

Exploring potential biomarkers for the correlation between inflammation and Age-Related Hearing Loss (ARHL)

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Hearing loss affects more than 5% of the global population and is projected to reach 10% by 2050. It mainly affects individuals over 65, with 33% undergoing its effects, and is known as age-related hearing loss (ARHL). ARHL is linked to cognitive decline, serving as a risk factor for dementia. It involves auditory neurodegeneration, related to apoptosis, inflammation, and metabolic dysfunction in the organ of Corti. Moreover, genetic, environmental, and nutritional factors influence the development of ARHL. Recent findings link changes in the gut microbiota to systemic inflammation impacting various organ systems, including the brain and inner ear. This suggests a potential correlation between hearing loss and microbiota changes. Our goal is to investigate genetic and molecular mechanisms of the gut-brain-cochlea axis, exploring antiinflammation molecules via comprehensive gut metabolic profiling in a premature ARHL *Dusp1* knockout mice model. Faecal samples from mice of different genotype, sex, and age underwent metabolomics analysis via liquid chromatography and capillary electrophoresis coupled to mass spectrometry. Untargeted and targeted strategies were used to analyse the entire metabolome, emphasizing on short-chain fatty acids, vital in the intestinal microbiota paradigm. Metabolic pathways mainly affected include fatty acids, amino acids, glutathione, and lipid metabolism. Compounds, such as sphingosine-1-phosphate, several lysophospholipids, and butyric acid are noted for their roles in inflammation signaling. These metabolites and proinflammatory cytokines may contribute to an inflammatory scenario that links changes in microbiota with the onset and progression of ARHL. Currently, there are no robust faecal biomarkers for evaluating ARHL. Our study data, combined with other omics platforms, will aid in identifying characteristic ARHL biomarkers and potential antiinflammatory molecules for this condition. Funding: THEARPY PID2020-115274RB-I00, FEDER/MICIN