

A FAST AND COST-EFFECTIVE APPROACH IN THE MOLECULAR DIAGNOSTICS OF CONGENITAL DEAFNESS (ARRAY CGC)

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Introduction: Congenital hearing loss/deafness is the most common birth defect and the most prevalent sensorineural disorder in developed countries but currently only a minority of genes is included in the genetic diagnostics. Genetic factors are considered to cause more than 50% of the cases of congenital deafness in children. Genetic deafness can be inherited, as an autosomal dominant, autosomal recessive, or X-linked recessive trait, as well as by mitochondrial inheritance. Over 400 genetic syndromes that include deafness have been described. In some syndromes deafness may appear as the first symptom, while other pathological manifestations may have a later onset during development. Molecular testing is a vital asset to complement the differential diagnosis between nonsyndromic and syndromic hearing loss and anticipate the onset of clinical features allowing a better planning for hearing rehabilitation.

Method: Using a custom microarray panel (ARRAY CGC – Pat. Pend.) we tested 312 point mutations, identified in the 31 main genes involved on congenital deafness (ACTG1, CDH23, COCH, CRYM, DFNAS5, DIAPH1, EYA1, GJA1, GJB2, GJB3, GJB6, KCNE1, KCNQ1, KCNQ4, MYO1A, MYO7A, OTOA, OTOF, PAX3, PCDH15, POU3F4, SIX1, SIX5, SLC26A4, SLC26A5, TECTA, TMC1, USH1C, USH1G and WFS1). With this approach it was possible to identify the molecular basis of the most common forms, both syndromic and nonsyndromic.

Results: We analyzed 163 cases and in 31 we detected mutations or sequence variants on CDH23, GJB2, GJB3, MYO1A, MYO7A, OTOF, SLC26A4, SLC26A5 and WFS1 genes. The samples analyzed were obtained from an already scrutinized population, so the most common genetic alterations were already excluded, mainly deletion/duplication analysis of GJB2 gene. Average turnaround time was one week after DNA extraction.

Conclusion: The usual trial and error diagnostic approach for congenital deafness needs to gain efficiency. With this approach we can drastically increase the number of genes/mutations analyzed maintaining accuracy but reducing turnaround time. This approach greatly enhances genetic diagnostics, allowing early decision-making process in patient management as well as new epidemiologic data regarding the genetics of congenital deafness that by the usual approach could not be obtained.