

Specific allelic diversity of the *SLC26A4* gene associated with hearing loss in the indigenous peoples of Southern Siberia (Russia)

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Motivation and Aim: Mutations in the *SLC26A4* gene (MIM 605646, 7q22.3) are considered to be the second common cause of hereditary hearing loss (HL) in many world populations. The *SLC26A4* mutation spectrum and prevalence were found to be very diverse around the world. We aimed to analyze for the first time the *SLC26A4* allelic diversity in deaf patients belonging to indigenous Turkic-speaking Siberian peoples.

Methods and Algorithms: Analysis of the *SLC26A4* gene sequence including all 21 exons and flanking regions was performed by Sanger sequencing in ethnically matched cohorts of deaf patients (170 Tuvinians and 62 Altaians).

Results: Contrast differences in the proportion of the *SLC26A4*-related HL caused by pathogenic variants c.919-2A>G, c.2168A>G, c.2027T>A, c.170C>A, c.2034+1G>A, c.1545T>G were found in Tuvinian (28.2 %) and Altaian (4.3 %) patients, despite their similar ethnogenesis and close residence in Southern Siberia. Along with pathogenic variants, both already known SNPs (c.225C>G, c.1790T>C, c.165-626T>A, c.165-546T>C, c.165-119A>T, c.165-113C>T, c.601-266T>G, c.1001+131G>T, c.1150-135C>T, c.1264-187C>T, c.1341+47T>C, c.1545-85G>C, c.1707+398T>C, c.1708-18T>A, and c.2319+243T>C) and novel variants (NC_000007.14: 107662833A>T, 107663118A>T, 107663208C>T, 107683478A>G, 107697874A>G, 107700976T>C, and 107701796C>T) were identified. We evaluated their frequencies in our samples and compared with available information from the Deafness Variation Database (<https://deafnessvariationdatabase.org/>). The frequencies of c.2319+243T>C (3.57 %), c.165-546T>C (0.40 %) in Tuvinians and c.225C>G (12.0 %), c.1545-85G>C (0.68 %), c.1707+398T>C (0.76 %) in Altaians significantly exceeded their world MAFs (0.04 %, 0.24, 0.09, 0.01, and 0.24 % respectively). The frequencies of c.601-266T>G (53.36 %), c.1150-135C>T (2.70 %), c.1341+47T>C (3.57 %) in Tuvinians, and c.1790T>C (2.27 %) in Altaians were comparable with their frequencies in East Asian populations (61.35, 3.30, 11.17, and 2.81 % respectively).

Conclusion: This work is the first study of the *SLC26A4* allelic diversity in Siberian indigenous populations. Analysis of the *SLC26A4* allelic frequencies in comparison with world populations revealed the affinity of Tuvinians and Altaians with East Asian populations. Obtained data significantly contribute to the information on the *SLC26A4* allelic diversity worldwide.

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