Molecular characterization of pathogenic *OTOA* gene conversions in hearing loss patients

Sacha Laurent[1], Corinne Gehrig[1], Thierry Nouspikel[1], Sami Amr[2], Andrea Oza[3], Elissa Murphy[3], Anne Vannier[1], Frédérique Bena[1], Maria Carminho-Rodrigues[1], Jean-Louis Blouin[1], Hélène Cao Van[1], Marc Abramowicz[4], Ariane Paolini-Giacobino[1], and Michel Guipponi[1]

[1]University Hospitals of Geneva
[2]Department of Pathology, Brigham & Women's Hospital and Harvard Medical School
[3]Partners Healthcare
[4]University Hospitals of Geneva

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Abstract

Bi-allelic loss-of-function variants of *OTOA* are a well-known cause of mild-to-moderate hearing loss. Whereas non-allelic homologous recombination-mediated deletions of the gene are well known, gene conversions to pseudogene *OTOAP1* have been reported in the literature but never fully described nor their pathogenicity assessed. Here, we report two unrelated patients with mild-to-moderate hearing-loss, who were compound heterozygotes for a converted allele and a deletion of *OTOA*. The conversions were initially detected through sequencing depths anomalies at the *OTOA* locus after exome sequencing, then confirmed with long range PCRs. Both conversions lead to loss-of-function by introducing a premature stop codon in exon 22 (p.Glu787*). Using genomic alignments and long read nanopore sequencing, we found that the two probands carry converted alleles of widely different lengths, suggesting that they originated from different mechanisms of gene conversion.

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