Exome sequencing data involve multiple genes and pathways in familial Meniere’s disease

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INTRODUCTION
- The prevalence of Meniere’s disease (MD) in European population is 0.05-0.1%.
- Familial Meniere’s disease (FMD) is found in 5-15% of cases in European population.
- We have identified 76 families with MD in Spain (1).
- Five different families with autosomal dominant inheritance pattern were selected.

AIM OF THE STUDY
- We present a combined strategy using multiple variant prioritization tools, phenotype ontology and pathway analysis to identify disease-causing variants and damaged genes in autosomal dominant diseases.

METHODS
- Whole-exome sequencing (WES)
- DNA was isolated from peripheral blood mononuclear cells in FMD patients. WES libraries were prepared with the Agilent's All Exon 50MB capture kit (Agilent Tech) and were carried out using a SOLID 5500x1 sequencing platform.
- Bioinformatics Tools
- Figure 1 shows four methods used to prioritize variants according to their effect on the protein structure, phylogenetic conservation, gene ontology and clinical phenotype.
- Gene ontology and Pathway analysis
- An analysis of genes carrying potentially pathogenic variants was performed by the Ingenuity Pathway Analysis software for each family (IPA, Ingenuity Systems, Redwood City, CA, USA)

RESULTS
- We have generated a gene list including the common genes from each family dataset according to the four prioritizing tools.
- A core analysis was performed for each pedigree and also another analysis for all merged familial datasets.
- Table 1 summarizes the 17 candidate canonical pathways obtained for FMD.
- Figure 2 shows the most significant pathways in merged datasets.

CONCLUSION
- Multiple pathways are probably involved in FMD.

REFERENCE

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