# Next-generation sequencing identifies rare pathogenic and novel candidate variants in a cohort of Chinese patients with syndromic or non-syndromic hearing loss


## Abstract:

- **Background**: Some disorders like Hearing Loss (HL) caused by mutations other than the hotspot mutations in the common disorder genes, which could be difficult, and need a lot of time to be discovered by the traditional ways of DNA analysis.
- The **problem**: Hotspot mutations in specific DNA regions are not necessarily the only deafness-causing genes, so more efficient technologies for another regions analysis is needed
- **Method**: In this paper, we analyzed clinical and molecular data from 21 Chinese deaf families who did not have hotspot mutations in the common deafness genes GJB2, SLC26A4, GJB3, and MT-RNR1.
- The kind of **algorithm** we are interested in is Targeted Next Generation Sequencing (TGS) of 127 known deafness genes, which have been applied to 12 families, while for the remaining nine families, whole-exome sequencing (WES) or trio-WES was used.
- **Results:** GJB2, CDH23, EDNRB, MYO15A, OTOA, OTOF, TBC1D24, SALL1, TMC1, TWNK, USH1C, and USH1G were found to have potential pathogenic mutations in a total of 12 deafness genes in 13 probands, with eight of the detected mutations being novel. Also, one proband with heterozygous deletion of chromosome 4p16.3-4p15.32 had a copy number variant (CNV).
- As a result, the overall diagnostic rate for our deafness patients using NGS was 66.67% (14/21).
- **Conclusions:** These observations expand the mutation scope of deafness-causing genes and encourage the use of NGS detection technologies in Chinese deaf populations for routine molecular diagnosis.


## Introduction:

- Hearing loss affects 1 in 300-1000 infants, besides nearly half of the patients with HL have a genetic cause that has been identified.
- HL can be the result of non-syndromic (70%) or syndromic (30%).
- Around 110 genes and 150 loci have been found to be associated with HL.
- GJB2 (121,011), SLC26A4 (605,646), mtDNA 12SrRNA (561,000), and GJB3 (603,324) are the most commonly detected genes in Chinese deaf populations, accounting for 30-50% of cases.
- In the remaining cases, Deafness is caused by rare mutations in known deafness genes or unknown etiologies.
- In this paper, we enrolled 21 Chinese patients with either syndromic or nonsyndromic HL who were previously evaluated also had no hotspot mutations in the common deafness genes GJB2, SLC26A4, MT-RNR1, or GJB3.
- Next-generation sequencing (NGS) technologies, including targeted NGS (TGS) and whole-exome sequencing (WES), were performed on the probands of each family to identify rare pathogenic mutations.
- The results of this study highlight the genetic heterogeneity of HL and the importance of using a next-generation sequencing (NGS) method in patients with complicated clinical phenotype.