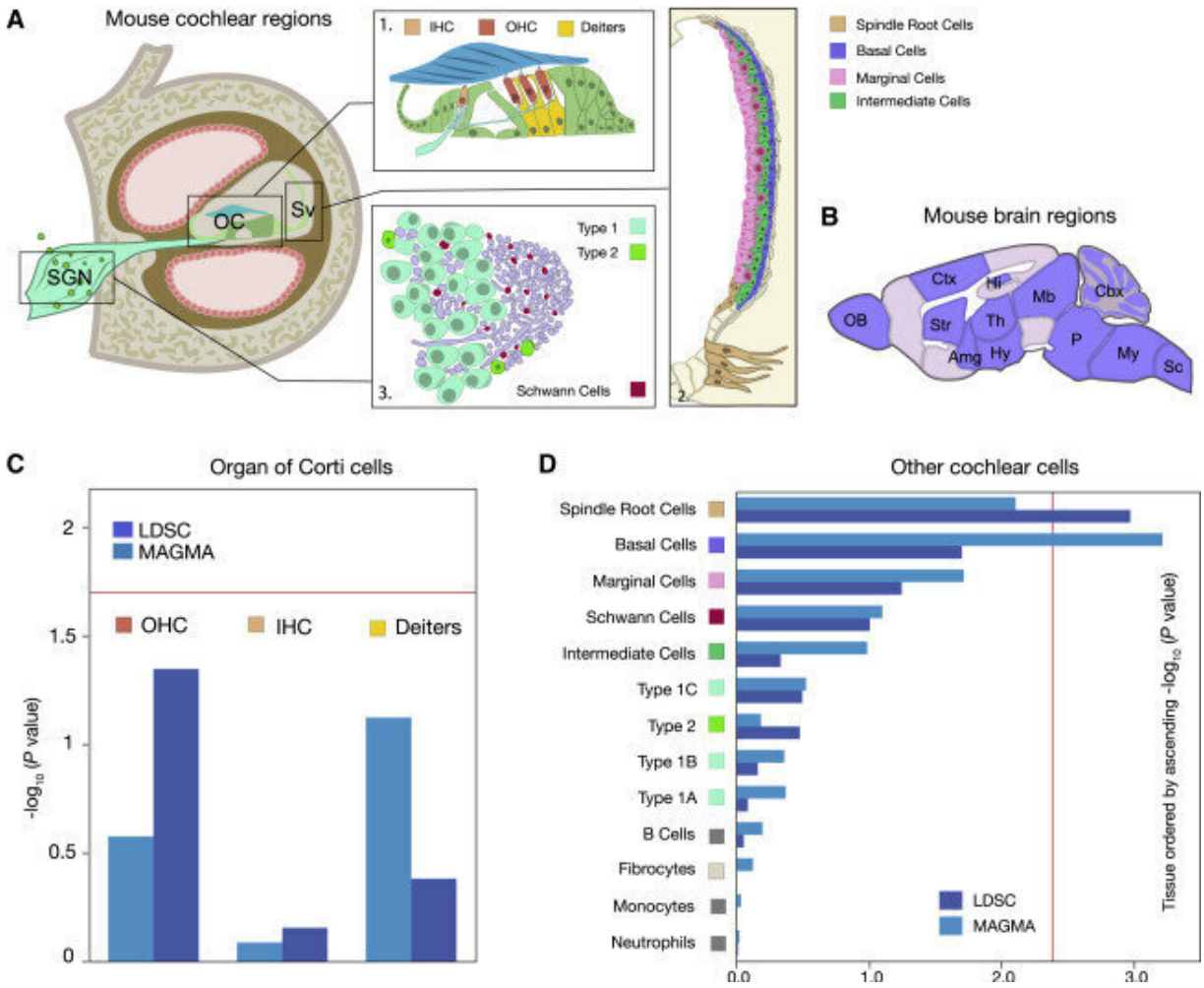
Hope for treatments against hearing loss as 10 genes identified

May 16 2022



Evaluation of enrichment of common-variant hearing loss GWAS results in scRNA-seq mouse datasets. Schematic of the mouse cochlea (A) and the mouse brain (B) regions used for the enrichment analysis. Abbreviations: Amg, amygdala; Cbx, cerebellum; Ctx, cerebral cortex; DC, Deiters' cells; Hi,

hippocampus; Hy, hypothalamus; IHC, inner hair cells; Mb, midbrain; My, medulla; OB, olfactory bulb; OC, organ of Corti; OHC, outer hair cells; P, pons; Sc, spinal cord; Str, striatum; Th, thalamus. OC is magnified in box 1 and illustrates the IHC, OHC, and DC, whose enrichment is shown in (C). A color box links a specific cell to the schematic. The red line is the Bonferroni significance threshold ($-\log_{10}$ p value 1.77). The enrichment analysis using cells from the stria vascularis (box 2) and the spiral ganglion neuron region (box 3) reveals a significant enrichment for spindle root cells and basal cells (D). All type 1 spiral ganglion neurons (type 1a, b, c) were all labeled the same color for sake of clarity. Given the broad and scarce distribution of immune cells (monocytes, neutrophils, and B cells), these are not shown on the schematic. The red line shows the Bonferroni significance threshold ($-\log_{10}$ p value 2.42) (E). Mouse nervous system cell type enrichment showing no significant enrichment. The red line shows the Bonferroni significance threshold ($-\log_{10}$ p value 2.89). Credit: *The American Journal of Human Genetics* (2022). DOI: 10.1016/j.ajhg.2022.04.010

Researchers led by King's College London, Karolinska Institute and Erasmus University have identified 10 new genes linked with hearing loss and located the part of the ear affected.

The findings, published today in *American Journal of Human Genetics*, cast doubt on the understanding that age-related hearing impairment originates mainly from sensory hair cells. Researchers argue that the stria vascularis, a part of the cochlea in the ear, is a new target for treatments to help people with hearing loss.

Many people gradually lose some of their hearing ability as they get older, and an estimated 2.4 billion individuals will have some form of hearing loss by 2050. Age-related hearing impairment is a top contributor to years lived with disability and is also an important risk factor for dementia.

The team studied genetic analyses previously carried out in centers around the world using samples from 723,266 people from 17 studies who had clinically diagnosed or self-reported hearing impairment. This meta-analysis is one of the largest conducted in hearing genetics to date. The researchers identified 48 genes linked to hearing loss, including 10 new variants newly linked to hearing.

Further analysis looking at mouse genetics indicated that age-related hearing loss is due to changes in the stria vascularis, which is necessary for hearing. The results provide targets for the basis of future research which could improve therapies against hearing loss.

Co-main author Frances Williams, Professor at King's College London, says that their "findings identify 10 genes newly linked with hearing loss. This study points to genes we could target for screening purposes, drug development and even gene therapy in the future. This study provides a solid foundation for ultimately improving therapies against hearing loss."

Co-main author Christopher R. Cederroth, Associate Professor at the Karolinska Institute, says that "it was hypothesized since the 1970s that the stria vascularis may play a role in hearing loss in humans, but the molecular evidence for this was missing until today."

More information: Natalia Trpchevska et al, Genome-wide association meta-analysis identifies 48 risk variants and highlights the role of the stria vascularis in hearing loss, *The American Journal of Human Genetics* (2022). DOI: 10.1016/j.ajhg.2022.04.010

Provided by King's College London