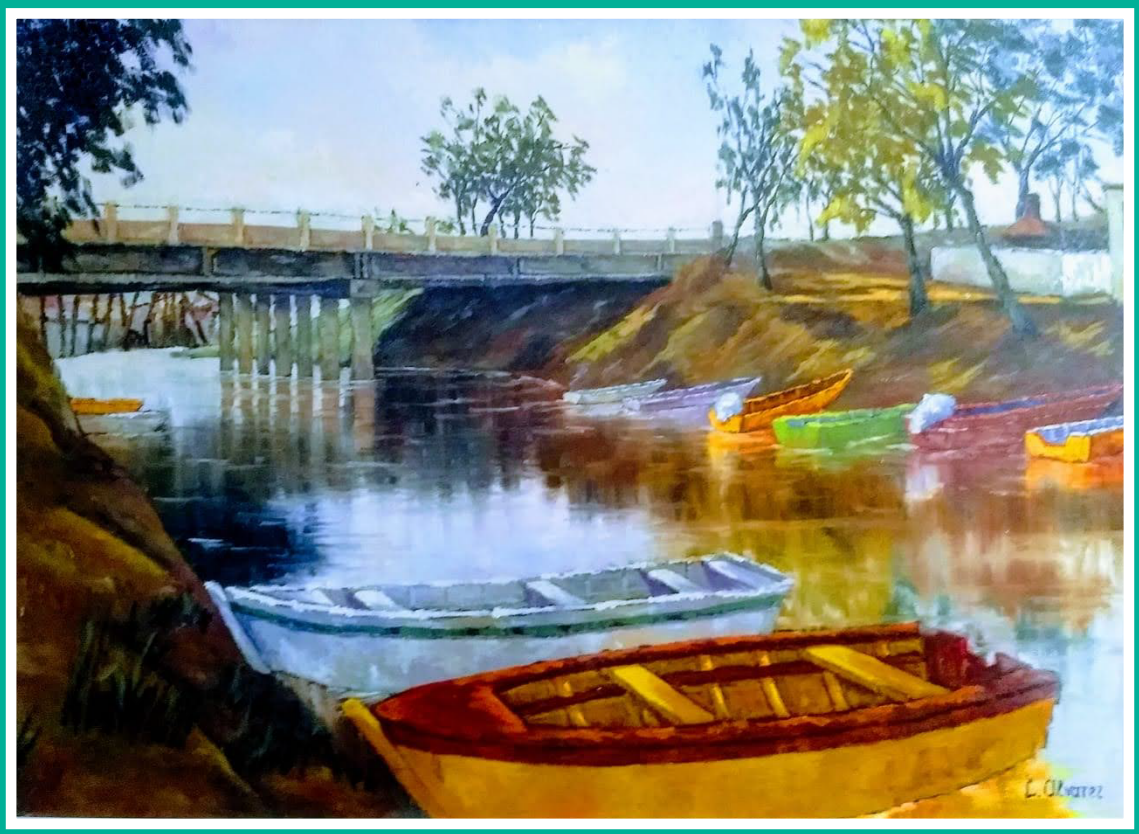
2020

medicina

BUENOS AIRES VOL. 80 Supl. V - 2020



MEDICINA

Volumen 80, Supl. V, Págs. 1-207

medicina

BUENOS AIRES, VOL. 80 Supl. V - 2020

La Tapa (Ver p 5)
Ludueña, 2016
María Luján Álvarez

MEDICINA (Buenos Aires) - Revista bimestral – ISSN 0025-7680 (Impresa) – ISSN 1669-9106 (En línea)

REVISTA BIMESTRAL
Registro de la Propiedad Intelectual N° 02683675
Personería Jurídica N° C-7497
Publicación de la Fundación Revista Medicina (Buenos Aires) Propietario de la publicación: Fundación Revista Medicina
Queda hecho el depósito que establece la Ley 11723

Publicada con el apoyo del Ministerio de Ciencia, Tecnología e Innovación Productiva.
MEDICINA no tiene propósitos comerciales. El objeto de su creación ha sido propender al adelanto de la medicina argentina. Los beneficios que pudieran obtenerse serán aplicados exclusivamente a este fin.
Aparece en *MEDLINE (PubMed), ISI-THOMSON REUTERS (Journal Citation Report, Current Contents, Biological Abstracts, Biosis, Life Sciences), CABI (Global Health), ELSEVIER (Scopus, Embase, Excerpta Medica), SciELO, LATINDEX, BVS* (Biblioteca Virtual en Salud), *DOAJ, Google Scholar y Google Books.*
Incluida en el Núcleo Básico de Revistas Científicas Argentinas del CONICET.

Directores Responsables:
Basilio A. Kotsias, Eduardo L. De Vito, Isabel Narvaiz Kantor, Guillermo B. Semeniuk

Secretaría de Redacción: Ethel Di Vita, Instituto de Investigaciones Médicas Alfredo Lanari, Combatientes de Malvinas 3150, 1427 Buenos Aires, Argentina
Tel. 5287-3827 Int. 73919 y 4523-6619
e-mail: revmedbuenosaires@gmail.com – http//: www.medicinabuenosaires.com

Vol. 80, Supl. V, Noviembre 2020

Diagramación y Diseño: Andrés Esteban Zapata - aez.sgi@gmail.com

REUNIÓN DE SOCIEDADES DE BIOCIENCIAS 2020

LXV REUNIÓN ANUAL DE LA
SOCIEDAD ARGENTINA DE INVESTIGACIÓN CLÍNICA (SAIC)

LXVIII REUNIÓN ANUAL DE LA
SOCIEDAD ARGENTINA DE INMUNOLOGÍA (SAI)

REUNIÓN ANUAL DE LA
SOCIEDAD ARGENTINA DE FISIOLOGÍA (SAFIS)

10-13 de noviembre de 2020

EDITORES RESPONSABLES
María Cristina Carrillo
Analía Trevani
Maria Cecilia Larocca

CD8+ (p=0.027M-W test) and CD4+ cells (p=0.012M-W test).
In MAFLD cases, the lymphocyte liver infiltrate composition differs between children and adults. Treg and Th17 balance seems to condition damage progression, denoting their important role in the pathogenesis.

GENÉTICA

83. (95) **BIOINFORMATIC ANALYSES OF KLF1 VARIANTS DETECTED IN ARGENTINEAN POPULATION WITH HEMOGLOBINOPATHIES**

Héctor M. Targovnik *(Instituto de Inmunología, Genética y Metabolismo (INIGEM), UBA-CONICET; Cátedra de Genética, FFYB, UBA)*, Karen Scheps *(Instituto de Inmunología, Genética y Metabolismo (INIGEM), UBA-CONICET; Cátedra de Genética, FFYB, UBA)*

KLF1 is an erythroid essential transcription factor. Sequence variants (mainly nonsense or substitutions in its Zinc finger domains) lead to distinctive phenotypes. The lack of KLF1 can lead to an inefficient β-globin cluster switch, which can increase the HbF and HbA2 fractions. In consequence, variants mapping in this gene can alter the clinical course of β-thalassemia.
Objectives: Perform structural predictive analyses of the missense variants detected in a group of Argentinean patients and carry out analyses to predict their impact as regulatory targets.
Patients and methods: The DNA from 3 individuals with moderately increased levels of HbA2 and 20 patients with thalassemia intermedia or severe β-thalassemia carriers was obtained and KLF1 was amplified by PCR and sequenced by the Sanger method. Since KLF1 has not been crystallized, predictive models were built with RaptorX contact prediction, their potential as regulatory sites was analyzed with RegulomeDB and their impact on the splicing of the mRNA with ESEfinder.
Results: Only 3 previously described missense variants with no or minor functional consequences were detected: rs112631212, rs2072597 and rs2072596. The first two could affect the structure locally, disrupting α-helixes. However, none affect the Zinc Finger domains. The second variant scored 0.3145 (2a category) in RegulomeDB 2.0. The latter 2 affect exonic splicing enhancers.
Discussion: The structural analysis of the variants matches the lack of effect described. It is unlikely that they could affect the default splicing of the KLF1 mRNA, since these SNPs map far from the exon-exon junctions. rs2072597 was the most frequent variant (11/46 alleles) and it could impact its role as a regulatory target; the ZFX transcription factor motif is disrupted and ChIP assays have demonstrated that this factor interacts with this region in K562 cells. Although this effect may not inhibit KLF1 expression, it could induce changes in its expression levels.

84. (153) **COMPREHENSIVE ANALYSIS OF GENETIC VARIANTS IDENTIFIED BY WHOLE EXOME SEQUENCING IN HEARING IMPAIRED PATIENTS IN ARGENTINA**

Paula Buonfiglio *(Instituto de Investigaciones en Ingeniería Genética y Biología Molecular Dr. Héctor Torres - INGEBI/CONICET. Argentina)*, Carlos David Bruque *(Centro Nacional de Genética Médica A.N.L.I.S. Dr. Carlos G. Malbrán)*, Vanesa Lotersztein *(Servicio de Genética del Hospital Militar Central Cirujano Mayor Dr. Cosme Argerich)*, Ernesto Goldschmidt *(Servicio de Genética del Hospital General de Agudos Dr. Juan A. Fernández)*, Paola Plazas *(Tercera Cátedra de Farmacología, Facultad de Medicina, Universidad de Buenos Aires)*, Ana Belen Elgoyhen *(Instituto de Investigaciones en Ingeniería Genética y Biología Molecular Dr. Héctor Torres - INGEBI/CONICET. Argentina)*, Viviana Dalamon *(Instituto de Investigaciones en Ingeniería Genética y Biología Molecular Dr. Héctor Torres - INGEBI/CONICET. Argentina)*

Hereditary hearing loss is the most common sensory disorder affecting 1:500 newborn children. It is a heterogeneous disease and more than 100 genes have been related to the pathology. This complexity led us to design a multistep diagnosis strategy with the use of Whole Exome Sequencing Technique (WES). The objective was identifying genetic variants in deaf patients and analyzed them through in-silico and in-vivo studies.
1250 patients were analyzed for frequent mutations in GJB2 and GJB6 genes by Sanger Sequencing, genotyping 25% of them according to worldwide reports. From undiagnosed patients, 29 families were selected to perform WES. After filtering and analysis, 45% of patients were genotyped, identifying 23 causative mutations (11 novel, 12 reported) classified according to ACMG/Hearing Loss-Expert Panel Standards.
Some of the novel variants were further studied in silico by structural, stability and motifs studies of the mutated proteins. In addition datasets from deafness and population databases were interrelated with protein motifs in order to predict the theoretical pathogenicity effect of the amino-acid changes. The pathogenic prediction of most of the variants was reinforced after analysis, and surprisingly in one case diminished the predictive deleterious effect.
On the other hand, knock down phenotype rescue assay in zebrafish is underway to accomplish in-vivo validation.
Preliminary results in zebrafish confirmed the pathogenicity of one novel variant in MYO6 gene which affected the hair cell function and hence, auditory system physiology.
This study shows that our algorithm is successful for deafness genetic diagnosis. Comprehensive analysis is crucial to strengthen the pathogenicity effect of variants and discard some of them. These findings highlight the importance of genetic studies followed by in silico and in vivo validation to better understand the genetic basis of hereditary hearing loss.

85. (187) **EVALUATION OF MITOCHONDRIAL DNA MASS IN WOMEN WITH POLYCYSTIC OVARY SYNDROME**

Rojo M[1,2]; Millan AL[1,2]; Velazquez ME[3]; Pautasso MC[1], Abruzzese GA[3], Motta AB[3], Cerrone GE[1,2].
1. Universidad de Buenos Aires – Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET). Instituto de Inmunología, Genética y Metabolismo (INIGEM). Laboratorio de diabetes y metabolismo.
2. Universidad de Buenos Aires. Facultad de Farmacia y Bioquímica. Cátedra de Genética.
3. Laboratorio de Fisiopatología Ovárica. Centro de Estudios Farmacológicos y Botánicos (CEFYBO). (CONICET)– Universidad de Buenos Aires (UBA).

Objective
Polycystic ovary syndrome (PCOS) is characterized by insulin resistance (RI) which can influence the content of mitochondrial DNA (mtDNA). Our objective was to evaluate the content of mtDNA in women with PCOS compared with control women and the relation with metabolic parameters.
Materials and methods:
We studied fifty women with PCOS and thirty-four control women aged 17 to 45 years. The determination of the number of copies of mtDNA was carried out in peripheral blood leukocytes by Quantitative real-time PCR. The results were calculated using the comparative-cycle threshold (ΔΔCtq) method. Statistical analysis were carried out by Student's t-test, correlation and linear regressions with a significance level of 0.05 (SPSS 25).
Results:
Compared to controls, PCOS patients have higher weight, body mass index (BMI), waist circumference (WC), also higher levels of TG, LDL, total cholesterol, fasting plasma glucose and lower levels of HDL cholesterol. By linear regression we observed that mtDNA was significantly lower in the presence of PCOS (135.57 ± 81.34 vs 190.37 ± 135.19; p = 0.023). A significant negative correlation was observed between the mtDNA content and telomere length (p = 0.034). Within PCOS patients, women with insulin resistance according to a HOMA index ≥ 2.5 have a lower mtDNA content compared to PCOS women with HOMA <2.5 (169.89 ± 105.3 vs 116.45 ± 53.2; p = 0.03).
Conclusion:
A decrease in mtDNA content occurs in the presence of PCOS and RI, which can be explained by the damage to mitochondrial DNA (mtDNA), proteins and lipids due to the oxidative stress associated with PCOS. More studies are required to determine the scope of the