V Reunião Brasileira de Citogenética e Citogenômica
5th Brazilian Meeting of Cytogenetics and Cytogenomics
30 e 31/Maio & 01 e 02/Junho de 2017

Gene interaction network analysis within the 4P16.3 critical region

Corrêa, T.[1]; Mergener, R.[1]; Leite, J.C.[2]; Galera, M.F.[3]; Moreira, L.M.A.[4]; Riegel, M.[1,2]

Abstract/Resumo

Deletions in the 4p16.3 region cause Wolf-Hirschhorn syndrome (WHS), a contiguous gene deletion syndrome involving variable size deletions. This study aimed to perform a gene interaction network analysis within the WHS critical region and to stablish the cytogenomic profile of the chromosome rearrangements involving the 4p16.3 regions. 16 samples from individuals with a clinical indication of WHS were retrospectively analyzed of which 11 had a cytogenetic visible deletion and 5 a submicroscopic deletion not previously identified. Using FISH, chromosomal microarray analysis, WGS and WES, we define the critical breakpoints within the 4p16.3 chromosome rearrangements. A gene interaction network analysis was performed using the Cytoscape (http://apps.cytoscape.org) platform.

In addition to 12 terminal deletions, we mapped 1 interstitial deletion, 2 ring chromosomes and 1 typical translocation 4;8. The deletions sizes ranged between 3.7 and 25.6 Mb. We present the genotype-phenotype correlation for each patient and characterize the type, the extension and the genomic position of the chromosome rearrangements as well. Previous genotype-phenotype correlations of the 4p16.3 regions have been hampered by the presence of other imbalances leading to duplication in part of the WHS critical region, which was a confounding factor in some of these correlations. In this study, only patients with 4p deletion due to different types of chromosome rearrangements were included, which enabled us to further refine the 4p critical region map and to explore new insights on mechanisms associated with CNVs within the 4p16.3 regions. The individuals in our study whose deletions encompass the terminal 875 kb 4p16.3 region were reported as having microcephaly and seizures, typical in the clinical context of the WHS. Focusing on the chromosome critical region defined in our sample, we explore, molecular interaction networks and biological pathways involving genes associated with the WHS.

Keyword/Palavras-chave: Microarray chromosome analysis; 4p16.3 chromosome rearrangements; Gene interaction network

1 PPG em Genética e Biologia Molecular, UFRGS, Porto Alegre, RS, *thiagocorrea252@gmail.com*
2 Serviço de Genética Médica, HCPA, Porto Alegre, RS.
3 Dept de Pediatria, UFMT, Cuiabá, MT.
4 PPG em Genética e Biodiversidade, UFBA, Salvador, BA.