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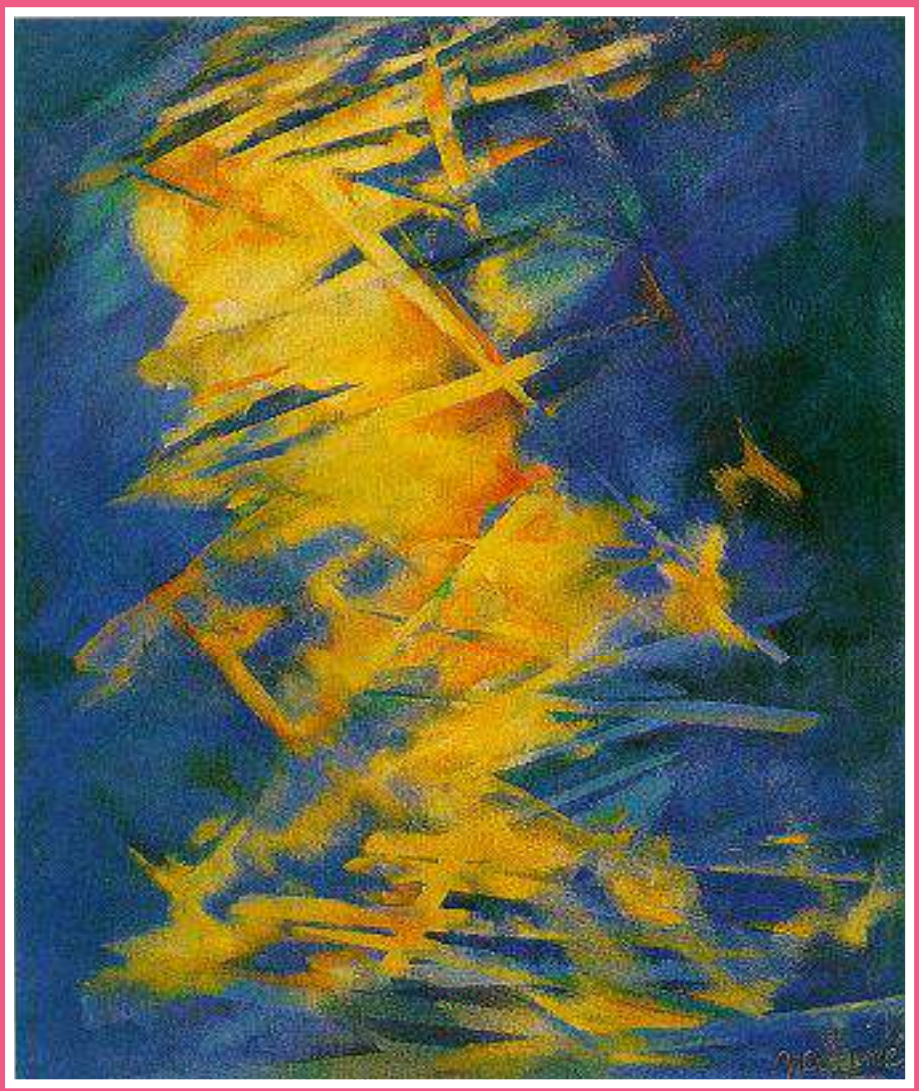

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and 100μM) or EGCG (20 and 40μM) for 24h. Cell proliferation was assessed using the WST-1 reduction kit, in presence or absence of E_2 and/or the estrogen receptor antagonist ICI 182,780. Levels of aromatase and estrogen receptor α expression were assessed by Western Blot. Both doses of RES inhibited aromatase expression ($p<0.01$) and 100μM RES reduced total estrogen receptor α levels ($p<0.05$) in both cell lines. In addition we found that both RES doses were able to inhibit the ECC-1 proliferation, even that induced by E_2 ($p<0.05$). Preliminary results on ECC-1 show that RES could be using more than one pathway, including that triggered by estrogen receptor. EGCG reduced the aromatase expression in T-HESC ($p<0.01$) as well as in ECC-1 ($p<0.05$) cell line. Besides, EGCG diminished total estrogen receptor α levels ($p<0.05$) in both cell lines. These results, taken together with our previously published ones, encourage us to investigate these compounds as novel strategies to treat endometriosis. More studies need to be undertaken to finally understand if RES and EGCG exert their inhibitory action through estrogen pathway inhibition which may represent an accurate therapeutic for an estrogen-dependent disease.

Keywords: Endometriosis, resveratrol, EGCG, aromatase, estrogen.

(1604) **STUDY OF THE IMMUNE RESPONSE ASSOCIATED WITH GENITAL INFECTIONS AND ITS RELATIONSHIP WITH INFERTILITY**

Romina Cecilia Russi (1), Paula Julieta Cepeda (1), Evelin Cáceres (2), Carla Bernasconi (2), María Ines García (1), German Henrich (2), Carolina Veaute (1)

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Chlamydia trachomatis (Ct), Mycoplasma hominis (Mh) and *Ureaplasma urealyticum (Uu)* are usually associated with infertility. Our aim was to study immunological factors induced by genital infections as a potential cause of infertility. Antisperm antibodies (ASA) were analyzed by ELISA and cytokines and master transcription factor expression were quantified by RT-qPCR using the ΔΔCt comparative method. Sperm parameters were analyzed by WHO recommendations. Vaginal washing were collected from 59 females, Infertile With Infection (IWI-f), Infertile Without Infection (IWoI-f), Fertile Without Infection (FWoI-f) and semen from 27 Infertile male With (IWI-m) and Without infection (IWoI-m). Categorical variables were analyzed by Fisher's Exact test, $P<0.05$ was considered statistically significant. We found a significant association between the type of infection and the patient's sex, for IWI-f with *Mh* and IWI-m with *Uu* infection. No significant difference in sperm parameters between IWoI-m and IWI-m were found. ASA analysis showed no correlation with infertility or infection. Cytokine expression exhibited a significant upregulation in IWoI-f compared to FWoI-f, for IL-6, IL-10, IL-17A, RORγt, FOXp3 and Tbet (Relative Expression [RE]: 5.9, 4.7, 4.4, 12.2, 4.9, 8.7; respectively). In IWI-f with *Mh*, IL-10 was significantly increased (RE: 3.2), while with *Uu,* INFγ, RORγt, FOXp3 were increased, versus FWoI-f (RE: 7.8, 10.7, 12.2, respectively). In IWI-f, the *Mh* and *Ct* were associated with a decrease for IL-17A, RORγt and Tbet, which were significant for *Mh* (RE: 0.25, 0.23, 0.13, respectively) but not for *Ct,* versus IWoI-f. In IWI-m with *Uu* IL-8 was significantly augmented (RE: 8.5) versus IWoI-m. Infertility is associated with an upregulation of several proinflammatory cytokines, in the absence of infection. Alterations in cytokine expression were observed in infertile patients with *Mh* and *Uu* infection. Cytokine disturbance may be associated with infertility.

Keywords: infertility, antisperm antibodies, cytokines, master transcription factors, genital infection

(1524) **THE HYALURONAN SYNTHESIS *INHIBITOR* 4-METHYLUMBELLIFERONE (4MU) EFFECT ON ENDOMETRIOSIS (EDT)**

Carla Noemi Olivares (1), Mariela Andrea Bilotas (2), Analía Gabriela Ricci (2), Laura Daniela Alaniz (3), Daniela Madanes (2), Luciana Ferella (1), Emilia Soledad Bogni (1), Inés Stella (4), Rosa Inés Barañao (2), Gabriela Fabiana Meresman (1)

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It is known from previous studies that 4MU has antiproliferative and antiangiogenic properties. We evaluated the effect of 4MU in EDT models. Stromal T-HESC and epithelial ECC-1 endometrial cell lines, were treated with different doses of 4MU (ranging 0-4mM) and cell proliferation (CP) by the WST-1 assay was evaluated. Mice were surgically induced with EDT and treated orally with 4MU during 28 days. Six groups were included in the in vivo experiment, two different time points for initiating the treatment (2 and 15 days) and two different doses of 4MU (80 and 200mg/kg) with the appropriate vehicle control groups. The number and size of developed lesions were evaluated, as well as vascularization, CP, infiltrating lymphocytes and collagen depot within the endometriotic lesions. CP of T-HESC was significantly inhibited with 2 and 4mM 4MU ($p<0.05$); preliminar results on ECC-1 show that all concentrations of 4MU tested inhibit CP. In vivo, there was a significant reduction in the number of developed lesions in the 200mg/kg group starting treatment at day 2 ($p<0.05$ vs. day 15) and the size of these lesions was significantly reduced too ($p<0.05$ vs. control). Vascularization, evaluated by von Willebrand Factor immunohistochemistry (IHC), did not differ after treatment. CP of epithelial or stromal endometriotic cells was unaltered as seen after PCNA IHC was performed. Lesion-infiltrating lymphocytes were homogenous along all treatment groups as well as collagen depot; demonstrated by hematoxilin eosin and Masson´s trichrome staining, respectively. In vivo, 4MU did not demonstrate to be an efficacious treatment option, although further studies are being held to elucidate what mechanisms have been altered that are reflected in an overall lesser lesion size and number for the 200mg/kg dose at day 2, while in vitro results are promising. Many more studies need to be undertaken to finally understand if 4MU can be thought of as an alternative treatment option in EDT.

Key words: endometriosis, cell proliferation, angiogenesis, hyaluronan inhibition

(704) **ANALYSIS OF *Ureaplasma urealyticum*, *Mycoplasma hominis*, AND *Chlamydia trachomatis* INFECTION OF THE MALE GENITOURINARY TRACT AND SEMEN QUALITY PARAMETERS**

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Male factors account for up to 50% of infertility cases, and infection in the genitourinary tract may play a contributing role in up to 15% of male infertility. In fact, several microorganisms have been proposed to play a pathogenic role in both genital infections and male infertility. Leukocytospermia is a well-known indicator of male urogenital infection or inflammation that can be deleterious to sperm.

This study aimed to analyze leukocytospermia and standard semen quality parameters from infected and non-infected young adult men. A total of 930 semen specimens were collected by masturbation from men attending to the Andrology clinic in a period of seven years. Analysis of *Ureaplasma urealyticum, Mycoplasma hominis,* and *Chlamydia trachomatis* infection were performed by molecular or culture methods. Semen analysis was assessed according to the World Health Organization guidelines. Non-parametric tests were used for statistical analysis.

Analysis of standard of semen quality parameters between non-infected and infected men showed that the presence of *Ureaplasma urealyticum* infection was associated with significantly increased semen leukocyte counts ($p<0.05$), low sperm concentration ($p<0.0001$) and abnormal sperm morphology ($p<0.0001$). On the other hand, the presence of *Mycoplasma hominis* or *Chlamydia trachomatis* in-

Daily Fe Intake (FeI), hem Fe intake (hem FeI) and Fe from flour enrichment (Ley 25630) were estimated by a "Food Consumption Frequency" questionnaire (ARGENFOODS and USDA National Nutrient Database on Standard Reference). sHep values (ng/mL) were: mean±SD (range): 33.6±20.9 (7-80); median: 25,0; 2.5th-97th Percentile: 8.85-68.9. Two donors (5%) showed sHep > 81 ng/mL, range assay upper limit. SF (ng/mL) and TS (%) were: mean±SD (range): 213±172 (42-753) and 32.6±12.8 (17.9-90.7), respectively. Criteria of Fe overload (SF>300 ng/mL and TS 50%) was observed in 5% of donors. FeI (mg Fe/d) was: mean±DS (range): 24.2±9.0 (10.0-47.2). No participant presented FeI lower than EAR (6 mg Fe/d), and one donor surpassed 45 mg Fe/d (UL) (NAS, 2001). Hem FeI and Fe from flour enrichment were 8.7% and 35% of daily FeI, respectively. A significant correlation was found between sHep and SF (r=0.52; p=0.00097), but not with FeI (r=0.014; p=0.9308), nor with hem FeI (r=0.194, p=0.263). These results show high FeI and a strong correlation between sHep and Fe stores. Therefore, local feeding habits (54.9 Kg meat/per capita/yr, FAO 2011) and mandatory flour fortification with Fe, could enhance adverse effects in individuals unaware of any family history of Fe overload. *Universidad de Buenos Aires, UBACyT 20720150100004BA*

Keywords: iron, hepcidin, biomarkers of iron status, iron intake; food fortification

(378) **BONE VASCULAR ACTIONS OF THE NUTRACEUTICAL GENISTEIN**

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Previously we reported that the phytoestrogen (PE) Genistein (Gen) prevents the atherosclerotic plaque genesis via estrogen receptor (ER) activation and the inhibition of the cellular/molecular events involved in vascular damage. Indeed, vascular muscle cell transdifferentation into osteoblasts (OB) like cells was also impaired. Here we studied the role of Gen on the bone-vascular axis interaction with focus on OB growth and angiogenesis. To that end, aortic rings (AR), primary cultures of aortic endothelial cells (EC) and calvaria OB isolated from female Wistar rats, exposed to Gen (10nM-1uM) were employed. OB proliferation and differentiation are regulated by several factors such as BMP-2, Runx2 and the bioactive compound NO. We showed that short term exposure of OB to Gen enhanced NO production (33-20% above C, 15-30 min treatment, p<0.05, Griess reaction). NO was involved in OB proliferation since in presence of a nitric oxide synthase inhibitor, L-NAME (10uM), OB growth was blunted (p<0.001). In RT-PCR assays we found that Gen significantly increased Runx2 and BMP-2 mRNA levels. The PE genomic action was extended to an up-regulation of alpha and beta ER mRNA expression (p<0.05). Angiogenesis depends on EC proliferation and migration that finally lead to capillary formation. These events were evaluated using conditioned medium (CM) obtained from OB exposed to Gen (72h). CM stimulated EC proliferation (0.47±0.07 vs 0.38±0.07, Gen vs C, p<0.02, MTT technique) and markedly enhanced EC migration (30;187% above C, Gen 10;100nM, p<0.05, wound healing assays). Capillaries formation was studied by seeding AR on a collagen matrix for 15 days in presence or absence of CM and quantified by optical microscopy. A high number of three-dimensional tubular structures around AR were detected. This work provided evidence of OB maturation induced by Gen with beneficial impact on vascular tissue promoting angiogenesis, crucial events involved in bone formation and remodeling.

Keywords: phytoestrogens, genistein, bone-vascular axis, angiogenesis

(964) **CALCIUM ABSORPTION EFFECTIVENESS OF PREBIOTICS IS AFFECTED BY THE NUTRITIONAL STATUS OF VITAMIN D**

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Vitamin D (VD) regulates Ca absorption (Abs) which is positively affected by prebiotics through lowering intestinal pH and increasing colonic cells growth. VD insufficiency could affect prebiotic effectiveness on CaAbs.

Galactooligosaccharides/Fructooligosaccharides (GOS/FOS®) effectiveness to increase CaAbs was evaluated in an experimental model of VD insufficiency and established osteopenia. Ovariectomized Wistar rats fed a VD-free (0 IU%) diet to become VD insufficient (-D) (n=32) or a normal VD diet (100 IU%) (+D) (n=16), during 45 days. Thereafter, for an additionally 45-days period D+ fed: AIN´93 (control diet) (+*D0.5%*); AIN´93 containing 0.3%Ca or 2.5%GOS/FOS® (9:1) (+*D0.3%P*) while D- fed: VD free-AIN´93 (-*D0.5%*); VD free-AIN´93 containing 0.3%Ca (-*D0.3%*); last diet containing 2.5% (-*D0.3%P*) or 5% GOS/FOS (-*D0.3%:2xP*). Food intake and faeces (F) were collected for CaI and CaF and CaAbs% calculated .

Results CaAbs% (mean±SD):.-D0.5%: 32.71±1.74; -D0.3%: 38.33±2.33; -D0.3%P: 44.71±1.84; -D0.3%x2P: 56.40±1.39; +D0.3%P: 87.45±1.82; +D0.5%: 67.80±2.21.

VD insufficiency reduced CaAbs% (-D0.5% and –D0.3% vs. +D0.5%; p<0.001) while GOS/FOS® effectiveness was negatively affected (-D0.3%P vs. +D0.3%P; p<0.001). CaAbs% of D- diets containing GOS/FOS® was improved by increasing dietary prebiotic % (-D0.3%P vs. -D0.3:2xP; p<0.01).

Effectiveness of prebiotics on Ca Abs was affected by VD nutritional status. Grants: UBACyT 20020130100091BA and PIP (CONICET) 11220130100199CO.

(998) **CONSEQUENCES OF MATERNAL FRUCTOSE INTAKE ON BROWNING POTENTIAL OF RETROPERITONEAL ADIPOSE TISSUE FROM ADULT OFFSPRING**

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Beige adipocytes are highly adapted to convert chemical energy into heat through the action of uncoupling protein-1 (UCP1). Cold exposure or β3 adrenergic agonist treatment stimulates generation of these cells in white adipose tissue (WAT). Our aim was to assess whether maternal fructose intake during pregnancy, affects browning capability of retroperitoneal adipose tissue (RPAT) from adult male offspring. On pregnancy day 1, dams were provided with either tap water alone (CTR, control) or containing fructose (10%w/v; FRD) and fed *ad libitum* with chow up to delivery. Lactating dams and their pups (between 21 and 60 days) received water and chow *ad libitum*. C and F indicate pups born to CTR and FRD dams. On experimental day (age 60 days) RPAT was dissected and stromal vascular fraction (SVF) cells were isolated. mRNA expression levels of beige and white adipogenic markers were assessed in RPAT SVF cells and pads. SVF cells were cultured and differentiation parameters were quantified by qPCR. Previously we found that pre-natal nutritional intervention decreased the adipogenic potential of adult RPAT precursor cells, favoring hypertrophic RPAT expansion and a distorted adipokine secretion pattern. Now, we found that F RPAT expresses lower levels (p<0.05 vs. CTR) of UCP-1, whereas those of Zfp423 (transcription factor involved in maintenance of white adipocyte identity and in inhibition of thermogenic program), leptin and enzymes involved in the lipolytic/lipogenic balance (LPL, HSL, and FAS) were higher (p<0.05 vs. CTR). Analysis of F SVF reveals lower expression levels of Pdgfr1α (a beige lineage marker) and CD34, and higher of Pref-1(p<0.05 vs. CTR). On F differentiated cells, UCP-1 and adiponectin expression was lower (p<0.05 vs. CTR) without changes in leptin or PPARg. Our data suggest that a decreased WAT browning potential could be involved in the adverse metabolic-endocrine dysfunction seen in F adult animals. (PICT2013-0930; PICT2015-2352).

Palabras Clave: WHITE ADIPOSE TISSUE, BEIGE ADIPO-