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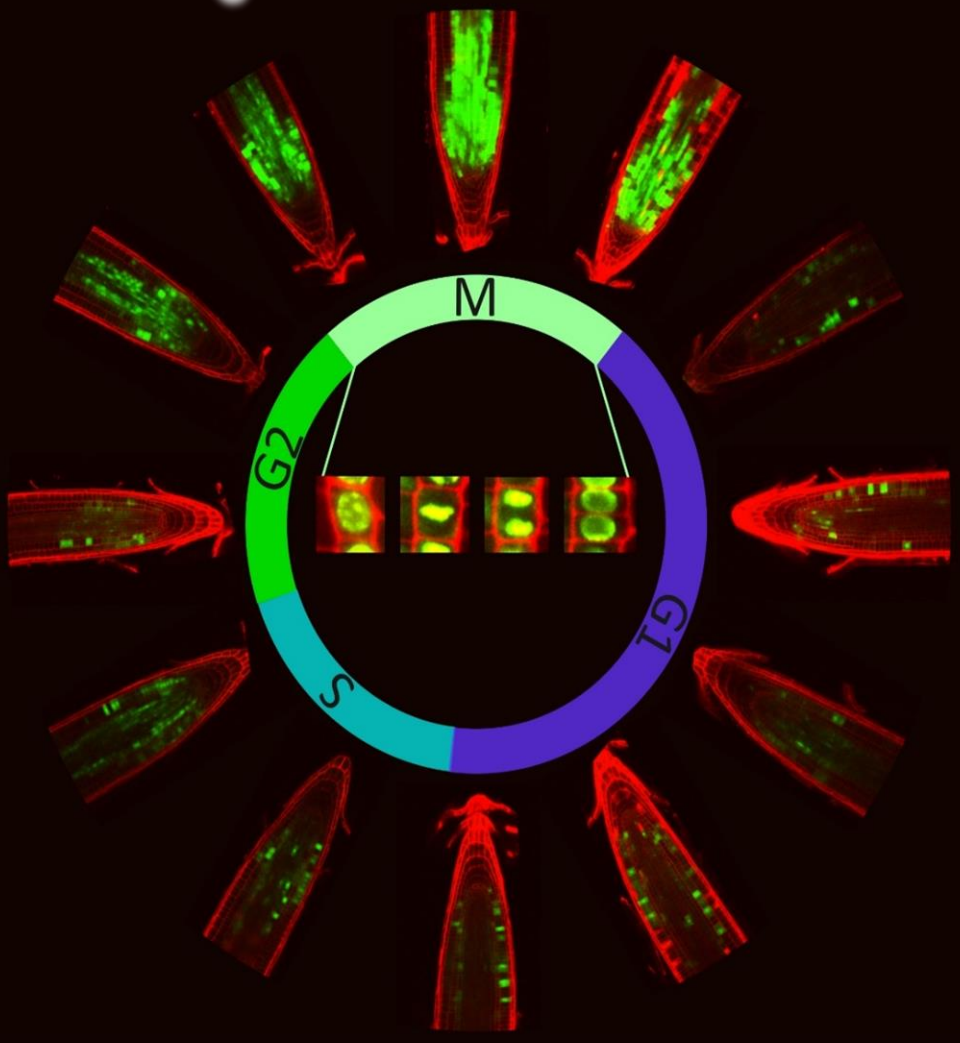

52TH ANNUAL MEETING

ARGENTINE SOCIETY FOR BIOCHEMISTRY AND MOLECULAR BIOLOGY

LII REUNIÓN ANUAL

Sociedad Argentina de Investigación en Bioquímica y Biología Molecular

Pabellón Argentina. Universidad Nacional de Córdoba

November 7-10, 2016

- SAIB -
52th Annual Meeting
Argentine Society for Biochemistry and Molecular Biology

LII Reunión Anual
Sociedad Argentina de Investigación en Bioquímica y Biología Molecular

November 7th–10th, 2016
Córdoba, República Argentina
Pabellón Argentina
Universidad Nacional de Cordoba

Cover Page:

Confocal microscopy images of Arabidopsis thaliana *root are displayed in the cover. The selected roots are expressing a GFP reporter of a mitotic cyclin (CYCB1;1-GFP, green), also they are counterstained with propidium iodide (IP, red) to display the cell structure. In order to follow the progression through the cell cycle phases, the root cells were synchronized in S phase using HU, and after pictures were taken every 2 hours. This type of experiment was also used to generate RNA samples to analyze the dynamics of different gene expression during the cell cycle. Inside the circle, which shows the cell cycle phases, images of cells expressing a histone fused to the fluorescent protein VENUS and stained with IP, are displayed. Those images allow following the steps of mitosis in vivo inside the root (PL-P56: Identification of cell cycle regulators inplants, by Goldy, C; Ercoli, MF; Vena, R; Palatnik, J, Rodriguez, Ramiro E.)*

Diseño de tapa: Natalia Monjes

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LI-P12
THE ROLE OF XBP-1 IN OSMOTIC ACTIVATED-LIPID SYNTHESIS.

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It is known that hypertonicity induces an abrupt synthesis of several osmoprotective proteins such as urea transporters, COX2, AQP2, AQP3, among others, and organic osmolytes. It is also known that a massive protein synthesis could cause endoplasmic reticulum (ER) stress. Previously, we showed that hypertonicity activates the expression of ER stress markers in MDCK cells subjected to high NaCl concentrations, XBP-1 and CHOP, among them. The active form of XBP-1 is a transcription factor that activates the expression of lipogenic genes which, in turn, activate membrane biogenesis and ER stress alleviation. As hypertonicity significantly increases lipid synthesis in renal cells, in the present work we evaluated whether XBP-1 is involved in such response. To do that, prior to hypertonicity treatment, MDCK cultures were treated with XBP1siRNA. After 24 h of hypertonic treatment, the synthesis of lipids and the expression of key lipogenic enzymes were assayed. NaCl treatment, significantly increased the synthesis of both phospholipids (PL) and triglycerides (TAG); XBP1 silencing reduced the levels 1,2 DAG and TAG formed. This finding was consistent with the decrease in the levels of Lipin2 and DGAT2 mRNA. Interestingly, PL synthesis was not affected. These results clearly evidence a major role of XBP1 in the regulation of lipid synthesis in renal epithelial cells.*Both last authors.

LI-P13
Tl(I) AND Tl(III) INDUCE ALTERATIONS IN LIPID METABOLISM IN DIFFERENTIATED MDCK CELLS

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Thallium (Tl) is a toxic heavy metal that contaminates the environment and affects human health. Tl intoxication affects several organs and tissues, being the kidney a main target of Tl toxicity. However, the molecular mechanisms are still poorly understood. Tl has two oxidation states, the monovalent (Tl(I)) and trivalent (Tl(III)) cations. Since most heavy metals disturb cell lipid homeostasis, in the present work we studied if Tl may affect lipid metabolism in differentiated renal epithelial (MDCK) cells. Confluent MDCK cells were differentiated in hypertonic medium for 72 h and further incubated for 48 h in the absence or presence of Tl(I) or Tl(III) (10 or 100 µM). After incubation, cells were collected, counted and lipids were extracted. Chloroformic extracts were resolved by TLC; phospholipids (PLs), cholesterol (Cho) and triacylglycerides (TG) contents were analyzed. Both Tl(I) and Tl(III) significantly increased PLs and Cho. Accordingly, microscopy images showed morphological alterations in cells. Together, results could suggest an expansion of membranes. Also, Tl(I) and Tl(III) significantly increased TG content along with an increased LD´s size and number. Also, Tl(I) and Tl(III) increased endogenous lipids biosynthesis. Obtained results indicate that Tl-mediated damage would involve severe alterations in lipid metabolism. *Both have to be considered as last authors.

LI-P14
ETHER-LINKED LIPIDS OF RAT DEVELOPING AND ADULT EPIDIDYMIS

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In mammalian tissues, glycerophospholipids (GPL) and tri-glycerides (TG) occur in three sublcasses, depending on wheth-er the chain at the sn-1 position of the glycerol backbone is a fatty acid, a fatty alcohol, or a fatty aldehyde. This study fo-cused on the ether-linked (EL) subclasses of GPL and TG, fol-lowing their changes during postnatal development in rat epidi-dymis and, in the adult, their distribution among epididymal caput, corpus and cauda regions. At postnatal day 30, in a still scarcely differentiated epithelium lacking spermatozoa, the epididymis already contained plasmanyl- and plasmenyl-ethanolamine (Pls-Et) with 22:4n-9 (DTA), the DTA-containing plasmenyl-choline (Pls-Cho) increasing with development and the presence of sperm. In the adult tissue, the DTA-Pls-Et con-centration per mg protein was highest in the corpus and higher than that of DTA-Pls-Cho in the three epididymal regions, sug-gesting a precursor-product relationship. The latter subclass is in turn the one to increase the most in rat spermatozoa as they mature. The epididymal EL-TG were even richer in DTA than the GPL, the 1-alkyl- predominating over the 1-alk-enyl- sub-class at all ages, their concentration being highest in the corpus. These results correlated well with the expression (mRNA) of a key peroxisomal enzyme involved in the biosyn-thesis of these lipids, alkylglycerone phosphate synthase

LI-P15
DISRUPTION OF THE CYTOSKELETON AND ALTERED LIPID METABOLISM IN SERTOLI CELLS

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Previous work demonstrated that exposures to mild hyperthermia results in altered lipid metabolism in cultured Sertoli cells (SC), as evidenced by accumulation of lipid droplets (LD), and that these changes concur with the disruption of SC cytoskeleton. To further investigate the relationship between cytoskeleton disruption and lipid perturbations, in this study SC cultures were exposed at a constant temperature to nocodazole (NCZ), an antineoplastic agent known to interfere with the polymerization of microtubules. As previously did hyperthermia, the cytoskeletal disarrangement induced by exposure to NCZ was accompanied by a significant alteration of the mitochondrial potential, an increase in triacylglycerol levels, a considerable accumulation of LD, and a functional cell impairment manifested in reduced expression of the SC-specific protein transferrin. As also seen after hyperthermia, the effects of NCZ on all these alterations were reverted after ending the exposures. The time-course of the changes suggest that the cytoskeletal disruption could be the primary cause of the SC mitochondrial alterations, which in turn may respond for the lipid metabolic

alterations, suggestive of intracellular recycling of membrane lipid components. The cytoskeleton is thus functionally relevant in maintaining the viability and survival of SC during metabolically adverse or stressful situations

LI-P16
DECREASED OXLDL UPTAKE AND CHOLESTEROL EFflUX IN THP1 CELLS ELICITED BY CORTISOL

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Data about glucocorticoids role in the development of atherosclerosis are controversial showing different effects in human than in experimental animal models. Atherosclerosis is the result of a chronic inflammatory response to an injured endothelium where an uncontrolled uptake of OxLDL (oxidized low density lipoprotein) by macrophages triggers the development of foam cells, the main component of fatty streaks in atherosclerotic plaque. There are few data about the direct effect of glucocorticoids in macrophages of atherosclerotic plaque. The aim of the study was to elucidate the role of glucocorticoids in the development of foam cells in atherosclerosis initiation. For this purpose we used THP1 cells differentiated to macrophages with phorbol esters and incubated with OxLDL alone or with cortisol or cortisone. Ours results showed that cortisol and cortisone decreased significantly the inflammation promoted by OxLDL, and also diminished the expression of genes involved in influx and efflux of cholesterol resulting in a reduced lipid accumulation. Our results indicate a direct effect of glucocorticoids on macrophages braking atherosclerosis initiation, reducing pro-inflammatory markers and OxLDL uptake and cholesterol re-esterification, but also inhibiting cholesterol output. These effects appear to be mediated, at least in part, by 11bHSD1 activity.

LI-P17
MOLECULAR CONSEQUENCES OF GPAT2 KNOCK-DOWN IN BREAST CANCER CELLS

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GPAT2, a glycerol-3P-acyltransferase isoform, is mainly expressed in pachytene spermatocytes and also highly expressed in certain tumor cells and tissues. We showed that GPAT2 expression promotes the tumorigenic phenotype of MDA-MB-231 cells, as its expression correlates to higher proliferation rate, lower apoptosis, and increased tumorigenic behavior, among others. To determine which genes and molecular pathways could be modified by GPAT2 in MDA-MB-231 cells we performed a transcriptomic analysis using an Agilent SurePrint G3 Human Gene Expression 8x60K v2 Microarray of GPAT2 silenced and control MDA cells. After filtering off for a FC>2 and p value<0.01, we found 616 differentially expressed genes (DEG; 326 up- and 290 down-regulated). Their functional enrichment analysis showed several molecular pathways and cellular processes affected by GPAT2 silencing. We focused on cancer-related pathways, particularly on WNT/Ca^{2+}, which is controversially considered as a tumor inductor or a tumor suppressor pathway, depending on the tissue and other conditions. In our model, several genes belonging to this pathway were significantly down-regulated upon silencing, ascribing to the Wnt/Ca2+ signaling the role of inductor rather than tumor suppressor. Further studies are needed to connect GPAT2 and WNT/Ca^{2+}, and to establish the impact of GPAT2 silencing on other cancer related genes.

LI-P18
STUDIES ON THE MOLECULAR CLOCK AND THE CIRCADIAN REGULATION OF HEPATIC TUMORAL CELL METABOLISM

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The circadian system comprising oscillators present in organs, tissues and even in individual cells temporally controls the body physiology. At the molecular level the “clock genes” (CGs) regulate their own expression and that of others “clock controlled genes” (CCGs). The clock liver controls the metabolism under a circadian base depending on feeding times; however, it is still unknown how liver works under a malignant growth. The aim of this project was to investigate the molecular clock work and the regulation of genes involved in the lipid metabolism in cultures of the human hepatoma cell line HepG2. We performed this study under two proliferative states, partial arrest and proliferation, maintaining cells with 0 or 5% of serum respectively after synchronization with dexamethasone (100 nM). We analyzed the expression of CGs (*Bmal, Per, Cry*), CCGs (*Rev-erb*) and the main enzymes involved in the glycerophospholipids (GPLs) biosynthesis (*Chk, Pcyt*) by qPCR. All genes assessed except *Chkα* showed oscillations under proliferation while no differences were observed in arrested cells except for *Pcyt2*. When we studied the endogenous content of GPLs in proliferation, we observed significant variations in the global and individual GPL levels at different times. These studies suggest that an active circadian control of metabolism takes place in proliferating HepG2 cells

LI-P19
NEUTRAL LIPIDS ARE INDUCED IN THE APPLE SNAIL *Pomacea canaliculata* BY CYPERMETHRIN PESTICIDE

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Lipids are involved in important cellular processes, they are essential for energy metabolism and their fate in organisms is regulated by environmental conditions. Lipid homeostasis could be altered in aquatic organisms exposed to stressors caused by anthropogenic