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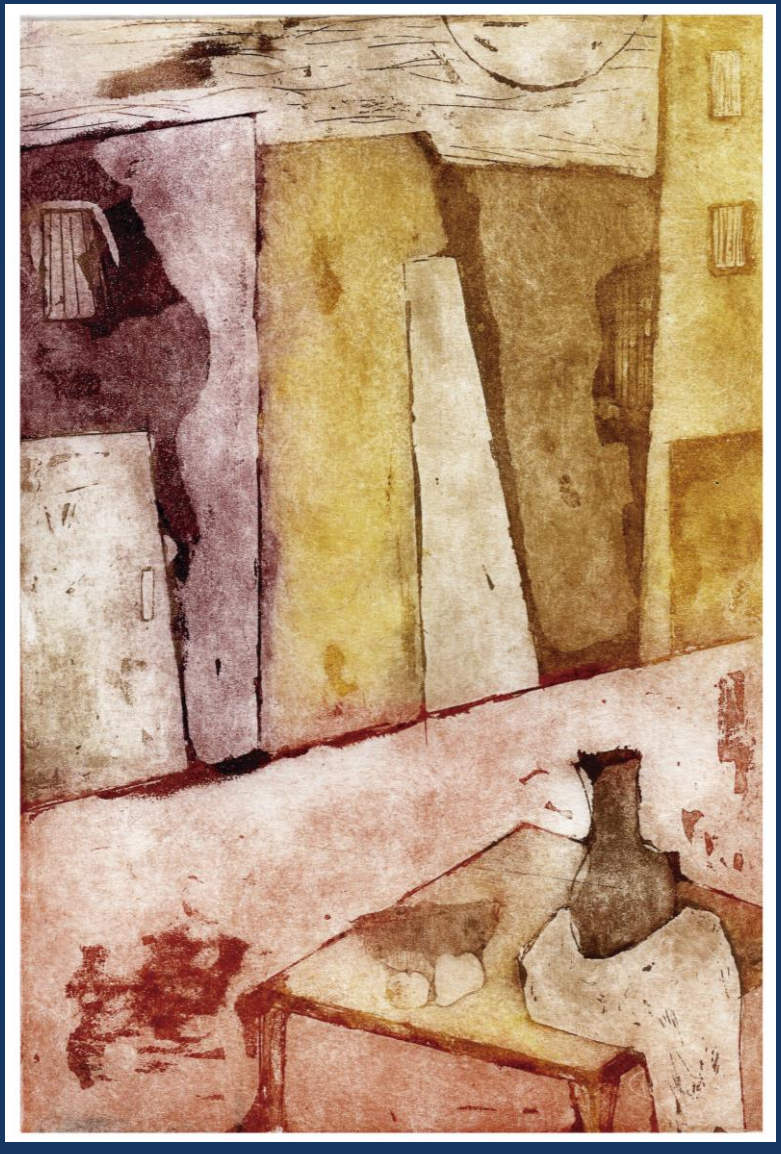

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La Tapa (Ver pág. 4)
Atardecer en la tarde
Antonella Ricagni

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REUNIÓN ANUAL DE SOCIEDADES DE BIOCIENCIA 2019

LXIV Reunión Anual de la
Sociedad Argentina de Investigación Clínica (SAIC)

LI Reunión Anual de la
Asociación Argentina de Farmacología Experimental (SAFE)

XXI Reunión Anual de la
Sociedad Argentina de Biología (SAB)

XXXI Reunión Anual de la
Sociedad Argentina de Protozoología (SAP)

IX Reunión Anual de la
Asociación Argentina de Nanomedicinas
(NANOMED-ar)

VI Reunión Científica Regional de la Asociación Argentina de Ciencia y Tecnología de Animales de Laboratorio (AACyTAL)

con la participación de
The Histochemical Society

13 - 16 de noviembre de 2019
Hotel 13 de Julio - Mar del Plata

EDITORES RESPONSABLES

Dra. Mónica Costas
Dra. Gabriela Marino
Dr. Pablo Azurmendi

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ANNUAL MEETING OF BIOSCIENCE SOCIETIES 2019

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CHIEF EDITORS

Dra. Mónica Costas
Dra. Gabriela Marino
Dr. Pablo Azurmendi

with previous results from our lab underlines sGC alpha1 as a relevant factor in tumor biology.

0474 - WHOLE EXOME SEQUENCING ANALYSIS OF CONSTITUTIONAL DNA IN ARGENTINEAN RETINOBLASTOMA PATIENTS

Diana Lidia PARMA (1) | Leonela LUCE(1) | Micaela CARCIONE(1) | Chiara MAZZANTI(1) | Marcela FERRER(2) | Florencia GILIBERTO(1) | Irena SZIJAN(1)

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Abstract/Resumen: Retinoblastoma (RB) is a pediatric tumor of the developing retina, caused by mutations in RB1 tumor suppressor gene. RB1 molecular alterations are small mutations in 80 % of cases and gross deletions/duplications in 20 %. In hereditary RB, identification of mutations is essential for genetic assessment. The purpose of this work was to detect small mutations in RB1 by whole exome sequencing (WES) in 7 Argentinean RB patients. WES was performed in leukocytes DNA from 2 familial and 1 sporadic bilateral and 4 early unilateral RB cases. The pathogenicity of the identified variants was determined according to: its presence in RB1 mutation database; its absence in sequence consortiums (ExAC and GnomAD); and predictive softwares. All pathogenic mutations were corroborated by Sanger Sequencing. Gross mutations were screened by MLPA. We have found an average of 13 sequence variants in RB1, 5 of them were present in all patients. We identified the disease-causing mutations in 2/7 cases. In one bilateral familial case, a nonsense mutation (g.70286C>A) in exon 12 was detected, the patient´s affected father showed the same mutation. The sporadic bilateral RB presented a substitution (g.5550G>A) in the last nucleotide of exon 2, according to previous reports this variant leads to aberrant splicing. In an unilateral RB patient, a likely benign inframe deletion was observed. The 4 unilateral and the other familial bilateral RB patients did not show pathogenic small mutations nor gross molecular alterations in RB1. Thus, screening was enlarged to genes associated with RB1 pathways and other tumors, but no deleterious variant was identified. We can conclude that WES was able to find constitutional mutations in RB1 gene, allowing confirmation of diagnosis and genetic assessment. Further studies must be performed in patients with no causative mutation found. Finally, the importance of this work relies on the fact that is the first one applying WES for RB molecular diagnosis in Argentina.

0482 - ESTABLISHMENT OF MAGEC2-KNOCKOUT CELLS THROUGH CRISPR/CAS9 TECHNOLOGY

Franco PASCUCCI | María Fátima LADELFA | Micaela ESCALADA | Martin MONTE

INSTITUTO DE QUÍMICA BIOLÓGICA DE LA FACULTAD DE CIENCIAS EXACTAS Y NATURALES (IQUIBICEN)

Abstract/Resumen: MageC2 is a member of the melanoma antigen gene (MAGE) family, specifically expressed in a wide variety of human cancers and associated with a non-favourable clinical course. It has been reported that MageC2 oncoprotein downregulates p53 and activates STAT3 transcription factors. Recently, we identified the Ras oncogene as responsible for MageC2 stability increase and phosphorylation through the MEK/ERK pathway. Then, our hypothesis is that Ras oncogene could regulate p53 and STAT3 by enhancing MageC2 protein levels. In order to analyze the functional consequences of endogenous MageC2 expression, we established a MageC2 knockout (KO) cell line through the CRISPR/Cas9 system in human melanoma A375 cells. All the obtained clones were probed for MageC2 protein expression by Western blot. Three clones were selected and sequenced for indel detection (KO1, gRNA1; KO2, gRNA1 and KO3, gRNA2). To validate the A375 MageC2 KO (A375-C2KO) clone behaviour, we quantified the mRNA levels of genes regulated by p53 or STAT3. Analysis of RT-qPCR data carried out in three pairs of biological replicates in A375-C2KO cells indicated enhanced transcription of p53 targets (p21waf1 and bax, $p<0.05$) and reduced levels of STAT3 targets (ccl2 and mmp2, $p<0.05$) when compared to A375 WT cells, as expected. These results indicate that A375-C2KO cells recapitulate the signalling behaviour reported by overexpression and RNA interference approaches, and are therefore suitable as biological model to investigate the role of endogenous MageC2 expression in cancer cells.

0487 - CHARACTERIZATION OF VEMURAFENIB-RESISTANT MELANOMA CELL LINES

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INSTITUTO MULTIDISCIPLINARIO DE INVESTIGACIONES BIOLOGICAS (IMIBIO-SL)

Abstract/Resumen: In the last years, the incidence of melanoma, the most aggressive skin cancer, has increased rapidly. Approximately half of melanoma patients display the V600E mutation in the BRAF protein, which stimulates ERK activation and promotes proliferation. The FDA approves the use of 4 therapeutic agents that reduce ERK activity: i) Vemurafenib (VEM) and Dabrafenib (BRAF inhibitors) and ii) Trametinib and Cobimetinib (MEK inhibitors). Indeed, VEM is approved by ANMAT in Argentina. Unfortunately, the durability of the response is limited and the tumors quickly become resistant. The aim of this work was to generate and characterize VEM-resistant melanoma cell lines as tools to study possible resistance mechanisms in tumor cells. VEM-resistant cell variants were obtained by continuous exposure of original parental cells to increasing concentrations (0,01 – 1 μM) of VEM during 3 months. Inhibition of ERK signaling was analyzed by western blot and viability was determined by MTT assay. In addition, cell migration was evaluated in a modified Boyden Chamber. As assessed by inverted microscopy, Lu1205 melanoma-resistant cells exhibit a bigger volume and more prolongations and lamellipodia than their sensitive parents. In agreement, VEM-resistant Lu1205 cells showed greater migratory capacity than their parents under normal culture conditions. Moreover, in the presence of VEM (1 μM), levels of phospho-ERK were higher in resistant cells. On the other hand, no changes were detected in phospho-Akt levels, indicating that VEM only affects ERK signaling. In conclusion, the VEM-resistant melanoma cells obtained in our laboratory constitute a good model to study possible mechanisms involved in the development of resistance to BRAF inhibitors. Moreover, it will be useful to develop new inhibitors that may improve the response and durability of current therapies against melanoma, and potentially diminish resistance occurrence.

0491 - HUMAN ADIPOSE TISSUE FROM KIDNEY TUMOR REGULATES EPITHELIAL-MESENCHYMAL TRANSITION OF TUMOR AND NON TUMOR RENAL EPITHELIAL CELLS

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Abstract/Resumen: In tumor development and maintenance of a cancerous phenotype, bidirectional communication between epithelial cells and stromal environment is necessary. We