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EDITORES RESPONSABLES
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VIP antagonist prior to the *in vitro* addition of 2-NBDG. We found that VIP antagonist impaired glucose uptake in placental explants ($p<0.05$) from WT mice. VIP+/- placental weight at gd17.5 did not differ from VIP+/+ placentas. Surprisingly, *in vivo* assays showed an increase of glucose uptake by VIP+/- placentas (0.57±0.11 nmol/gplac vs. 0.38±0.04 nmol/gplac; $p<0.05$) in line with an increase of GLUT1/mTOR expression in placental/fetal tissue, however transplacental transport remained constant. VIP treatment tended to restore mTOR/GLUT1 expression. These results suggest that while VIP regulates at the cellular level Tb glucose uptake, VIP deficiency *in vivo* triggers compensatory mechanisms at both the placental and fetal tissues that would contribute to placental metabolic adaptations in order to restore fetal growth.

319. (60) **PARTICIPATION OF SIRT1 IN THE REGULATION OF MATURE SERTOLI CELL (SC) ENERGY METABOLISM**

Gorga A[1], Rindone GM[1], Centola CL[1], Pellizzari EH[1], Camberos MC[1], Riera MF[1], Galardo MN[1], Meroni SB[1].
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SCs provide structural and nutritional support for germ cells (GC) development. SC metabolism has particular characteristics. It converts glucose to lactate, the main energy substrate for GC, and uses fatty acids (FA) as its own energy source. SC is also capable of synthesizing triglycerides and storing them in lipid droplets (LD). In this context, the simultaneous regulation of lipid metabolism and lactate production may be relevant to the seminiferous tubule physiology. Sirtuins (SIRT1-7) belong to a NAD^+-dependent enzymes family that act as cellular energy sensors. SIRT1, the most studied member, plays an important role in processes ranging from cell cycle regulation to energy homeostasis. The aim of this work was to evaluate the participation of SIRT1 in the regulation of lactate production and of FA metabolism in SCs. SC cultures obtained from 20-day-old rats were incubated in the absence (B) or presence of resveratrol 50 μM (RSV, SIRT1 activator). Results are expressed as X±SD of three independent experiments (*$p<0.05$). It was observed that RSV increases lactate production (B: 3.62±0.73; RSV: 5.24±0.76*μg/μg DNA) and glucose consumption (B: 21.34±5.21; RSV: 40.14±5.71*μg/μg DNA). Possible mechanisms involved in the increase of lactate production after SIRT1 activation were evaluated and it was observed that treatment with RSV augments GLUT1 mRNA levels (1.86±0.44* fold variation respect to B). Regarding FA metabolism, RSV treatment decreases LD content (B: 0.52±0.06; RSV: 0.13±0.02* LD/cell) and increases the expression of FA transporter FAT/CD36 (2.01±0.47* fold variation respect to B). In addition, RSV increases Acetyl CoA Carboxylase phosphorylation levels, which is related to active FA oxidation. Taken together, these results suggest that SIRT1 activation would play an important role in the regulation of SC glucose and lipid metabolism, essential for a normal spermatogenesis (PICT2014-0945; PIP2015-0127).

320. (77) **DISRUPTION IN THE SPERM QUALITY OF THE OFFSPRING CAUSED BY MATERNAL OVERNUTRITION IN RATS**

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Obesity has increased in recent years and is the most important noncommunicable chronic disease. Maternal overnutrition may induce multiple pathologies in both women and their offspring. Our previous studies showed that male offspring from high-fat-fed rats exhibited higher body and testis weight and altered puberty. Also, we found a lower number of germ cells, percentage of motile sperm and capacitation. Thus, the aim of the present study was to evaluate the effects of maternal overnutrition, induced by high-fat diet, on the quality and function of sperm in the offspring.To this end, maternal overnutrition were induced by a high-fat palatable (cafeteria) diet, which was supplied continuously until weaning of their offspring, including pregnancy and lactation. Male offspring from rats fed standard (OSD) or cafeteria diet (OCD) were fed with a standard diet, inspected periodically, and euthanized at 60 days of age. In the germ cells we examined the presence of the reactive oxygen species by flow cytometry using a fluorescent probe (2,7-dichlorofluorescein diacetate), DNA fragmentation by TUNEL kit, mitochondrial function using the probe 3.3-diaminobenzidine, the membrane functional status by hypoosmotic swelling test, and the presence of abnormal chromosomes by cytogenetic assay (Evan test). Compared with OSD rats, OCD group showed a lower percentage of the hypoosmotic-reacted sperm (15±1 vs 23±2, $p<0.01$) and an increase in the abnormal metaphases (6±1 vs 2.1±0.7, $p<0.001$). No differences were found in the TUNEL positive cells, but OCD exhibited higher fluorescein intensity expressed as relative units (577±74, $p<0.01$) compared with OSD (233±27). Finally, 50% of OCD rats displayed a lower mitochondrial function, expressed as relative units (94.8±4 vs 97.7±0.4 from OSD, $p<0.01$).These results indicate that diet-induced maternal overnutrition may contribute to disorders in the fetal programming, particularly in the germ cell quality.

321. (172) **HYPERTHYROIDISM INCREASES MILK IMMUNE CELLS AND IMPAIRS OFFSPRING DEVELOPMENT IN EARLY LACTATION**

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Hyperthyroidism (H) reduced milk ejection and quality, impairing maternal behavior and mammary gland development. However, it remains unclear if H impacts in milk immune cells numbers. Our aim is to assess the influence of H on i) pup maturation and development ii) prolactin secretion and iii) milk immune cells. For this purpose, 10-12 weeks old *Wistar* rats were injected daily with T_4 (0.25 mg/kg until day 18 of gestation, then 0.1 mg/kg until day 2 of lactation L2) to induce H or with vehicle in control group. Rats were mated 8 days after starting T_4 treatment and euthanized L2 (after ketamine/xylazine sedation and oxytocin stimulation for milking). Afterwards, milk and mammary gland samples, minced to reach single cell suspension, were dyed with fluorophore labeled mAbs ($CD45^+$, $CD3^+$, $CD11b/c^+$) and analyzed by flow cytometry. Offspring weights on L1 and 2, head circumference and body length (L2) were measured. Serum of dams and offspring was obtained to determine total T_4 and prolactin levels by RIA. Our results show that H mothers had more implantation sites and pup number ($p<0,05$) and higher pup mortality rate than controls ($p<0,001$). The H pups had lower weight on days 1 and 2 ($p<0,001$), less weight gain, and diminished length and head circumference ($p<0,001$). H group T_4 and prolactin levels were increased in dams ($p<0,01$; $p<0,001$) but T_4 reduced in the pups ($p<0,001$). The H group had increased % of $CD45^+$ cells ($p<0,05$) and % and absolute quantity of $CD3^+$ cells/μl compared with control while the number of CD11 b/c^+ cells was diminished ($p<0,05$). No changes were observed in mammary gland resident immune cells. These results suggest that T_4 impairs pup development on early lactation. Additionally, milk leukocytes are modulated by H with a cell-lineage specific response. These data suggest that then maternal immune protection transferred through milk to the offspring may be altered in H and highlight the need of evaluating thyroid status in pregnancy and lactation.
Área temática: Reproducción.

322. (186) **PRESENCE OF SHIGA TOXIN PRODUCING *ESCHERICHIA COLI* IN ENDOCERVIX OF ASYMPTOMATIC PREGNANT WOMEN: NOVEL PATHOGEN RESPONSIBLE FOR ADVERSE PREGNANCY OUTCOMES?**

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E. coli can colonize the vagina, usually asymptomatically, although epidemiologic studies have showed that the presence of this bacterium in the endocervix microbiota could be a risk factor for pregnancy. We have previously reported that Shiga toxin (Stx) producing *E. coli* (STEC) infections during pregnancy may cause maternal or fetal damage mediated by Stx2 in rats in early or late stage of gestation. **The goal** of this study was to detect STEC in the endocervix from asymptomatic pregnant women. Endocervical swabs from 103 asymptomatic pregnant women with gestational age of 12 to 30 weeks from the National Hospital Posadas were enrolled. Swab samples were enriched in Tryptic Soy Broth and then streaked on sorbitol-MacConkey (SMAC) agar. *E. coli* was confirmed by the presence of *uidA* gene detected by polymerase chain reaction PCR. The positive samples for *E. coli* were analyzed for STEC virulence factors genes such as: *stx1, stx2, eae, rfb*$_{O157}$, *lpfA*$_{O113}$ and *hcpA genes*. The *stx2* positive *E. coli* samples were grown in Luria-Bertani Broth and the filter-sterilized bacterial supernatants (SN) were used to evaluate Stx2 activity on Vero, Swan and Hela by cell viability assay. **Our results** showed that 14.6% (15/103) of the endocervical samples were positive for *uidA* gene. Additionally, we found that 8.7% (9/103) was positive for *stx2* and 5.8 % (6/103) for *lpfA*$_{O113}$ and *hcpA* genes. The SN of one of them expressing *stx2* gene had a high cytotoxic activity on Vero, Swan 71 and HeLa cells. Stx2 identity was checked using an anti-Stx2 antibody in order to neutralize the cytotoxic effects. **In conclusion**, we demonstrate that STEC can be asymptomatically present in the endocervix and that can potentially express Stx2. This study may open a new perspective to understand whether STEC can be a novel pathogen involved in adverse pregnancy outcomes.

323. (197) **OVARIAN PROTEOME OF VIZCACHAS (LAGOSTOMUS MAXIMUS, CAVIOMORPHA, RODENTIA) IS MODULATED BY ENVIRONMENTAL FACTORS**

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Proteome is the complete set of proteins expressed by an organism, and it actively changes in response to both internal and external conditions. Since estradiol levels of pregnant vizcachas strongly correlate with climate variables we aimed to study the effect of such variables on the ovarian proteome. For this, ovarian protein extracts from two groups of pregnant females (n=2 each group) with 105±6 days of gestation were used for proteomic analysis. The years of capture of each group, 2011 and 2015, were characterized by low temperature/high precipitation and high temperature/low precipitation levels respectively. Briefly, equal amounts of protein extracts were analyzed using MALDI-TOF/MS and then, LC-ESI/MS (Orbitrap). The resulting peptides were identified with Proteome Discoverer Software using the Rodentia UniProt Database, and functional enrichment analysis was performed using DAVID, STRING and FunRich softwares. Proteins differentially expressed in each year were plotted on a volcano plot (t-test, p <0.05). Through functional enrichment analysis it was corroborated that apoptosis regulation and platelet degranulation processes prevailed in 2011-ovaries, while in the 2015-ovaries signal transduction was favored. In addition, the interactomes defined by the overexpressed proteins showed a very distinct topography in 2011 vs 2015, with different nodal peptides in each situation. This is the first large-scale data analysis of the vizcacha proteome. The present work showed an ovarian expression profile that significantly varies under different climatic conditions. Finally, this work provides new markers for future investigations on the modulation of ovarian function. Grants: Fundación CIentífica Felipe Fiorellino; PIP (CONICET)110/14

324. (223) **RESVERATROL IMPAIRS CELLULAR MECHANISMS ASSOCIATED WITH ENDOMETRIOSIS DEVELOPMENT**

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Endometriosis (EDT) is a benign gynecological disease with no available effective treatment due to its adverse side effects. Resveratrol (RES) is a natural polyphenol with well-known anticarcinogenic properties found abundantly in grapes, peanuts, and berries. We and others have shown its inhibitory effect on EDT development but its molecular mechanism is still unknown. The aim of this study was to evaluate the effect of RES (50-100μM) on the proliferation, migration and apoptosis of endometriotic epithelial cell line 12Z and endometrial stromal cell line St-T1b. We also studied its effect on gene expression related to cell migration and angiogenesis, and on the maintenance of stem cell pluripotency in both cell lines and in primary endometrial epithelial cell cultures (EEC). RES significantly decreased cell viability after 48h in both concentrations and both cell lines ($p<0.01$), and reduced wound healing size after 8h and 20h with 100μM and 50 μM RES respectively ($p<0.05$). The number of apoptotic cells, assessed by FITC Annexin V/PI, was increased after 24h ($p<0.01$) as well as cleaved caspase-3 levels, assessed by Western Blot ($p<0.05$). On the other hand, real time PCR showed that treatment with 100μM RES reduced MMP2 and increased Timp1 mRNA expression in both cell lines ($p<0.05$). Angiotensin1 mRNA levels decreased with both RES doses ($p<0.05$). Besides, 100μM RES decreased VEGF mRNA levels only in St-T1b ($p<0.05$). EEC treated with 100μM RES displayed an increase of Timp1 and a decrease of MMP2, VEGF and Angiotensin1 mRNA levels ($p<0.05$). Among the stem cell pluripotency markers, 100μM RES provoked an increase in Notch1, Snail1, KLF4, Sox2 and Tert mRNA levels in both cell lines and in EEC ($p<0.05$). Also, the expression of Oct4 mRNA increased in St-T1b and EEC ($p<0.05$) and Vimentin mRNA exerted a significant upregulation only in EEC ($p<0.01$). These findings revealed that RES treatment affects several signaling events implicated in EDT development and progression.

325. (280) **GLUCOCORTICOID RECEPTOR CHARACTERIZATION AND DEXAMETHASONE LEPTIN REGULATION IN PLACENTAL CELLS**

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Leptin is a key hormone in placental physiology. It regulates trophoblast survival and fetal maternal tolerance by the induction of HLA-G in placental cells. The expression of leptin in trophoblastic cells is regulated by different endogenous signals. Previous results from our lab demonstrated that estradiol (E2) regulates leptin expression. In this study we aimed to characterize glucocorticoid receptor (GR) and analyze the effect of the synthetic glucocorticoid dexamethasone (DEX) on leptin expression in human placental cells. BeWo cells cultured under standard conditions, and human placental explants were used as well. Western blot immunofluorescence and transient transfection analysis were carried out. We analyze (GR) expression in placental explants. Two isoforms of 67 and 56 KDa were characterized and the smaller one was increased after E2 treatment.