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La Tapa (Ver p 5)
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LXVIII ANNUAL MEETING OF
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November 10-13, 2020

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LA TAPA

María de Luján Alvarez. Ludueña

Técnica: óleo sobre tela

Medidas: 60 x 40 cm, año 2016

Gentileza de la autora

La obra de tapa refleja un lugar típico rosarino. El arroyo Ludueña nace en los campos de las afueras de Rosario y finaliza en el barrio Arroyito de la ciudad, donde desemboca en el Río Paraná.

María de Luján Alvarez es Bioquímica y Doctora en Ciencias Biológicas. Es investigadora adjunta (CIC-CONICET) en el Instituto de Fisiología Experimental (IFISE-CONICET) y docente en el área Morfología de la Facultad de Ciencias Bioquímicas y Farmacéuticas de la Universidad Nacional de Rosario (UNR). Alumna del taller de arte Tunkeyén, estudió con la pintora rosarina Ana Petrini. Ganó el segundo premio en el 12º Salón de Pintores Nóveles de la Sociedad Argentina de Artistas Plásticos de Rosario (2004), el primer premio en el 2º Salón Pintando Argentina de Rosario (2010), una mención al trabajo realizado en el 2º Encuentro de Pintores de Rosario organizado por la Asociación Cultural Museo Ambrosio Gatti (2018) y el tercer premio en el Concurso de Pinturas 150 años de la Sociedad Filantrópica Suiza (2018). Participa frecuentemente en muestras colectivas de diferentes salones pictóricos rosarinos y sus obras han sido expuestas en espacios de arte organizados por CONICET y la UNR.

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gene. RB may be hereditary (bilateral tumors) or non-hereditary (mostly unilateral tumors). The first mutation can be germinal (RB hereditary) or somatic (RB non-hereditary), the second mutation is always somatic. RB is a potentially curable cancer depending on early diagnosis and treatment. Besides, patients with hereditary RB can transmit the predisposition to their offspring. The aim of our work is the identification of *RB1* mutations, for risk assessment in the offspring and siblings of bilateral patients and for discrimination between hereditary and non-hereditary RB in unilateral patients. Out of a total of 215 patients with RB studied in our lab, the results of 2 bilateral and 2 unilateral are presented here. Mutational detection was conducted by a combined approach of Exome analysis and MLPA. Variants in donor splicing sites were detected in the 2 bilateral patients: c.1389+1G>A and c.2106+1del. Moreover, a newly born sibling could be excluded from RB risk. One of the unilateral patients showed a homozygous deletion of *RB1* entire gene and surrounding genes (*ITM2B-5,RCBTB2-8,DLEU1-2*) in the tumor; this mutation was not present in blood DNA, denoting a non-hereditary RB. The other unilateral patient displayed a heterozygous germline deletion of whole *RB1* gene and neighboring genes (*ITM2B-5,RCBTB2-8,DLEU1-2,PCDH8-3,PCDH8-2*), denoting a hereditary RB and a likely contiguous deletion syndrome. The 3' end was not found, that is, the deletion continues beyond *PCDH8*.
Identification of *RB1* mutations allows detection of RB predisposition in patient´s offspring and siblings which provides access to early treatment to preserve survival and vision. Identification of germinal mutations in unilateral patients allows detecting the risk of tumor development in the other eye and its absence eliminates the need for frequent eye *exams under anesthesia*.

313. (561) **MELANOMA XENOGRAFTS GROWTH INHIBITION BY SOLANUM TUBEROSUM ASPARTIC PROTEASES 3 (*St*AP3) TREATMENT**

Ibañez IL[1], Muñoz F[2], Zoppi J[3], Abaurrea R[4], Scandogliero E[4], Durán H[1,5,6], Guevara MG[2]
1. Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET) – Instituto de Nanociencia y Nanotecnología (INN) – Nodo Constituyentes, Buenos Aires, Argentina.
2. Consejo Nacional de Investigaciones Científicas y Técnicas – Instituto de Investigaciones Biológicas (IIB) – Centro Científico Tecnológico CONICET – Mar del Plata, Universidad Nacional de Mar del Plata, Mar del Plata, Argentina.
3. Hospital Privado de la Comunidad, Mar del Plata, Argentina.
4. Laboratorio de Análisis Clínicos y Bacteriológicos (BAS), Mar del Plata, Argentina.
5. Comisión Nacional de Energía Atómica (CNEA), Buenos Aires, Argentina.
6. Universidad Nacional de San Martín (UNSAM), Buenos Aires, Argentina.

The swaposin domain is present in plant aspartic proteases (APs) inserted into the C-terminal domain as an extra region known as plant-specific insert (PSI). The PSI domain interacts with the plasma membrane, causing cell permeabilization, thus killing plant and human pathogens. A typical Solanum tuberosum AP (*St*AP) named as *St*AP3 was demonstrated to have cytotoxic activity against cancer cells and no effect in normal cells in vitro. The toxicity of *St*AP3 was assessed in a mice model, showing no signs of systemic toxicity. Malignant melanoma (MM) is one of the most aggressive cancers, with high metastatic ability and resistant to therapies. Thus, the pursuing of novel agents against MM is still challenging. Herein, we aimed to evaluate the *in vivo* antitumor effect of *St*AP3 in MM. Subcutaneous A375 human melanoma xenografts in athymic nude mice were induced. Once tumors developed (mean larger dimension = 3.8 ± 0.09 mm), mice were treated with *St*AP3 (6 μg/mg body weight, subcutaneously under the tumor at a single dose) or physiologic solution (controls). Animal experiments complied with the ARRIVE guidelines and were performed with protocols approved by the Argentine National Atomic Energy Commission Animal Care in accordance with the EU Directive 2010/63/EU and NIH Publications No. 8023, revised 1978. A significant inhibition of MM tumors growth was observed in *St*AP3-treated mice ($p < 0.05$) *vs.* controls. This was detected immediately after treatment and was sustained until 15 days post-treatment, with a maximum inhibition of 76%, when control tumors reached 200 mm^3 and animals were sacrificed. As far as we know, this is the first report showing the *in vivo* effect of a plant AP whose action mechanism would be mediated by membrane destabilization, which may be explained by the plasma membrane composition with high levels of phosphatidylserine in the outer leaflet of cancer cells. These results suggest the potential of these plant proteases as anticancer agents.

314. (394) **HYALURONAN MODULATION BY 4-METHYLUMBELLIFERONE (4MU) CONFERS CHEMO SENSIBILITY TO LUNG CANCER STEM CELLS**

Díaz MA[1], Bezazian A[1], Roselló, P[2], Escribano A[1], Fusco M[1], Braga Menéndez J[1], Fiore E[2], Bayo J[2], Rizzo MM[1], Malvicini M[1].
1. Laboratorio de Inmunobiología del Cáncer, Instituto de Investigaciones en Medicina Traslacional, Universidad Austral.
2. Instituto de Investigaciones en Medicina Traslacional, Universidad Austral.

Taxane-platin chemotherapy is widely used for non-small cell lung cancer (NSCLC). However, the majority of patients will progress or relapse. In the tumor microenvironment (TME) cancer cells co-exist with cellular and non-cellular components that drive tumor processes such as chemotherapy resistance. Cancer stem cells (CSCs) are tumor initiating cells identified by CD133, CD44 and ALDH1 among others markers, which form residual niches involved in tumor recurrence. It has been partly described how the TME hyaluronan (HA) regulates CSCs function. We have demonstrated that 4-Methylumbelliferone (4Mu), a modulator of HA synthesis, reduces CSCs properties in hepatocarcinoma. Here, we observed that HA was present on mice Lewis Lung Carcinoma (LLC) tumors. We found HA+ LLC cells; thus cancer cells produced, at least in part, the HA observed in tumors. We observed about 6.58 ± 0.83 % of CD133+ CSCs on *in vitro* cultured LLC cells. Isolated CD133+ cells showed higher expression of HA and CD44 in comparison with non-CSCs population ($p<0.05$). Analysis of HA synthases (HAS), hyaluronidases (HYAL) and the CSCs transcription factors KLF4 and SOX2 expression from NSCLC patients using The Cancer Genome Atlas data showed that while HAS3 positively correlates with levels of KLF4 and SOX2, HYAL2 inversely correlates with SOX2 expression. Also, HAS3 correlates with a shorter disease-free survival when it is highly expressed. Also, 4Mu treatment of whole, CD133+ or CD133- LLC cells showed an inhibitory concentration 50 (IC50) of 0.90mM, 0.60mM and 1.06mM respectively, while non tumor cells showed an IC50 of 4.22mM ($p<0.01$). When CD133+ cells were treated with 4Mu plus chemotherapy we observed a significant decrease in viability with an IC50 of 0.32nM pemetrexed (Pe) vs. 0.15nM Pe+4M, and 7.52nM paclitaxel (Pa) vs. 0.50nM Pa + 4Mu. Our results suggest that targeting HA could turn tumors, particularly CSCs, more susceptible to chemotherapy promoting an effective antitumoral response.

REPRODUCCIÓN

315. (22) **EFFECT OF ZN ON SPERM PHYSIOLOGY**

Fernández Beato L[1], Cane F[2], Piskulic L[3], Marini PE[1,4], Teijeiro JM[1,5]
1. Laboratorio de Medicina Reproductiva. Facultad de Ciencias Bioquímicas y Farmacéuticas. Universidad Nacional de Rosario.
2. Medax. Chañar Ladeado. Santa Fe.
3. Área de Estadística y Procesamiento de Datos. Facultad de Ciencias Bioquímicas y Farmacéuticas. Universidad Nacional de Rosario
4. IBR-CONICET
5. CONICET

Optimal preservation of boar sperm for artificial insemination (AI) is at 16°C. At this temperature, neither cellular metabolism nor microbiological growth conditions can be effectively reduced in seminal doses. Under the hypothesis that Zn's effect on sperm physiology could improve their preservation at lower temperatures, the ob-