mutation (FM) in the *FMR1* gene. About 50% of females carrying a FM present with some degree of ID, usually less severe. As there are few studies on female FM carriers, the aim of this study was to describe the clinical and molecular characteristics of these females and to outline the genotype-phenotype correlation. Data from all female cases observed at our genetics consultation that had a FM in the *FMR1* gene diagnosed at our lab was collected. A checklist was designed based on medical experience and literature reports with the most frequent signs and symptoms easily detected through clinical exam. Whenever necessary, molecular study was re-evaluated and completed with different techniques. In all cases, the pattern of X-chromosome inactivation was performed using HUMARA assay. From 12 cases identified, 10 were included in the study, belonging to 7 families. The mean age at FXS diagnosis was 18,3 years (ranging from 6 to 47). In 6 cases the female patient was the index case, under investigation for neurodevelopmental disorder, and in 3 cases the index case was an affected male relative. All cases had learning difficulties, 2 of them with moderate ID; 3 cases had ADHD and none had ASD. Six cases presented with nonspecific dysmorphic features. The main manifestation was behaviour disturbance. Molecular test revealed a FM in *FMR1* gene, ranging from 250 to 600 CGG repeats. In 7 cases the mutation was maternally inherited and in 3, heredity was unknown. Eight cases showed random X-chromosome inactivation pattern, and remaining cases are in progress. All findings were consistent with previous literature reports. Mild dysmorphic features and absence of systemic manifestations make the diagnosis more difficult, so it should be suspected in females with learning difficulties/ID, with or without behaviour alterations. The authors wish to stress that this molecular diagnosis requires specific laboratory techniques and that FM is not detectable by *array*-CGH or NGS tests used in ID diagnosis workout nowadays.

P44| Correlation between peripheral cytopenias and cytogenetic changes in the bone marrow in a paediatric population. Experience of 22 years.

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The haemogram is the most frequent request and an essential tool in the diagnosis of different pathologies in paediatric age, especially in haematological diseases. Peripheral cytopenias is the first laboratory finding suggestive of haematological disease, such as myelodysplastic syndrome, idiopathic thrombocytopenic purpura, among others. Confirmation of these pathologies should include the study of bone marrow, with analysis by different methodologies, including conventional cytogenetic karyotype analysis. In this work, we intend to present and establish a correlation between the results obtained by conventional cytogenetics in bone marrow samples and observation of peripheral cytopenias in a paediatric population over 22 years. A retrospective 22-year series (1995–2017) of 154 bone marrow samples from a paediatric population was analysed, which at the initial diagnosis presented peripheral cytopenia. The samples were process according to the established protocol for chromosome analysis in bone marrow, including cell culture, for each biological product, followed by a cytogenetic study to identify the karyotype. In the 154 samples analysed with peripheral cytopenias, 31 were bicytopenias, 33 pancytopenias, 21 neutropenias, 11 anaemias and 58 thrombocytopenias, of which 22 were of idiopathic origin. We identify 15 samples with abnormal karyotype, some of which presented a complex karyotype. Samples with abnormal karyotypes had pancytopenia or bicytopenia at the same time. Peripheral cytopenias are extremely important for suspicion of paediatric haematological diseases, especially in myelodysplastic syndrome. Conventional cytogenetic analysis of the bone marrow plays a fundamental role in the confirmation of these pathologies, their clinical evolution and the choice of proper therapy, However, micro-arrays should be performed with the aim of identifying micro-deletions / duplications or loss of heterozygosity that are characteristic in this group of pathologies.

P45| Fanconi anemia: still an underdiagnosed disease? Retrospective analysis based on 25 years of cytogenetic evaluation

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Fanconi anemia (FA) is a recessive disorder clinically characterized by progressive bone marrow failure (BMF) and congenital abnormalities with variable presentation. The rarity of the disease, its phenotypic variability and the late onset of BMF generate a consensus that considers FA as a disease susceptible to underdiagnosis/late diagnosis. This collides with the benefits inherent to a timely diagnosis, which is decisive both for patient's outcome and appropriate genetic counseling. An effort is being carried out, among the clinical specialties involved with the morbility of FA, to promote a timely diagnostic accuracy. Despite the recent research advances about genetic diversity and pathophysiology of FA, the evaluation of DEB-induced chromosome instability still remains the first line diagnostic test. The ICBAS Cytogenetics Laboratory has been a reference laboratory in the application of this test since 1992. A total of 667 DEB-tests requested for suspicion/exclusion of FA were performed, with 66 patients diagnosed with FA. In the present work we evaluated the evolution of the diagnostic accuracy over 25 years on the basis of the following parameters: clinical specialties that requested the test; number of tests/year; number of diagnosis/year; age at the time of diagnosis. The main specialties that requested DEB-tests were Hematology and Pediatrics, and the relation between them evolved in favor of the second over the time. The number of tests/year increased over the years. The number of diagnoses/year, whose overall mean (2.4) was higher than the expected (according to FARF estimative), remained stable over the years, as opposed to the age at diagnosis, which decreased during the same period. In conclusion, the results point to an improvement in diagnostic accuracy. The number of tests/year increased, revealing greater clinical sensibility to FA diagnosis, with progressive intervention of other specialties than Hematology. As a result, we observed a significant decrease of the age at diagnosis. The high overall mean of diagnoses/year may be due to the presence of a gypsy population where there is a founding effect associated with consanguinity.

P46| Genome-wide association study in chronic obstructive pulmonary disease (COPD): associations between genetics and clinical measures

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Chronic Obstructive Pulmonary Disease (COPD) is common and progressive condition with increasing relevance in Western countries. Patient's genetic background is bound to play a role in this disease since clinical variables are not sufficient to explain its onset and/or progression. Our goal was to study the genetic profile of these patients and explore association with clinical measures commonly associated with a deterioration of symptoms (e.g., number of exacerbations) in order to pinpoint genetic variants that could help clinicians predict COPD prognosis. A pilot study of 40 patients with stable COPD (68 ± 9 years old) was conducted. Patients were recruited from routine pulmonology appointments and primary health care centres. Sociodemographic, anthropometric and general clinical data were collected. DNA was extracted from saliva samples and genotyped with the Illumina Beadchip array. Individual variants were tested for association with clinical variables (Airway obstruction levels (FEV1pp) and number of exacerbations) and interactions with smoking behavior was tested through a Genome-wide association study (GWAS). FEV1pp was associated with 2 SNPs (mapped to 2 genes) and the number of exacerbations was affiliated with 195 SNPs (mapped to 29 genes). Gene enrichment analysis using the GO term revealed an enrichment of genes associated with the inflammatory response. In addition, a greater number of relevant SNPs / genes resulted from inclusion in the GWAS of the patients' smoking status, which suggests a better stratification of the subjects based on this additional information. This pilot study showed significant genetic variations in patients with COPD, related to several clinical variables considered relevant for this disease. Further studies will be conducted with a larger set of patients and matched healthy controls, as a way to further characterize this population and to explore the interplay between genetics and COPD progression. Our ultimate goal shall be to identify potential new biomarkers for personalized interventions in COPD.

P47| Cancer challenges: common pathogenic *ATM* variants

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Ataxia-telangiectasia (AT) is caused by biallelic pathogenic variants in *ATM* gene, which encodes a protein kinase that plays an important role in cellular responses to DNA damage. Classic AT is characterized by early childhood-onset cerebellar ataxia, telangiectasias of the conjunctivae, immunodeficiency, radiosensitivity, and a predisposition to malignancy. Non-classic forms of AT include adult-onset AT and AT with early-onset dystonia. The study of AT patients' families have shown a 2 to 5-fold increased risk of breast cancer for females who are monoallelic carriers. Men who are monoallelic carriers have an increased risk of prostate cancer. Monoallelic carriers also have an increased chance to develop pancreatic cancer and possibly other cancers, like gastric, colorectal and ovarian cancer. Clinical and molecular characterization of all cases with monoallelic *ATM* variants observed at the Familial Cancer Risk Clinic of Instituto Português de Oncologia de Lisboa Francisco Gentil, based on retrospective analysis of patient medical records. Next-generation sequencing was performed in all cases. We report 6 patients, 5 females and 1 male. Four of the female patients had breast cancer and the male had Hodgkin's lymphoma. The other female does not have history of cancer and was a relative of an affected female patient. In all families, there were several female relatives with breast cancer, not tested yet. To our knowledge, no family has an AT case. At this moment, we cannot rule out that Hodgkin' lymphoma is from the spectrum of cancers caused by pathogenic *ATM* variants. *ATM* gene investigation results are being released every month, with fresh insights, making it difficult to update patients' management in a fair, coherent and cost-effective process. As far as we know, carrier frequency for pathogenic *ATM* variants is about 1%. As such, this can pose a serious healthcare challenge, further aggravated by the massification of genetic testing. Genetic counselling should be offered to these patients and genetic testing of their partners should be discussed, especially if they also have a suggestive family history of cancer.

P48| High performing AmplideX PCR/CE for Myotonic Dystrophy type I is concordant with a combination of PCR and Southern Blot analysis

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Myotonic dystrophy type 1 (DM1) is among the most common adult-onset forms of inherited neuromuscular disorders, with a prevalence of ~1/8000 individuals worldwide. It is a triplet repeat disorder caused by an expansion of >50 CTGs in the 3'UTR of the *DMPK* gene. Somatic mosaicism is common and the number of repeats can be different within and between tissues in a single individual, and this number can change over time. The age of onset and severity of the condition are roughly correlated with the size of the expansion. The conventional diagnostic strategy is based on a Fluorescent-PCR (FP-PCR) and/or a Triplet-Primed-PCR (TP-PCR), both of which rarely amplify above 100 repeats. This is followed by Southern Blot (SB) analysis to resolve apparent homozygous genotypes and to quantify the size of the expansion. We evaluated the AmplideX PCR/CE *DMPK* kit as part of an early access program. This technology combines PCR and capillary electrophoresis (CE) to size of alleles with up to 200 repeats, with an optional agarose gel electrophoresis (AGE) protocol to size larger alleles. The kits were tested on gDNA samples extracted from peripheral blood, amniotic fluid, chorionic villi and cell cultures, from a total of 101 patients and 5 controls that had been previously genotyped by conventional methods. Genotyping with the AmplideX PCR/CE assay was 100% concordant with previous results, showing 100% sensitivity and specificity, including zygosity resolution. CE profiles enabled clear differentiation between normal and expanded alleles while simultaneously identifying repeat mosaics. The high sensitivity enabled molecular analysis of samples with limited amounts of gDNA. The AmplideX *DMPK* technology resolves zygosity and demonstrates high accuracy in both sizing of up to 200 repeats and detecting expansions of >200 repeats, as well as low abundance mosaics. Sizing of alleles with over 200 repeats can be achieved using an AmplideX PCR/AGE *DMPK* assay protocol. This technology is a simpler and faster approach than the combination of conventional techniques previously required for the molecular diagnosis of DM1.