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Antibodies were used for ligand detection, and absorbance was determined at 405 nm. CHO-ldlA7 cells were transfected with wt LDLR plasmid and incubated with FITC-labeled LDL to determine LDL binding and uptake by flow cytometry.
Results: p.(Gln4316*) and p.(Glu4387Asnfs*7) alterations from exon 29 showed reduced affinity for the LDL receptor. Uptake and binding assays results were similar, so these variants may affect the binding of apoB to the LDL receptor. The alterations studied were not present in a normolipidemic panel.
Discussion: APOB variants studied in this work produce truncated forms of apoB, but they are unlikely to lead to nonsense-mediated decay processes due to their location near the end of the gene. Functional studies can provide important evidence for variant pathogenicity assessment being these essential to provide an accurate diagnosis. These assays can confirm the clinical diagnosis by highlighting the cause of disease, and contribute to a personalized treatment and stratify patient associated cardiovascular risk.

P18 - STUDY OF THE CONTRIBUTION OF GENES NERVOUS SYSTEM RELATED TO HEART FAILURE

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Introduction: HF is a clinical syndrome due to a structural and functional abnormality of the heart that results in elevated intracardiac pressures and inadequate cardiac output at rest or during exercise. This syndrome is a major public health problem and one of the main causes of mortality. Moreover, it can be amplified by pathology associated with the Nervous System.
Aim: This study aims to investigate the contribution of variants in genes BDNF (rs6265), NTRK2 (rs2289656), NGF (rs6330), NOS2 (rs9282801 and rs2297518) and ADRB2 (rs1042713) to HF development.
Material and methods: A case-control study was conducted with a population of 508 individuals, of which 268 had HF and 240 were controls. Among the HF group, the disease was divided into non-preserved ejection fraction (EF) and preserved EF. Variants related to the NOS2 and ADRB2 genes were performed using the RFLP-PCR technique, the remaining variants were analyzed using the Genotyping Endpoint PCR technique. Statistical analysis was performed using IBM software® SPSS® Statistics 28.0, with a statistical significance level set at $p < 0.05$.
Results: For the rs2289656 variant (NTRK2), the presence of the A allele was found to be protective for HF [OR (CI, 95%) = 0.393 (0.184 – 0.837); p = 0.015]. Regarding all the other variants, no statistically significant differences were found between patients and controls. When the analysis between non-preserved EF and controls was carried out, again the presence of the A allele emerged a as protection factor [OR (CI, 95%) = 0.294 (0.116 – 0.746); p = 0.010)]. These results were adjusted for age, BMI and gender.
Discussion: These results show an association between the NTRK2 gene and HF in general, and non-preserved EF. The identification of genetic variants that can somehow influence the development and severity of HF may allow its faster diagnosis and the application of methodologies for disease prevention. Moreover, the results of this study will contribute to define a genomic profile associated with the role of the nervous system in HF.

P19 - STUDY OF THE CONTRIBUTION OF MODULATORS OF IRON HOMEOSTASIS IN HEART FAILURE

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Introduction: Heart failure (HF) is considered one of the biggest public health problems, affecting 2% of the world's population. Is defined as a clinical syndrome due to a structural and/or functional abnormality of the heart that results in elevated intracardiac pressures and/or inadequate cardiac output at rest and/or during exercise. It can be influenced by several genetic modulators, in particular genes responsible for the balance of iron (Fe) metabolism, such as the HFE, SLC40A1 and TMPRSS6 genes.
Aims: To investigate the contribution of common genetic variants in HFE (C282Y - rs1800562 and H63D - rs1799945), SLC40A1 (rs1439816 and rs2304704) and TMPRSS6 (rs855791) to HF.
Material and Methods: The study included a population of 301 HF patients and 361 controls. The polymorphic analysis of the HFE gene variants (C282Y and H63D) was realized using the Multiplex PCR-ARMS technique, while the Endpoint Genotyping PCR technique was used for the remaining variants. Statistical analysis was done using SPSS software, version 28.0, with a statistical significance level of $p<0.05$.
Results: Statistically significant differences were found between patients and controls, in relation to the frequency of the C282Y genotypes. The presence of the Y allele [OR (CI, 95) = 3.127 (1.223-7.995); p = 0.017] was considered a risk factor for HF development.
Discussion: Based on the results obtained, the HFE gene was shown to modulate HF. This investigation not only provides a better understanding of the role of HFE in the etiology of HF and is a step forward in personalized medicine, but also underlines the importance of the iron homeostasis in HF. It proposes and reaffirms that the study of iron – related biomarkers as well as HFE common variants should be performed in patients with HF.

P20 - UNVEILING SCA2 DISEASE PHENOTYPE: A NEW MOUSE MODEL REVEALS MOTOR DEFICITS AND NEUROPATHOLOGY

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Introduction: Spinocerebellar ataxia type 2 (SCA2) is a neurodegenerative rare disorder, characterized by an abnormal repeat of the cytosine-adenine-guanine (CAG) trinucleotide within the coding region of the human ATXN2 gene. While healthy individual typically display 22-23 CAG repetitions, when these exceed 33 repeats, people will be affected by the disease. The mutant gene is then translated into the protein ataxin-2 bearing an abnormally long tract of glutamines (polyQ). The molecular mechanisms by which the mutant ataxin-2 leads to neurodegeneration are not fully understood. However, it is known that mutant forms of ataxin-2 bearing abnormal polyQ expansion are responsible for a wide-range of cellular disturbances that include protein aggregation, RNA toxicity, enhanced oxidative stress, aberrant calcium released or autophagy impairment. People affect by SCA2, experience numerous debilitating motor symptoms that culminate in premature death. Currently, there are no therapies able to cure nor delay the natural course of SCA2 disease, and affected people rely only on symptomatic and supportive treatment. Additionally, more than 80% of all therapies that are in clinical trials fail to reach the market, mostly due to poor pre-clinical evidence. This urgent unmet medical need highlights the necessity to create new and more refined tools to studies disorders, in order to develop novel, better and more sustainable therapies. While several SCA2 mouse models were already developed, they fail to recapitulate the disorder phenotype, either because disease-related motor symptoms are mild and late stage, or neurodegeneration is not present.
Methodology: Fallowing this rational, and to advance our understanding of SCA2, we have developed a novel transgenic mouse model that expresses a human form of the ATXN2 gene, bearing 129 CAG repeats