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REUNIÓN CONJUNTA DE SOCIEDADES DE BIOCIENCIAS

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LIII REUNIÓN ANUAL DE LA SOCIEDAD ARGENTINA DE INVESTIGACIÓN BIOQUÍMICA Y BIOLOGÍA MOLECULAR (SAIB)

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JOINT MEETING OF BIOSCIENCE SOCIETIES

LXII ANNUAL MEETING OF ARGENTINE SOCIETY OF CLINICAL INVESTIGATION (SAIC)

LIII ANNUAL MEETING OF ARGENTINE SOCIETY OF BIOCHEMISTRY AND MOLECULAR BIOLOGY (SAIB)

LXV ANNUAL MEETING OF ARGENTINE SOCIETY OF IMMUNOLOGY (SAI)

MEETING OF ARGENTINE SOCIETY OF ANDROLOGY (SAA)

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MEETING OF ARGENTINE SOCIETY OF HEMATOLOGY (SAH)

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lecular level, 90% of all ccRCC patients show mutations in Von Hippel Lindau (VHL) gen which is involved in Hypoxia Inducible Factor 1α expression. Current research has shown that several metabolic alterations are associated with RCC, during tumor progression and metastasis. Mammalian cell metabolomics has emerged as a promising tool for studying cellular biochemistry and investigate altered metabolic networks that contribute to cell proliferation, growth and survival in RCC.

In this study, we have optimized a protocol for harvesting, extraction, lyophilization and reconstitution of metabolites present in conditioned media derived from human ccRCC cell lines 786-O ($VHL^{-/-}$) and Caki-1 ($VHL^{+/+}$), and the non-tumor human cell line HEK-293 (n=22); and we have profiled the exometabolome using a discovery-based metabolomics approach by means of ultraperformance liquid chromatography coupled to quadrupole-time-of-flight mass spectrometry (UPLC-QTOF-MS). Metabolic features (Rt, *m/z* pairs) were analyzed using a cross-validated orthogonal projection to latent structures-discriminant analysis model, using a genetic algorithm variable selection method. A panel of 12 discriminant features with tentative chemical identification allowed differentiating the three cell lines with 100% specificity, sensitivity and accuracy. In addition, 5 of these compounds were present in 10 human serum samples from ccRCC patients and healthy controls. Discriminant metabolic features suggest alterations of the glutathione and phenylalanine metabolism, tryptophan degradation and the pentose phosphate pathway. Current work involves validation of the tentative identification of the compounds with chemical standards.

Keywords: untargeted metabolomics, conditioned media, statistical multivariate analysis, mass spectrometry

(1747) **GENDER DIFFERENCES IN RENAL RESPONSE TO HIGH SODIUM INTAKE IN ADULT NORMOTENSIVE WISTAR RATS**

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There is a gender difference in the regulation of renal function and blood pressure in humans and also in several experimental animal models. We studied the renal response to high sodium intake in male and female Wistar rats.

The experiments were performed in intact male (IM), female (IF) and Gonadectomized (GX) Wistar rats at 150 days of life. Half of them were Orchidectomized (ORX) or ovariectomized (OVX) at 60 days of life and supplemented or not with testosterone propionate (ORXTo), 17β estradiol 3-benzoate (OVXE2) or medroxyprogesterone acetate (OVXP4) at 138 days of life , using cholesterol (CHO) as vehicle. During the last 5 days of the study, half of rats received normal sodium (NS, NaCl 0.24%) or high sodium diet (HS, NaCl 1% in drinking water). Glomerular filtration rate (GFR), renal plasma flow (RPF), sodium excretion (mmol/d/g kw) and mean arterial pressure (MAP, mmHg) were measured. To analyze the response of renal function upon HS, mRNA (Atpa1a) expression by RT-PCR and dephosphorylated Na+,K+-ATPase (dNKA), dopamine-D1-receptor (D1R), cytochromeP450A (CYP4A), Na+,K+,2Cl- (NKCC2) and Na+/Cl- (NCC) cotransporters were determined in renal tissue by western blot.

Under HS, both IM and IF do not change MAP and IF excrete more sodium and showed lower medulla dNKA, Atpa1a, cortical NCC and NKCC2 than IM. OVX excrete less sodium and ORX excrete more sodium than their intact ones and both increase MAP (all $p<0.05$).

The increase of MAP in OVX is a consequence of a defective D1R-CYP4A pathway, which results in more active dNKA and to a higher expression of NKCC2 and NCC, whereas it could be due to changes in GFR and RPF in ORX. E2, but not P4 or To prevented the increase in MAP.

There is a sexual dimorphism in renal function and blood pressure. Gonadectomized rats behave as a model of salt sensitivity. Findings provide a better understanding of gender differences in renal function.

Keywords: renal Na+,K+-ATPase; gonadectomy; dopamine; sex hormones; salt-sensitive hypertension.

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(1725) **ALBENDAZOLE METABOLITES IN SERUM AND URINE: A FIRST STEP IN DEVELOPING AN INDICATOR OF TREATMENT COMPLIANCE IN MASS DRUG ADMINISTRATION PROGRAMS**

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Soil Transmitted Helminth (STH) infections directly impact nutritional status, educational development, individual productivity, and physical and mental development in human populations. Currently, these infections are controlled through mass drug administration (MDA) programs using albendazole (ABZ) or mebendazole. However, not all programs have demonstrated expected impact on prevalence or intensity of infections. These failures may be related to poor programmatic coverage, suboptimal adherence or the exposure of parasites to sub-therapeutic drug concentrations due to poor drug dissolution, insufficient gastrointestinal absorption and/or systemic availability of the active ingredient.

The aims of the present work were to characterize the serum disposition kinetics and pattern of urinary excretion of ABZ and its main metabolites, ABZ sulphoxide (ABZSO) and ABZ sulphone ($ABZSO_2$) in human volunteers, and to determine the optimal time point where ABZ and/or its metabolites can be measured in urine as an indirect assessment of an individual's adherence to treatment. Venous blood and urine samples were collected from eight (8) volunteers between 2 and 72 h for HPLC analysis of ABZ/metabolites, following administration of a single postprandial oral dose of ABZ (400 mg). The ABZSO metabolite was the main analyte recovered either in serum and urine samples from ABZ-treated human. ABZSO serum concentrations reached its peak concentration (Cmax= 1.20 **±** 0.44 µg/mL) at 4.75 h post-treatment. In urine, ABZSO Cmax value was 3.24 ± 1.51 **µg/mL,** reached at 6.50 h post ABZ administration. The urinary AUC value resulted higher (2.3 fold) compared to that measured in serum. The overall, PK-based information reported here demonstrates that the measurement of ABZSO concentrations both, in serum and urine, could be useful to confirm compliance to ABZ treatment and an objective measurement of program coverage.

(1766) **AZILSARTAN AND ITS Zn(II) COMPLEX. SYNTHESIS, ANTICANCER MECHANISMS OF ACTION AND INTERACTION WITH BOVINE SERUM ALBUMIN**

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Azilsartan is the eighth approved member of angiotensin II receptor blockers for hypertension treatment. Considering that some drugs have additional beneficial effects on health when administered, we