modifications in glomerular ultrastructure. Structural alterations might lead to RDS dysfunction and subsequent development of hypertension induced by sodium retention in this experimental model.

0580 - SUPPLEMENTATION WITH DOCOSAHEXAENOIC ACID PLUS HYDROXYTYROSOL PREVENTS WHITE ADIPOSE TISSUE IMPAIRMENT BY IMPROVING MITOCHONDRIAL ACTIVITY AND THE EXPRESSION OF NRF2, NF-Kß, SREBP-1C AND PPAR-GAMMA IN MICE FED A HIGH-FAT DIET

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Abstract/Resumen: Overnutrition, lead to white adipose tissue (WAT) expansion, adipocyte hypertrophy, antioxidant defense depletion, inflammation, insulin resistance and dysregulated lipolysis. Docosahexaenoic acid (C22:6n-3, DHA) have beneficial effects on metabolic disorders linked with obesity. The hydroxytyrosol (HT), a polyphenol that provides antioxidant and anti-inflammatory protection, also impact positively on metabolism. Both bioactive compounds can modulate the activation of transcription factors and gene expression involved in lipid, antioxidant and inflammatory responses. Previously we found that HT improved the antioxidant system and inflammation of altered WAT in mice. Thus, the aim of our work was test if DHA+HT co-administration could avoid adiposity increase and WAT deterioration in a mouse model of high-fat diet (HFD)-induced obesity and the possible action mechanisms related. Male C57BL/6J mice received: control diet (CD) (10 % fat), CD+DHA, CD+HT, CD+DHA+HT, high fat diet (HFD) (60 % fat), HFD+DHA, HFD+HT or HFD+DHA+HT for 12 weeks constituting 8 experimental groups (Doses: DHA, 50 mg/kg/day; HT, 5 mg/kg/day). In WAT we evaluate: oxidative stress damage; mRNA levels and antioxidant enzymes activities; citrate synthase, mitochondrial Complex I and II activities; binding activity and gene expression of transcription factors: nuclear factor erythroid 2-related factor 2 (Nrf2), nuclear factor-kß (NF-kß), sterol regulatory element-binding protein 1c (SREBP-1c) and peroxisome proliferator-activated receptor gamma (PPAR-gamma). The treatment with DHA+HT avoid the increase of adipose mass; maintained the levels of TBARS, F-2 isoprostanes and protein carbonyl compared to CD group; increased enzymatic activity of superoxide dismutase and catalase; preserved mitochondrial activity; up-regulated Nrf2 and PPAR-gamma; and down-regulated the NF-kß and SREBP-1c. Co-administration of DHA+HT prevent the development of obesity conserving mitochondrial function and preventing the dysregulation of WAT.

0641 - PROBIOTIC ADMINISTRATION TO DOG PETS WITH GASTROENTERITIC SYMPTOMS IN A CONTROLLED, RANDOMIZED, DOUBLE BLIND TRIAL

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UNT (1); CONICET (2)

Abstract/Resumen: There is a renewed interest in the design of formulas containing probiotic or beneficial microorganisms for the prevention of infections and animal welfare, exerting a physiological effect (ISAPP). The objective of this work was to determine the effect of the oral administration of four strains previously selected by their beneficial properties: Lactobacillus johnsonii CRL1693, L murinus CRL1695, L mucosae CRL1696 and L salivarius CRL1702 to dog pets (from 1-4 months old) with gastrointestinal symptoms (diarrhea, fever, vomiting). The randomized, double blind placebo-controlled trial was conducted at a veterinary center in Tucumán (June 2018-July 2019) in a Treated TG (n= 60) and Placebo PG (n= 60) groups. The probiotic was administered as freeze-dried bacteria (10^8 CFU) or excipients for 7 days by oral route. Race, weight, sex, type of feeding and previous sickness were registered, while clinical protocols were applied for diagnostic and treatment. Fecal stools were collected for microbiological and parasitological evaluation at days 0 and 8. No significant differences were observed between the two groups at the beginning of the trial. Pets' recovery was significantly different between the groups, having an excellent score (less than 3 days) in TG, while not as good in the PG (more than 7) (Fisher, $p<0.0001$). The stools consistency (by Bristol-adapted stools test) was harder in most of the TG after 7 days, but softer in PG (Fisher, $p= 0.024$). No significant differences were obtained in the number of cultivable mesophylls, lactic acid bacteria, enterobacteria and enterococci, or parasitological evaluation after the treatments. The dead animals were 3 and 4 in the TG and PG, respectively. The pets died after 6 days in the TG, but at days 2-4 in the PG. The results indicate that probiotic administration exerts a positive effect on the recovery of pets, and can be used as adjuncts for diarrhea treatment, supported by the stopped symptoms and high recovery levels.

0685 - ARTERIAL HIPERTENSION INDUCED BY SALINE OVERLOAD: ROLE OF CHLORIDE ANION

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Abstract/Resumen: A chronic saline (as sodium chloride) overload (SO) in the diet induces a renal inflammatory response and oxidative stress, which lead to the development of hypertension. The aim of this work was to demonstrate the hypothesis that chloride anion (Cl^-), besides sodium cation (Na^+), is involved in these inflammatory and oxidative responses. These alterations might be diminished if Cl^- is replaced by other anion (like citrate), or if Na^+ is replaced by other cations. Male Wistar rats were randomly divided into four experimental groups (n= 8): control (C); SO (NaCl 8% W/W); high Na^+ without Cl^- (Na: $Na_3C_6H_5O_7$ 11,8%); high Cl^- without Na^+ (Cl: $CaCl_2$ 3.80 %; KCl 3.06 % and $MgCl_2$ 1.30 %). After three weeks, systolic blood pressure (SBP) was measured, and rats were housed in metabolic cages in order to collect 24-hour urine to assess renal function. Oxidative stress parameters were measured in renal cortex: TBARS production andantioxidant enzymes activities and expression: superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPx). In all the experimental groups we observed a significant increase of diuresis (*$p<0.05$ vs. C) while SBP was increased only in those rats fed with Cl^- (mmHg, C: 125 ± 9; NaCl: 164 ± 8*; Na: 133±4; Cl: 152±7*). These changes were accompanied by an increase in TBARS production in renal cortex (mol TBARS/mg protein) ($x10^{12}$): C:1.30 ± 0.10; NaCl: 1.82 ± 0.18*; Na: 2.01 ± 0.32*; Cl: 1.91 ± 0.34*. No changes were observed on the activity or expression of SOD and CAT. Despite the fact that GPx expression was unaltered, the enzyme activity was increased in those groups with Cl^- (µmol GSSG/mg protein .min, C:1.34 ± 0.14; NaCl: 2.31 ± 0.37*; Na: 1.30 ± 0.14; Cl: 2.77 ± 0.52*). These results suggest a relevant role of

Cl^- in the development of hypertension, independently on Na^+. Saline overload, and both ions separately, induced lipid oxidative damage. Nevertheless, only Cl^- salt diets produced an increase in GPx activity, resulting in a high prooxidant state in kidney.

0818 - PARTICIPATION OF GUT MICROBIOTA ON THE METABOLIC CHANGES INDUCED BY HIGH FAT DIET

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Abstract/Resumen: Environmental factors, such as a fat-enriched diet are among the causes of the great prevalence of obesity and type 2 diabetes in the population. Recent studies have shown that diet-induced alterations the gut microbiota composition play a pivotal role in the development of obesity. Changes in the predominant gut bacterial phylums: Bacteroidetes and Firmicutes (B-F) characterizes different metabolic phenotypes. Our objective is to study in a high fat diet (HFD) feeding model of obesity if the treatment with probiotics induces changes in glycidic metabolism and B-F DNA. Four week-old male C57B6/6J mice were fed with a normal chow diet (fat content: 7.5 g/100 g) or an HFD diet (fat content: 31 g/100 g, butter and lard). When HFD mice reached a 5 % weight gain with respect to the controls (p= 0.07, n= 12) and a cumulative increase in food intake of 19 % kcal (week 16), probiotic treatment was started. We used two type of probiotics (P1 and P2) in two concentrations: 10^7 CFU and 10^8 CFU, supplied in drinking water. Genomic DNA of gut microbiota was isolated from feces samples and were analyzed by real time PCR reactions using selective primers. HFD induced an increment in basal (Gb) and after 2 hours of glucose administration (G2h) glycemia. Lower dose probiotic treatment did not produce changes in those parameters, however the higher dose induced an improvement in Gb and G2h (ANOVA Gb p= 0.0204, G2h p= 0.022, n= 4) being P2 most effective. No changes were observed in body weight and food intake. Concerning gut microbiota, we observed a non-significant increase in the Bacteroidetes DNA under treatment with HFD and P1 (interaction diet probiotic p= 0.06, n= 4). We conclude that probiotic treatment improved metabolic parameters that were altered during HFD treatment. These data suggest the importance of gut microbiota as a therapeutic target in the treatment of obesity complications.

Bioinformática, genoma, proteoma y nuevas tecnologías / Bioinformatic II

Chairs: David Brudke/ Alberto Penas Steinhardt

0117 - CYTOTOXICITY OF METHYL VANILLATE AND METHYL DIVANILLATE IN BREAST CANCER CELLS

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Abstract/Resumen: Breast cancer is the most common cancer among women worldwide, with over 1.3 million new cases per year resulting in about half a million deaths. Current treatment strategies are based on surgical removal of the tumor and/or radiotherapy followed by chemotherapy, which are usually associated to harmful side effects. Regarding this, there is a constant search for new selective and low toxicity drugs. Phytochemicals and their chemically modified derivatives are potential candidates in this scenario. Recently, some studies have evaluated the antioxidant properties of vanillic acid and its esters in which methyl vanillate has been found to have higher antioxidant activity than vanillic acid itself and vanillin. This effect was related to their higher lipophilicity and self-dimerization that occurs when they react with free radicals, as vanillin. Considering previous studies with vanillin and vanillic acid and the fact that there are no reports in the literature about the effects of methyl vanillate and its dimer methyl divanillate on human breast cancer cells, the aim of this work was to study the cytotoxic and antitumor effects of these compounds on MCF-7 and MDA-MB-231 cancer cell line, estrogen dependent and triple negative, respectively. For cytotoxicity assays, MTT reduction viability assay, flow cytometry cell apoptosis, and Hematoxylin/Eosin and DAPI/Phalloidin stains were performed. The MTT reduction assay showed that divanillate was 15-fold more cytotoxic than vanillate for MCF-7 and 9-fold higher for MDA-MB-231 cell lines ($p<0.05$). The cells incubated with the average of IC50 and IC25 values were stained and showed lower cell damage for IC25. This concentration was chosen for the apoptosis assay, which showed higher cytotoxicity for the MCF-7 than MDA-MB-231. In conclusion, divanillate presents higher cytotoxicity than vanillate and the MCF-7 strain is more sensitive to both compounds.

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0318 - GENETIC DIAGNOSIS OF CONGENITAL HYPOPITUITARISM BY MOLECULAR INVERSION PROBES SEQUENCING: NOVEL PATHOGENIC VARIANTS

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Abstract/Resumen: Congenital hypopituitarism (CH) is a life-long and threatening disease, associated with an abnormal pituitary development. CH is highly variable comprising a spectrum of disorders that range from isolated growth hormone deficiency (IGHD) to combined pituitary hormone deficiency (CPHD). Mutations in at least 30 genes have been implicated in CH, but at present, precise diagnosis remains a challenge. In the present study, we report variants found in pediatric patients with CPHD (n= 116) or IGHD (n= 55) from Argentina using the molecular inversion probes sequencing (MIPS) method and our own custom designed gene panel. We identified pathogenic, likely pathogenic or variants with uncertain significance but predicated to be damaging for at least 3 independent software in about 23 % of the cases. We have identified a number of phenotypes associated with mutations in known genes that cause hypopituitarism (HESX1, LHX3, LHX4, GLI2); in less frequently reported genes (BMP4, FGFR1, GLI3, TGIF1, FOXA2) and in genes that require additional evidence about causality (ARNT2, ZSWIM6, GPR161, PNPLA6, CDH2). We have identified de novo heterozygous variants in LHX3 and LHX4, transcription factors involved in the development of the pituitary. Two variants on LHX3 (p.L220S and p.P187S) were found in a patient with IGHD and a patient with CPHD, micrognathia, chiasm hypoplasia and bilateral cryptorchidism. LHX4 variants (p.Q100H, p.W204L and