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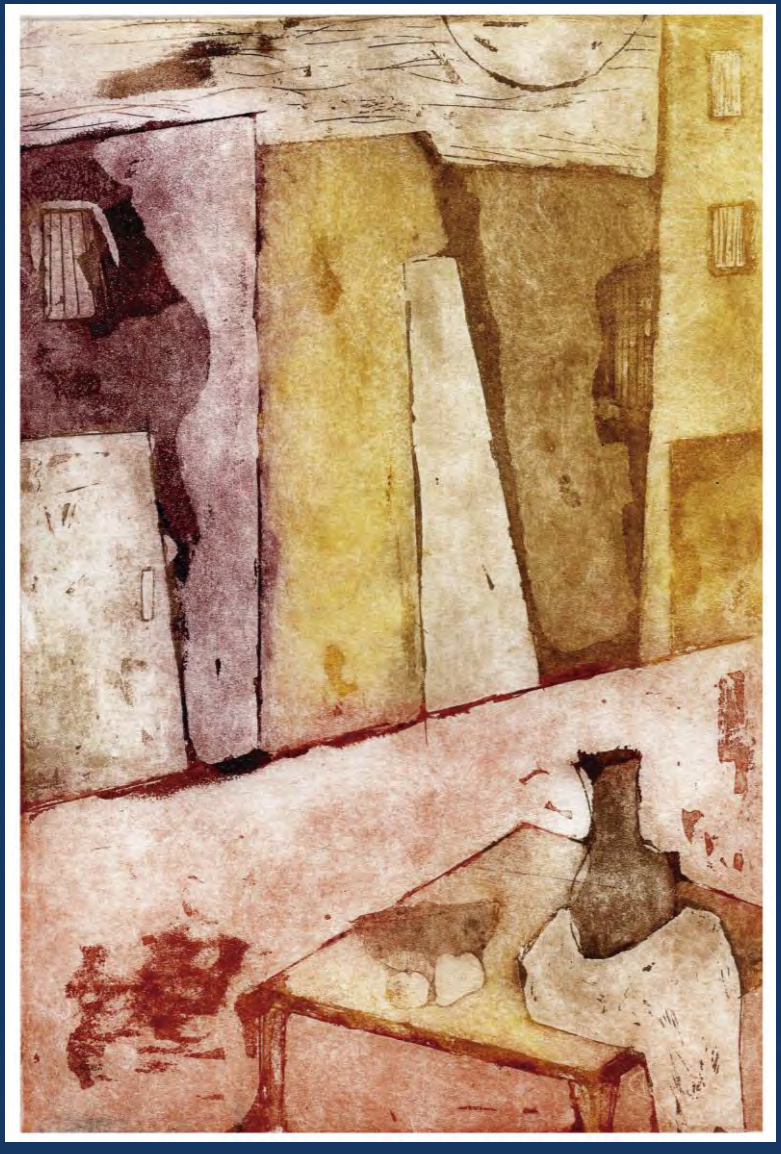

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La Tapa (Ver pág. 4)
Atardecer en la tarde
Antonella Ricagni

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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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(NANOMED-ar)

VI Regional Scientific Meeting of Asociación Argentina de Ciencia y Tecnología de Animales de Laboratorio (AACyTAL)

with the participation of
The Histochemical Society

November 13th – 16th, 2019
Hotel 13 de Julio - Mar del Plata

CHIEF EDITORS

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

effects. Eu-VAN bactericidal activity was evaluated by killing curves. VAN and free-drug Eu were assayed for comparison purposes. Eu-VAN at 4xMIC of VAN caused 99.9 % killing within 360 min and bacterial erradication was observed within 24 h, whereas VAN needed 4-fold higher concentration for the same efficacy. Free-drug polymer (Eu) exhibited limited antimicrobial activity as population of bacteria was still viable after 24 h. Eu produces switch in sign of superficial net charge in S. aureus (Z potential measure) and a concentration-dependent membrane depolarization as determined by flow cytometry using DiBAC4, a potential sensitive probe. In addition, morphological changes were observed and these were confirmed by TEM. Fluorescence microscopy using a fluorescent conjugates of VAN (BODIPY-FL®) allowed to demonstrate increased binding of VAN to S. aureus when bacteria is treated with Eu-VAN as compared to free VAN. The difference was statically significant. The interaction of the cationic polymer with the bacterial cell led to improved antimicrobial efficacy of VAN. This result provides a feasible alternative to avoid or combat antimicrobial resistance. Therefore, more studies are needed to define its potential use.

0954 - ALLOPREGNANOLONE DUAL MODULATES THE SEROTONERGIC AND GABAERGIC SYSTEM IN A RAT AGGRESSION MODEL

Maria Belen MULLE BERNEDO | Sebastina GARCIA | Victor ASTORGA | Ricardo Jorge CABRERA

IMBECU

Abstract/Resumen: The serotonergic system is involved in a wide variety of physiological and behavioral functions. Serotonergic axons have been shown to target GABAergic inhibitory neurons and vice-versa. Also, the serotonergic system is influenced by changes in plasma and brain levels of neuroactive steroids. Progesterone derivative, allopregnanolone (Allo) enhances GABAA receptors sensibility, acting as an allosteric modulator on the function of GABA. This receptor acts as heteroreceptor in serotoninergic neurons. Allo, also modulates negatively 5-HT3 receptors. This neurosteroid influences a wide range of behaviors, among others, like aggressive behavior in rodents. This work aimed to evaluate modulatory Allo effects in an aggressive behavior rat model. Male Sprague-Dawley rats 60 days old were used. On a postnatal day 60 (PND), the rats were cannulated in the 3rd ventricle (icv). On PND 66, the rats received once pCPA (300 mg/kg, i.p) injection in order to generate aggressive behavior. On PND 72, the rats were divided randomly into groups, 1) Allo; 2) Bicuculine (Bic)+Allo; 3) Bic 4) 5-HT 5) Allo+ 5-HT. Moreover, 30` before resident intruder test (RVI) receive the drug icv. The behavioral activity of all groups was video recorded and was analyzed by the researchers. Aggressive behavior was evaluated as the presence of tromping, bites, attempted mounts, and lateral threats (AB). We also measured non-social interaction (lying and sitting), social interaction (sniffing and grooming) and locomotor activity. All data were expressed as a mean+ SEM and analyzed by ANOVA I and Tukey post hoc test. Allo positively modulates the GABAergic system by decreasing aggressive behavior ($p < 0.01$). This decrease was reversed by the blockage of this system with Bicuculin ($p < 0.01$). The administration of 5HT icv did not modify the aggressive behavior induced by pCPA depletion. Moreover, the previous administration of Allo to 5HT icv significantly increased this behavior ($p < 0.05$). We conclude that Allo is a neurosteroid modulator of aggressive behavior in rats. This modulatory effect would be mediated by GABAergic and serotonergic mechanisms oppositely, thus proposing a duality in its modulatory capacity not described above, for this type of aggressive behavior in rats.

SAFE AWARD II

PHARMACOLOGY RESEARCH

Juries - Alicia Fuchs | Adrian Lifschitz | Victoria Lux-lantos | Miriam Wald

Chair - Carlos Reyes Toso

1036 - DIISOPROPYLPHENYL-IMIDAZOLE (DII): A NEW COMPOUND THAT EXERTS ANTHELMINTIC ACTIVITY THROUGH NOVEL MOLECULAR MECHANISMS.

María Gabriela BLANCO (1) | María Soledad VELA GUROVIC(2) | Gustavo Fabián SILBESTRI(3) | Andrés GARELLI(1) | Sebastián GIUNTI(1) | Diego RAYES(1) | María José DE ROSA (1)

INIBIBB-CONICET, DEPTO. BIOLOGÍA, BIOQUÍMICA Y FARMACIA-UNS (1); CERZOS-CONICET, DEPTO. BIOLOGÍA, BIOQUÍMICA Y FARMACIA-UNS (2); INQUISUR, DEPARTAMENTO DE QUÍMICA, UNIVERSIDAD NACIONAL DEL SUR (UNS)-CONICET (3)

Abstract/Resumen: Nematode parasites cause infections that affect approximately one-third of the world´s population and considerable losses in livestock and food crops. Paradoxically, the repertoire of effective anthelmintics for treating these parasitoses is very limited, as drug development has been delayed for decades. Moreover, resistance to currently available drugs is a global concern in livestock parasites and is an emerging issue for human helminthiasis. Therefore, anthelmintics with novel mechanisms of action are urgently needed. Taking advantage of Caenorhabditis elegans as an established model system for developing agents, in this project we synthesized and screened the anthelmintic potential of novel imidazolium and imidazole derivatives. We found that one of these derivatives, diisopropylphenyl-imidazole (DII), is lethal to C. elegans at both mature and immature stages. Toxicity appears to be specific because DII concentrations which are lethal to C. elegans do not induce significant lethality on bacteria, Drosophila melanogaster, and HEK-293 cells. Our analysis of DII action on C. elegans mutant strains determined that, in the adult stage, null mutants of unc-29 are resistant to the drug. Muscle expression of this gene completely restores DII sensitivity. UNC-29 was reported as an essential constituent of the levamisole-sensitive muscle nicotinic receptor (L-AChR). Nevertheless, null mutants in unc-63 and lev-8 (essential and non-essential subunits of L-AChRs, respectively) are as sensitive to DII as the wild-type strain. Therefore, our results suggest that DII effects on adult nematodes rely on a previously undescribed AChR. This novel AChR is composed by UNC-29 (a non-alfa subunit incapable of forming homomeric receptors) and other unidentified subunits. To completely elucidate its stoichiometry, we are analyzing DII resistance in different strains containing null mutations in AChR subunits. Since DII mechanism is different from those of currently used anthelmintics, it could constitute a therapeutic option when traditional anthelmintic agents fail. Interestingly, DII targets appear to be different between larvae and adults, as unc-29 null mutant larvae are sensitive to the drug. The existence of more than one target could delay resistance development. The specificity and novel mode of action of DII, which includes differential targeting in larvae and adult nematodes, support its potential as a promising drug candidate to treat helminthiasis.

1037 - ISCHEMIC CARDIOMYOPATHY AND THYROID ALTERATIONS: FROM THE ENERGETICS OF CALCIUM HOMEOSTASIS TO CARDIOPROTECTION IN RAT CARDIAC MODELS.

Matías BAYLEY(1) | Sofía LÓPEZ(1) | **María Inés RAGONE** (1) | COLABORADORES: Alicia CONSOLINI(1) | Patricia BONAZZOLA(2)

CÁTEDRA DE FARMACOLOGÍA; DEPARTAMENTO DE CS BIOLÓGICAS; FACULTAD DE CS. EXACTAS; UNLP (1); INSTITUTO DE INVESTIGACIONES CARDIOLÓGICAS, FACULTAD DE MEDICINA, UBA-CONICET (2)

Abstract/Resumen: Thyroid diseases affect cardiac Ca^{2+} homeostasis and induce long-term pathologies. The consequences of cardiac ischemia-reperfusion (I/R) are still worse in a hyper- or a hypothyroid patient. The aim of this project is to characterize the myocardial mechanisms of hyperthyroidism (HypT) and hypothyroidism (HypoT) in the postischemic dysfunction, especially the mitochondrial role in two models of stunning due to I/R. HypT rats were obtained by daily SC injection of triyodothyronine, and HypoT rats by drinking methymazol, both during 15 days. Results were compared with euthyroid rats (EuT). Ventricles were perfused in a flow calorimeter and exposed to one of two models of I/R: moderate (20 min I) or severe (30 min I) followed by 45 min R (mI/R or sI/R, respectively). Intraventricular contractile pressure (P, mmHg), diastolic contracture (ΔLVEDP) and total heat rate (Ht, mW.g-1) were measured, and the total muscle economy (Eco= P/Ht) was calculated. HypT was cardioprotector in mI/R because it increased the post-ischemic contractile recovery (PICR) and Eco with low ΔLVEDP. Clonazepam (Clzp, inhibitor of mitochondrial Na^+/Ca^{2+}-exchanger, mNCX) or 5-hydroxidecanoate (5-HD, blocker of mitochondrial ATP dependent-K^+ channels, mKATP) reduced the PICR and Eco in HypT but not in EuT. Ru-360 (blocker of mitocondrial Ca^{2+} uniporter, UCam) strongly reduced PICR and Eco in both hearts. HypT was not cardioprotector in sI/R. It was reversed by Cys-A (inhibitor of mitochondrial permeability transition pore, mPTP). HypoT was cardioprotector in mI/R and sI/R. In models, mI/R and sI/R, HypoT improved PICR and Eco and reduced ΔLVEDP, but Clzp reversed these effects. In sI/R, 5-HD, wortmanine (PI3K/Akt inhibitor) and chelerythrine (PKC inhibitor) worsened PICR and Eco in HypoT. L-NAME (NOS-inhibitor) was cardioprotector. However, adrenaline reduced the HypoT cardioprotection, and it was prevented by oral 20 mg/kg/day carvedilol (β-blocker). Conclusions: a) The HypT was cardioprotector only in mI/R, and it was due to activation of mNCX and mKATP which reduced Ca2+ overload, while in sI/R the mPTP opening cause dysfunction; b) The HypoT was cardioprotector in both models of I/R. In sI/R, cardioprotection was related to activation of PI3K/Akt and PKC pathways and reduction of Ca^{2+} overload; c) The NOS-activation and adrenaline perfusion avoided cardioprotection, but carvedilol prevents the adrenergic dysfunction.

Supported by UNLP X-795 grant.

1038 - NON-CONVENTIONAL CITOPROTECTIVE EFFECTS OF DRUGS AGAINST EXPERIMENTAL MODELS OF SEPSIS.

Julieta RONCHI | Gabriela OLEA | **Tania STOYANOFF** | COLABORADOR: María Victoria AGUIRRE

LABORATORIO DE INVESTIGACIONES BIOQUÍMICAS, HOSPITAL ESCUELA "JOSÉ DE SAN MARTÍN". UNNE.

Abstract/Resumen: Currently, sepsis is defined as an organic dysfunction caused by a deregulated host response to infection and is one of the main causes of morbi-morbility in intensive care units. This pathogenesis is complex, multifactorial and is associated with organic dysfunction and inflammation, hypoxia, microvascular disorders and injury due to apoptosis. This highlights the importance of studying new therapeutic strategies to mitigate these effects. The preliminary work of our group showed that the administration of recombinant Erythropoietin (EPOrh) attenuates cardiac lesions in a murine model of Doxorubicin-induced injury, improving both; the tisular damage and the enzymatic changes. On the other hand, there were several drugs, such as Eporh, that exert histoprotective, anti-apoptotic, anti-inflammatory, proangiogenic and/or antioxidant actions in experimental models of injury. In this sense, our field of research aims to dilucidate the cellular and molecular non-canonical mechanisms of various drugs involved in the histoprotection in pre-clinical models of sepsis. Thus EPOrh, sildenafil and dexmedetomidine (DEX) were used in experimental sepsis induced by lipopolysaccharide (LPS) and cecal ligation and puncture (CLP). We have demonstrated that the administration of EPOrh has renoprotective effects in an LPS-induced AKI model through several mechanisms: a) anti-apoptotic: by modulating the intrinsic and extrinsic pathways; b) pro-angiogenic: increasing the VEGF/VEGFR-2 pair and the expression of PeCAM-1; c) anti-inflammatory/antioxidants: by decreasing iNOS expression and inflammatory infiltration and d) attenuation of tisular hypoxia by decreasing the expression of HIF-1α. These effects are associated with the overexpression of EPO-R in the hypoxic context of the injured renal tissue. Likewise, EPOrh attenuates both pulmonary and renal injury in an experimental CLP model through the modulation of the EPO/EPO-R and VEGF/VEGF-R2 systems. Concurrently, we determined that sildenafil also mitigates pulmonary injury (ALI) and acute renal injury (AKI). Furthermore, we have established the protective dose of DEX and verified significant improvements in renal and hepatic functionality post-endotoxemia. In addition, DEX attenuates histopathological alterations in kidney, lung and liver, through the modulation of Bax/BclxL expressions. Currently, we are focused in the study of the additional molecular mechanisms involved in the histoprotection by DEX. Our next purpose in this field is the study of flavonoid's cytoprotective effects in these experimental sepsis models from native species of the Northeastern of Argentine for their potential application in phytomedicine.

RESÚMENES DE LAS COMUNICACIONES

Cardiovascular y Respiratorio / Cardiovascular and Respiratory I

Chairs: Bruno Buchholz | Nicolás Kouyoumdzian | Ana María Puyó

0165 - EFFECT OF THE INFUSION OF LIGARIA CUNEIFOLIA OR ARGENTINE MISTLETOE ON THE LIPID PROFILE AND HEMORRHEOLOGICAL PARAMETERS IN PATIENTS WITH HYPERCHOLESTEROLEMIA

Mariana Paula FERRERO (1) | Maria José SVETAZ(2) | Constanza GIACOSA(1) | Marcelo WAGNER(3) | Juan BELOSCAR(4) | Cristina Ester CARNOVALE(5) | Alejandra Nora LUQUITA(1)

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Abstract/Resumen: Ligaria cuneifolia (Lc) is a plant used in Argentine folk medicine to lower excess cholesterol and increase blood flow, improving the hemorrological profile. Previously we observed that intraperitoneal Lc-treatment in Wistar rats, leads