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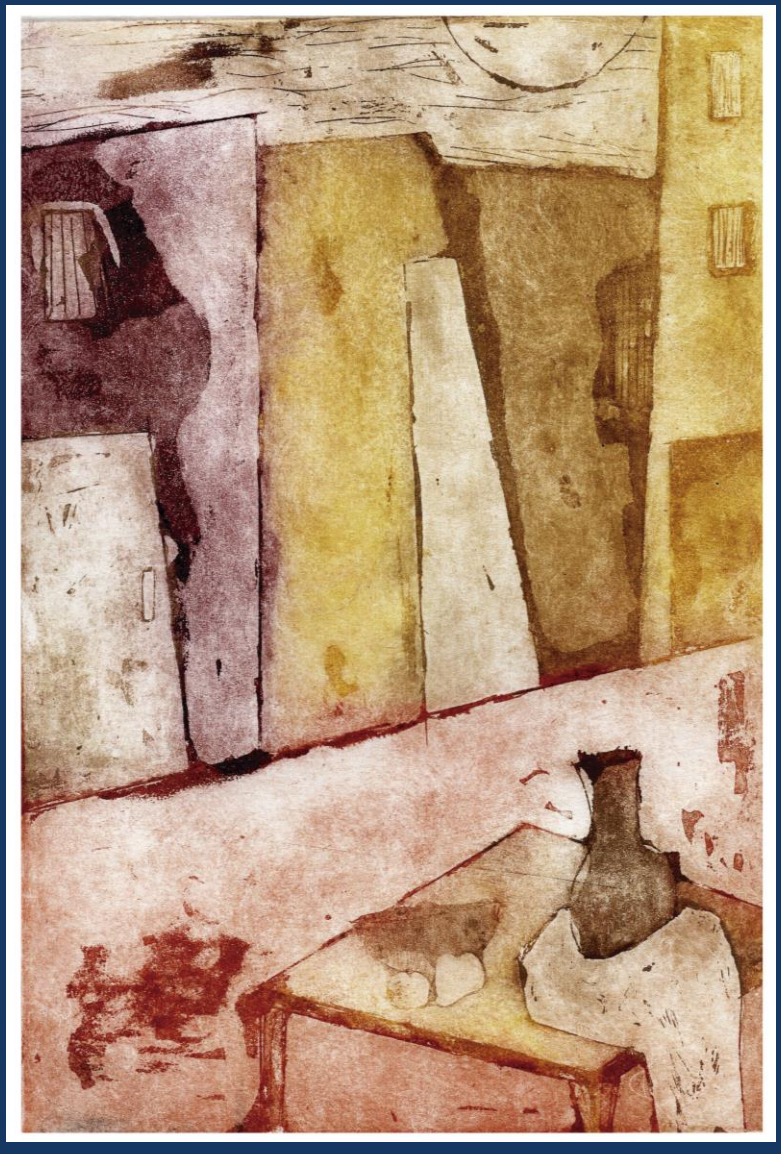

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LXIV Reunión Anual de la
Sociedad Argentina de Investigación Clínica (SAIC)

LI Reunión Anual de la
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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

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Dra. Mónica Costas
Dra. Gabriela Marino
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ANNUAL MEETING OF BIOSCIENCE SOCIETIES 2019

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(NANOMED-ar)

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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

0.6/s, n= 6, p< 0.05; K^+ 20: control 162.0 ± 11.25/s, probenecid 224.2 ± 16.3/s, n= 4, p< 0.001), whereas at 30 mM K^+, probenecid decreased MEPP frequency (Control 286.2 ± 17.3/s, probenecid 233.8 ± 10.8/s, n= 5, p<0.05). These results suggest that, at mammalian neuromuscular junction, non-vesicular endogenous ATP coming from muscle fibers through pannexins contribute to the modulation of ACh release. The increase in MEPP frequency observed at 10-20 mM K^+ when pannexins were blocked could indicate the lack of ATP/adenosine action on inhibitory receptors. On the other hand, as A2A facilitatory receptors are only activated when high adenosine concentration is present at the synaptic cleft (30 mM K^+), the reduction of MEPP frequency recorded at this K^+ concentration in the presence of probenecid, would suggest that these receptors are being less activated.

Infectología y Parasitología / Infectology and Parasitology III

Chairs: María Fernanda Franke | María Elena Nader | Carolina Poncini | Alan Talevi

0045 - ANTIPROLIFERATIVE EFFECT OF TRICLABENDAZOLE AND CLOFAZIMINE ON TOXOPLASMA GONDII GROWTH, A REPURPOSING APPROACH.

Agustina GANUZA(1) | Lucas ALBERCA(2) | Roque DIETRICH(2) | Luciana GAVERNET(2) | Alan TALEVI(1) | **Maria CORVI** (1)

INSTITUTO TECNOLÓGICO DE CHASCOMÚS (INTECH) (1); FACULTAD DE CIENCIAS EXACTAS, UNIVERSIDAD NACIONAL DE LA PLATA (2)

Abstract/Resumen: Toxoplasmosis is an infection caused by the parasite Toxoplasma gondii. Although healthy individuals present few symptoms, the disease could have a high impact in immunocompromised individuals and in congenital infection, leading to serious health problems. Although the combination of pyrimethamine with a sulfonamide is still very effective for treatment of toxoplasmosis, the use of these two drugs in immunocompromised individuals for long periods of time frequently leads to adverse reactions. As such, there is a need for alternative therapeutic options. Recently, by application of in silico drug repurposing it was reported that cisapride (gastroprokinetic agent), cinnarizine (antihistamine used to treat travel sickness), clofazimine (antimycobacterial compound), triclabendazole (antihelminthic drug) and paroxetine (antidepressant) inhibit putrescine uptake in Trypanosoma cruzi. Given that T. gondii is auxotroph for polyamines, here we evaluated these compounds on T. gondii growth in vitro. All the tested compounds presented anti-toxoplasmic effect. The calculated IC50 for paroxetine, cinnarizine and cisapride were 2.42, 3.12 and 4.72 µM, respectively. However, triclabendazole and clofazimine presented a higher selectivity towards T. gondii inhibition growth: selectivity index of 15.67 and 10.3, respectively (IC50 0.61 µM for triclabendazole and 0.3 µM for clofazimine) without showing a cytotoxic effect on host-cells. Our results suggest that target and drug repurposing are valid approaches for the study of putative antiparasitic compounds, especially for neglected diseases.

0055 - IDENTIFICATION OF POLYAMINE TRANSPORT INHIBITORS: REPURPOSING ANTIPSYCHOTIC DRUGS FOR CHAGAS DISEASE

Chantal REIGADA | Edward VALERA VERA | Melisa MARTINEZ SAYE | Mariana MIRANDA | Claudio PEREIRA

INSTITUTO DE INVESTIGACIONES MEDICAS A LANARI (UBA - CONICET)

Abstract/Resumen: In Trypanosoma cruzi, the etiological agent of Chagas disease, the uptake of polyamines constitutes a promising target to design specific inhibitors with tripanocidal effects, since it is essential for parasite survival. In a previous study, Ant4, a 9-anthracenylmethyl-putrescine conjugate, designed for cancer treatment, inhibited the polyamine transport in T. cruzi parasites and also presented a strong trypanocidal effect on trypomastigotes, the bloodstream stage of T. cruzi. Considering the effects of Ant4 in the parasite, and that is not approved for use in humans, in this work we proposed to identify, using in silico and in vitro strategies, trypanocidal drugs approved for the treatment of other diseases that have similar structure and activity to Ant4. Initially, we performed a similarity ligand-based virtual screening in the SWEETLEAD database containing world's approved drugs and natural products, using Ant4 as reference molecule. Applying this strategy, four antipsychotic tricyclic drugs were identified to be used in experimental assays in T. cruzi parasites. Three of them; promazine, chlorpromazine and clomipramine, showed to be effective inhibitors of polyamine uptake in epimastigotes and trypomastigotes. The drugs also revealed a high trypanocidal activity against amastigotes (IC50 values of 3.8, 1.9 and 2.9 µM, respectively) and trypomastigotes (IC50 values of 3.4, 2.7 and 1.3 µM, respectively) while in epimastigotes the IC50 were significantly higher (34.7, 41.4 and 39.7 µM, respectively). Taking advantage of the intrinsic fluorescence signal of Ant4 and chlorpromazine, we demonstrated that both compounds are incorporated into the parasite, suggesting the existence of additional intracellular targets. In conclusion, these polyamine transport inhibitors are promising trypanocidal drugs, in addition they are approved for use in humans, which could reduce significantly the requirements for their possible applications in the treatment of Chagas disease.

0135 - BROADENING THE SPECTRUM OF IVERMECTIN: EVIDENCES OF ITS EFFECT ON EPIMASTIGOTES OF T. CRUZI

María Daniela RUIZ | Agustina CLAUSI | Luciana LAROCCA | Verónica DE PINO | Carolina CARRILLO | **Laura FRACCAROLI**

ICT MILSTEIN - CONICET

Abstract/Resumen: Chagas disease is an endemic parasitosis originally from Latin America, caused by the protozoan Trypanosoma cruzi (T. cruzi). The current therapies are limited in efficacy and show multiple side effects. Thus, there is a need to identify new effective and specific trypanocidal strategies. Ivermectin (IVN) is a broad-spectrum antiparasitic drug of human and veterinary use. It is used for both ecto- and endo-parasite treatments and presents low toxicity in humans. These factors, along with its relative low cost, make IVN an interesting drug candidate for Chagas disease treatment. In previous studies, IVN has shown an effect against T. brucei and Leishmania in animal infection models. Beginning our evaluation of IVN as a potential trypanocidal drug, the aim of this work was to analyze the effects of IVN on T. cruzi epimastigotes and other trypanosomatids proliferation and viability. To approach this aim, we performed growth curves of epimastigotes of the Y-GFP strain in the presence of IVN (0 - 200 µM). The cultures were evaluated both by cell counting in Neubauer chamber and optical density at 630 nm for 8 days. IVN dose dependently reduced the proliferation of the parasites. The relative density and the viability (assessed by MTT) significantly decreased while duplication time increased at day 4 of culture. The IC50 calculated at day 4 of culture was 12.53 µM (10.83 - 14.49 µM). In related trypanosomatids, preliminary results showed that IVN affected the proliferation of Phytomonas Jma, with an estimated IC50 of 5.5 µM, while it did not affect to Crithidias fasciculata. The results presented herein showed that IVN affects the proliferation and viability of T. cruzi epimastigotes suggesting that Ivermectin could be a potentially viable drug to study in the Chagas disease context.