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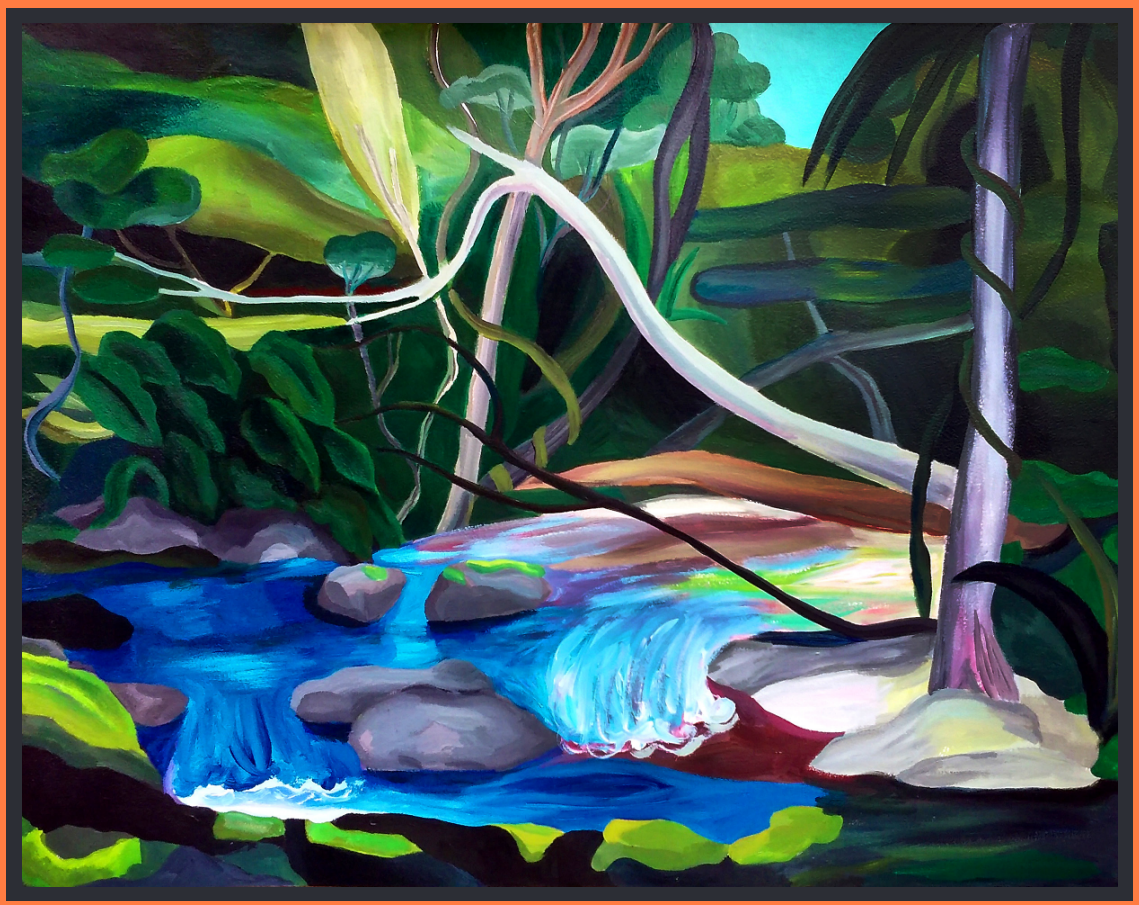

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e-mail: revmedbuenosaires@gmail.com – http//: www.medicinabuenosaires.com

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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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accompanied by a significant decrease in diameter and an increase in the number of spheres (P<0.05). The qPCR analysis of retinoid system genes revealed a significant increase in RARγ (nuclear retinoic receptor involved in stemness) in both ATRA and combination treatment. The cytotoxic effects on cell monolayers observed in previous studies, with the effects evidenced on CSCs of Lapatinib, either alone or in combination with ATRA in both triple-negative breast cancer models, provide further in vitro evidence of the potential repositioning of these drugs for the treatment of HER2-negative breast cancer.

394. 428. **THE PROTUMORAL ROLE OF P300 IN THYROID CANCER**

Valentina Clemente[1,2], Agustina Ibarra[1,2], Exequiel G. Alonso[1,2], Jessica A. Carballido[3], Guillermina A. Gallardo[1,2], María J. Ferronato[1,2], Eliana N. Alonso[1,2], Georgina P. Coló[1,2], Alejandro C. Curino[1,2], María E. Fermento[1,2], María M. Facchinetti[1,2].

1.- Laboratorio de Biología del Cáncer – Instituto de Investigaciones Bioquímicas Bahía Blanca (INIBIBB) Universidad Nacional del Sur (UNS-CONICET). Departamento de Biología, Bioquímica y Farmacia.

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

3.- Instituto de Ciencias e Ingeniería de la Computación (ICIC), Universidad Nacional del Sur (UNS)-CONICET, Bahía Blanca, Argentina.

Thyroid Carcinoma (TC) is the most prevalent endocrine tumor worldwide. p300 is a protein that functions as a transcriptional cofactor, histone acetyltransferase, and lysine acetyltransferase for proteins involved in functions other than transcription. A relationship of p300 with cancer has been demonstrated, however, its role is still unclear since it has been documented as a tumor suppressor and/or as an oncoprotein. In our laboratory, we have established an association between p300 and breast cancer, observing a protumoral role. Due to the limited studies on p300 and TC, it is interesting to investigate the expression and the cellular and molecular mechanisms through which this protein could be involved in the oncogenesis and tumor progression of TC. The objective of this work was to study the expression of p300 and the effect of inhibiting the acetylase function on the processes of apoptosis and metastasis in human TC cells. We observed through In silico assays that p300 is expressed (both RNA and protein) in these tumors. The treatment of human papillary TC cell line, TPC-1, with VV59 (inhibitor of p300 acetylase function) or its vehicle (DMSO) produced a decrease in the number of cells compared to the vehicle (crystal violet assay and manual counting, p<0.0001). When we analyzed the cell cycle by flow cytometry, we detected an increase in the sub G0/G1 phase and a decrease in the G0/G1 phase in the cells treated with VV59 compared to those treated with the vehicle (p<0.001). On the other hand, we detected that pharmacological inhibition of p300 decreases migration (wound healing assay, p<0.0001), invasion (matrigel assay, p<0.0001), and cell adhesion (crystal violet assay, p<0.0001). Taken together, these results demonstrate an antitumoral role for pharmacological inhibition of p300 acetylase function in the human TC cell line.

395. 519. **TARGETING ANGIOGENESIS IN OSTEOSARCOMA: ADDITION OF REPURPOSED HEMOSTATIC DRUG DESMOPRESSIN TO BEVACIZUMAB AS A THERAPEUTIC STRATEGY**

Solernó Luisina M.[1,2], Saud Zahira Y.[1,2], Llavona Candela[1,2], González Morán Florencia[1], Gottardo M. Florencia[1,2,3], Andersen Melisa[1], Georgina A. Cardama[1,3], Alonso Daniel F.[1,2,3], Garona Juan[1,2,3].

1. *Centro de Oncología Molecular y Traslacional (COMTra), Unidad de Oncología Traslacional, Universidad Nacional de Quilmes.*

2. Centro de Medicina Traslacional (Unidad 6), Hospital de Alta Complejidad en Red El Cruce "Dr. Néstor Carlos Kirchner" S.A.M.I.C.

3. Consejo Nacional de Investigaciones Científicas (CONICET).

Angiogenesis plays a crucial role in osteosarcoma (OSA) progression, the most common primary malignant bone tumor. In these highly metastatic and vascularized tumors overexpression of VEGF correlates with poorer outcomes. Although promising, adding anti-VEGF bevacizumab to chemotherapy didn't provide significant clinical benefits in OSA. Desmopressin (dDAVP) is a repurposed hemostatic drug in oncology that acts as a selective agonist for the AVPR2 receptor present in blood microvessels and some cancer cells. dDAVP has shown potent angiostatic and antimetastatic activity in other aggressive tumors but its antiangiogenic effect in OSA has never been studied. The objective of this work was to evaluate dDAVP effects on OSA-associated angiogenesis, alone or in combination with bevacizumab. After exploring interactive gene expression web servers GEPIA2 and TIMER2.0 (SARC-TCGA/n=257), AVPR2 showed a positive prognostic impact on overall and disease-free survival in sarcoma patients, and negatively correlated with proangiogenic genes (VEGFA, MEK, MTOR), as well as protumoral immune infiltrates (MDSCs and M0 macrophages). Its expression also correlated with different antitumoral immune cells such as NK cells, M1 macrophages, mast cells and CD4+ T cells. Moreover, AVPR2 was detected in human MG-63 OSA cells by qPCR and IHC. In an *in vivo* modified matrigel plug assay, dDAVP treatment (12 μg/kg i.v., 3 doses/week) notably reduced early angiogenic response in MG-63 incipient lesions. In nude mice bearing growing MG-63 xenografts treatment with dDAVP (12 μg/kg i.v., 3 doses/week) in combination with bevacizumab (5 mg/kg i.p., 2 doses/week) significantly inhibited tumor progression, enhancing the anti-OSA effects of both monotherapies. Results were significant at p<0.05 (t test or ANOVA, GraphPad Prism). dDAVP plus bevacizumab exhibits cooperative antiangiogenic activity in OSA, revealing an interesting correlation between AVPR2, angiogenic markers and the tumor immune landscape.

396. 525. **SYNERGISTIC ANTIPROLIFERATIVE EFFECT OF THE COMBINATION OF 2'NITROFLAVONE AND GEFITINIB IN TRIPLE NEGATIVE BREAST CANCER CELLS**

Julieta R Cebrón[1,2]; Mariana A Bojorge[1,2]; Viviana C Blank[1,2]; Mariel Marder[1,2]; Johanna G Miquet[1,2].

[1] Departamento de Química Biológica, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires (UBA).

[2] Instituto de Química y Fisicoquímica Biológica (IQUIFIB), UBA/CONICET.

Gefitinib is an epidermal growth factor receptor (EGFR) inhibitor used for the treatment of cancer which has recently been proposed for the treatment of certain types of breast cancer. 2'nitroflavone (2'NF) is a synthetic flavone that was obtained in our institute which has previously demonstrated to affect the EGFR pathway activation as well as the expression of receptors related to EGFR activity in breast cancer cells. As EGFR is associated with tumorigenesis and is believed to be involved in the mechanism of action of flavonoids, a combinatory therapy between 2'NF and gefitinib is proposed. The aim of our investigation is to analyze if there is a synergistic effect that justifies the combination of these two molecules for the treatment of breast cancer. To assess our objective, MDA-MB-231 breast cancer cells were treated with 2'NF, gefitinib or a combination of both for 48 h. The effect on cell proliferation was determined by hexosaminidase assay using concentrations in a range between 0.1 μM and 150 μM. Afterwards, the synergistic effect was determined using Compusyn software that calculates a combinatory index (CI) which value must be under 1 to have a synergistic effect. Besides, the results were confirmed by flow cytometry using concentrations of 5 μM and 10 μM. Results were analyzed by ANOVA, p<0.05 was considered statistically significant. Results showed an CI of 0.62 which according to the software refers to the category of synergism (n=6). The software also indicates that due to this synergism the IC_{50} can be reduced 2.95 times for 2'NF and 3.49 times for gefitinib. These results were reconfirmed by flow cytometry showing a significative increase in cell death when the molecules are combined.
In conclusion, a combinatory treatment using 2'NF and gefitinib demonstrated to have a synergistic effect on breast cancer cells which justifies the use of them together as a potential new therapy.