

SKELETAL DYSPLASIA DIAGNOSED BY A CUSTOM MOLECULAR MICROARRAY (ARRAY CGC)

Purificação Tavares¹, Adosinda Rosmaninho², Jorge Saraiva³, Formosinho Sanches⁴, Márcia Martins^{5,6}, Osvaldo Moutinho⁵, Susana Pereira⁷, Tavares Silva⁸, Francisco Valente⁹, Ana Franco¹⁰, Dora Mayén¹¹, Lina Ramos¹², Maria Orera¹, Heloísa Santos¹, Aida Palmeiro¹, Paula Rendeiro¹ ¹CGC Genetics (www.cgcgenetics.com), Newark, New Jersey, United States, ²Centro Hospitalar do Alto Ave, Guimarães, Guimarães, Portugal, ³Hospital Pediátrico de Coimbra, Coimbra, Coimbra, Portugal, ⁴Maternus, Lisboa, Lisboa, Portugal, ⁵Centro Hospitalar Trás-os-Montes e Alto Douro, Vila Real, Vila Real, Portugal, ⁶Centro Hospitalar do Porto, Maternidade Júlio Dinis, Porto, Porto, Portugal, ⁷Hospital de S. Teotónio, Viseu, Viseu, Portugal, ⁸Hospitais da Universidade de Coimbra, Coimbra, Coimbra, Portugal, ⁹Centro Hospitalar de Vila Nova de Gaia/Espinho, VN Gaia, Porto, Portugal, ¹⁰Hospital de Faro, Faro, Faro, Portugal, ¹¹Hospital Ángeles Lomas, Huixquilucan, Edo de México, Mexico, ¹²Maternidade Bissaya Barreto, Coimbra, Coimbra, Portugal

Introduction:

Osteochondrodysplasias, also known as Skeletal Dysplasias (SD) account for more than 400 different genetic diseases with bone involvement but variable clinical characteristics, whose diagnosis is based on clinical examination, radiological findings, histo-pathological and molecular analysis. They represent around 5% of genetic diseases of the newborn and are a major cause of problems for families and patients due to its morbidity, high lethality and complex medical problems, emerging since the prenatal period, having a high risk of recurrence in children or siblings. Genetic testing improves clinical diagnosis and is essential for a differential diagnosis. The molecular characterization of genes responsible for SD, is extremely important for establishing a precise diagnostic evaluation, namely during the prenatal period. Here we report our experience using this custom methodology.

Method:

Using a customized microarray panel (ARRAY CGC – Pat. Pend.) we tested 50 point mutations, identified in the 6 main genes involved in SD: FGFR3 (Achondroplasia, Thanatophoric Dysplasia), COL2A1 (Achondrogenesis type II), SLC26A2 (Achondrogenesis type IB), CRTAP (Osteogenesis Imperfecta, recessive type), LEPRE1 (Osteogenesis Imperfecta, recessive type) and SOX9 (Campomelic Dysplasia). With this approach it is possible to identify the molecular basis of the most frequent and severe forms of SD.

Results:

From 46 cases analyzed (16 amniotic fluids, 15 peripheral bloods, 9 DNA samples, 3 cell cultures, 1 CVS, 1 Umbilical cord blood, 1 paraffin block, and 1 tissue sample from a kidney fetal biopsy; one case was tested by CVS and fetal biopsy, confirming the previous result), 13 had a positive result. Five were heterozygote for the mutation c.742C>T (p.Arg248Cys) in the FGFR3 gene, four heterozygote for the c.1138G>A (p.Gly380Arg) mutation, one heterozygote for the c.2420G>C (p.Ter807Ser) mutation, one homozygote for the c.835C>T (p.Arg279Trp) in the SLC26A2 gene and one with c.532C>T (p.Arg178Stop) and c835C>T (p.Arg279Trp) mutations in the SCL26A2 gene, both in heterozygosity.

Conclusion:

This customized array panel drastically reduces turnaround time (one week after DNA extraction), maintaining accuracy and liability. The results are achieved independently of the sample type. Faster diagnostic is achieved, allowing early decision-making process in patient management, being particularly relevant in prenatal diagnosis.