Title: Exploring the Biological Mechanisms of Transforming Growth Factor (TGF) for Inflammation and the Ageing Processes of the Inner Ear

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Introduction. Previous research suggests that inflammation is a contributor to the biological mechanisms of age-related hearing loss (ARHL-presbycusis), a highly prevalent medical disorder. The cochlear amplifier resides in the outer hair cells (OHCs), and has reduced activity with aging and inflammation. The TGF family, involved in inflammatory modulation, is also involved in noise-induced hearing loss (NIHL). Following upon this, we investigated the TGF family and its associated receptors (TGFRs and epidermal growth factor receptors-EGFRs) to determine their role in OHC functionality and ARHL.

Methods. Auditory brainstem responses (ABRs) and distortion product otoacoustic emissions (DPOAEs) were recorded to characterize auditory function in young adult (Y, 7 months, n=4) and old (O, 24-31 months, n=4) CBA/CaJ mice. Following auditory testing, organ of Corti (OC) cochlear tissue (*in vivo*) samples were dissected from the cochleae, and extracted RNA was then analyzed for gene expression levels using qPCR. For *in vitro* experiments HEI-OC1 cells were used; and cisplatin and hydrogen peroxide were administered to them for a period of 24 hours to mimic cochlear aging and inflammation. Extracted RNA samples were then analyzed for the following candidates: TGFα, β1, β2, β3, TGFβR1, TGFβR2, TGFβR3 and EGFR.

Results. ABRs and DPOAEs revealed elevated hearing thresholds with aging (24-31 months) compared to young adult animals. The gene expressions of the TGF family and associated receptors were examined in HEI-OC1 cells and the *in vivo* OC cochlear tissue. *In vivo* samples showed some disagreement with the *in vitro* samples, as only the *upregulated* TGFβ2 and TGFβR1 were matched between *in vivo* tissue samples and *in vitro* results for both stimulants. However, TGFβ3, TGFα, TGFβR3, and EGFR exhibited match *in vitro* and *in vivo* results *upregulation* or *downregulation*. TGFβ1 and TGFβR2 showed no agreement in observed changes between the *in vivo* and *in vitro* samples. These differential findings indicate there may be subtle mechanistic variations in inflammatory reactions between HEI-OC1 cells and the more general organ of Corti *in vivo* tissue responses.

Conclusions and Future Work: Our findings strongly suggest that the TGF family and their associated receptors are involved in cochlear ARHL. These cytokines can be both anti-inflammatory and pro-inflammatory depending upon the biological feed-back pathway mechanisms involved. Future work will explore mechanistic pathways and therapeutic potentials of anti-inflammatory drugs in the treatment and prevention of ARHL.

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Poster or Podium

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