2018

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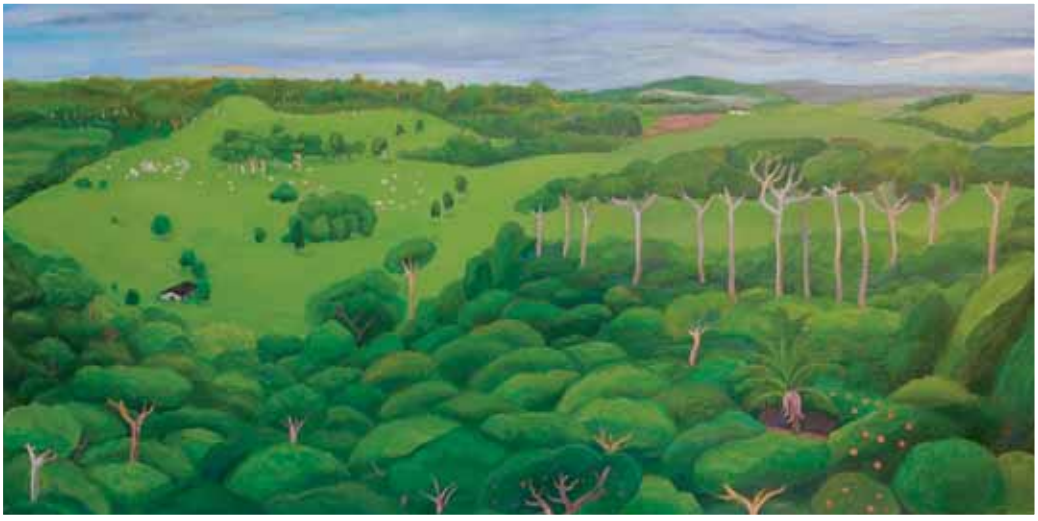

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La Tapa (Ver p xx)
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# REUNIÓN CONJUNTA SAIC SAI SAFIS 2018

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**14-17 de noviembre de 2018**
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# JOINT MEETING SAIC SAI SAFIS 2018

## LXIII ANNUAL MEETING OF

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Claudia Pérez Leirós
Pablo Baldi
Alberto Crottogini

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LA TAPA

**Los palos rosas**, 2015

Daniela Kantor

Técnica: Acrílico sobre bastidor. Medidas: 35 x 70 cm

Daniela Kantor es diseñadora gráfica (FADU-UBA), historietista, ilustradora y pintora. Desde 2014 es docente en la materia Ilustración, cátedra Roldán, FADU, y da talleres para niños (Filbita 2017, taller de comics librerías Matilda-Tigre, taller de historietas CCK, etc.) Estudió con el maestro Alberto Breccia dibujo de historieta y con Carlos Gorriarena realizó el Curso de color. Asistió al Taller de acuarela y pastel de Carlos Nine y realizó clínicas de pintura con Mariano Sapia y Tulio de Sagastizábal. Además de ilustrar muchos libros para niños y adolescentes (Editoriales Troquel, Abran Cancha, Puerto de Palos, Santillana, etc.), es parte de la revista de historietas El tripero, publica en revistas (Barcelona, Zona de obras, Crisis, suplemento Ñ, entre otras). Publicó su primera novela gráfica: Mujer primeriza (2014). Su proyecto de segundo libro de historietas Naturalella obtuvo la primera mención del Premio Nueva Historieta Argentina (2016) y fue publicado en parte en Dis-tinta, el compilado de Liniers y Martín Pérez (Ed. Sudamericana, 2016). Expone sus pinturas desde 2003; recientemente exhibió en Cic.edu.ar

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between patients with and without BCR post radical prostatectomy. We obtained a list of 1021 genes differentially expressed (adjusted p<0.05). In order to increase the confidence of the results, we ran the stability selection algorithm on the 1021 genes selected on the previous step. This algorithm is a resampling procedure to assess the stability of variables for high-dimensional data. We obtained a set of 4 genes that resulted as differentially expressed in >40% of the subsamples. The selected genes were: CRISP3, APOE, CEL and DDTL; and they all were significantly overexpressed in the tumors of patients who relapsed. The analysis of BCR-free survival showed significant poorer survival for patients with high-tumoral expression of these genes. Moreover, the risk of BCR is >2-fold for patients with high-tumoral expression compared to patients with low expression. The analysis of the combined expression showed a HR=15 (95%CI=3.5-63.9) for patients with high-tumoral expression for two or more genes. In conclusion, the expression signature of these genes might have the potential to detect aggressive tumors and predict BCR at the time of radical prostatectomy.

**43.** (364) **THE MIRNAOME ASSOCIATED TO CTBP1 AND METABOLIC SYNDROME IMPACTS ON THE OUTCOME OF BREAST CANCER PATIENTS.**
Rocío Belén Duca, Paula Lucia Farre, Karen Daniela Graña, Guillermo Nicolás Dalton, Georgina Daniela Scalise, Cintia Massillo, Adriana De Siervi, Paola De Luca
*Laboratorio de Oncología Molecular y Nuevos Blancos Terapéuticos - IByME – CONICET*

Breast cancer (BrCa) is the leading cause of cancer death in women and metabolic syndrome (MeS) constitutes a risk factor for this disease. C-terminal binding protein 1 (CTBP1) is a co-repressor of tumor suppressors activated by low $NAD^+$/NADH ratio. Previously, we generated a MeS model by chronically feeding mice with high fat diet. We found that CTBP1 and MeS induced tumor growth and progression regulating the expression of let-7e-3p, miR-494-3p, miR-146a-5p, miR-194-1-5p, miR-381-5p and miR-378a-3p in BrCa xenografts. The aim of this work was to investigate the role of the miRNAs modulated by CTBP1 and MeS in BrCa. We analyzed the effect of the CTBP1/MeS-associated miRNAs in survival of BrCa patients through the bioinformatics tool PROGmiR. We found that in almost all cases, miRNAs effects depend on ER and PR status. Thus, low expression of let-7e-3p correlated with diminished survival in patients with BrCa $ER^+$ and $PR^+$, while high expression levels are associated with a lower metastasis-free survival in patients with BrCa $ER^-$. Low expression of miR-494-3p is associated with decreased metastasis-free survival in patients with BrCa $PR^+$. Low expression of miR-146a-5p correlated with low metastasis-free in $ER^+$ BrCa patients. In BrCa $PR^-$ patients, miR-146a-5p and miR-194-1-5p expression is related to increased relapse-free survival, while miR-381-5p expression is associated with reduced metastasis-free survival. Interestingly, miR-378a-3p expression is associated with low metastasis-free survival in BrCa global population. Based on this, we selected miR-378a-3p to evaluate its effects in proliferation, adhesion and migration of BrCa cells through *in vitro* assays. Thus, miR-78a-3p was cloned into the expression vector pSM30. We generated MDA-MB-231 stable-transfected cells with overexpression of miR-378a-3p or control cells and selected positive MDA-MB-231-derived clones by RT-qPCR. To identify microRNAome associated with tumor growth and progression constitutes the first step for the development of targeted therapies for BrCa associated to MeS.

**44.** (414) **THEORETICAL AND BIOLOGICAL STUDY OF NEW POTENTIAL BRAFV600E INHIBITORS**
Ludmila Campos, Francisco Garibotto, Celia Perez, Cristian Falcón, Sergio Alvarez, Daniel Enriz
*IMIBIO-SL, CONICET, San Luis, Argentina*

Around 50% of melanoma patients express the mutated protein kinase BRAFV600E which in turn induces cell survival and proliferation through ERK pathway activation. Lately, two small BRAF inhibitors (BRAFi) have been approved for the treatment of metastatic melanoma: Vemurafenib and Dabrafenib. Considering that tumors become resistant after a few months of treatment and in some cases tumors are intrinsically resistant to BRAFi, new therapeutic options should be analyzed. Thus, by a combination of theoretical and experimental studies our aim was to find new potential BRAF inhibitors. Based on virtual screening, docking and molecular dynamics approaches we selected a panel of 20 different compounds. To test its potential BRAFi activity, biological assays were conducted in melanoma cell line Lu1205 which express the mutant kinase BRAFV600E, and Vemurafenib was employed as positive control of all the experiments performed. In particular, ERK phosphorylation, an indirect measure of BRAFV600E activity, was determined by western blot. In addition, MTT assay was conducted to study the effect of the compounds on cell viability. Our results show that 6-OH-2-carboxianilide derivatives 10C and 10F reduce significantly ERK phosphorylation at 1 μM (p<0.05). In addition, compound 10C also reduce cell viability (p<0.001). Taking together, these results allowed us to identify the compound 10C as a new potential BRAFi that reduce ERK phosphorylation and cell viability. Moreover, this compound can be modified in order to design new chemical structures with improved activity.

**45.** (322) **TUMOR ORGANIZATION: A MULTIDIMENSIONAL APPROACH**
Marina Belen Cuenca, Lucía Canedo, Carolina Perez Castro, Hernán Edgardo Grecco
*Instituto de Investigación en Biomedicina de Buenos Aires (IBioBA) - CONICET - Partner Institute of the Max Planck Society*

Tridimensional (3D) culture of cancer cells has become a useful technique to replicate as close as possible the conditions found in living tissue. Along with it came new methodological challenges to visualize cell organization and progression. We present an open source Python toolbox applied to transmission and fluorescence 2D/3D images, obtained with a variety of techniques such as Confocal and Single Plane Illumination Microscopy (SPIM). Using glioblastoma multicellular spheroids, we were able to quantify their morphology through time with automatic segmentation based on object recognition. We expect, by making this tool available to the scientific community, to improve 3D cell culture characterization to assess the effect of drug screening assays.
Supported by ANPCyT, CONICET and FOCEM (COF 03/11)

**46.** (295) **STUDY OF AHCYL1 GENE IN A TUMOR CELL PLASTICITY MODEL**
Melina Muñoz Bernart, Nicolás Budnik, Carolina Perez Castro
*Instituto de Investigación en Biomedicina de Buenos Aires (IBioBA) - CONICET - Partner Institute of the Max Planck Society*

Development and tumorigenesis involve cell plasticity events, where cells may undergo differentiation/dedifferentiation processes. TGF-beta/SMAD proteins and the core transcriptional factors (Oct4, Sox2 and Nanog) modulate the behaviour of stem cells as well as the tumor cells. Our aim is to study oncogenic reprogramming as a cell plasticity model and we chose A549 human lung adenocarcinoma cell line. This cell line is capable of growing as three-dimensional (3D) culture (a property of stem-like cells) and is induced to undergo TGFbeta-driven Epithelial-Mesenchymal Transition (EMT). We have developed INSECT, a bioinformatic tool to identify genes potentially co-regulated by the core factors and SMAD proteins in stem-like cells. Using this tool we identified several candidate genes and we selected and started to characterize the high-scored gene Ahcyl1. Results showed that after 48-hour-TGFbeta1 treatment Ahcyl1 transcriptional variant A is downregulated while Snail expression as a known target is enhanced. Moreover, we found that in 3D-culture vs. monolayer assays Ahcyl1 expression is downregulated in A549 spheres, suggesting its expression could be associated with a more differentiated phenotype. These results are consistent with INSECT in silico predictions about Ahcyl1 expression being modulated by TGFbeta1 and associated with cell plasticity events.
Supported by ANPCyT, CONICET and FOCEM (COF 03/11)