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浙江省非综合征型耳聋患者12S rRNA突变频谱分析

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摘要 线粒体DNA (Mitochondrial DNA，mtDNA)突变是引起耳聋的重要原因之一。尤其是12S rRNA基因是药物性耳聋与非综合征型耳聋相关的突变热点区域。文章收集了浙江省各地区非综合征型及药物性耳聋患者标本318例，对其进行临床和分子遗传学评估。12S rRNA基因突变分析发现34个变异位点，已知的1555A>G、1494C>T和1095T>C突变分别占9.1%、0.6%和1.25%。结构和种系发生分析显示，839A>G和1452T>C突变位于12S rRNA基因的高度保守区域且未在449例正常对照组中发现，可能增加了耳毒性药物的敏感性。其他变异位点为多态性位点。文章数据支持了12S rRNA基因是耳毒性药物的作用靶点之一这一理论，为预测个体耳毒性的发生风险，提高氨基糖甙类药物治疗安全性提供了有价值的信息，以期降低耳聋的发生。

关键词： 线粒体12S rRNA基因 非综合征型耳聋 氨基糖甙类药物 突变频谱听力损失

Abstract： Mitochondrial DNA (mtDNA) mutations are one of the important causes of deafness. In particular, the 12S rRNA gene is the hot spots for mutations associated with both aminoglycoside ototoxicity and nonsyndromic deafness. In this report, a total of 318 Chinese pediatric hearing-impaired subjects were recruited from otology clinics in the Zhejiang Province, China. These subjects underwent clinical, genetic evaluation and molecular analysis of 12S rRNA gene. Mutational analysis identified 34 variants in the 12S rRNA gene in this cohort. The incidences of the known deafness-associated 1555A>G, 1494C>T and 1095T>C mutations were 9.1%, 0.6% and 1.25% in this cohort, respectively. Other mtDNA variants were evaluated by structural and phylogenetic analysis. Of these, the 839A>G and 1452T>C variants could confer increased sensitivity to aminoglycosides or nonsyndromic deafness as they were not present in 449 Chinese controls and localized at highly conserved nucleotides of the 12S rRNA. However, other variants appeared to be polymorphisms. These data further support the idea that mitochondrial 12S rRNA is one of major targets for aminoglycoside ototoxicity. These data have been providing valuable information to predict which individuals are at risk for ototoxicity, to improve the safety of aminoglycoside antibiotic therapy, and eventually to decrease the incidence of deafness.

Keywords： mitochondrial 12S rRNA gene, non-syndromic deafness, aminoglycoside antibiotics, mutation spectrum, hearing loss

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