2013-09-16

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Congresso Brasileiro de Genética, 59., p. 161, 2013, Águas de Lindóia, São Paulo.
http://www.producao.usp.br/handle/BDPI/45640

INVESTIGATING DEAFNESS GENES AS A CAUSE OF SUDDEN SENSORINEURAL HEARING LOSS

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Keywords: Deafness, sudden sensorineural hearing loss, mitochondrial genes, deafness genes.

Hearing loss is a very heterogeneous genetic condition, meaning that identical or similar phenotypes result from mutations in many di erent genes, with diverse inheritance mechanisms. Sudden sensorineural hearing loss (SSNHL) is an emergency de ned as sensorineural hearing loss (SNHL) equal to or greater than 30 dB HL, a ecting at least three consecutive tonal frequencies, with sudden onset and occurring within three days. - e estimate incidence is 5 to 20 within 100.000 people by year, but despite the extensive list of potentially etiologic factors described, its pathophysiology is poorly understood. Some individuals with deafness due to mitochondrial mutations were described as having SSNHL. In mitochondrial DNA, genes encoding for transporter and ribosome RNA are hot candidates to explain hearing loss due to the large number of mutations associated with deafness already described in them. - e main mitochondrial mutations associated with non-syndromic deafness are A1555G, ΔT961insCn, T1095C, C1494T in MTRNR1 gene, that encodes the 12S subunit of rRNA; and A7445G, 7472insC, T7510C and T7511C in MTTS1 gene, that encodes the tRNASer(UCN). Regarding the MTTL1 gene, mutations are more frequently associated to mitochondrial syndroms that can include deafness as a symptom. Besides, mutations c.35delG and c.167delT in the GJB2 gene, del(GJB6-D13S1830) and del(GJB6-D13S1854) deletions near the GJB6 gene and the A1555G mitochondrial mutation in the 12S rRNA gene are described as the most frequently molecular diagnosis among individuals with hearing loss. - e aim of this work was to investigate the role of genetic factor in the etiology of SSNHL. In order to achieve this, the screened the mutations in the GJB2 and GJB6 gene and sequenced the mitochondrial genes MTRNR1, MTTS1 and MTTL1 in 53 individuals with SSNHL, associated or not with other symptoms. Mutations c.35delG, c.167delT, the deletions del(GJB6-D13S1830) and del(GJB6-D13S1854) were not found in the sample. Variants in MTTS1 and MTTL1 genes were not detected, either. Regarding the MTRNR1 gene, 15 di erent variants were found, 13 of which were already described as having no phenotypic e ect. Two novel mutations (m.806C>T and m.986G>A) were not reported in SNP database. - ey were not found in a Brazilian control sample of 104 normal hearing individuals (Abreu-Silva et al., Ann Hum Biol, 2011, 38(2):210-8), and their meaning still needs to be clari ed through population studies. Although molecular screening did not point to a signi cant role of the tested genes in SSNHL, it is noteworthy that 20 (37,7%) of the 53 subjects reported a positive familial history of hearing loss. while 18% of people in the control sample reported a ected relatives. – ese data suggest genetic susceptibility to hearing loss in this group, probably resulting from multifactorial mechanism. Financial support: Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) – CEPID, and Conselho Nacional de Desenvolvimento Cientí co e Tecnológico (CNPQ).