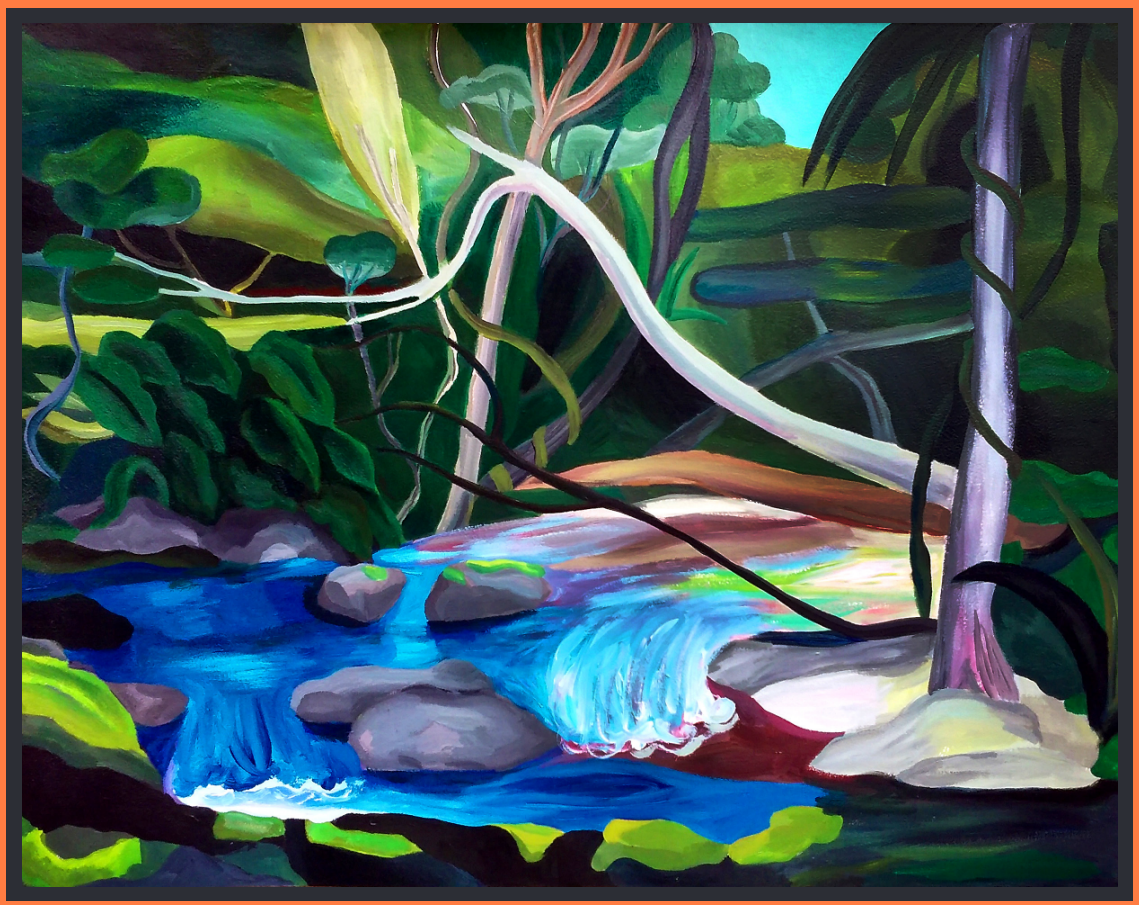
2023

medicina

BUENOS AIRES, VOL. 83 Supl. V - 2023



MEDICINA

Volumen 83, Supl. V, Págs. 1- 262

medicina

BUENOS AIRES, VOL. 83 Supl. V - 2023

La Tapa
Todo, 2016
Daniela Kantor

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

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.
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Vol. 83, Supl. V, Noviembre 2023

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

REUNIÓN CONJUNTA SAIC SAB AAFE AACYTAL 2023

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

XXV JORNADAS ANUALES DE LA SOCIEDAD ARGENTINA DE BIOLOGÍA (SAB)

LV REUNIÓN ANUAL DE LA ASOCIACIÓN ARGENTINA DE FARMACOLOGÍA EXPERIMENTAL (AAFE)

VIII REUNIÓN CIENTÍFICA REGIONAL DE LA ASOCIACIÓN ARGENTINA DE CIENCIA Y TECNOLOGÍA DE ANIMALES DE LABORATORIO (AACYTAL)

15-17 de noviembre de 2023
Hotel 13 de Julio – Mar del Plata

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of disease progression and provide a rapid parameters for treatment management. We used an *in vivo* xenograft model to validate the correlation between tumor burden and BM' concentration. 2-We generated three ddPCR panels to detect the major mutations that lead to EGFRi resistance: a.On-target EGFR mutations T790M and S797X; b.BRAF V600E and PI3K E545K; c.CNV of EGFR, HER2, and MET. We have confirmed the proper detection of each BM using liquid biopsy. This approach will offer an affordable tool to personalized therapies based on identified mutations, enabling broader, earlier, and proactive management of available therapeutic options. With these tools we expect to contribute to the improvement of patient treatment outcomes.

327. 455. **COMBINATION THERAPY OF PACLITAXEL AND UVB1 IN HNSCC AND TNBC CELLS**

Agustina Ibarra [1,2], Valentina Clemente [1,2], Karen Schweitzer [1,2], Georgina Pamela Coló [1,2], Eliana Noelia Alonso [1,2], María Eugenia Fermento [1,2], María Marta Facchinetti [1,2], María Julia Ferronato [1,2], Alejandro Carlos Curino [1,2].

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2. Departamento de Biología, Bioquímica y Farmacia, Universidad Nacional del Sur (UNS), Bahía Blanca, Argentina.

Head and Neck Squamous Cell Carcinoma (HNSCC) and Triple Negative Breast Cancer (TNBC) are heterogeneous and aggressive tumors with high mortality and difficult clinical management. Conventional chemotherapy remains as the main clinical management with the concomitant undesirable side effects for patients and time-limited positive responses. Further research is needed to find novel therapeutic strategies that prolong the patient survival and ensure a better quality of life. The aim of the present study was to evaluate the antitumor potential of the combination of the conventional chemotherapeutic agent Paclitaxel (PTX) with the non-hypercalcemic Calcitriol analog UVB1 in HNSCC and TNBC cells. Cell viability was evaluated by crystal violet assays in human HN13 and HN12 HNSCC and murine 4T1 TNBC cell lines treated with vehicle, UVB1, PTX or combination of drugs. The results show that UVB1 (1µM) with low concentrations of PTX displayed a greater reduction in viability with respect to control and monotherapies in all cell lines tested (120h of treatment, $p<0.001$). Apoptosis analyses were performed in 4T1 cells by flow cytometry with Propidium Iodide and Annexin V-FITC staining. The percentage of cells in early apoptosis was higher in cells treated with UVB1 or UVB1 (1µM) + PTX (1nM) compared to PTX alone or vehicle ($p<0.001$). In order to evaluate the Vitamin D Receptor (VDR) role in these antitumor effects, VDR was overexpressed in 4T1 cells with a pcDNA3-VDR plasmid. Transfected cells were selected and the overexpressed of VDR was checked by RT-qPCR, WB and IFI. The viability studies carried out with these cells showed that PTX displayed a higher antitumor effect in 4T1-pcDNA3-VDR cells compared to 4T1-pcDNA3-CTL cells ($p<0.001$). These results encourage us to continue evaluating this combination therapy in HNSCC and TNBC cells, as well as VDR role in the antineoplastic effects of these chemotherapeutic drugs.

328. 457. **EFFECT OF PHARMACOLOGICAL INHIBITION OF P300 ON THE EXPRESSION AND LOCALIZATION OF P53 IN TRIPLE NEGATIVE BREAST CANCER**

Guillermina Ana Gallardo[1,2], Valentina Clemente[1,2], María Julia Ferronato[1,2], Eliana Noelia Alonso[1,2], Georgina Pamela Coló[1,2], María Marta Facchinetti[1,2], María Eugenia Fermento[1,2], Alejandro Carlos Curino[1,2].

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Triple-negative breast cancer (TNBC) is a heterogeneous group of tumors that lack specific molecular targets. Therefore, it is necessary to investigate potential tumor markers for this subtype of BC. A relationship between p300 and cancer has been demonstrated; but its role remains unclear, as it has been documented both as a tumor suppressor and an oncoprotein. p300 functions as a transcriptional coactivator, histone acetyltransferase, and acetylates lysines of proteins involved in functions beyond transcription. This protein acts as a transcriptional coactivator of p53, regulating its activity through acetylation mechanisms in various tumor types. Hence, we decided to study whether the regulation of p53 mediated by p300 can influence its cellular localization and the alteration of its functions in TNBC. The aim of this work was to evaluate the effect of pharmacological inhibition of p300 on the expression and localization of p53 in TNBC cell lines (MDA-MB-231 and 4T1). The cell lines were treated with VV59 (an inhibitor of p300 acetylase function) or DMSO (vehicle) for 24 hours. In western blot assays, no significant differences were observed in p53 expression levels in either cell lines. However, a decrease in acetylated p53 levels was noted in the MDA-MB-231 cells treated with VV59 compared to control cells ($p=0.0370$). Through immunofluorescence, we observed that p300 inhibition reduced nuclear expression and localization of p53 ($p<0.0001$), accompanied by an increase in cytoplasmic p53 localization, compared to the vehicle, in both cell lines ($p<0.0001$). In silico assays revealed interaction pathways and high affinity between p300 and p53. These findings suggest that the acetylase function of p300 impacts the expression and localization of p53, providing potential insights into p53 regulation in TNBC cells.

329. 544. **CHARACTERIZATION OF R-SPONDIN3 GENE EXPRESSION REGULATION IN HUMAN BREAST CANCER CELLS**

Ana Laura Ortiz*[1], Carla María Felcher*[1], Pedro Javier Salaberry[1], Edith Claudia Kordon[1,2]

1 Instituto de Fisiología, Biología Molecular y Neurociencias-CONICET-UBA Argentina, 2 Departamento de Química Biológica-Universidad de Buenos Aires.

** Ana Laura Ortiz and Carla Maria Felcher contributed equally to this study.*

We have determined that R-spondin3 (RSPO3), a secreted protein that potentiates Wnt signaling pathway, is a key modulator of tumor progression and stem cell behavior in basal-like breast cancer (BL-BC) cells. Although the highest RSPO3 expression has been detected in cells of this cancer subtype, immunohistochemical analysis showed that a high proportion of human breast luminal tumors are positive for RSPO3. We have also found that blocking RUNX-CBFβ activity inhibited RSPO3 expression in the BL-BC cell line MDA-MB-231. In these cells it has been determined that RUNX1 binds to its DNA motif at the end of RSPO3 first intron, which constitutes a relevant putative regulatory region of the human RSPO3 gene, as indicated by combined bioinformatic studies of publicly available data from chromatin immune-precipitation and assay for transposase-accessible chromatin with sequencing (ChIP-seq and ATAC-seq) as well as transcription factor (TF) binding motives in the human genome. The goal of our present project is to analyze RSPO3 expression in a set of human BC cell lines, which includes both luminal (T47D and MCF-7) and basal (MDA-MB231 and BT-549) phenotypes, to determine relationships with information provided by publicly available data-sets about transcription modulators differentially recruited by the promoter and the intronic regulatory region in the human RSPO3 locus. Our results suggest that not only RUNX1, but also the estrogen receptor (ER), STAT3, co-repressor Groucho as well as the SWI/SNF chromatin remodeling complex may exert relevant differential roles in regulating RSPO3 expression in various breast cancer molecular subtypes.

330. 586. **EVALUATION OF A NOVEL BODIPY-BASED BORONATED COMPOUND FOR BORON NEUTRON CAPTURE THERAPY IN MELANOMA CELLS**

Cristian Cascardo[1,2], Oriana N. Beraldi[3], Verónica Mestre Ahumada[2], María Silvina Olivera[4], Irene L. Ibañez[1,2], Luciana Giordano[3], Hebe Durán[1,2,5]

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