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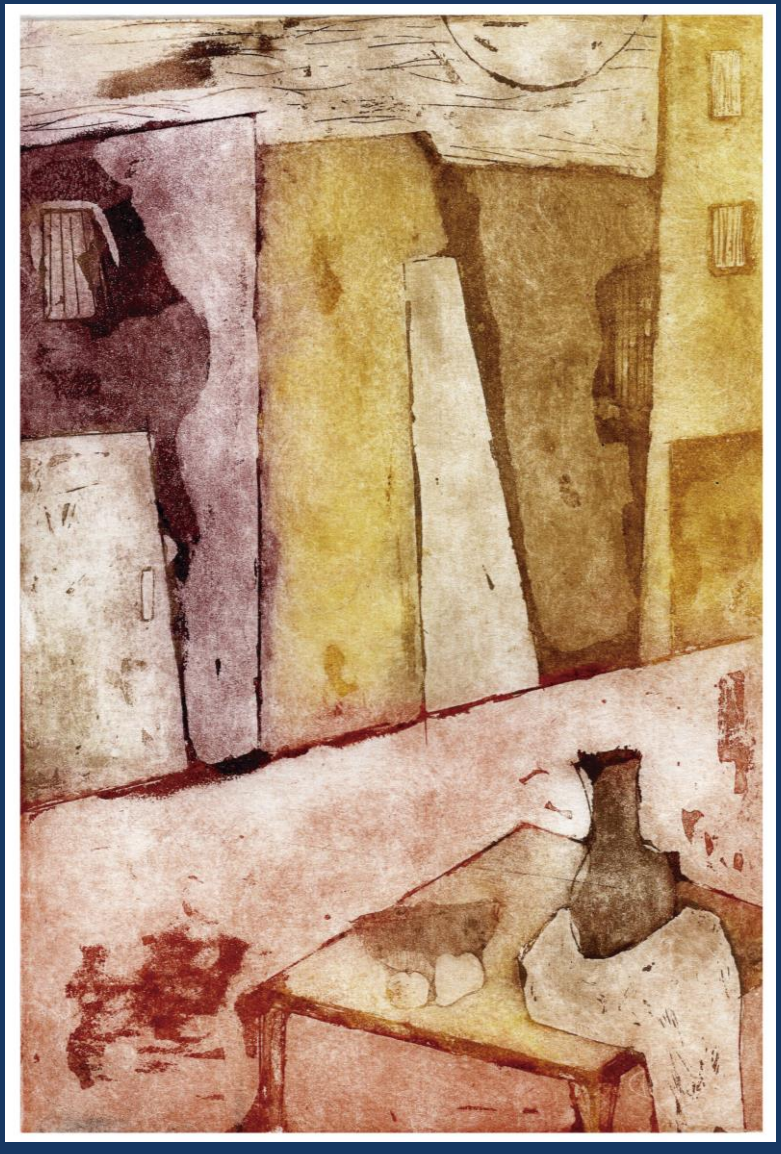

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La Tapa (Ver pág. 4)
Atardecer en la tarde
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BUENOS AIRES, VOL 79 Supl. IV - 2019

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
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cells (CSC) is associated with the above-mentioned resistance, and the retinoic acid system, among other systems, has been implicated in the maintenance and expansion of CSC. In order to evaluate the involvement of retinoic acid (ATRA) in growth modulation in a chemoresistance context, we have developed a cisplatin-resistant variant from NSCLC A549 cell line (A549cpr). Monolayers of parental and cisplatin-resistant A549 cells were treated with ATRA (0.3 - 70 μM) and/or Cisplatin for 72 h. While the Cisplatin treatment IC50 (6.87 ± 1.04 and 18.08 ± 1.03 μM for A549 and A549cpr, respectively) induce growth inhibition, ATRA addition did not modify proliferative capacity. Although both cell lines express all nuclear retinoic acid receptors, A549cpr cells showed lower levels of the RARβ isotype, involved in differentiation (determined by RT-qPCR). Moreover, ATRA treatment (1 μM) increased RARβ levels in both A549 variants, indicating that retinoic system is active. Finally, we studied the CSC component of A549 and A549cpr cells through an oncosphere culture. Although no differences were observed in oncosphere formation capacity, A549cpr cells present larger oncosphere colonies. This phenomenon was accompanied with higher Nanog mRNA expression levels, involved in cell pluripotentiality. In all cases, Nanog expression was higher in oncospheres than in the respective monolayers. Our results reinforce the hypothesis that cisplatin resistance may be mediated by an increase in CSC renewal. These findings lead us to propose different combination therapies for targeting CSC.

0666 - CFTR IS INVOLVED IN COLORECTAL CANCER STEM CELL PHENOTYPE

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Abstract/Resumen: CFTR is a chloride channel expressed in many epithelial cells and there is a relationship between this channel and cancer. The cancer stem cells (CSC) are responsible of tumorigenesis, secondary focus formation in metastasis and chemoresistance. We previously found that CFTR is expressed in colorectal cancer cells HCT116 and is associated with cancer stem cells (CSC). To further investigate this, we inhibited CFTR activity with CFTR inhibitor-172 or downregulated CFTR expression with two different shRNA (shCFTR1 or shCFTR2) in HCT116 cells. When these cells were transfected with the shCFTRs, we observed a downregulation of both CFTR protein and mRNA by Western blot, immunofluorescence and RT-PCR. Then we determined the clonogenic growth, a property of CSC, of control HCT116 cells and when CFTR is inhibited after seven days of platting at low density. The number of colonies was diminished in cells where CFTR was inhibited ($p<0.05$). Next we analyzed the expression of CSC markers in these cells. A lower amount of the colon cancer stem cell marker CD133, Nanog, c-Myc and Oct-4 were detected by immunofluorescence staining of HCT116 cells when CFTR is inhibited. From these and our previous results we confirmed that the channel CFTR expression and activity are associated with CSC, indicating that CFTR could have an influence on the CSC properties at least in human colorectal cancer.

0682 - RUNX1 PARTICIPATION IN CHEMOTHERAPY RESISTANCE ON TNBC

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Abstract/Resumen: Triple negative breast cancer (TNBC) is associated with early recurrence and low survival rates. Treatment options are limited due to the lack of specific therapeutic targets and are consequently managed with chemotherapy. This highlights the urgent need for new specific therapeutic targets for this group of patients. TNBC is associated with epithelial-mesenchymal transition (EMT) and enrichment in breast cancer stem cell population. Growing evidences strongly suggest that EMT might be involved in tumor chemoresistance. Our group has shown that RUNX1 could be involved in the aggressiveness of ER-/PR- breast tumor. We reported that RUNX1 is able to promote cell migration and regulate tumor related-gene expression, like RSPO3 and GJA1, in a FOXP3-dependent manner. ChIP assays done in our lab on MDA-MB-231 cell line revealed that RUNX1 has the potential to regulate other transcription factors, such as SOX4, involved in EMT process. Besides, we observed a significant up regulation of RUNX1 gene expression in murine tumor cell lines treated with TGFß. Moreover, RUNX1 has been reported to correlate with poor patient prognosis in human samples of TNBC. Our hypothesis is that RUNX1 promotes EMT in TNBC cells, which make them become chemoresistant while leading metastasis to distant organs. The aim of this study was to investigate RUNX1 participation in the generation of chemotherapy resistance in TNBC. To do this, we used TNBC cell lines, doxorubicin (a clinically used drug) and loss of RUNX1 function assays. Here we show that RUNX1 ($p= 0.0067$) and GJA1 ($p<0.0001$) gene expression are significantly up regulated in doxorubicin-treated MDA-MB-231. Interestingly, we observed that loss of RUNX1 transcriptional activity strongly enhance doxorubicin toxicity on MDA-MB-231 ($p<0.05$), showing an improvement in drug's sensitivity. Therefore, RUNX1 may be involved in TNBC chemotherapy resistance, pointing out this transcription factor as a possible new therapeutic target in TNBC.

0729 - A COMBINATION OF IN SILICO AND WET-LAB STRATEGIES TOWARDS THE IDENTIFICATION OF BIOMARKERS OF ENDOMETRIAL CANCER PROGRESSION AND AGGRESSIVENESS

María Cecilia ARGIBAY | Luciana MONTIVERO | María José BESSO | **Monica VAZQUEZ DE LEVIN**

INSTITUTO DE BIOLOGÍA Y MEDICINA EXPERIMENTAL (IBYME-CONICET)

Abstract/Resumen: Endometrial cancer (EC) is the 2nd most frequent gynecological neoplasm, expecting a > 50% increase in the next 20 years. Current diagnosis is based on abnormal uterine bleeding, transvaginal ultrasound or uterine biopsy or curettage with or without hysteroscopy. Final diagnosis and tumor classification is done during hysterectomy. Although highly relevant, there are no established EC molecular biomarkers. Objective: Combine bioinformatics tools to identify potential biomarkers of EC progression and aggressiveness and test their expression in EC cell models. An in silico and wet-lab basic research study was conducted. Bioinformatics: DisGeNET (text mining), GEO, TCGA, HPA databases (data mining), ToppGene (gene priorization), and Statistics: Kaplan-Meier Method, Odds Ratio and Cox Proportional Risk Model (Statistical models) approaches. Cell culture, end-point/Q-RT PCR. Data base analysis of a transcriptomic study (GSE17025; GEO platform) from EC samples identified 39 differentially-expressed genes, based on comparing tumor versus non-tumor; ECC versus NEEC, Grade 1,2 versus 3. Text database (DisGeNET) analysis identified 962 EC-associated genes. Gene prioritization analysis (ToppGene) selected 33 genes. Genes were subsequently assessed in an EC TCGA dataset and evaluated using clinical parameters statistical models ($p<0.05$), selecting 6 genes. Four genes were finally selected based on ToppGene prioritization and HPA data: PLEKHH1, PTCH1, TMPRSS2 and TPX2. Their differential expression was confirmed in EC cell models of aggressiveness (Hec1a-ETV5 and Ishikawa-ETV5) and controls (Hec1a and Ishikawa) (Colas et al, Oncogene 2012). Strategies combining bioinformatics and cell culture/molecular biology approaches identified potential biomarkers of EC progression and aggressiveness. Current studies are assessing their expression in EC patient samples to validate their clinical use.