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different lipid metabolic pathways. Statins, as simvastatin (SV), are HMG-CoA reductase (HMGCR) inhibitors used primarily for hyperlipidemia, but have also been studied as anticancer agents. In the present work we studied the antiproliferative and hypolipogenic action of the combination of SV and *L. alba* EO (LEO) in HepG2 and A549 cells. CP was evaluated using MTT and neutral red assays , cells were treated with LEOs of four CHMs alone or combined with SV. All LEO-SV associations induced synergistic CP inhibition rather than treatments alone. For tagetenone LEO (TLEO)-SV combination, lipid composition and incorporation of ^{14}C-acetate into total, unsaponifiable and phospholipids (PL) were evaluated. The amount of HMGCR was also quantified by western-blot. TLEO-SV increases HMCR quantity, decreases cholesterol, PL and triglycerids synthesis and lipid content, instead of each drug separately. Our results suggest that LEO-SV synergism may be used as a novel cancer therapeutic regimen and as a more effective dyslipidemia control than statins alone.

LI-P19
METABOLIC LINK BETWEEN LIPID SYNTHESIS AND LIPID DROPLETS MORPHOLOGY INDUCED BY OLEIC ACID

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Nuclear lipid droplets (nLD) are a new nuclear (N) domain where neutral lipids are stored and organized. These droplets would be built up around a hydrophobic core of TAG and CE enriched in oleic acid and surrounded by a monolayer of polar lipids along with C (cholesterol) and associated proteins. nLD could be involved in nuclear-lipid homeostasis and provide or incorporate lipids and proteins involved in signaling pathways and transcription factors. The aim of the present work was to determine if nLD reversibly respond to external stimuli. The addition of oleic acid (OA) to HepG2 cells or primary culture of rat hepatocytes determined cellular shape modification, thus increasing TAG and CE content and cLD and nLD (number + size) , LD increments would be reverted if OA was excluded. cLD and nLD induction by OA was prevented by ACS (acyl-Co-A synthetase) inhibitor (TriacsinC) involved in lipid biosynthesis. nLD and cLD were stained with BODIPY and N with DAPI.
In conclusion, 1) nLD are a dynamic nuclear domain, 2) nLD number, size and lipid content are reversibly induced by OA, 3) nLD and cLD have a coordinated metabolism with a cellular regulation, 4) nLD and cLD are induced by OA by a reversible mechanism that involves ACS activity and TAG and CE biosynthesis.

LI-P20
INDOMETHACIN EFFECT ON BMMC MIGRATION: PROSTAGLANDIN SYNTHESIS INHIBITION OR PPARγ ACTIVATION?

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We have previously described the reorganization of major myelin and axonal proteins during sciatic nerve demyelination, as well as the migration of bone marrow mononuclear cells (BMMC) exclusively to the injured nerve. Once in the ipsilateral nerve, some BMMC colocalize with Schwann cell and nerve fiber markers. In this context, BMMC accelerate the degeneration process and, as a consequence, promote the onset of regeneration. The aim of the present work was to determine whether lesion-associated inflammation is involved in cell recruitment. To that end, animals subjected to sciatic nerve crush and transplanted or not with BMMC, were treated with indomethacin or vehicle and sacrificed at different survival times. Then BMMC migration, COX expression and prostaglandin (PGs) biosynthesis were evaluated. Results showed an injury-mediated induction of COX-2 expression. Treatment with indomethacin blocked BMMC migration but did not inhibit PG synthesis as evidenced by an increase in PGJ2. In the light of these results we can suggest that indomethacin action on BMMC migration occurs through an independent PG-mediated mechanism such as the PPARγ pathway. Further experiments are necessary to elucidate indomethacin effect on BMMC migration.

LI-P21
HEAT STRESS AFFECTS THE METABOLISM OF LIPIDS OF EPIDIDYMAL EPITHELIAL CELLS

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Frequent exposures of testes to hyperthermia are known to result in germ cell death, and, although not lethal to Sertoli cells, we previously showed that such exposures damage them structurally and functionally. Here we studied the

consequences of heat stress on the epididymis by assessing its effects on epithelial cells from its three regions (caput, corpus, and cauda) in primary culture. All of them had abundant lipid droplets (LD) rich in triacylglycerols (TAG), similar in size and numbers in vivo and in culture. Temperature-treated (a 15 min exposure once a day to 43ºC for 5 days) and control cells were incubated for 1 h with [3H]20:4 on the 5th day. In the three regions, TAG were faintly labeled, most of the fatty acid being taken up by phospholipids. Caput-derived cells exhibited the highest rate of lipid labeling. Due to heat exposures, caput and corpus cells showed a significant increase in the label from [3H]20:4 in diacylglycerols (DAG), concomitant with a decrease in the label in phosphatidylinositol (PI), phospatidylethanolamine phosphatidylglycerol (PE-PG), and little change in phosphatidylcholine (PC). Quite the opposite occurred in cells from cauda: the label in DAG decreased, while that in PI, PE-PG and PC increased. Our results suggest that epididymal cells are differentially susceptible to short but periodical exposures to mild hyperthermia

LI-P22
SPHINGOMYELINS WITH VERY LONG CHAIN PUFA ARE EXCLUDED FROM RAFT MEMBRANE DOMAINS IN MALE GERM CELLS

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The synthesis of sphingomyelins (SM) and ceramides (Cer) with nonhydroxy and 2-hydroxy very long chain PUFA (n-V and h-V) is a trait of differentiation in male rat germ cells. Here we evaluated how these lipids distribute among cell membranes as differentiation proceeds from pachytene spermatocytes to round and late spermatids, in relation to glycerophospholipids (GPL) and cholesterol. A small light (L) and a larger heavy (H) fraction, both derived from the plasma membrane, and a bulky fraction containing intracellular membranes were obtained. In the three cell stages, the L fraction concentrated Flotillin-1, indicating the existence of rafts membrane domains. This fraction had relatively more SM and more cholesterol than the H fraction in spermatocytes, and also more SM, but less cholesterol, in the two spermatids. In the three cases, the SM of L was rich in saturated fatty acids (SFA), whereas that of H contained virtually all the n-V and h-V of the plasma membrane. The GPL of L and H contained SFA and PUFA, respectively. The intracellular membrane fraction of the three cells contained most of the n-V and h-V Cer species of the cells, likely precursors of the SMs that in due course are incorporated in their plasma membranes. Thus, the global lipid composition and the distribution of lipids among cell membranes are significantly transformed during male germ cell differentiation.

LI-P23
GPAT2 SILENCING ALTERS ARACHIDONATE DISTRIBUTION IN MDA-MB-231 CELLS

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Glycerol-3-phosphate acyltransferases (GPATs) catalyze the first step in the de novo glycerolipid biosynthesis. Although mouse GPAT2 gene was first cloned by sequence homology to GPAT1, we have demonstrated that GPAT2 is notably different to the other GPATs. In order to elucidate its role in lipid metabolism, we explored the arachidonate (AA) distribution among membrane phospholipids in MDA-MB-231 control (scr-MDA) versus GPAT2 stably knocked down (sh-MDA) cells. Fatty acid composition of phospholipids (PL) and triacylglycerols (TG) was evaluated by GLC after a 3-day- incubation with 50 µM AA; AA content in PL and TG of sh-MDA cells was increased (13.6% vs. 6.8% and 13% vs. 3 % respectively). Endogenous AA-containing PL species were measured by LC/MS/MS. sh-MDA cells showed higher amounts of most AA-containing PC and PE species and lower amounts of (18:1/20:4)PI and (18:2/20:4)PI compared to scr-MDA cells. 2[H]-AA incubation for 30 min showed that sh-MDA cells incorporated higher amounts of AA in PC species and lower amounts in (18:0/ 2H 20:4)-PI and (18:1/2H20:4)-PI than scr-MDA cells. Phospholipase A specific activity was also measured and it was 50% lower in sh-MDA than in scr-MDA cells. In conclusion, GPAT2 expression in MDA-MB-231 cells diminished AA content in PC and PE and incorporation of exogenous AA in PC. Results presented here suggest a novel enzymatic activity for GPAT2.