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COMMENTARY

A commentary on '*TECTA* mutations in Japanese with mid-frequency hearing loss affected by Zona Pellucida domain protein secretion'

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The authors detected *TECTA* mutations in 3.6% (5/139) of Japanese families with autosomal-dominant hearing loss. Of the mutations detected, those in the zona pellucida domain of alpha-tectorin (T1866M and I1997T) were associated with mid-frequency hearing loss. Fusion recombinant alpha-tectorin protein with mutations in the zona pellucida domain abnormally aggregated in the cytoplasm of transfected cultured cells, experimentally supporting the phenotypic impact of these missense mutations, which is consistent with previous reports in Caucasian and original in Japanese population.

Alpha-tectorin (Tecta) is a major non-collagenous protein of the tectorial membrane that covers the hair cells in the organ of Corti. The tectorial membrane is in contact with the hair bundles of sensory cells and has an important role in sound transduction in the inner ear.

Associations between *TECTA* and autosomal-dominant, non-syndromic hereditary hearing loss (NSHL) were first demonstrated by mapping in an Australian family,[1] as well as candidate gene approach and linkage analysis in Belgian and Austrian families (DFNA8/12) in 1998.[2] Mutations in *TECTA* have been identified in autosomal-dominant NSHL families in Sweden,[3] Netherlands[4] and Korea.[5] *TECTA* mutation is the most frequent genotype identified in autosomal-dominant NSHL in Caucasian populations.[6] *TECTA* mutations are also associated with autosomal-recessive NSHL (DFNB21) in Lebanese and Iranian families.[7]

The article by Usami and colleagues[8] provides significant clinical impact and raises further questions. They demonstrated that *TECTA* mutations are frequently associated with progressive, autosomal-dominant NSHL in Japan. Generally, autosomal-dominant NSHL is postlingual and progressive, and is often undetectable by audiologic screening in newborns. In Japan, a mutation-specific oligonucleotide screening panel (invader assay) that covers 47 mutations in 10 genes is available in current clinical practice supported by public health care, and this panel detects specific mutations in approximately 30% of the patients;[9] however, this leaves the etiology unknown in more than half of the cases. It has been shown that *TECTA* mutation is a frequent genotype in progressive, autosomal-dominant NSHL; thus, screening for *TECTA* mutations is an efficient strategy for identifying associated mutations for this type of hearing loss. It is also possible that novel *TECTA* mutations will be added to the screening panel in the future.

Usami and colleagues note that mutations in the zona pellucida domain of *TECTA* in the Japanese population are associated with mid-frequency hearing loss, which is consistent with reports in Caucasian populations.[10] The molecular basis of this phenomenon is supported by findings in *TECTA*-targeted mice.[11] The genetic basis or mutations in NSHL are heterogeneous, but the phenotype is generally solely sensorineural hearing loss. Audiometric profiling of the affected frequencies may be the only possible strategy for selecting candidate genes for NSHL basing on its phenotype. Along with the future recruitment of genome-wide screening realized by second-generation sequencing in clinical practice, conventional screening and molecular analysis of specific mutations remain indispensable. This report on *TECTA* mutations and phenotypes of mid-frequency hearing loss may provide a basis for the efficient screening of specific mutations in Japan. As *TECTA*-associated hearing loss is postlingual and progressive, identification of *TECTA* mutations would provide clinical insights into prognosis and interventions, such as hearing aids and cochlear implants.

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