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FAMILIAL Xp22 MICRODUPLICATION (INCLUDING THE RPS6KA3/RSK2 GENE) STUDIED IN THREE GENERATIONS OF A FAMILY AND CAUSING A BORDERLINE TO MILD NON-SYNDROMIC MENTAL RETARDATION

M^a Isabel Tejada¹, Cristina Martínez-Bouzas¹, Ainhoa García-Ribes², M^a Asun López-Aríztegui,³

Molecular Genetics Laboratory-Biochemical Department, Cruces Hospital, Barakaldo-Bizkaia, SPAIN¹

Neuropaediatrics Consultation- Paediatrics Department, Cruces Hospital, Barakaldo-Bizkaia, SPAIN²

Cytogenetics Laboratory-Biochemical Department, Cruces Hospital, Barakaldo-Bizkaia, SPAIN³

Mental retardation is the only clinically consistent manifestation in patients with non-syndromic forms of XLMR and, when families are too small for performing linkage analysis, the diagnosis of these families become very difficult. Multiplex ligation-dependent probe amplification (MLPA) has been demonstrated to be a fast and cost-efficient tool for screening patients with XLMR and has allowed detecting of new cryptic chromosome aberrations responsible for XLMR. During the last three years, we re-studied more than 100 male MR patients suspected to be XLMR searching for copy number changes of several genes on the X-chromosome using the MLPA P106 MRX kit. Among the anomalies found (work in preparation), here we describe a familial Xp22 microduplication (including the RPS6KA3/RSK2 gene) causing a borderline-to-mild non-syndromic mental retardation in a three generation family: A male infant, born in 2000 was referred to our genetic consultation because of a developmental delay and a similar clinical history in two maternal uncles. Karyotype, FMR1 gene and subtelomeric rearrangements were normal. After finding the microduplication in Xp22.11-22.2 by MLPA, we designed a specific CGH microarray that allowed us to determine the extent of the duplication: from 19410850 to 20460348, containing 10 genes, RPS6KA3/RSK2 being the only gene that could be related to MR. The same duplication was also observed in the younger brother, mother and grandmother all three being normal. The two maternal uncles also carried the microduplication. The re-examination of the 4 males in this family showed that they exhibited none of the features typical of Coffin-Lowry Syndrome and furthermore, the two maternal uncles presented with border-line mental retardation, are living normal, independent lives. In contrast to the numerous well-known microdeletion syndromes, only a few microduplications have been described and, to our knowledge, this is the first case with this duplication.

Acknowledgements: We thank the members of this family for their help with this research and BIOEF Foundation for supporting it (BIO06/DI/005).