P-02

NEXT GENERATION FRAGILE-X TESTING: GETTING AWAY FROM SOUTHERN BLOTS

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Fragile X syndrome (FXS) is the most common form of intellectual disability in the general population, usually caused by an expansion of a trinucleotide CGG repeat in the 5' untranslated region of the *FMR1* gene. In most cases, expansions over 200 repeats, termed full mutations, cause silencing of *FMR1* gene due to methylation of its promoter, and consequently loss of protein product. Expansions with 55-199 CGG repeats called pre-mutations or others even smaller (45-54 CGG repeats) named intermediate, do not cause FXS, but are frequently associated with late-onset neurological and/or reproductive disorders (FXTAS/FXPOI). Southern Blot (SB) is still considered the gold standard for molecular diagnosis of FXS, because it is able to clearly characterize size and methylation status of full and pre-mutated *FMR1* alleles (following DNA digestion with methylation sensitive enzymes). Nevertheless, SB is a very time-consuming technique and requires a large amount of intact and high-molecular weight DNA. As such, several methodologies have been developed to replace SB and overcome its disadvantages. The aim of this work was to test different techniques which can substitute totally or partially the SB, by comparing (1) their ability to quantify or discriminate normal, pre-mutated and fully mutated alleles; (2) the maximum number of CGG repeats detected; (3) their capacity to determine the DNA methylation state; (4) their power to discriminate size and methylation mosaics; and (5) the amount of DNA required for each technique. The tested techniques were High Resolution Melting Curve Analysis (currently in experimental process with prototype reagents), the FragilEase™ assay from PerkinElmer®, the Amplidex® FMR1 mPCR Protocol from Asuragen® and a multiplex assay developed by our group, for the simultaneous screening of 3 genes - *FMR1*, *AFF2* e *ARX*. For this work we tested 7 DNA samples from patients previously characterized at the molecular level in our laboratory: 6 from females and 1 obtained from a chorionic villus sample of a male fetus. These samples were previously characterized as normal (n=2), fully mutated (n=3), pre-mutated (n=1) and a size mosaic (n=1). Although using a very small number of samples, this work aims to describe and compare four different methodologies in an attempt to establish if they can adequately replace SB.

P-03

PORTUGUESE PATIENT REGISTRY FOR DUCHENNE/BECKER MUSCULAR DYSTROPHY

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Duchenne/Becker muscular dystrophy (D/BMD) collectively known as the dystrophinopathies, is one the most frequent neuromuscular diseases with onset during pediatric age, having an estimated incidence of about one in every 3500 to 5000 boys. Over the last two decades, the Molecular Genetics Unit of CGMJM has performed the genetic characterization of over 360 D/BMD patients, leading to the identification of 189 mutations, including 46 novel variants. Comprehensive analysis also involved expression studies at the mRNA level, the identification of splicing changes and ultimately providing evidence for apparent exceptions to the reading-frame rule. Considering the recent mutation-based therapeutic approaches, *DMD* gene analysis has gone beyond the molecular confirmation of the clinical diagnosis and is now also crucial for patient inclusion in disease registries and in ongoing clinical trials. In 2007, the network of excellence for the neuromuscular field - TREAT-NMD - started a global patient registry for D/BMD. This registry depends entirely on data gathered at the national level in country-specific disease registries using the same database items (mutational and clinical). This standardization enables consensus and facilitates clinical research, the development of new therapeutic approaches and clinical trials for new drugs. These trial-ready registries are also useful for phenotype/genotype correlations and epidemiological profiles of the disease. In response to this international endeavor, we developed the Portuguese D/BMD registry which is currently located in the CGMJM, Centro Hospitalar do Porto. The Portuguese registry is based on the Leiden Open Variation Database (LOVD) software and follows the TREAT-NMD charter for patient database/registry, abiding by National and European legislation concerning data. The national registry uses the clinical reporting model, where three medical coordinators from major hospital centers (Porto, Coimbra and Lisbon) were assigned to data collection (personal, clinical and pathological data) and patients' regular clinical (re)evaluation. Registry inclusion is completely voluntary and requires a specific informed consent. All the information, namely data sent by the clinician, consent and

the genetic data obtained in the laboratory, is assembled by the D/BMD registry curators and added to the database after validation. The registry was officially launched in 2012 and until now eighteen patients have been included in the database.

P-04

"ENTRE OS GENES E A MENTE" - SÍNDROMA DE TURNER E MANIFESTAÇÕES PSICOPATOLÓGICAS

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A Síndrome de Turner (ST) é uma cromossomopatia caraterizada pela monossomia total ou parcial do cromossoma X. Ocorre de forma esporádica, afetando 1 em cada 2000-5000 recém-nascidos do género feminino, associando-se habitualmente a baixa estatura, disgenesia gonadal, anomalias congénitas e adquiridas e sinais dismórficos. Estão igualmente presentes alterações neuropsiquiátricas como dificuldades cognitivas, distúrbios de perceção espacial e temporal, memória visual, atenção, reconhecimento e interpretação de emoções. São relatadas na literatura algumas doenças psiquiátricas em doentes portadoras de Síndroma de Turner, de que são exemplo as Perturbações do Humor, a Esquizofrenia e a Anorexia Nervosa. No entanto, parece não haver risco aumentado de psicopatologia grave. Verifica-se, por seu lado, maior risco de dificuldades psicossociais, dificuldades específicas de aprendizagem, problemas de comportamento e baixa autoestima. Tratando-se de uma "doença crónica", compreende-se, ainda, o possível impacto emocional. A propósito de uma adolescente com Síndrome de Turner, internada no Departamento de Psiquiatria da Infância e Adolescência do CHP, revêem-se os dados existentes na literatura sobre as manifestações psicopatológicas da Síndrome de Turner.

Palavras-chave: Síndrome de Turner; cromossomopatias; psicopatologia.