



Poster 26. A MULTIPLEX ASSAY FOR X-LINKED INTELLECTUAL DISABILITY ASSESSMENT.

Autores: Paula Jorge, Isabel Marques, B Oliveira, Rosário Santos.

Afilições: Unidade de Genética Molecular (UGM), Centro de Genética Médica Doutor Jacinto de Magalhães (CGMJM), Centro Hospitalar do Porto (CHP), Porto, Portugal.

Contatos: Paula Jorge, PhD, Técnica Superior de Saúde, ramo de Genética, UGM, CGMJM, CHP.
E-mail: paula.jorge@insa.min-saude.pt

INTRODUCTION: X-linked intellectual disability (XLID) represents a common cause of monogenic mental retardation affecting mostly males. However it is not uncommon to have X-linked disorders with variable degrees of penetrance or a skewed X-inactivation, phenomena that hamper prediction of the phenotype. Based on the clinical presentation, XLID can be categorized into three classes: syndromes, encompassing multiple congenital anomalies compromising other organs beyond the brain; neuromuscular disorders presenting neurological and/or muscular symptoms such as epilepsy, dystonia, spasticity and muscle weakness in the absence of malformations; nonspecific conditions, where ID is the only consistent clinical sign and their discrimination depends entirely on the determination of the causative gene. Among the genetic causes involved, mutations in FMR1, AFF2 and ARX genes emerge as important causes. FMR1 and AFF2 genes contain polymorphic repetitive regions susceptible to suffer dynamic mutations, which may give rise to pathogenic expansions. In the ARX gene, the second exon represents a mutational hotspot as it contains repetitive regions coding for alanine stretches. Among those present in polyalanine tracts, c.429_452dup24 is the most frequent.

OBJECTIVES: To characterize a population at risk for ID.

MATERIAL AND METHODS: Aiming for the characterization of a population at risk for ID, a multiplex molecular screening technique was developed targeting mutational hotspots in FMR1, AFF2 and ARX.

RESULTS: The assay was used to screen over 4500 intellectually-disabled individuals.

CONCLUSIONS: The present work represents the first retrospective study of a Portuguese population where Fragile-X Syndrome was excluded, screened by this three gene cluster-based approach. This method should improve the detection of genetic conditions associated with these three genes, which are likely to be underdiagnosed.