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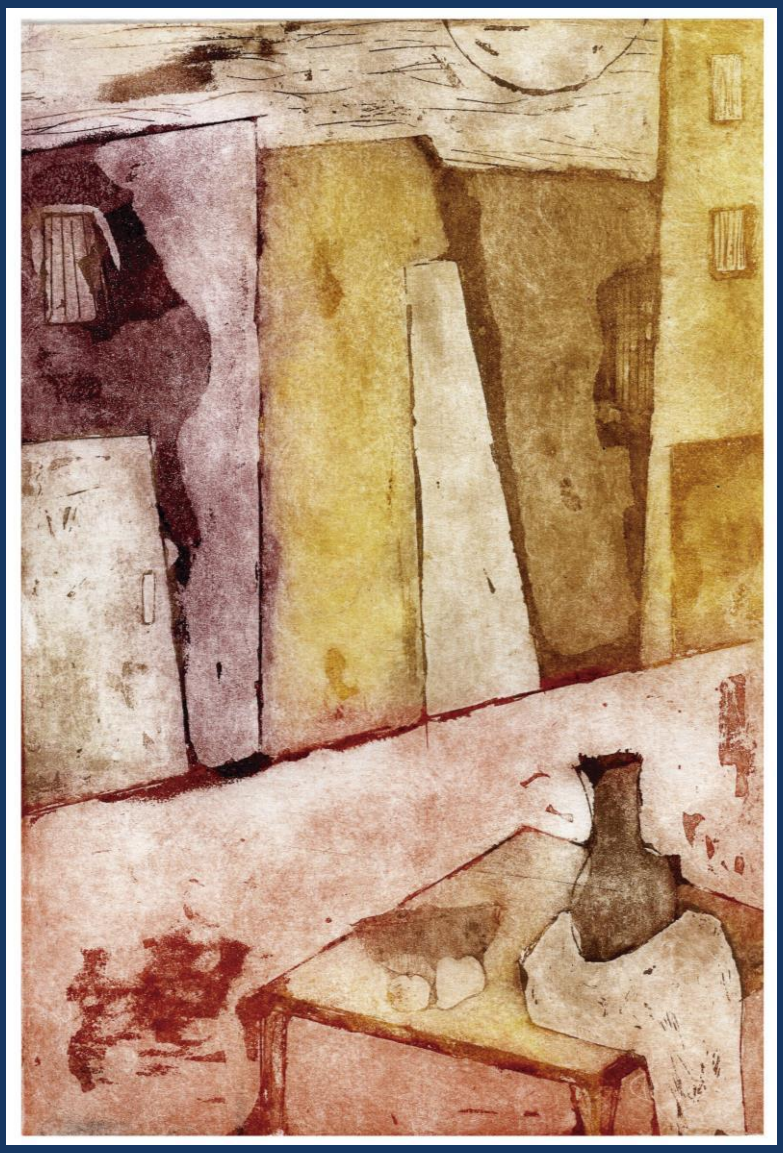

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La Tapa (Ver pág. 4)
Atardecer en la tarde
Antonella Ricagni

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medicina
BUENOS AIRES, VOL 79 Supl. IV - 2019

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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CHIEF EDITORS

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

Stx2 in combination with STEC and free fecal Stx2 in stool culture considerably can improve diagnosis. Supported by ANPCyT (PICT 0617), CONICET (PUE2017-IFIBIO Houssay) and Universidad de Buenos Aires (UBACyT 2017) grants.

0231 - ELIGLUSTAT, AN INHIBITOR OF GB3 RECEPTOR SYNTHESIS, PROTECTS HUMAN MICROVASCULAR ENDOTHELIAL CELLS FROM SHIGA TOXIN TYPE 2 CYTOTOXICITY.

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Abstract/Resumen: Hemolytic Uremic Syndrome associated to Shiga toxin (Stx)-producing E. coli infection is the most common cause of acute renal failure (ARF) in children in Argentina. Stx2 binds the globotriaosylceramide (Gb3) receptor and causes direct damages on human renal microvascular endothelial cells (HGEC). In this work, we assayed the action of a Gb3 synthesis inhibitor, Eliglustat (EG), to prevent the Stx2 cytotoxicity on human renal cells. Cell viability was analyzed by neutral red uptake and data are expressed as mean ± SEM. Cell morphology analysis was evaluated by light microscopy after staining with H&E. Cell counts were performed on five fields and cell area values were obtained using Image J software. Necrosis and apoptosis were detected by flow cytometry after Annexin V-FITC/PI double staining assay. Non-cytotoxic concentrations of EG were established on HGEC treated with EG (0.05 – 50 µM) for 120 h. While EG (50 µM) caused a significant decreased of cell viability (8.3 ± 0.9% vs. Ctrl: 100 ± 2.7 %, n= 3, $p<0.05$), EG (0.05 – 25 µM) did not exhibit any cytotoxic effect. Next, HGEC were pre-treated with non-cytotoxic EG concentrations at different times (2, 4, 6, 24 and 48 h) and then incubated with Stx2 (0.5 ng/ml) for 72 h and in the presence of EG. At all the times, EG (0.5 - 10 µM) prevented the decrease in HGEC viability caused by Stx2 (n= 5, $p<0.05$) and pre-incubation with EG (5 µM) for only 2 h was enough to protect the HGEC viability in about 73 %. The maximum protection (100 %) was obtained after 24 and 48 h of pre-treatment with 5 µM EG (EG 24 and 48 h: 100.0 ± 2.6 vs. Stx2: 49.0 ± 7.9 %, n= 5, $p<0.05$). Furthermore, EG (5 µM, 24 h) prevented the cell detachment in 80 % and the swelling in 81 %. Finally, a significant prevention (86 %) of necrosis induced by Stx2 was obtained with EG (1 µM, 24 h). We propose EG as a therapy to avoid the renal damage and the consequent ARF.
Supported by ANPCyT (PICT 0617), CONICET (PUE2017-IFIBIO Houssay) and UBA (UBACyT 2017) grants.

0376 - POTENTIAL ROLE OF INTERLEUKIN 10 ON THE EFFECTS OF FENOFIBRATE IN AN EXPERIMENTAL MODEL OF CHAGAS DISEASE.

Maria Jimena RADA (1) | Martín DONATO(2) | Azul Victoria PIERALISI(1) | Ágata Carolina CEVEY(1) | Federico Nicolás PENAS(1) | Ricardo J GELPI(2) | Catalina ALBA SOTO(1) | Gerardo Ariel MIRKIN(3) | Nora Beatriz GOREN(1)

INBIRS, CONICET, FAC. MEDICINA-UBA (1); INSTITUTO DE FISIOPATOLOGÍA CARDIOVASCULAR, DEPARTAMENTO DE PATOLOGÍA, FACULTAD DE MEDICINA, UBA (2); IMPAM (UBA-CONICET) (3)

Abstract/Resumen: Chagas disease, caused by Trypanosoma cruzi (Tc) infection, is conditioned by the presence of the parasite and the development of an inflammatory response. PPARa ligands, such as fenofibrate (fen) modulate inflammation and restore ventricular function. Interleukin 10 (IL10) is produced by a variety of cells and plays an important role in the resolution of inflammatory processes. We evaluated the potential role of IL10 in the effects of fen on the modulation of the immune response and on cardiac remodeling and function, in BALB/c IL10 knockout (IL10-/-) mice infected with a non-lethal Tc strain. The ejection fraction (EF) and the shortening fraction (SF) were measured by echocardiography, which were diminished in Tc in comparison with uninfected mice ($p<0.05$) at 4 weeks post infection (wpi). Fen treatment was given from the 5th to 9th wpi. When the treatment finished, EF and SF were evaluated again, fen restored them to levels of uninfected mice ($p<0.05$). The expression of IL6, TNFa and NOS2 was analyzed at 9 wpi in the heart, using RTq-PCR. Infection increased the expression of IL6, TNFa and NOS2 ($p<0.05$), and fen inhibited them ($p<0.05$). While Tc infection induced the release of IL17, IL6 and TNFa to serum (ELISA $p<0.05$), fen inhibited it ($p<0.05$). The inflammatory reaction was also studied in heart sections. Fen was not capable to decrease the inflammatory infiltrates neither fibrosis (p= NS) in IL10-/- mice. Furthermore, expression of the M2 profile markers was evaluated in the heart of IL10-/- mice. Fen did not modify the expression of Mannose Receptor, FIZZ and YMI (RTq-PCR p= NS) unlike what had been observed for these markers in wild type mice. These results suggest that IL10 is required to induce an M2 profile and modulation of fibrosis and inflammatory infiltrates by fen. On the other hand, fen effects on heart function and modulation of proinflammatory mediators seem to be IL10-independent. Therefore, fen exerts IL10-dependent and IL10-independent effects.

0384 - A TRANSCELLULAR GB3 DEPENDENT PATHWAY IS MAINLY RESPONSIBLE FOR SHIGA TOXIN-2 CYTOTOXICITY AND TRANSLOCATION ACROSS HUMAN INTESTINAL EPITHELIAL CELLS INFECTED WITH E. COLI O157:H7

Nicolas GARIMANO | Maria Marta AMARAL | Cristina IBARRA

LABORATORIO DE FISIOPATOGENIA, IFIBIO-HOUSSAY (UBA-CONICET), FACULTAD DE MEDICINA-UBA

Abstract/Resumen: Shiga toxin-2 (Stx2) is produced and released by E. coli O157:H7 (O157:H7) into the intestinal lumen after colonization, and is able to translocate to the circulatory system and reach target cells causing hemolytic uremic syndrome. Our aim was to elucidate which pathways were involved in Stx2 endocytosis and translocation across intestinal cells infected with STEC. HCT-8 cells grown on 96-well plates were preincubated with specific endocytosis inhibitors such as Eliglustat (EG), Dynasore (DY), MßCD or Amiloride (AM). Then, cells were washed and incubated for 4 h with 100 ng/ml Stx2 alone or in the presence of O157:H7 mutant lacking stx2 gene (O157:H7Ðstx2). Stx2 uptake was measured by flow cytometry and its cytotoxic effect by neutral red uptake assay. Translocation of Stx2 was evaluated by inhibitor preincubation of HCT-8, grown as monolayers on Millicell inserts, and incubated with O157:H7Ðstx2+ Stx2. Then Stx2 cytotoxicity was quantified in lower chamber media by neutral red uptake, To analyze inhibitors effect on bacteria attachment, bacterial adherence assays were performed on HCT-8 monolayers cultured on 24-wells plates. EG caused the maximum decrease of Stx2 cytotoxic activity, followed by MßCD. AM and DY significantly neutralized Stx2 cytotoxicity but only in presence of O157:H7Ðstx2. Furthermore, Stx2 uptake was reduced when cells were pre-incubated with EG or MßCD, compared to DY or AM ($p<0.05$), indicating that Stx2 uptake may depend on Gb3 receptor, and, to a lesser extent, on cholesterol, which is consistent with a necessary interaction between Stx2 and its receptor to cause cytotoxicity. Moreover, both dynamin-dependent endocytosis and Gb3-independent macropinocytosis became relevant only when bacteria were present, suggesting that these mechanisms are sensible to bacterial infection. Taken together, our study suggests that the mechanisms responsible for enhanced cytotoxicity and transcytosis during infection may have the same endocytic origin.

0397 - ANTIBACTERIAL ACTIVITY OF EXTRACTS OF ILEX PARAGUARIENSIS ST. HIL AGAINST METHICILLIN-RESISTANT AND METHICILLIN-SENSITIVE STAPHYLOCOCCUS AUREUS