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

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**IX Reunión Anual de la
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acidosis and hypoglycaemia post endotoxemia. Mice demonstrated AKI by elevation of serum creatinine and renal histologic damage. Similarly, LPS-induced ALI was evident by parenchymal lung histopathologic alterations. DEX attenuates renal dysfunction ($p < 0.01$) and ameliorates kidney and lungs histopathologic changes. Additionally, DEX administration caused a decreased in the Bax/Bcl-xL ratio within the 24h post LPS accompanied by a significant increase in VEGF expression. This study demonstrates that DEX exerts protective effects in AKI and ALI in endotoxemic mice through the reduction of Bax/Bcl-xL ratio and the regulation of the VEGF expression.

Farmacología/ Pharmacology IV

Chairs: Andrea Errasti | Alejandro Español

0164 - HIGH-THROUGHPUT SCREENING ASSAY FOR CAMP TRANSPORT INHIBITORS: SEARCHING FOR A NEW DRUG FOR PDAC TREATMENT.

Ramiro Hector CERVIÑO | Natalia GÓMEZ | Samanta Nerea GANCEDO | Carlos DAVIO | Agustín YANEF

ININFA, UBA-CONICET

In a previous work, we validated the inhibition of MRP4-dependant cAMP extrusion process as a promising therapeutic strategy for pancreatic ductal adenocarcinoma. MRP4 inhibition abrogated proliferation in vitro by both, augmenting intracellular cAMP and diminishing extracellular cAMP. In this work we sought to study the activity of a large series of compounds as cAMP transport inhibitors. In view of this objective, we first analyzed the available information about the inhibitory effect of different molecules on MRPs and classified them according to their chemical structure and their transporter-substrate specificity. Since the data set of cAMP transport inhibitors is scarce, we developed a microplate high-throughput Förster resonance energy transfer (FRET) assay that monitors the real-time kinetics of intracellular cAMP levels in cell monolayers, using the EPAC-SH187 biosensor. We established a HEK293T-EPAC-SH187 clone that stably expresses this sensor, which exhibited a wide dynamic range and high sensitivity (2-fold delta FRET in a concentration range of 0.01–500 μ M cAMP). Using this technique, we analyzed 60 compounds, with diverse chemical structures and pharmacological uses, which were previously identified in literature as substrates or inhibitors of MRP4. We identified 25 compounds that functioned as inhibitors of cAMP transport and characterized them by performing concentration-response experiments. These set of compounds include traditional MRP4 inhibitors as probenecid and MK571, channel blockers, protease inhibitors, nucleotide analogs and non-steroidal anti-inflammatory drugs. The emerging results will serve as a basis for the further development of specific inhibitors of MRP4-mediated cAMP transport potentially applicable in the treatment of PDAC.

0310 - AT1 RECEPTORS IN STRIATUM DA-UPTAKE: CRUCIAL ROLE AND RELEVANCE IN AN AMPHETAMINE-SENSITIZATION MODEL OF SCHIZOPHRENIA

Oswaldo Martin BASMADJIAN (1) | Antonella E MONTEMERLO(2) | Gustavo A. RIVAS(2) | Gustavo BAIARDI(3) | M. Dolores RUBIANES(2) | Claudia BREGONZIO(1)

UNC, FCQ, DEPARTAMENTO DE FARMACOLOGÍA - IFEC, CONICET (1); INFIQC-CONICET, DEPARTAMENTO DE FÍSICOQUÍMICA, FACULTAD DE CIENCIAS QUÍMICAS, UNC (2); IIBYT, CONICET, UNC (3)

Limbic dopamine (DA) hyperactivity, a hallmark of amphetamine (AMPH) exposure, it is considered as a neurochemical feature involved in the expression of schizophrenic positive symptoms. DA

neurotransmission dynamics is regulated by the uptake of extracellular transmitter at presynaptic neurons through specific transporter. Angiotensin II, through AT1 receptors (AT1-R), modulates DA neurotransmission at limbic areas. Herein, we studied AT1-R involvement after AMPH exposure on: a) development and expression of behavioral sensitization, b) in vitro striatum DA uptake. To these purposes male Wistar rats (250-300 g) were daily administered with d-AMPH (2.5 mg/kg i.p.) for 5 days. After 3 weeks of withdrawal, the behavioral sensitization was evaluated measuring locomotor activity. The AT1-R blocker, Candesartan (CV 3 mg/kg p.o.), was administered daily for 10 days, starting 5 days prior to the first AMPH injection in the prevention sensitization protocol. In the reversion protocol, either, CV or aripiprazole (antipsychotic drug widely use partial agonist of D2 receptors), were administered for 5 days starting 2 weeks after the last AMPH injection. DA uptake was measured in homogenized striatum using an electrochemical sensor, based on glassy carbon electrode modified with carbon nanotubes and polyethylenimine by amperometry. The results were analyzed by 2-way ANOVA followed by Bonferroni test or t-test. We found that behavioral sensitization was prevented and reversed by AT1-R blockade more efficiently than aripiprazole. Moreover, 5 days of CV administration increased DA uptake fact that could account for the behavioral results. We conclude that the lesser DA signaling, as a result of the increasing of its uptake, would explain the beneficial effects of AT1-R blockade in the behavioral neuroadaptations induced by AMPH.

0328 - POTENTIALLY INAPPROPRIATE MEDICATION USE IN OLDER ADULT AFFILIATES OF A SOCIAL SECURITY INSTITUTE IN CORRIENTES CITY. 2018

Maria Teresa ROCHA | Mirta Liliana MIEREZ | Sergio Daniel MORALES | María Carla ZIMMERMANN | Lorena DOS SANTOS ANTOLA

UNIVERSIDAD NACIONAL DEL NORDESTE. FACULTAD DE MEDICINA

To identify potentially inappropriate medication in older adults' affiliates of a Social Security Institute in Corrientes city. Observational descriptive transversal study, also classified as a prescription-indication medications usage study. MPI prescriptions classified as "non clinical evidence for indication" were considered. Based on STOPP-START criteria, 60 years and older adults with polymedication (more than four drugs) belonging to the Social Security Institute of Corrientes city during 2018 were included in the present study. Variables analyzed: sex, age, drug prescription and diagnosis. Were included 192 prescription; with an average of seven drugs per patient (4-21 drugs range), age average 68 years old (60-91 age range), 61% male (n=118). More frequent diagnosis: hypertension, dyslipidemia, diabetes mellitus, hypertensive cardiopathy, gastropathy and ocular diseases. Were identify 28 MPI: multivitamin B complexes (8) associated to paresthesia, muscle cramps, hypopotassemia, and others with non-precise indication; beta-escin (3) for varicose veins; unproteneized calf blood extract (3) for diabetes retinopathy and corneal dystrophy; ascorbic acid (2) with no diagnosis association; silymarin (1) for diabetes; vitamin E (1) for irritable bowel; purified flavonoids (1) for irritable bowel; and others with no precise diagnosed indication (6). In 10% patients (n=20) MPI was detected, drugs with no scientific evidence or with no clinical relation to the patient diagnosis. MPI in Elder adults, who are habitually polymedicated due to their multiple pathologies, increases the risk to adverse effects or harmful drugs interactions and expose patients to a higher morbidity and mortality, also increasing health care expenses.

0365 - CHARACTERIZATION OF EXOSOME-LIKE VESICLES DURING DRUG TREATMENT OF CYST ECHINOCOCCOSIS

M. Celeste NICOLAO* | Magalí B COCCIMIGLIO* | Christian R. RODRIGUEZ* | Andrea Carina CUMINO