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between archival blood spot material and fresh blood DNA from Fragile X symptomatic and asymptomatic individuals, premutation carriers and healthy controls. Given that there is increasing evidence for the benefits of early diagnosis and treatment for FXS, the FREE methylation test offers an attractive solution to the technical and ethical problems that have prevented the introduction of FXS newborn screening.

P_07-044

A multiplex assay for X-linked intellectual disability assessment

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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 intellectual disability (ID) is the only consistent clinical sign and their discrimination depends entirely on the determination of the causative gene. Among the genetic causes involved in XLID, 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. 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. The assay was used to screen over 4500 intellectually-disabled individuals. 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.

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Against All Odds: Genetic Screening In Brazilian Patients With Intellectual Disability

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Background: Mental retardation or intellectual disability affects 2% of the general population, but in 60% to 70% of cases the real cause of this retardation is not known. An early etiologic diagnosis of intellectual disability can lead to opportunities for improved educational interventions, reinforcing weak areas and providing a genetic counseling to the family. Objective: To investigate etiological factors in mental retardation in one educational institution APAE (Associação dos Pais e Amigos dos Excepcionais) for mental impaired patients (adults and children) in Limeira, Sao Paulo State, Southeast of Brazil. Methods: A detailed clinical, cytogenetic, biochemical and molecular survey was undertaken on 400 patients with no previously recognized cause of retardation (patients with clinical diagnosis of Down syndrome were excluded from this evaluation). The etiological study was based on a clinical genetic approach with special attention to dysmorphology and neurological findings. Results: The patients had a female: male ratio of 1:2 and their ages varied from 10 months to 48 years. The patients were classified as having mental retardation of unknown origin, i.e. patients with apparently normal pre-, peri- and postnatal histories who had neither dysmorphism nor affected first-degree relatives, and had a normal karyotype and metabolic screen. Among the 243 males, 151 of them were selected to molecular screening (FRAXA and FRAXE) and G-banded chromosome analysis, 17 had positive molecular screening (PCR) and/or Southern blotting for X-fragile syndrome. Of all patients, 19 had abnormal chromosome findings; it was worthy to note that Triple X syndrome was noted in 4 girls with minor dysmorphisms, 35 patients had features of MCA/MR syndromes and 69 had features of non-syndromic X-linked mental retardation based in the family's pedigree. The former group of MCA/MR syndromes may include unidentifiable chromosomal aberrations, uniparental disomy, mutations and multifactorial factors. ArrayCGH was only performed in a selected group of patients (12) and 7