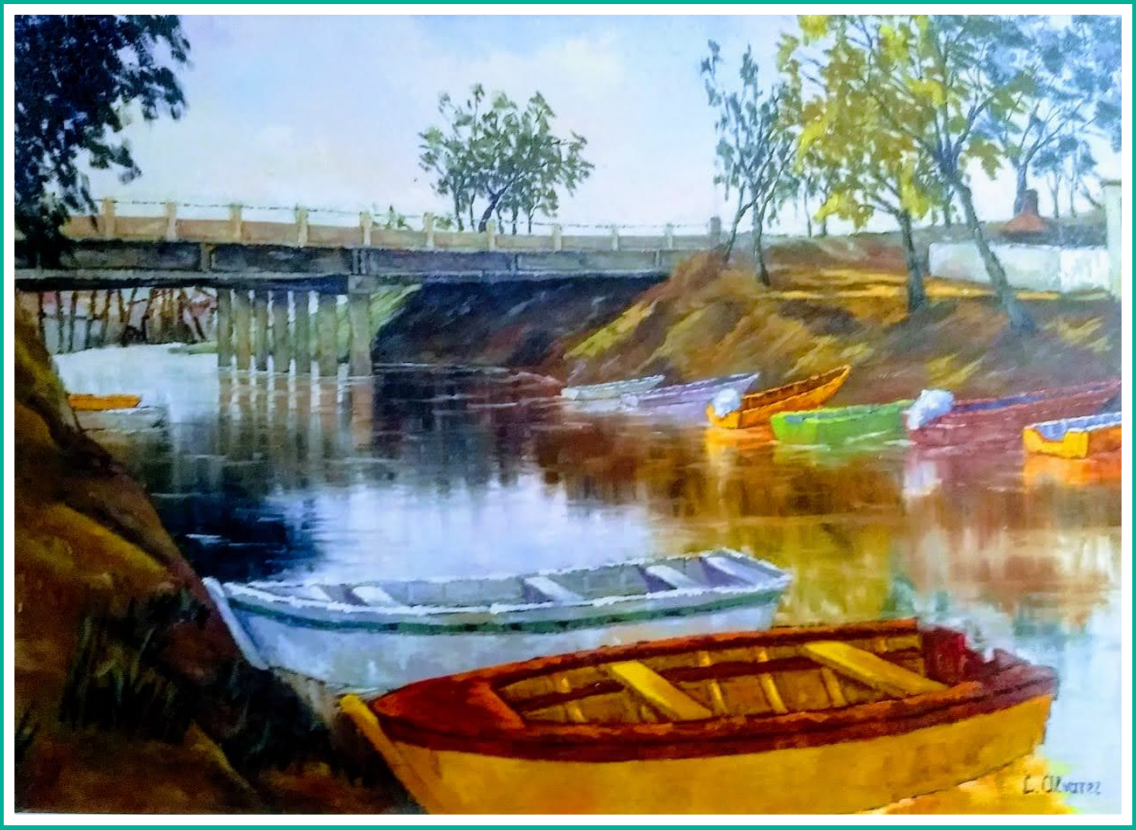
2020

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.
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Incluida en el Núcleo Básico de Revistas Científicas Argentinas del CONICET.

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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

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ANNUAL MEETING OF BIOSCIENCE SOCIETIES 2020

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November 10-13, 2020

RESPONSIBLE EDITORS
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el consisted in the chemotherapeutic challenge of adrenal cancer NCI-H295R and breast cancer MCF-7 cells, two lines characterized by low aggressive phenotypes and low expression of the ACSL4, ABCG2 and ABCC4 proteins. We evaluated cell functionality using proliferation (BrdU) and viability (MTT) assays, and compound exclusion (efflux) using fluorescent Hoechst 33342. ACSL4 and ABC transporters were evaluated by western blot (WB). NCI-H295R cell treatment with doxorubicin (20 nM) and cisplatin (200 nM) increased the expression of ACSL4 (WB-p <0.001), ABCG2 (WB-p <0.001) and ABCC4 (WB-p <0.05). The treatments also improved fluorescent compound exclusion (efflux-p <0.01), an effect reversed by the action of ABGC2 transporter inhibitor KO143. Combined treatments (chemotherapeutic agents and ACSL4 inhibitor) reduced the proliferation of NCI-H295R cells (BrdU-p <0.05). MCF-7 cell treatment with doxorubicin and cisplatin increased the expression of ACSL4 (WB-p <0.001) and ABCG2 (WB-p <0.05) and the phosphorylation of pAKT (WB-p <0.05) and pS6 (WB-p <0.01), components of the AKT/mTOR pathway. These results are in line with our previous observation that ACSL4 regulates ABGC2 expression through the regulation of the AKT/mTOR pathway. Therefore, ACSL4 may constitute a therapeutic target at the initial stages of chemotherapeutic treatment to prevent the activation of pathways associated with increased tumor aggressiveness.

238. (46) **HEMEOXYGENASE-1 IN THYROID CANCER PROGRESSION**

Alonso EG[1], Pichel P[2], Mascaró M[1], Fernández Chávez L[1], Peros, I[1], Schweitzer K[1] Coló GP[1], Recio S[2], Carballido JA[3], Arévalo J[1], Castellano L[4], Facchinetti MM[1], Gandini NA[1], Curino AC[1].

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4.-Servicio de Patología, Hospital Municipal de Agudos "Dr. L. Lucero", Bahía Blanca, Argentina.

Previous work from our group shows that Hemeoxygenase-1 (HO-1) is overexpressed in several types of tumor and the enzyme can be located in cell cytoplasm and/or nucleus. This subcellular distribution is caused by the cleavage of the C-terminus of HO-1 by calpain 1 (CAPN1), calpain 2 (CAPN2), cathepsin B (CTSB) and signal peptide peptidase (SPP). In thyroid cancer (TC), HO-1 potential utility as biomarker remains underexplored. The aim of this work was to study HO-1 expression in TC and its correlation with clinical-pathological data. Tumor biopsies (N=64) and fine needle aspiration biopsies (FNAB) (N=22) were used to asses HO-1 expression by inmunohistochemistry (IHC) and inmunocytochemistry (ICC), respectively. In addition, mRNA expression of HO-1, CAPN1, CAPN2, CTSB and SPP were analyzed by using GEPIA2 and Kaplan-Meier Plotter databases in *in silico* assays. In TC biopsies, overexpression (OE) of HO-1 by IHC was found in the tumor (T) respect to non-malignant areas to the tumor (NMT) (Mann Whitney test, p<0.0001). In T, HO-1 was expressed in the cytoplasm while in NMT, nuclear expression was found. HO-1 expression correlated with histological subtype by IHC (Chi^2, p=0.0006) and Bethesda classification by ICC (Chi^2, p=0.0470). *In silico* studies (ISS) corroborated IHC results in papillary TC (ANOVA, p<0.001). Stage IV female patients with HO-1 OE were associated with lower overall survival (Log rank, p=0.032). ISS showed that stage III male patients with OE of CTSB and female patients with OE of CAPN1 correlated with greater survival (Log rank, p=0.017; Log rank, p=0.027 respectively). However, in female and male stage IV patients, OE of CAPN2 was associated with lower survival (Log rank, p=0.0015; Log rank, p=0.039 respectively). Furthermore, SPP OE correlated with lower survival in female patients (Log rank, p=0.041). So far our results show that HO-1, CAPN2 and SPP overexpression together could be used as unfavorable biomarkers in TC.

239. (64) **δ-TOCOTRIENOL POTENTIATES THE INHIBITORY EFFECTS OF INTERFERON ALFA 2-B (IFN A) ON PROLIFERATION, MIGRATION, INVASION AND INCREASES APOPTOSIS IN HUMAN HUH7 HEPATOCARCINOMA CELLS.**

Lucci A, Vera M, Comanzo C, Lorenzetti F, Ferretti A, Ceballos MP, Quiroga AD, Alvarez ML, Carrillo MC

Instituto de Fisiología Experimental (IFISE-CONICET)

Our group has previously postulated that δ-tocotrienol supplementation to interferon alfa (IFN α) therapy can be used as a strategy against liver cancer cells because combined treatment produced growth inhibition and induced apoptosis in SK Hep-1 tumor cells. According to our preliminary results in SK-Hep1 cells, we decided to check if they were repeated in another liver tumor cell line (HuH7), doing additional migration and invasiveness studies.

Cells were treated with 20000 IU/L IFN α and 25 uM δ-tocotrienol, an isomer of vitamin E (combined IFN-E-group). Also, treatments with each single compound were made (IFN-group and E-group). MTT assay was performed to determine cell viability at 72 h of treatment; wound healing assay was done at 24 h to determine cell migration. Invasion studies at 24 h were made in transwell chambers, and annexin v/propidium iodide assay was performed to determine apoptosis at 72 h. As expected, IFN-E-group showed a higher decrease in cell viability (-70%$^{*\#}$) compared with monodrug therapy: IFN-group (-10%*), E-group (-15%*). IFN-E-group displayed a significant decrease (-44%$^{*\#}$) in migratory activity compared with each individual treatment: IFN-group (-21%*) and E-group (-22%*). Also, IFN-E-group showed a significant diminution (-75%$^{*\#}$) in cell invasiveness compared with monodrug therapy: IFN-group (-25%*) and E-group (-55%*). Finally, IFN-E-group showed a higher increase in total apoptosis (+160%$^{*\#}$) compared with individual therapy: IFN-group (-40%*) and E-group (-43%*),(*p≤0.05 vs. control untreated cells; $^{\#}$p≤0.05 vs IFN-group and E-group). In summary, we demonstrate that the addition of δ-tocotrienol to IFN α therapy enhances the reduction of cell proliferation and migration/invasiveness capacities of Huh7 cells, as well as potentiates the increase in apoptotic cell death. In this regard, combined treatment of immunochemicals together with natural products, might open a potential clinical aproach for HCC treatment in the future.

240. (81) **miR-34a AND miR-137 AND THEIR TARGET PROTEINS WERE FOUND TO BE DOWNREGULATED IN ACUTE LYMPHOBLASTIC LEUKEMIA CELLS**.

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Acute Lymphoblastic Leukemia (ALL) is the most frequent cancer in children, characterized by clonal proliferation of early B- and T-lymphocyte progenitors. Up to 25% of children and more than 50% of adults suffer a relapse of the disease which significantly reduces patient's survival. Therefore, it is important to identify new biomarkers, which can be used to improve the disease prognosis and/or to predict treatment efficacy. Non-coding RNAs have been shown to play a key role in the development and progression of tumors. Recent studies point out that aberrant miR-34a and miR-137 expression leads to an increase in cell proliferation, as well as an abnormal response to chemotherapy in various types of cancer. Thus, we aimed to elucidate the role of this two microRNAs in ALL, specifically to study their association to tumor development and disease