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Next generation sequencing of patients with hereditary neurosensory hearing loss to clarify the genetic cause of hearing impairment

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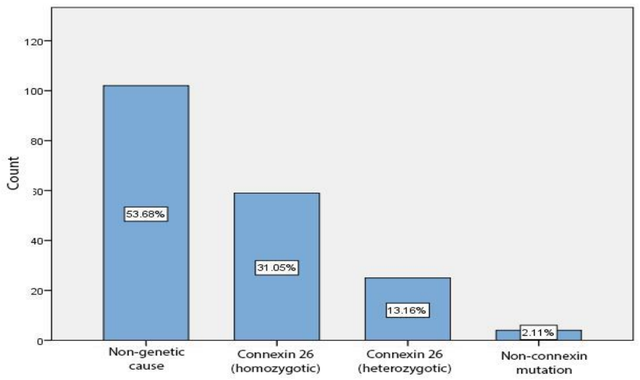
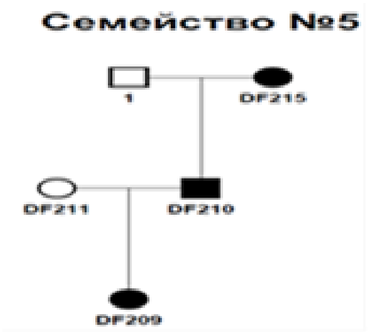
Introduction: The purpose of the study is a clinical and genetical diagnostics of families with family history of neurosensory hearing loss (NSHL), defining clinical and genetical characteristics of the hearing damage by conducting a targetted next generation sequencing (NGS). There were examined patients with NSHL who rejected frequent genetical mutation such as mutations in connexin genes – Cx26, Cx30, Cx31 and mitochondrial mutations.



Found genetic mutations

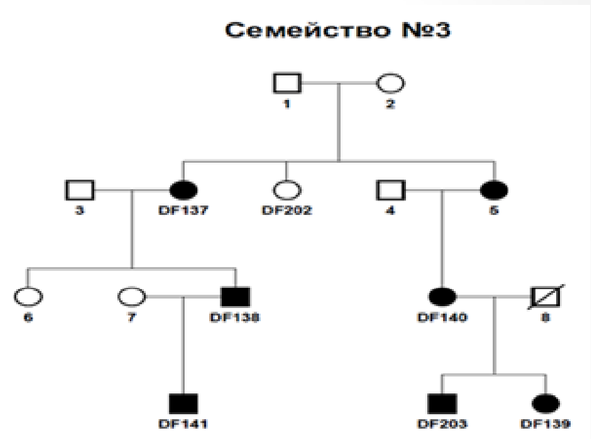
Methods: We studied a total of 193 patients with hystory of family NSHL. First we did PCR to screen for mutations in Cx26. Those patients without mutations in Cx26, were subsequently investigated for mutations in Cx30, Cx31 and mutations in mitochondrial DNA. We select five patients in which any mutations were not found and all of them have family history of NSHL. Targetted NGS was performed in these five cases and their families.



Family tree of the 5th proband – DF210

Results: A genetic cause for hearing loss was found out in two of the patients. When examining DF210 the variant c.853G>A(p.Gly285Ser) in exon 6 of the KCNQ4 gene was found. The mutations in it are connected with the development of an autosomal dominant hearing loss. A genetic cause for a formation of NSHL is assumed and for patient DF139, in whom, with the help of CNV analysis, was found a duplication of 51 basic pairs in OTOA gene (16:21679026-21679076), affecting exon 3 and partly intron 1-2 and intron 2-3. This is associated with a clinical phenotype in the autosomal recessive hearing loss.

As regards to the other three selected patients-in two of them(DF60 and DF182) were found variants which are insufficient to be associated with the particular clinical picture. There are not found pathological variants in one of the investigated pationts(DF84) in whom AD inheritance is assumed.



Family tree of the 3th proband – DF139

Discussion: Reasons for the inability to register genetic causes for the development of hearing loss are unclear. There have not been found all the genes causing a hearing loss up to the moment. Structural, mutational and epigenetic modifications related to the development of hearing loss have not been fully explained.

Conclusion: The literary date until now reports that detailed diagnostics through NGS dives excellent results in clinical practicce as a diagnostic method for deafness. The discovery of a hereditary model of inheritance enables affected families to obtain onformation on the presence and extent of risk in the next generations.

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