Proteomic and Transcriptomic Insights into Noise-Induced Hearing Loss

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Over 1.5 billion people globally suffer from hearing loss (HL), with about 5% of Brazilians affected. Sensorineural HL, caused by cochlear degeneration, is irreversible and can result from inherited or acquired conditions, including noise exposure. Investigating the mechanisms behind noise-induced hearing loss (NIHL) is essential for understanding its biological foundations. Proteins play a crucial role in the inner ear\'s response to acoustic stress, influencing processes such as cell apoptosis, inflammation, and cell regeneration. Proteomic analysis is a useful tool for detecting and characterizing these proteins, offering a complete understanding of the biological alterations that occur in response to noise.

Previous mass spectrometry (MS) and statistical analyses identified 81 differentially expressed proteins (DEP) in the cochlea of mice (P28-30) with normal hearing (NH) vs those with NIHL. The aim of this study was to perform in-silico characterization of DEP after acoustic trauma to identify key proteins and signaling pathways, providing new insights into the mechanisms of auditory damage.

Gene ontology over-representation analyses significantly grouped proteins by biological process and cellular component, particularly the mitochondria. Biological pathway enrichment analyses indicated a significant association with oxidative stress pathways.

We leverage omics data from previous studies to evaluate the expression and determine the specific cell types in which the proteins or their coding genes are enriched. Using MS studies from cochleae from mice (P30) with NH, we confirmed that 35/81 proteins were enriched in the organ of Corti (sensory epithelium responsible for transducing sound into electrical impulses) and 17/81 in the stria vascularis (recycling ions and maintaining homeostasis and endocochlear potential). After reuse of the scRNA-seq data, we discovered that 49/81 genes coding these proteins were enriched in supporting cells (SC), hair cells (HC), and auditory neurons. Integrating the data, we validated the gene and protein expression of 12/81 DEP in the cochleae of NH mice.

NIHL results from a complex interaction involving damage to the organ of Corti, dysfunction of the lateral wall (especially the stria vascularis), axonal retraction of spiral ganglion neurons, and activation of the immune response. The organ of Corti comprises supporting cells (SC) and two types of hair cells (HC): inner hair cells (IHC) and outer hair cells (OHC), with these cells being the first to degenerate in response to noise overexposure. Like this, we chose MS and scRNA-seq studies of mice cochleae with NIHL and confirmed 38 proteins out of 81 in cochlear extracts and 23 coding genes were differentially expressed in SC, OHC and neurons. Thus, 14 out of 81 DEP showed altered gene and protein expression in the murine cochlea after noise exposure.

Finally, four orthologous proteins in humans were described as enriched in the cochlear perilymph of patients with HL and/or vestibular schwannoma, with one protein associated with hearing deterioration. Phenotype ontology analysis revealed five proteins associated with altered hearing phenotypes.

These findings provide new insights into the molecular mechanisms of NIHL and highlight

potential therapeutic targets for intervention and diagnostic biomarkers. Further research is needed to validate these targets and explore their potential in cochlear regeneration strategies.

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