

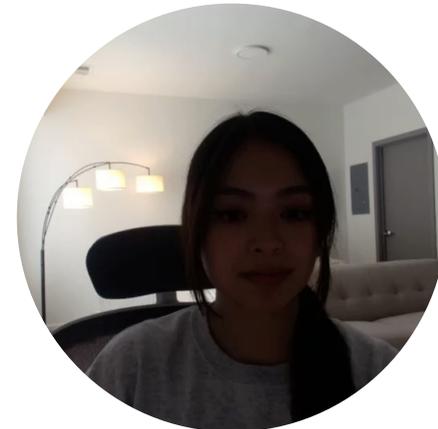
Indiana Clinical and Translational Sciences Institute

2023 Annual Meeting

Reduced Endocochlear Potential in vivo Prevents Hair Cell Degeneration in Tmprss3-deficient Mice

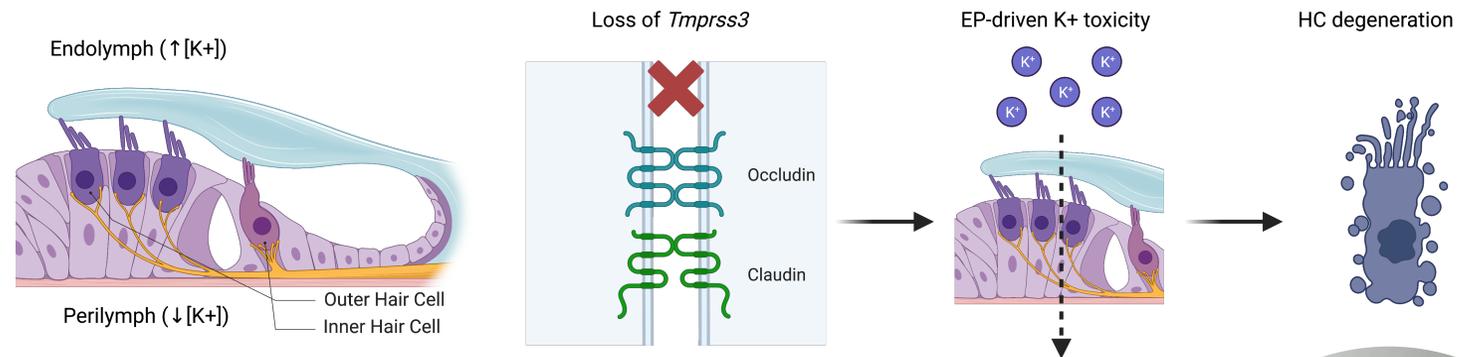
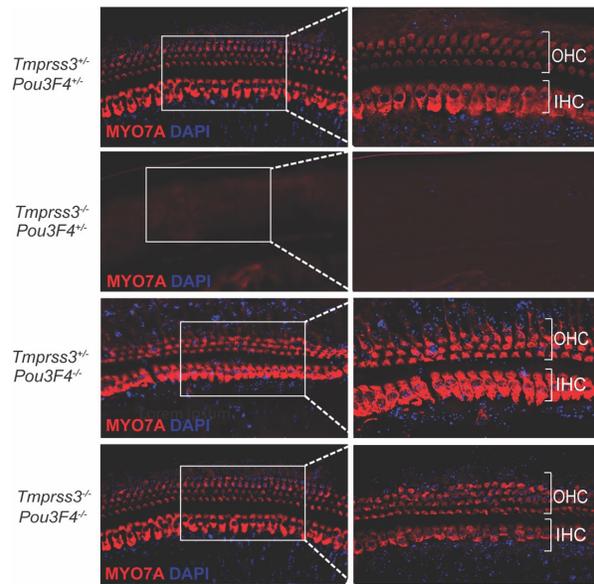
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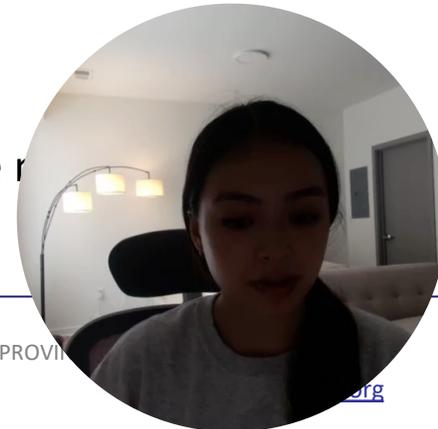


Our Findings

- We were able to discover a single factor, reduced endocochlear potential, that allowed for hair cell survival in mice deficient in the gene *Tmprss3*.
- This discovery shows us that hair cell death in *Tmprss3*-deficient mice is mediated by high endocochlear potential, through the mechanism of K⁺ paracellular leakage to the basolateral side of hair cells, implicating the role of TMPRSS3 in apical tight junction regulation.

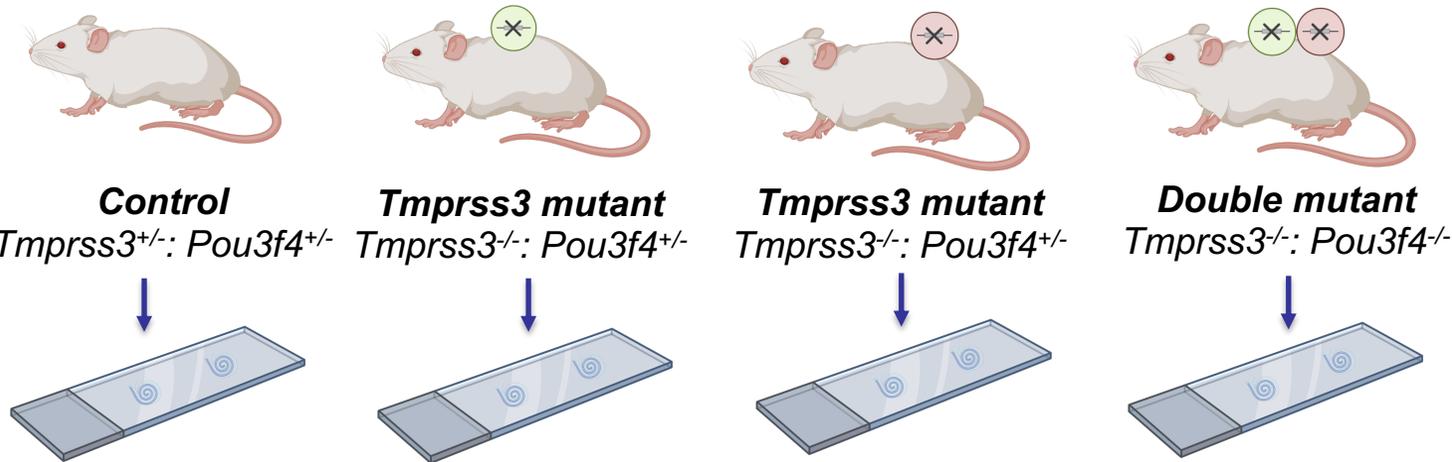


- These findings are incredibly significant because this brings us one step closer to elucidating the role of TMPRSS3, which is a major cause of deafness in patients with cochlear implants.



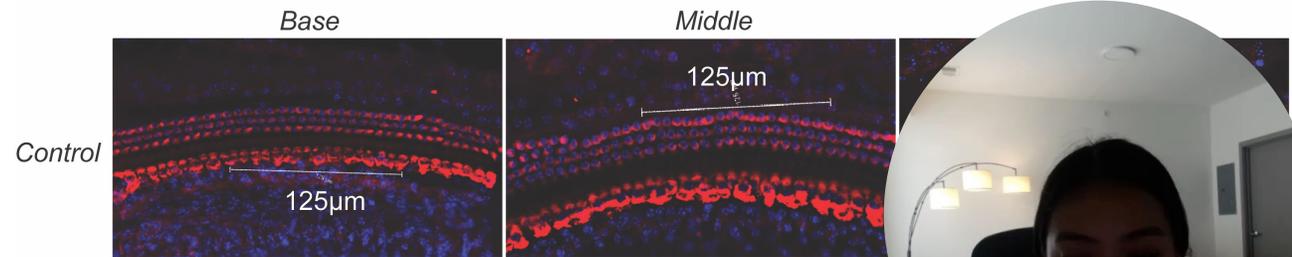
Methods

- *Pou3f4^{del-J}* mice
 - *Pou3f4* → transcription factor necessary for normal EP generation
 - *Pou3f4^{del-J}* mice have early onset hearing loss without HC degeneration and have reduced EP



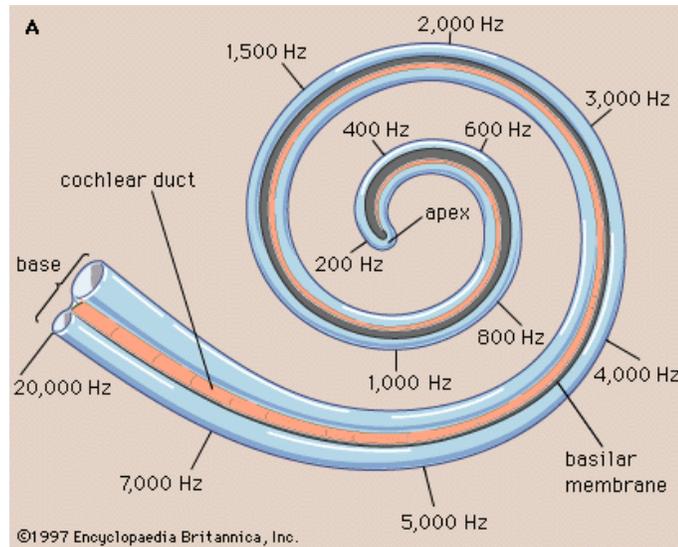
Antibody
 Myo7A → Cells stained IHCs & OHCs
 Sox2 → Supporting cells
 DAPI → Cells with nuclei

- Cell counts (IHC and OHC) were performed on stained slides in triplicates in a span of 125µm. Two-tailed unpaired t tests were performed with a significance of 0.05 (Figure below).

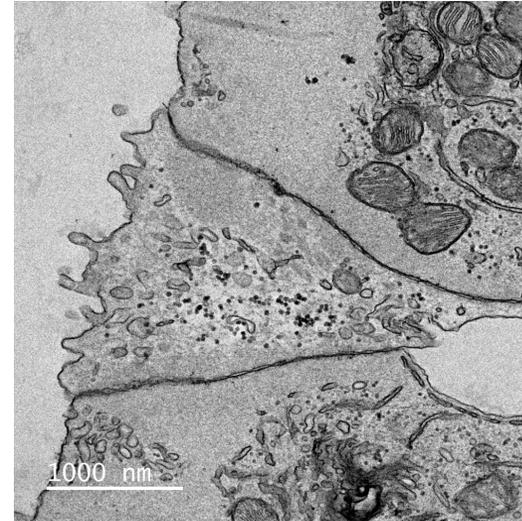


Future implications for patients or the community/ or next steps

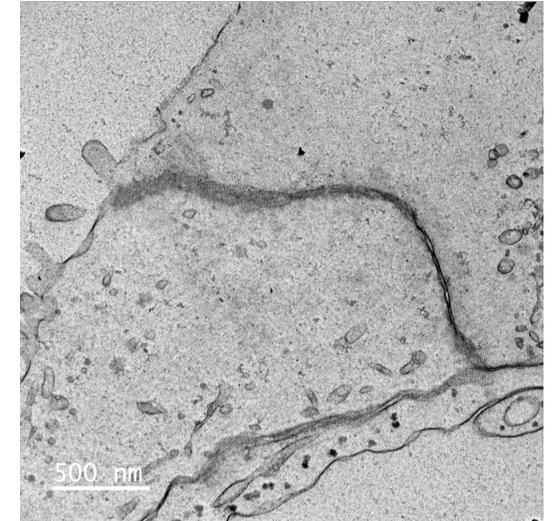
- Reducing EP to buy time before hair cells degenerate
- Patients with partially functional TMPRSS3 → hearing loss at higher frequencies due to base having slightly higher EP → modulate expression of endogenous gene



- Assessment of tight junction structure within *Tmprss3*-mutant mice using TEM and immunofluorescence.

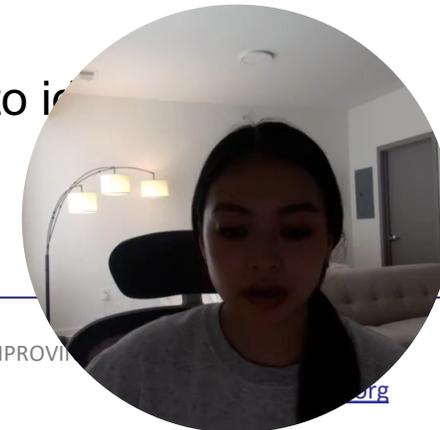


Tmprss3^{-/-}



Tmprss3^{+/-}

- Protein-protein interaction studies to identify substrates for TMPRSS3.



Grant Acknowledgement

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