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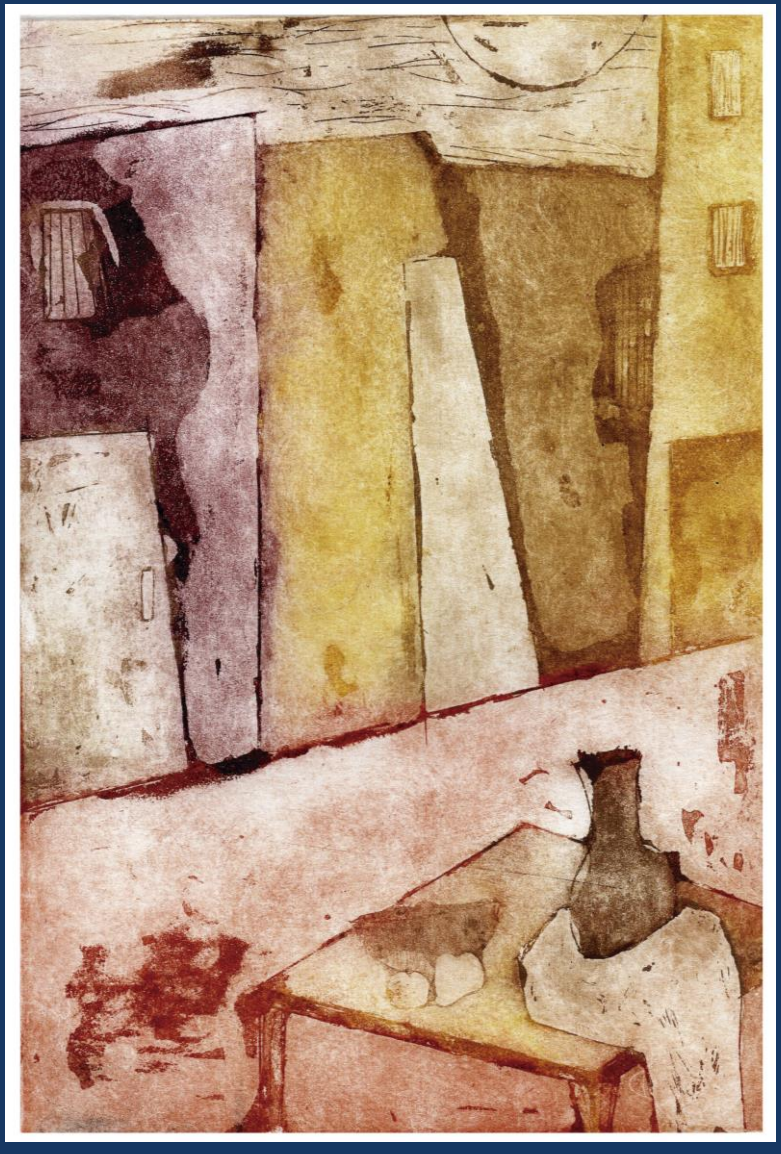

MEDICINA

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Porphyromonas gingivalis (Pg) is a prevalent pathogen of periodontal disease that was implicated in adverse pregnancy outcome although the mechanisms involved are still unclear. The aim of this study was to examine the effect of lipopolysaccharide from (Pg-LPS) on trophoblast cell function and trophoblast-neutrophil interaction. Human trophoblastic cell line Swan-71 was treated with Pg-LPS (10 ng/ml). Cytokine and chemokine expression was evaluated by RTqPCR and ELISA, glucose uptake by flow cytometry using the fluorescent analogue 2-NBDG and cell invasion assessed in Matrigel-covered transwells. Peripheral blood neutrophils were purified from healthy donors and cultured with conditioned media of trophoblast cells pretreated (PgLPS-CM) or not with LPS (TbCM); apoptosis was determined by fluorescence microscopy and CD11b and reactive oxygen species (ROS) were evaluated by flow cytometry. Regulatory T cell induction was evaluated after 48h of neutrophil-PBMC coculture. Pg-LPS treatment reduced trophoblast cell invasion, glucose uptake and modulated cytokine production (IL1ß; secretion X ± SE basal 11.4 ± 4.3; Pg-LPS 21.4 ± 5.4; $p<0.05$). PgLPS-CM induced neutrophil activation with higher CD11b expression and ROS synthesis (basal Neutrophil: 13,930 ± 2,830; Neutrophil+TbCM: 10,721 ± 2,298 Neutrophil+PgLPS-CM: 19,816 ± 3,543; $p<0.05$). Neutrophil exposed to TbCM favored the induction of CD4+ Foxp3+ T cell after 48 h of coculture with PBMCs. There was no Treg induction when neutrophils were preconditioned with PgLPS-CM (% CD4+FoxP3+cells PBMCs-Neutrophil: 3.8 ± 0.6; PBMCs-TbCM Neutrophil: 10.0 ± 3.4 and PBMC-PgLPS-CM Neutrophil: 5.7 ± 0.9 %; $p<0.05$). In line with this result, lower percentage of Foxp3-GFP+ Treg cells within CD4+ cells is observed in implantation sites of WT mothers treated at 6.5 gestation day with PgLPS compared with control mice. PgLPS impairs trophoblast cell function and abolishes their deactivating effect on neutrophils. This might contribute to the pathogenic mechanisms of Pg infection during placentation.

0761 - INTERPLAY BETWEEN VIP AND MTOR IN TROPHOBLAST CELL NUTRIENT UPTAKE. IMPACT ON THE TROPHOBLAST-IMMUNE INTERACTION

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Abstract/Resumen: The transport of nutrients by cytotrophoblast cells regulates placental metabolism throughout pregnancy. The mammalian target of Rapamycin (mTOR) functions as a placental growth signaling sensor and modulates nutrient transporters expressed on trophoblast cells (Tb). A decreased placental mTOR activity was reported in pregnancies complicated by placental insufficiency and intrauterine growth restriction. We have previously shown that the vasoactive intestinal peptide (VIP) stimulates human cytotrophoblast cell glucose and amino acid uptake along with increased GLUT1/3 and SNAT1 expression. Accordingly, a murine pregnancy model with VIP-deficient Tb cells presented reduced fetal weight at day 14.5. Here we deepened into the mechanisms of nutrient transport induced by VIP in cytotrophoblast cells focusing on the interplay between exogenous/endogenous VIP and mTOR activity. Also, based on the close regulatory interaction of cytotrophoblast cells and maternal leukocytes at the early maternal-placental interface, we explored glucose uptake by monocytes conditioned by VIP and Tb cell factors. The human Tb cell lines Swan-71/BeWo were used. VIP knocking-down was carried out with a VIP siRNA. System A activity was measured by 14C-MeAIB incorporation and VIP/mTOR expression by qRT-PCR and flow cytometry. mTOR phosphorylation was studied by western blotting. Glucose uptake in CD14+ monocytes isolated from peripheral blood was assessed by flow cytometry using the fluorescent analog 2-NBDG. VIP stimulated Na+-dependent 14C-MeAIB uptake in Tb cells ($n= 4$; $p<0.05$) and induced mTOR phosphorylation ($n= 3$; $p<0.05$). In VIP-knocked down Tb cells, mTOR mRNA and protein expression was reduced ($n= 3$; $p<0.05$). Finally, VIP and Tb conditioned media modulated glucose uptake by monocytes. Our findings support an interplay between endogenous/exogenous VIP and mTOR in nutrient uptake by Tb cells. A metabolic conditioning of maternal leukocytes by trophoblast cells is also proposed.

0878 - HIPPOCAMPAL HORMONE RECEPTORS EXPRESSION IN LATE PREGNANT AND LACTATING RATS: EFFECT OF MILD HYPERTHYROIDISM

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Abstract/Resumen: Thyroid disorders are associated with anxiety, depression and disturb responses to stress. The effect of stress is associated with functional changes in hippocampus (HpC) and hypothalamus by activating the hypothalamic-hypophysis-adrenal axis (HHA) and glucocorticoid release induced to stress. This response is physiologically attenuated during lactation. We found that mild hyperthyroidism (HyperT) increases stress-induced serum prolactin (PRL) and corticosterone secretion in lactating rats suggesting that HHA remains activated in lactation. To explore possible causes of this effect we studied the expression of thyroid receptors (TR), the long isoform of PRL receptor (PRLRl), members of the PRL signaling pathway, estradiol receptor (ER) and glucocorticoid receptor (GR) in HpC of Wistar female rats in different reproductive states (day 19 of gestation (G19), 2 (L2, early lactation) and 12 (L12) of lactation) in control (Co) and HyperT rats. Mild HyperT was induced with T4 (0.1 mg/kg/day, s.c.), a dose that allows the maintenance of lactation. HpC mRNA was obtained and the expression of receptors TRa1, TRa2, TRb1, TRb2, ERa, GR and PRLRl and members of the PRL signaling pathway (STAT5b, SOCS1 and SOCS3) was determined by RT-qPCR. HpC mRNA content of TRs, STAT5b (activator of PRL signaling) and SOCS1 (supressor of PRL signaling) decreased from G19 to L12 in Co and HyperT rats ($p<0.05$). HyperT induced increases of TRa2 ($P< 0.05$ vs Co) and TRb2 in L2 ($p< 0.01$ vs. Co) without changes in others isoforms. HyperT increased STAT5b in G19 ($p<0.05$ vs. Co). ERa and PRLR mRNAs were unchanged by treatment or reproductive state while GR increased in L12 in both groups ($p<0.05$ vs. G19).These results indicate a physiological decline in HpC responsiveness to thyroid and PRL hormones in the transition from pregnancy to lactation in Co, while the increases observed in TRa2, TRb2 and STAT5b described in HyperT rats may be involved in the persistence of high HHA axis reactivity.

Endocrinología / Endocrinology III

Chairs: María Sonia Baquedano | Silvina Gutiérrez Oschmann

0066 - THE PHTALATE DEHP DOWNREGULATES THE PITUITARY ESTROGEN RECEPTOR ALPHA EXPRESSION AND IMPACT ON LACTOTROPH AND GONADOTROPH CELL PROLIFERATION

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Abstract/Resumen: The normal functioning of the pituitary gland is the result of a balanced mechanism capable of