Conclusions: Our results point to a regulatory role of VIP in modulating placental metabolism and glucose transplacental transport in vivo. Endogenous VIP sustains placental glucose and amino acid uptake whereas VIP deficiency triggers compensatory pathways that would contribute to placental metabolic adaptations. The apparently compensatory actions are not sufficient to sustain normal fetal growth and could result in complications later in life.

#35 Anandamide and cyclooxygenase-2 participate in vascular remodeling at the maternal-fetal interface

Vanesa A. Cañumil[1,*], Leopoldina Scotti[2], Ana M. Franchi[1], Gabriela Meresman[2], Fernanda Parborell[2], María L. Ribeiro[1]

[1]Center for Pharmacological and Botanical Studies (CEFYBO), CONICET – University of Buenos Aires, C1121ABGB Buenos Aires, Argentina; [2]Institute of Biology and Experimental Medicine (IBYME), CONICET, C11429 Buenos Aires, Argentina. * canumilvanesa@gmail.com

Successful implantation and placentation requires vascular transformation of the uterus. A dynamic interaction between cells at the maternal-fetal interface is crucial for these processes. Anandamide (AEA) is an endocannabinoid that regulates embryo implantation and many of the placental functions. The uterine levels of AEA are primarily regulated by fatty acid amide hydrolase (FAAH), its degrading enzyme. Using *in-vivo* and *in-vitro* approaches we investigated the role of anandamide in the vascular remodeling of the uterus at early gestation. Also, ciclooxigenase-2 (COX-2) participation was studied. First, Wistar rats received an intrauterine injection of URB-597 in day 5 of gestation (day of implantation). URB-597 is a highly selective inhibitor of FAAH. Control horns were injected with vehicle. Animals were euthanized in day 8. We observed that: (1) URB-597 increased fetal resorptions and induced aberrant embryo spacing and abortions, (2) URB-597 augmented the cross-sectional length of the uterine and arcuate arteries, and (3) Meloxicam (a highly selective COX-2 inhibitor) prevented URB-597 effects. Afterward, we studied the effect of AEA in the interaction between the endometrial stromal fibroblasts and the endothelial cells of the maternal vessels. Thus, human endometrial stromal cells (T-hESC) were incubated with AEA or AEA + meloxicam. AEA stimulated T-hESC migration in a concentration-dependent manner and COX-2 mediated this effect. To test endometrial fibroblasts-endothelial crosstalk, the endothelial cell line EA.hy926 was incubated with T-hESC conditioned medium. The conditioned media from AEA-induced T-hESC migration stimulated endothelial cells migration. Soluble factors derived from COX-2 pathway were involved in T-hESC and EA.hy926 interaction. Collectively, our results show the participation of AEA in the vascular remodeling that takes place in the uterus during early gestation by a mechanism that involves the COX-2 isoform.

#39 Detection of Shiga toxin producing Escherichia coli in endocervix of asymptomatic pregnant women: novel pathogen responsible for adverse pregnancy outcomes?

María Luján Scalise[1,*], Nicolás Garimano[1], Melina Porporato[1], Patricia Leonino[2], Adriana Pereyra[2], José A. Ferreiros[2], Roberto Casale[2], María Marta Amaral[1], Cristina Ibarra[1], Flavia Sacerdoti[1]

[1]Laboratorio de Fisiopatogenia, Departamento de Ciencias Fisiológicas, Instituto de Fisiología y Biofísica, IFIBIO-Houssay (UBA-CONICET), Facultad de Medicina, Universidad de Buenos Aires, C1121ABG Buenos Aires, Argentina; [2]Departamento Materno Infantil, Servicio de Obstetricia, Hospital Nacional "Profesor Alejandro Posadas", C1684 Buenos Aires, Argentina. * lujan.scalise@gmail.com

Brief Introduction: Some studies have demonstrated that vaginal E. coli colonization may produce complications during pregnancy. We have previously reported that Shiga toxin-2 (Stx2) secreted by enterohemorrhagic E. coli can produce abortion and premature delivery in animals and can impair human trophoblast *in vitro*.

Objective: The aim of this study was to detect virulence factor genes from Shiga toxin producing E. coli (STEC) in the endocervix of asymptomatic pregnant women. Methods: Endocervical swabs were collected from 103 pregnant

women (12 to 30 weeks of pregnancy) during their antenatal examination. Swab samples were enriched in Tryptic Soy Broth overnight at 37 °C and then streaked into selective and differential medium, Sorbitol MacConkey agar. E. coli detection was confirmed by identification of uidA gene by PCR assay. Then, positive samples for E. coli were analyzed for STEC virulence factors genes: stx1, stx2, eae, rfbO157, lpfAO113 and hcpA. After that, positive E. coli samples for stx2 gene were grown in Luria-Bertani Broth medium in order to evaluate Stx2 cytotoxic activity. For that, the bacterial supernatants were filter-sterilized and cytotoxicity was evaluated on Vero, Swan 71 and HeLa cells.

Results: Our results showed that 14.5% of the endocervical samples were positive for E. coli (positive for uidA gene). Furthermore, 9/15 (60%) of the E. coli-positive samples carried the stx2 gene and 6/15 (40%) carried the lpfAO113 and hcpA genes. One bacterial supernatant from an E. coli-positive endocervical sample carrying stx2 and lpfAO113 genes exhibited high cytotoxic activity on the cells evaluated due to Stx2 production confirmed by specific neutralization of Stx2 with an anti-Stx2 antibody.

Conclusions: The novelty of this report is the presence of STEC in the endocervix of asymptomatic pregnant women. This opens a new perspective with respect to the possible role of this pathogen in woman reproductive health care.

#42 AQP9-mediated lactate transport: an alternative source of energy in placenta

Medina Yollyseth[1,*], Szpilbarg Natalia[1], Reppetti Julieta[1], Damiano Alicia Ermelinda[1,2]

[1]Laboratorio de Biología de la Reproducción, Facultad de Medicina, IFIBIO-CONICET, UBA, C1121 Buenos Aires, Argentina; [2]Cátedra de Biología Celular y Molecular, Dpto. de Ciencias Biológicas, Facultad de Farmacia y Bioquímica, C1121ABG UBA, Argentina. * yollysethm@gmail.com

Introduction: Emerging evidence shows that placental AQP9 is not involved in the transfer of water between the mother and the fetus. AQP9 is an aquaglyceroporin that also permeates other solutes such as lactate. In other tissues, AQP9 may transport lactate as an alternative energy substrate, having important participation as a nutrient sensor, detecting the availability of nutrients in the cell.

Objective: Our aim was to evaluate the participation of AQP9 in the lactate transfer across the human placenta.

Methodology: This study was approved by the ethics committee of the Hospital Nacional Dr. Prof. A. Posadas. Explants from normal term placentas were cultured in low glucose with or without L-lactate, and in presence and absence of AQP9 inhibitors (0.3 mM HgCl2, a general blocker of AQPs, or 0.5 mM Phloretin, to block AQP9). Medium supplemented with glucose was used as control. Cell viability was assessed by MTT assay and LDH release. Apoptosis indexes were analyzed by Bax/Bcl-2 protein expression ratio and TUNEL assay.

Results: In low glucose medium, MTT decreased while LDH release did not change compared to controls, suggesting that cell death is not due to necrosis. Moreover, Bax/Bcl-2 ratio and apoptotic nuclei increased ($n = 5$, $p < 0.02$) and the blocking of AQP9 did not abrogate apoptosis. However, when explants were cultured in low glucose medium supplemented with L-lactate, explant viability and apoptotic indexes were similar to controls indicating that L-lactate could be replacing glucose as an energy substrate. In this case, the blocking of AQP9 resulted in an increase in cell death ($n = 4$, $p < 0.05$).

Conclusions: Our results show that placental AQP9 may have a key role in lactate transport as an alternative energy substrate on nutritional stress conditions. Thus, the blocking of lactate transport mediated by AQP9 negatively affects the survival of trophoblast cells in these conditions.

#45 Endocannabinoid system from maternal-fetal interface is involved in preterm birth induced by LPS

Carolina Marvaldi[1,*], Julieta A Schander[1], Julieta Aisemberg[1], Ana M Franchi[1], Manuel L Wolfson[1]

[1]Center for Pharmacological and Botanical Studies, CEFYBO, UBA-CONICET, School of Medicine, C1121ABG Buenos Aires, Argentina. * carolinamarvaldi@gmail.com