

Abstract 88

A NOVEL NONSENSE MUTATION IN JARID1C GENE IN A BRAZILIAN MENTAL HANDICAPPED MALE

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Mutations in Jumonji AT-rich interactive domain 1C (*JARID1C/SMCX*) gene, located at Xp11.22, are emerging as a frequent cause of X-linked mental retardation (XLMR). Recent breakthroughs have pointed that *JARID1C* encodes for a member of an ARID protein family that harbors conserved DNA-binding motifs and acts as a histone H3 lysine 4 demethylase, suggesting a potential role of it in epigenetic regulation during development, cell growth and differentiation. In this study, we performed a mutation screening of the exon 15 of *JARID1C*, one of the most commonly mutated, in 97 probands with idiopathic mental retardation from families with a probable history of XLMR, in which at least two affected males were present. All patients had normal karyotypes and mutations in *FMR1*, *FMR2*, *ARX* and *MECP2* genes were previously ruled out by our group. Genomic DNA was obtained from peripheral blood and molecular analysis of exon 15 and flanking intronic regions was performed by standard PCR, followed by bidirectional direct sequencing. In a 12-year-old boy, we identified a novel single-nucleotide substitution (c.2172C>A), which replaces the normal cysteine by a termination codon at position 724 of the protein (p.Cys724X) in the evolutionarily conserved C5HC2 zinger finger domain. The proband, who has two affected brothers and a cognitively impaired mother, exhibits speech delay, hyperactivity and high palate, besides mental retardation. Although other *JARID1C* regions remain to be investigated, our preliminary results extend the number of *JARID1C* mutations implicates with XLMR and highlight its promise for understanding neural function and unexplained cases of XLMR.

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