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].
[1] Centro de Investigaciones Endocrinológicas "Dr. César Bergadá" (CEDIE) – Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET) – FEI – División de Endocrinología, Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina.

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**

Meneghini MA, Flores Quiroga JP, Cortez AE, Faletti AG
Centro de Estudios Farmacológicos y Botánicos (CEFYBO-CONICET), Facultad de Medicina, Universidad de Buenos Aires.

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**

Sánchez MB[1,2], Moreno Sosa MT[1,2], Neira FJ[1,2], Soaje M[1,2], Pietrobon EO[1,2], Farias H[1,2], Jahn GA[1,2], Valdez SR[1,2], Mackern-Oberti, JP[1,2].
1. Instituto de Medicina y Biología Experimental de Cuyo (IMBECU-CCT-CONICET)
2.Universidad Nacional de Cuyo (UNCuyo). Mendoza, Argentina. E-mail: sanchezbelen564@gmail.com

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?**

Scalise ML[1]; Garimano NE[1]; Porporato M[1]; Leonino P[2]; Pereyra A[2]; Ferreiros JA[2]; Casale R[2]; Amaral MM[1]; Sacerdoti F[1]; Ibarra C[1].
1. Laboratorio de Fisiopatogenia, IFIBIO-Houssay (UBA-CO-