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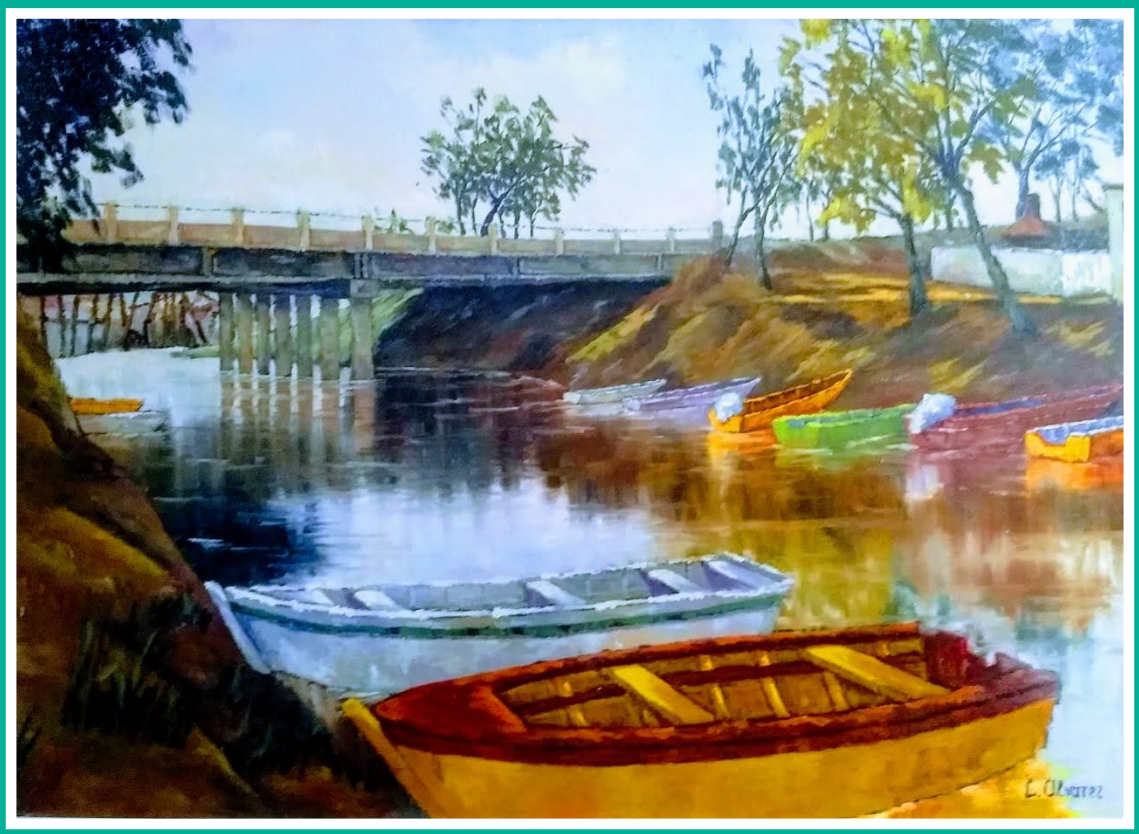

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LXV REUNIÓN ANUAL DE LA
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10-13 de noviembre de 2020

EDITORES RESPONSABLES
María Cristina Carrillo
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the generation of reactive oxygen species (ROS) and the induction of autophagy. Neutrophils were obtained from heparinized peripheral blood from HD and tuberculosis patients (TB) and cultured (2x10^{6}cells/ml) with a *Mycobacterium tuberculosis* lysate (*Mtb*-Ag, 10µg/ml) ± PGE2 (2µM). ROS production and PD-L1/PD-L2 surface expression were determined by flow cytometry. Confocal microscopy and flow cytometry were used to evaluate autophagy levels. P-values < 0,05 were considered significantly different.
We found that *Mtb*-Ag stimulation increased PD-L1 expression on neutrophils from HD (p=0,041, Ag-stimulated *vs.* unstimulated neutrophils) and PGE2 decreased it (p=0,041). Additionally, we measured significantly lower PD-L1 levels on *Mtb*-Ag stimulated neutrophils from TB patients than on HD´s stimulated cells (p=0,014). Besides, neither *Mtb*-Ag nor PGE2 treatment modulated PD-L2 expression on human neutrophils. Moreover, we observed that PGE2 did not modify ROS production in *Mtb*-Ag stimulated neutrophils. Furthermore, significant higher levels of autophagy were detected in *Mtb*-Ag stimulated neutrophils from HD as compared to TB patients (p=0,042) but PGE2 treatment did not modify these levels. Taken together, our findings indicate that PGE2 treatment could alter PD-L1 surface expression on HD´s neutrophils, but had no effect on the levels of autophagy induced by *Mtb*-Ag, at least in our experimental conditions. Therefore, further experiments are required to determine the precise role of PGE2 on human neutrophils during active tuberculosis.

414. (423) **EFFECT OF PGE2 ON THE FUNCTIONS OF NEUTROPHILS DURING HUMAN TUBERCULOSIS**

Martin C[1,2], Pellegrini JM[1,2], Morelli MP[1,2], Tateosian NL[1,2], Amiano NO[1,2], Ciallella L[3], Palmero DJ[3], García VE[1,2].
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Neutrophils have been associated with tuberculosis (TB) protection but also with excessive inflammatory burden. Previously we showed that PGE2 decreased CD11b expression in *Mtb*-Ag stimulated neutrophils from healthy donors (HD). Here we investigated the potential role of PGE2 on human neutrophils´ response during active TB. We evaluated the expression of immunoreceptors (PD-L1, PD-L2), the generation of reactive oxygen species (ROS) and the induction of autophagy. Neutrophils were obtained from heparinized peripheral blood from HD and tuberculosis patients (TB) and cultured (2x10^{6}cells/ml) with a *Mycobacterium tuberculosis* lysate (*Mtb*-Ag, 10µg/ml) ± PGE2 (2µM). ROS production and PD-L1/PD-L2 surface expression were determined by flow cytometry. Confocal microscopy and flow cytometry were used to evaluate autophagy levels. P-values < 0,05 were considered significantly different.
We found that *Mtb*-Ag stimulation increased PD-L1 expression on neutrophils from HD (p=0,041, Ag-stimulated *vs.* unstimulated neutrophils) and PGE2 decreased it (p=0,041). Additionally, we measured significantly lower PD-L1 levels on *Mtb*-Ag stimulated neutrophils from TB patients than on HD´s stimulated cells (p=0,014). Besides, neither *Mtb*-Ag nor PGE2 treatment modulated PD-L2 expression on human neutrophils. Moreover, we observed that PGE2 did not modify ROS production in *Mtb*-Ag stimulated neutrophils. Furthermore, significant higher levels of autophagy were detected in *Mtb*-Ag stimulated neutrophils from HD as compared to TB patients (p=0,042) but PGE2 treatment did not modify these levels. Taken together, our findings indicate that PGE2 treatment could alter PD-L1 surface expression on HD´s neutrophils, but had no effect on the levels of autophagy induced by *Mtb*-Ag, at least in our experimental conditions. Therefore, further experiments are required to determine the precise role of PGE2 on human neutrophils during active tuberculosis.

415. (448) **PLATELETS-MONOCYTES AGGREGATES IN COVID19 PATHOGENESIS**

Paletta AL[1], Di Diego García F[1], García J[2], Cisneros JC[2], Varese A[1], Cabrerizo G[1], Mazzitelli I[1], Ludueña G[3], Finochieto P[3], Bleichmar L[1], López Malizia A[1], Pérez P[1], Leicaj MJ[1], Adamczik A[1], Geffner J[1], Remes Lenicov F[1], Ceballos A[1]
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2. Hospital de Infecciosas Francisco Javier Muñiz
3. Hospital de Clínicas José de San Martin

There is an urgent need to understand the pathogenesis of coronavirus disease 2019 (COVID19). In particular, thrombotic complications in patients with COVID19 are common and contribute to organ failure and mortality. It has been reported that COVID19 patients present increased platelet activation. Our aim was to evaluate if activated platelets from COVID19 patients form aggregates with monocytes and modulate their activation and functionality.
Samples from whole blood and PBMCs were obtained from healthy donors or COViD19 patients. PBMCs were purified by ficoll-paque and washed platelets were obtained from plasma by centrifugation with 200 nM of prostaglandin I_2. Phenotype and cytokine production was evaluated by flow cytometry and ELISA. The viral production was measured by cytopathic effect in Vero cells.
We observed that COVID19 patients presented an increased percentage of platelet-monocyte aggregates compared to control samples (7,1 ± 1,9, n=10; 44,3 ± 3,9, n=30, p<0,0001). We did not observe a correlation between platelet-monocyte aggregates and severity of the disease. When we analyzed the functionality of monocytes we found that COVID19 patients presented an increased production of IL8 (n=4, p<0,05) in monocytes aggregated with platelets but not of TNFα and IL6 (n=6).
We also evaluated the role of platelets in the dissemination of the virus. Interestingly, we observed that COVID19 platelets but not control platelets, inhibited the infection of SARS-CoV-2 in Vero cells (n=2, p<0,05).
These results show that patients COVID19 present increased platelet-monocyte aggregates. Further studies are required to evaluate the role of these aggregates and platelets in SARS-CoV-2 pathogenesis.

416. (452) **IMMUNE ALTERATIONS IN ARGENTINE PATIENTS WITH CONGENITAL UREA CYCLE METABOLIC DISORDERS**

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3. Fundación para el Progreso de la Medicina, Córdoba, Argentina.
4. Sección Enfermedades Metabólicas, Hospital de Niños de la Santísima Trinidad, Córdoba, Argentina.

Background. Urea Cycle Disorders (UCD) comprise a group of metabolopathies sharing similar clinical phenotypes, in which acute hyperammonemia (HA) crises often occur. Among others, intercurrent infections have been empirically proposed as the main precipitants. Moreover, acute HA events following infections are clinically different from those triggered by other precipitants, representing a distinct clinical entity with increased morbidity. As infections are concurrent with HA events, we hypothesized that HA may *per se* induce an immunocompromised state that would be causal of the observed recurrent infections.
Methods. Different phenotypic and functional immune function parameters were assessed in UCD patients and healthy control volunteers. *In vitro* lymphoproliferation against different polyclonal and memory recall cell antigens, T helper cell subset frequencies, cytokine secretion in culture supernatants, total immunoglobulin serum levels, and the glycosylation status of leukocyte cell surface proteins were assessed.