ASSESSMENT OF *STRC* DELETION PREVALENCE IN HEARING-IMPAIRED BRAZILIAN PATIENTS

PARAMO-NETO,M.E.; DIOGO-CAVASSANA,S.; ALENCAR-COUTINHO,D.; ABREU-OBERHUBER,R.; BENTO, R.F.; OITICICA, J.; BATISSOCO, A.C. ; LEZIROVITZ, K.
Laboratório de Otorrinolaringologia Genética Molecular, Celular e Translacional – LIM32 – HCFMUSP
Faculdade de Medicina Universidade de São Paulo – FMUSP

INTRODUCTION

The STRC gene (15q15.3) encodes the structural protein stereocilin that links stereocilia to each other and to the tectorial membrane in the inner ear, thereby ensuring the integrity and proper function of cochlear stereocilia. Loss-of-function variants in STRC cause autosomal recessive non-syndromic sensorineural hearing loss (ARNSHL), typically presenting as bilateral, symmetric, congenital hearing impairment of mild to moderate severity.

A major challenge in STRC analysis is the presence of its highly homologous pseudogene (pSTRC), which shares 99.6% sequence identity with the functional gene. This extensive similarity complicates variant detection by conventional sequencing methods, including Sanger sequencing and NGS, often requiring specialized strategies such as MLPA, TaqMan qPCR, or long-range PCR coupled with nested PCR to achieve reliable discrimination between STRC and pSTRC.

In Brazil, STRC-related hearing loss remains substantially underdiagnosed due to these technical limitations. Nevertheless, available epidemiological evidence suggests that STRC deletions are among the most frequent genetic causes of hearing loss in the population. Notably, larger homozygous deletions that extend into the adjacent CATSPER2 gene cause Deafness–Infertility Syndrome (DIS) in males.

AIM

This study aimed to investigate STRC gene deletions in patients with mild to moderate hearing loss, thereby contributing to advances in genetic diagnosis and to a better understanding of the epidemiology of hearing loss in Brazil.

METHODS

Samples were obtained from individuals with non-syndromic hearing loss. Only patients lacking a conclusive diagnosis after screening for common mutations or broader NGS panels were included. Copy number variations (CNVs) were assessed using MLPA (Multiplex Ligation-dependent Probe Amplification SALSA, P461-B1 kit), and deletions were subsequently confirmed by qPCR and multiplex PCR.

RESULTS AND DISCUSSION

A total of 109 samples were analyzed from patients with mild to moderate hearing loss using MLPA (Fig. 1).

Deletions involving the STRC and CATSPER2 genes were identified in eight samples (7%). Of these, three carried heterozygous STRC deletions (2%), while five harbored homozygous deletions (4%). Importantly, not all STRC deletions are of equal size: among the 13 chromosomes with STRC deletions detected in this study, ten also involved CATSPER2, while three were restricted to STRC alone (Fig. 2 and 3).

Deletions encompassing STRC and CATSPER2 in homozygosis are associated with Deafness-Infertility Syndrome (DIS). Notably none of the presenters was homozygous for the CATSPER2 deletion.

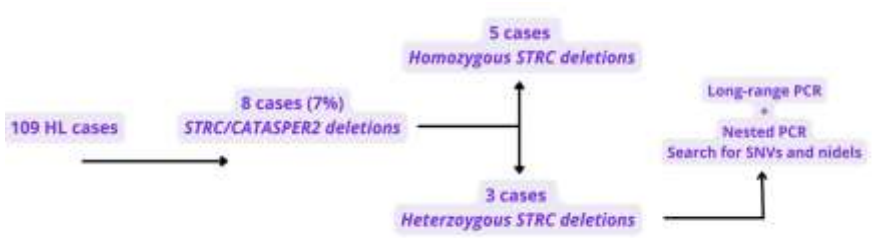

FIG1. Workflow for the detection, validation, and analysis of STRC gene deletions.

Despite the challenges posed by the highly homologous pSTRC pseudogene, the combined use of MLPA and complementary methods allowed reliable detection of STRC deletions.

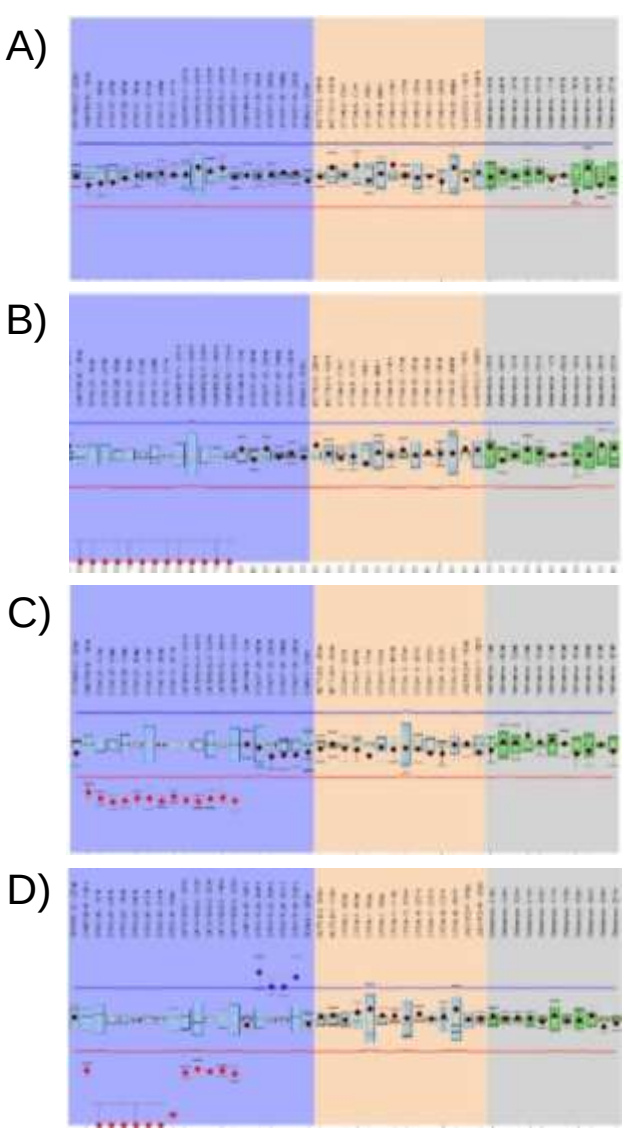

FIG2. Ratio chart output from Multiplex Ligation-dependent Probe Amplification (MLPA) analysis, showing representative profiles for: (A) negative control with normal copy number;(B) homozygous deletion of both STRC and CATSPER2;(C) heterozygous deletion of STRC and CATSPER2; and(D) homozygous deletion of STRC with a heterozygous deletion of CATSPER2.

FIG3. Schematic representation of chromosome 15, highlighting 13 affected regions.

CONCLUSION

These findings highlight the importance of incorporating STRC analysis into diagnostic workflows for hereditary hearing loss in Brazil. They contribute to improving molecular diagnosis, optimizing patient management, and strengthening genetic counseling strategies.

REFERENCES

Vona B, *et al.* 2015. DFNB16 is a frequent cause of congenital hearing impairment: implementation of STRC mutation analysis in routine diagnostics. Clin Genet 87(1):49-55. **PMID: 26011646.**

E-mail: eduardamarsola@gmail.com

AGRADECIMENTOS: AOS PACIENTES