Meeting Abstracts

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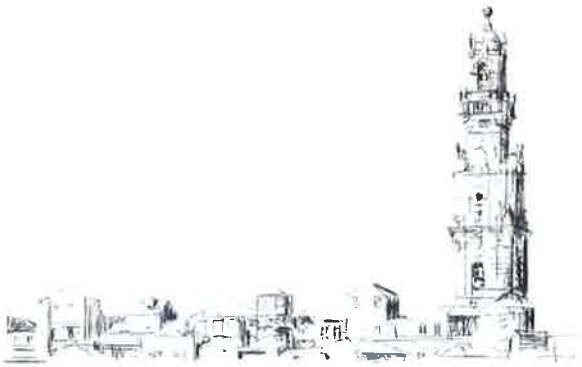

INTRODUCTORY NOTE

The Portuguese Society of Human Genetics (SPGH - *Sociedade Portuguesa de Genética Humana*) was founded in 1996 by a group of 68 medical and clinical laboratory geneticists. Its mission, statutes and governance resemble those of societies of similar ilk. Aligned with these and with the European Society of Human Genetics, so too the SPGH has organized annual meetings, constituting a major event that brings together professionals and students from all over the Country. In 2018, from the 15th to the 17th November, Porto hosted the SPGH's 22nd Annual Meeting. Recent developments in several fields of human genetics were brought to discussion, with the spotlight on epigenetic regulation and dysregulation, the revolutionary role of immunotherapy in cancer treatment, advances in etiologic diagnosis and therapy of neurological disorders, as well as the ethical implications of genome editing. These were addressed in the format of plenary lectures, thematic sessions or Panel discussions (detailed proceedings available at www.spgh/net/reuniao-anual/22a-reuniao/). The programme included several Satellite meetings and three sessions each of oral and poster presentations, selected from a total of 97 Abstracts. The high scientific standard was set by the excellence of the guest speakers, all renowned experts in the respective fields, while the vivid discussions, exchange of ideas and new collaborations are a measure of the meeting's success. The event was rounded off with the usual SPGH prize-giving ceremony, with five awards: best presentations in Basic Research, Clinical Research, Clinical Case Reports, the Amândio Tavares Young Scientist Award and the ESHG Fellowship Award.

Rosário Santos
(SPGH President, 2018)

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Lectures

The genetic landscape of Intellectual disability

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Intellectual disability (ID) is characterized by significant impairment of intellectual and adaptive functions with onset during childhood. The level of such deficits is commonly measured by standardized tests and a value below 69–75 of the resulting, normally distributed intelligence quotient (IQ) is defined as ID. Boosted by broad applications of whole-exome sequencing (WES), more than 1000 genes affecting a variety of pathways with a large spectrum of associated phenotypes have been identified as underlying monogenic causes in about 50% of patients with otherwise undiagnosed neurodevelopmental disorders. As an explanation of variability in ID severity within the same disorders, there is growing evidence that next to mutation specific effects, familial genetic background and polygenic risk variants known to be associated with normal IQ distribution may influence expressivity of monogenic defects or may even mimic the latter in a minority of cases. While in offspring of consanguineous couples, autosomal recessive genes are commonly found as disease causes, a major distribution of de novo pathogenic variants in outbred populations was shown. Nevertheless, recent data indicate, that compound heterozygosity for autosomal recessive disorders may also significantly contribute to ID, but is difficult to diagnose due to the plethora of inherited variants of unknown functional significance. Further explanations for monogenic pathogenic variants escaping WES diagnoses are parental mosaicism or de novo variants in recessive alleles leading to unwarranted neglecting of pathogenic variants by trio-approaches, as well as imprinting and repeat expansion disorders, and larger indels not reliably detectable by WES. A further unresolved question is the contribution of non-coding variants for which causality is difficult to proof.

References:

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3. Finucane-B et al. "Shift happens: family background influences clinical variability in genetic neurodevelopmental disorders" Genetics in Medicine 2016.

4. Kochinke-K et al. "Systematic Phenomics Analysis Deconvolutes Genes Mutated in Intellectual Disability into Biologically Coherent Modules" Am J Hum Genet 2016.

5. Deciphering Developmental Disorders Study "Prevalence and architecture of de novo mutations in developmental disorders" Nature 2017.

control group genotype frequencies of GSTT1*0 were: 49 (30.6%) and GSTT1+ were: 111 (69.4%). The GSTT1*0 is more frequent among asthmatics (p=0.001). In asthmatics genotype frequencies of GSTM1*0 were: 51 (53.1%) and GSTM1+ were: 45 (46.9%); in control group genotype frequencies of GSTM1*0 were: 72 (45.0%) and GSTM1+ were: 88 (55.0%). There is no statistical differences (p=0.258). The genotype GSTT1*0 confers a risk of being asthmatic of 2.747 times when compared with GSTT1+ genotype and adjusted for age: OR[b]: 2.747 [1.602–4.713]; p<0.001. The genotype GSTT1*0 confers a risk of being allergic asthmatic of 4.863 times when compared with GSTT1+ genotype and adjusted for gender: OR[b]: 4.863 [1.137–20.788]; p=0.033. According to our results GSTT1*0 polymorphisms could lead to different genotype specific response to therapy and different endotypes/phenotypes among asthmatic patients.

P25| Effects of cryopreservation on spermatic parameters, DNA integrity and mitochondrial activity: a preliminary study

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Cryopreservation is a routine technique used in assisted reproductive technology (ART). The aim of the study was to compare the impact of cryopreservation on spermatic parameters, DNA integrity and mitochondrial activity between normozoospermic men (group N) and men with altered spermatic parameters (group A). This study used 26 sperm samples from men who attended the infertility consultation. Motility, vitality, morphology, sperm concentration (according to WHO, 2010), DNA damage (Comet Assay) and mitochondrial activity (MitoTracker™ Red FM) were assessed before and after cryopreservation. DNA fragmentation (TUNEL) was assessed before, and SOD and GR enzymes activity after cryopreservation. In fresh samples, the motility and normal morphology were significantly higher in samples of group N (p<0,05). The DNA integrity, measured by Comet Assay (N=94,8 AU vs A=79,6 AU; p=0,247) and TUNEL (N=4,6% vs A=6,5%; p=0,258), was similar between the two groups, but the percentage of spermatozoa with active mitochondria was significantly lower in group A (N=71,4% vs A=59,1%; p=0,035). The results showed that the motility, vitality, midpiece abnormalities, DNA damage and active mitochondria tend to be more affected by cryopreservation on group A. The DNA damage (N=163,6 AU vs A=180,7 AU; p=0,471) increased 126,8% in group A and 72,6% in group N (p=0,057), and spermatozoa with active mitochondria (N=25,8% vs A=16,1%; p=0,021) decreased 72,9% in group A and 63,9% in group N (p=0,165). SOD and GR enzymes activity were slightly higher on group A. Spearman correlation coefficients reinforced that the better the quality of fresh samples is, the less the quality becomes affected by cryopreservation (p<0,05). As expected and despite the small number of samples, sperm samples with altered spermatic parameters tend to have higher DNA damages/fragmentation, less active mitochondria and a higher oxidative stress, demonstrating a lower resistance to cryopreservation. Concerning the implications of our results, it's also urgent to enhance efficiency of freezing systems.

P26| Study of genetic variations associated with channelopathies in cases of sudden death

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Sudden Death (SD) is a public health problem that has taken on a growing concern in the general population and has raised awareness of the need for a precise autopsy diagnosis with genetic information that may be useful in preventing other family members' deaths. In young people (≤ 40 years), victims of SD, studies report that a complete medical-legal autopsy does not reveal a cause of death in 30% of cases and these events are designated as cases of Sudden Unexplained Death (SUD). For these unexplained cases, an important diagnostic contribution may be provided by genetic analysis, which should be conducted during the investigation about the cause of death. It is estimated that 1/3 of the SUD can be explained by channelopathies which are hereditary pathologies caused by mutations in genes that lead to dysfunctions in the cardiac ion channels. The main phenotypes seen in patients with these dysfunctions are: Long QT Syndrome, Short QT Syndrome, Brugada Syndrome, and Catecholaminergic Polymorphic Ventricular Tachycardia. In this study will be used peripheral blood samples from SUD cases. Genetic analysis will be performed by Next Generation Sequencing in *KCNQ1, KCNH2, SCN5A, CACNA1C, CACNB2b, SCN10A, KCNJ2, RyR2* and *CASQ2* genes, that according to the literature are associated with channelopathies. In cases of SUD in which variations are detected in the genes analyzed, a DNA sample will be requested from the direct relatives of these victims in order to assess the risk of having a genetic condition that makes them susceptible to SD. With the results of this scientific investigation we hope to demonstrate the viability and the feasibility of the conducted genetic studies, in the medical-legal investigation of SUD cases in young people in Portugal, in order to reduce considerably the inconclusive diagnoses about the etiology of death. In addition, with the genetic evaluation of relatives of SUD victims, we intend to contribute to an effective prevention of new cases of SD.

P27| Human Epidermal Growth Factor Receptor 2 at one Portuguese district hospital

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The human epidermal growth factor receptor 2 (HER2) plays an important role in the development of some types of cancer and is considered a prognostic biomarker. The accuracy in determining HER2 status is essential because there are anti-HER2 targeted therapies that are able to reduce recurrence and improve survival. This new era for cancer patients is only possible thanks to Human Genetics. Observational prospective study conducted between August 18th of 2016 to September 19th of 2018. Sample of the patients tested for HER2 status in the Genetic Laboratory of the Centro Hospitalar de Trás-os-Montes e Alto Douro. The technique applied to determine HER2 was Fluorescence in situ Hybridization (FISH) and was performed