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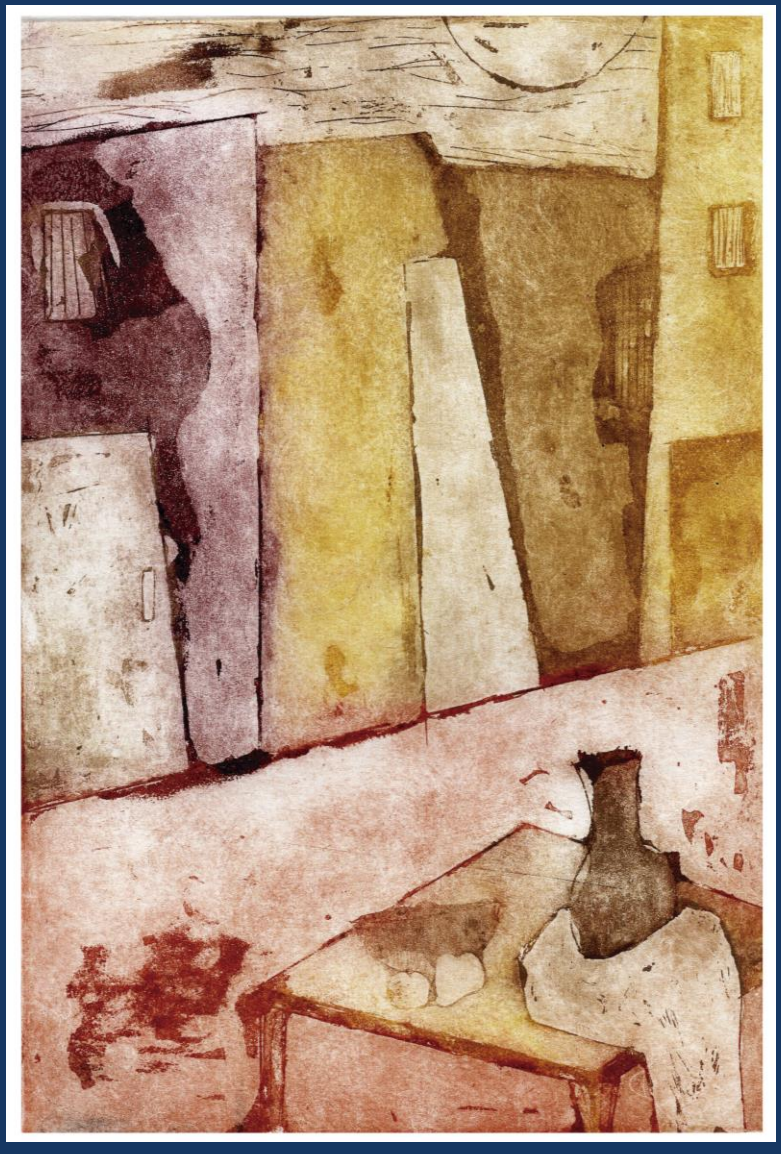

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REUNIÓN ANUAL DE SOCIEDADES DE BIOCIENCIA 2019

LXIV Reunión Anual de la
Sociedad Argentina de Investigación Clínica (SAIC)

LI Reunión Anual de la
Asociación Argentina de Farmacología Experimental (SAFE)

XXI Reunión Anual de la
Sociedad Argentina de Biología (SAB)

XXXI Reunión Anual de la
Sociedad Argentina de Protozoología (SAP)

IX Reunión Anual de la
Asociación Argentina de Nanomedicinas
(NANOMED-ar)

VI Reunión Científica Regional de la Asociación Argentina
de Ciencia y Tecnología de Animales de Laboratorio
(AACyTAL)

con la participación de
The Histochemical Society

13 - 16 de noviembre de 2019
Hotel 13 de Julio - Mar del Plata

EDITORES RESPONSABLES

Dra. Mónica Costas
Dra. Gabriela Marino
Dr. Pablo Azurmendi

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ANNUAL MEETING OF BIOSCIENCE SOCIETIES 2019

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de Ciencia y Tecnología de Animales de Laboratorio
(AACyTAL)

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November 13th – 16th, 2019
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CHIEF EDITORS

Dra. Mónica Costas
Dra. Gabriela Marino
Dr. Pablo Azurmendi

0858 - SCREENING AND IDENTIFICATION OF METACASPASE INHIBITORS, EVALUATION OF INHIBITION MECHANISM AND TRYPANOCIDAL ACTIVITY

Brian Daniel PÉREZ LÓPEZ | Emir SALAS-SARDUY | Vanina Eder ALVAREZ

IIBIO-UNSAM

Targeting proteases is a common strategy to identify new antiparasitic agents due to their essential contribution to parasite growth and development. Metacaspases (MCAs) are cysteine proteases (Clan CD) present in fungi, protozoa and plants. These enzymes, which are associated with crucial events in protozoa parasites (i.e. cell death and cell cycle progression), are absent in the human host, thus arising as attractive drug targets. To find new MCAs inhibitors bearing trypanocidal activity, we adapted a continuous fluorescent enzymatic assay to a medium-throughput format and carried out the screening of different compounds collections, followed by the construction of dose-response curves for the most promising hits. We used MCA5 from T. brucei (TbMCA5) as a model for the identification of inhibitors from the GlaxoSmithKline HAT and CHAGAS chemical boxes; two collections grouping 404 non-cytotoxic compounds with high antiparasitic potency, drug-likeness, structural diversity and scientific novelty. We also assessed a third collection of 9 compounds from Maybridge database identified by virtual screening as potential inhibitors of the cysteine peptidase falcipain-2 (Clan CA) from Plasmodium falciparum. As a result, 4 hits from the HAT and CHAGAS boxes showed modest IC50 values in the range 79-142 µM. Remarkable, HTS01959 (Maybridge collection) resulted the most potent inhibitor with IC50 of 14.39 µM; also inhibiting other MCAs from T. brucei and T. cruzi (TbMCA2= 4.14 µM, TbMCA3= 5.04 µM and TcMCA5= 151 µM). HTS01959 behaves as a reversible, slow binding and noncompetitive inhibitor of TbMCA2, where the mechanism of action includes RedOx components. Importantly, HTS01959 displays trypanocidal activity against bloodstream forms of T. brucei and trypomastigotes forms of T. cruzi, with non-cytotoxic effect on VERO cells. Thus, HTS01959 seems to be a promissory starting point to develop more specific and potent chemical structures to target MCAs from trypanosomatids parasites.

0860 - PROTEINS INVOLVED IN DNA HOMOLOGOUS RECOMBINATION REPAIR IN TOXOPLASMA GONDII: BRCA2 AND RAD51 CHARACTERIZATION

Constanza CRISTALDI | Ana María SALDARRIAGA CARTAGENA | Agustina GANUZA | Sergio ANGEL | Laura VANAGAS

INSTITUTO DE INVESTIGACIONES BIOTECNOLÓGICAS "DR. RODOLFO UGALDE", UNIVERSIDAD NACIONAL DE SAN MARTÍN

Toxoplasma gondii is an obligate intracellular parasite, belonging to the phylum Apicomplexa and is responsible of toxoplasmosis infection. Although there are treatments against toxoplasmosis, due to the toxicity of the drugs used there is an intensive search for new treatments against the parasite and innocuous to the host cell. There are conserved components of the homologous recombination DNA repair (HRR) pathway in T.gondii that could present unique characteristics which make them attractive therapeutic targets. Among them, a putative T. gondii BRCA2 was identified in silico because of the presence of conserved domains with the human homologous. In higher eukaryotes BRCA2 interacts with the recombinase RAD51, which is also present in T. gondii, generating an essential complex for the HRR. T. gondii BRCA2 and RAD51 genes were cloned and expressed in bacteria to obtain recombinant proteins used to produce specific mouse polyclonal antibodies. RAD51 was expressed as an entire recombinant protein, but for BRCA2 only the OB1 domain was expressed due to its high mass, near 480 kDa. The antibodies were titrated by ELISA, and used to detect their presence in T.gondii by Western blot (WB) and their subcellular localization by indirect immunoflourescence (IFA) either in normal conditions or using DNA damaging agents such as phleomycin and metylmethanesulfonate (MMS). The results showed no differences in the protein expression by WB in a DNA damage context, compared to non-treated parasites, for both proteins. When parasites were analyzed by IFA TgBRCA2 showed a spotted distribution along the whole parasite (nucleus included) in normal and DNA damage conditions. The antibodies obtained against these two important proteins will allow us to make progress in the understanding of the complex BRCA2-RAD51, which is fundamental to study the DNA repair by HRR observed in other eucaryotes.

0884 - HISTOLOGICAL DEMONSTRATION OF APOPTOSIS ACTIVATION IN THE LIVER FLUKE (FASCIOLA HEPATICA) FOLLOWING CLOSANTEL TREATMENT OF EXPERIMENTALLY-INFECTED SHEEP

Silvana SCARCELLA (1) | Maria Victoria SOLANA(1) | Florencia BIANCO(1) | Hugo SOLANA(1) | Daniel LOMBARDO(2)

CIVETAN CONICET (1); FCV- UBA (2)

The apoptosis can be by DNA damage, cytokine expression, etc. The study of apoptosis has application for the understanding of biological events, such as the tumorogenesis, the action mechanism to drugs, etc. For the apoptosis detection in different cell lines and tissues there are methods such as TdT-mediated dUDP nick end labelling (TUNEL) or directly the immunolocalization of Caspase-3. Closantel is an antiparasitic halogenated salicilanilide for the treatment of Fasciola hepatica infestation in farm animals. Its action mechanism is not fully known. It's known decouple the oxidative phosphorylation but the probable degree of contribution of apoptosis is unknown. In this work, were used the Caspase-3 detection and TUNEL techniques to assess the probable involvement of the closantel in the generation of apoptosis in Fasciola hepatica. Fourteen lambs were infected orally with 200 metacercariae of Fasciola hepatica. At 16 weeks post-infection, 10 lambs were treated orally with closantel (10 mg/kg.). Adult flukes were recovered from the liver of individual lambs at 0 (no treated n= 4), 24 (n= 5) and 36 h (n= 5) post treatment. The flukes were processed for usual histological analysis. There were no injuries at the controls. The F. hepatica at 24 h PT showed minor damage to the posterior end of syncytium. Those of 36 h PT lost large areas of the syncytium in the posterior and dorsal end with cell depletion in testis and vitelline follicles and the oocytes appear rounded with condensed cytoplasm, indicating apoptosis. In testis, ovary and vitelline follicles, defects in closantel-treated trematodes were aligned with failure in the energy-demanding processes of mitosis and differentiation. These changes could be attributed to anthelmintic-induced blockage of intermediary metabolism and neuromuscular paralysis. This work confirms that closantel activates apoptosis being too this phenomenon its mechanism of action.

0886 - MODE OF ACTION OF THE SESQUITERPENE LACTONE EUPATORIOPICRIN ON TRYPANOSOMA CRUZI

Orlando German ELSO(1) | Vanesa Rocio PUENTE(2) | Patricia BARRERA(3) | Miguel SOSA ESCUDERO(3) | **Valeria SULSEN** (1) | Maria Elisa LOMBARDO(2)

IQUIMEFA. UNIVERSIDAD DE BUENOS AIRES, FACULTAD DE FARMACIA Y BIOQUÍMICA (FFYB) (1); CENTRO DE INVESTIGACIONES SOBRE PORFIRINAS Y PORFIRIAS (CIPYP) (2); IHEM-UNCUYO (3)

Eupatoriopicrin is a sesquiterpene lactone isolated from Stevia maimarensis (Asteraceae), an endemic plant species from northern Argentina. This compound has shown promising trypanocidal activity and selectivity against epimastigotes, trypomastigotes and