as CD86 expression, as determined by flow cytometry. Our results suggest that DC precursors obtained from tumor-bearing mice retain the features of their normal counterparts.

51. (157) **SIRNA TARGETED KNOCK-DOWN OF NOX4 DECREASES MIGRATION IN AN ANAPLASTIC THYROID CARCINOMA CELL LINE.**

Romina Oglio, Luciano Rossich, Leonardo Salvarredi, Mario Alberto Pisarev, Guillermo Juvenal, Lisa Thomasz
National Atomic Energy Commission

BACKGROUND:
Overexpression of NADPH oxidase isoform 4 (NOX4) has been implicated in promoting cell survival, migration and invasion in many cancers. Anaplastic thyroid cancer (ATC) is one of the most lethal human malignancies. In the present study, we studied the effect of suppressing NOX4 by RNA silencing on the survival and migration on the ATC cell line, 8505C.
METHODS:
Small interfering RNA (siRNA) constructs targeting NOX4 were validated and used to develop clonal derivatives of the ATC cell line, 8505C. Cell viability was measured by MTT (thiazolyl blue tetrazolium bromide) assay. The wound healing assay was used to determine the migration of cells in culture. The expression of mesenchymal markers such as vimentin and E-cadherin was detected by Western blot. Transforming growth factor β1 (TGF-β1), FOXO1 and FOXO3 expression was determined by quantitative RT-PCR
RESULTS:
Targeting NOX4 expression in 8505C cells caused a 30 % decrease in migration and Western Blot analysis shows an increase of E-cadherin expression. However the cell viability has not changed. NOX4 siRNAs decreased mRNA levels of TGF-β1 (30%) and increased FOXO1 (20%) and FOXO3 (90%) mRNA expression.
CONCLUSION:
Targeting NOX4 in combination with other tumor-targeted drugs could be enhances the anticancer therapies in ATC.

52. (177) **4-METHYLUMBELLIFERONE EXERTS ANTI-TUMORAL EFFECTS IN A DEPENDENT AND INDEPENDENT MANNER TO HYALURONAN SYNTHESIS INHIBITION IN HUMAN GLIOBLASTOMA CELLS.**

Daniela Poodts, Matías Pibuel, Mariángeles Díaz, Élida Álvarez, Silvia E. Hajos, Silvina Lompardía
Instituto de Estudios de la Inmunidad Humoral, Facultad de Farmacia y Bioquímica-UBA-CONICET

4-methylumbelliferone (4MU) is a non toxic coumarins derivative that shows anti-tumoral effects on several neoplasms. Despite being widely used as hyaluronan (HA) synthesis inhibitor, HA-independent effects have been recently reported. HA is the main glycosaminoglycan of extracellular matrix and it is strongly involved in tumor progression, favoring cell proliferation and migration, processes that are directly related with glioblastoma, the most common primary tumor of central nervous system. Given that current therapy for this type of cancer is ineffective and highly toxic, new drugs are required for glioblastoma treatment. Our hypothesis is that 4MU exerts anti-tumoral effects on glioblastoma as a consequence of dependent as well as independent mechanisms of hyaluronan synthesis. Therefore, the aim of this work was to evaluate the effect of 4MU, alone and in combination with hyaluronan, on cell migration and metabolic as well as metalloprotease (MMP) activity in LN229 and U251 human glioblastoma cell lines. Metabolic activity was evaluated by XTT assay, migration by wound healing assay, MMPs activity by zymography and cell death by FDA/PI using flow cytometry. 4MU reduced metabolic activity in a dose dependent manner in both cell lines ($p<0.05$), however this drug slightly modified the percentage of PI+ LN229 and U251 cells. Besides, 4MU decreased gap closure and MMP-2 activity in both cell lines ($p<0.05$). Furthermore, the addition of HA partially prevented the 4MU effect on migration and MMP-2 activity ($p<0.05$) without modifying metabolic activity respect to 4MU alone in LN229 and U251 cells. In conclusion, we demonstrate that 4MU anti-tumoral effects on glioblastoma cell migration and MMP-2 activity seem to be dependent of hyaluronan synthesis inhibition, while 4MU effect on metabolic activity showed signs of being independent of hyaluronan metabolism. Altogether, these results highlight the potential use of 4MU for glioblastoma therapy.

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53. (227) **FATTY ACID COMPOSITION OF HUMAN EPICARDIAL ADIPOSE TISSUE: FROM LIPOPROTEINS TO ADIPOCYTES.**

Magali Barchuk, Veronica Miksztowicz, Jessica Luquez, Rosario Mecozzi, Graciela Lopez, Marta Aveldaño, Miguel Rubio, Laura Schreier, Maria del Carmen Fernandez Tome, Gabriela Berg
Universidad de Buenos Aires. Facultad de Farmacia y Bioquimica, *Universidad de Buenos Aires. Facultad de Farmacia y Bioquimica*, *CONICET-Universidad de Buenos Aires*, *CONICET-Universidad nacional del sur*, *INIBIBB-CONICET*, *Universidad de Buenos Aires. Facultad de Farmacia y Bioquimica*, *CONICET-IQUIFIB*, *Hospital de Clinicas Jose de San Martin*

Epicardial adipose tissue (EAT) is a visceral AT, surrounding and infiltrating myocardium and coronary arteries. An increase in EAT volume is directly related to coronary artery disease (CAD); this increase would be in part a consequence of greater fatty acids (FA) influx to adipocytes from lipoproteins, which hydrolysis is mediated by Lipoprotein Lipase (LPL). It is known that FA species in AT would determine its properties. To date, little is known about LPL behavior in EAT, and whether FA released from lipoproteins would determine its composition. Our aim was to evaluate LPL activity and FA composition in EAT, and their association to circulating lipoprotein characteristics and FA profile.
Methods: in EAT and subcutaneous AT (SAT) from patients undergoing coronary artery bypass graft (CAD, n=40) or valve replacement (No CAD, n=24) LPL activity was evaluated by a radiometric assay. Serum lipid profile and glucose were assessed. Circulating VLDL and HDL were isolated by ultracentrifugation and characterized in their lipid and protein composition. FA composition from EAT and lipoproteins were assessed by Gas Chromatography. The study was approved by the Ethic Committee of the Hospital de Clínicas, UBA.
Results: LPL activity was higher in EAT than in SAT in both groups ($p<0.001$). EAT LPL activity was higher in CAD compared to No-CAD ($p=0.01$). No differences were observed in VLDL and HDL characteristics between groups. EAT, but not SAT, LPL activity was inversely associated to VLDLs TG content ($R=-0.529$, $p=0.05$), mass ($R=-0.541$, $p=0.04$) and TG/protein index ($R=-0.691$, $p=0.05$). No differences in FA species was observed in EAT nor lipoproteins between groups, although FA pattern was conserved between EAT and lipoproteins.
Conclusion: The increase in EAT LPL activity in CAD would be responsible of VLDL catabolism, supplying FA to the tissue. Deeper knowledge in FA from EAT would help understand its behavior in CAD.

54. (232) **IS ENDOTHELIAL LIPASE A SUPPORTING ACTOR OF LIPOPROTEIN LIPASE? STUDY FROM THE GENE TO THE ACTIVITY IN AN OBESITY MODEL.**

Magali Barchuk, Veronica Miksztowicz, Ágata Carolina Cevey, Valeria Zago, Graciela Lopez, Rosario Mecozzi, Silvia Maria Friedman, Nora Goren, Celina Morales, Laura Schreier, Gabriela Berg
Universidad de Buenos Aires-Facultad de Farmacia y Bioquimica, *Universidad de Buenos Aires. Facultad de Farmacia y Bioquimica*, *Universidad de Buenos Aires. CONICET*, *Universidad de Buenos Aires. CONICET*, *Universidad de Buenos Aires. Facultad de Odontologia*, *Universidad de Buenos Aires. Facultad de Medicina*

Lipoprotein lipase (LPL) and endothelial lipase (EL) are involved in lipoproteins metabolism. In insulin-resistance (IR), with visceral adipose tissue (AT) expansion and cardiac steatosis, this enzymes behavior is altered. Peroxisome Proliferator Activated Receptors

(PPARs) and apoproteins (apo)CII and CIII could be partly responsible for these alterations. Aim: evaluate LPL and EL mRNA, protein levels and activity in AT and heart, association with lipoprotein profile and the role of PPARs and apoCs in an obesity model.
Methods: Male Wistar rats were fed with standard diet (Control,n=14) or High Fat Diet (HFD,n=14) during 14 weeks. Glucose, lipoprotein profile and IR markers were measured. Histological studies were performed in heart and epididymal AT. LPL and EL mRNA levels were assessed by RT-qPCR, proteins levels by Western Blot and enzymes activities by radiometric assays. Cardiac and AT PPARs expression were measured by Western Blot and hepatic apoCs mRNA by RT-qPCR. The study was approved by CICUAL-FFYB(UBA).
Results: In HFD, fat depots were observed in hearts, whereas AT presented higher adipocyte size. In heart and AT, no differences were found in EL mRNA levels between groups, while AT LPL mRNA and protein levels were decreased in HFD (p=0.04 and p=0.01,respectively), without differences in heart. In both tissues, EL protein levels and activity were increased (p=0.05 and p=0.001,respectively) and inversely associated with decreased LPL activity(heart: R=-0.64,p<0.001,AT: R=-0.53,p=0.004), being partially responsible for the atherogenic lipoprotein profile in HFD. PPARγ expression in AT was decreased in HFD, without differences in cardiac PPARδ expression and hepatic apoCs mRNA.
Conclusion: This is the first time that three levels of regulation of EL and LPL are reported. The increase in EL activity could be an alternative pathway for fatty acids release from lipoproteins and uptake in tissues with decreased LPL activity. In adipose tissue, PPARγ could be involved in enzymes regulation.

55. (249) **SATURATED FATTY ACIDS DIETS AND THE EFFECT OF SUPPLEMENTATION WITH DIFFERENT SOURCES OF OMEGA 3 FATTY ACIDS. STUDY IN EXPERIMENTAL MODEL.**

Anabel Impa Condori, Paula Perris, Inés Fernandez, Nora Slobodianik, María Susana Feliu
University of Buenos Aires, Faculty of Pharmacy and Biochemistry, Dept. Nutrition, Buenos Aires, Argentina

A balanced and varied diet is important to maintain optimal health status and prevent diseases. Diet's fatty acids profile has an essential function as immune regulator. Thymus is a biological marker of nutritional disorders.
The objective was to analyze the effect of diet containing butter, as fat source, with and without the supplementation with omega 3, on serum and thymus' fatty acid profiles of growing rats. Weanling Wistar rats received during 10 days normocaloric diet; fat was provided by butter (B). The others groups received the same diet supplemented with 24mg/day of fish oil (BF) or chía oil (BCh). Control group (C) received diet AIN´93. Serum and thymus fatty acids profiles were determined by gas chromatography. Statistical analysis used ANOVA and Dunnett test. Results were (%Area):
SERUM: OLEIC B:17.21±1.68b BF:18.85±2.66b BCh:20.07±2.94b C:10.36±1.85a. LINOLEIC(LA) B:7.82±1.83b BF: 8.23±0.88b BCh:8.82±0.59b C:19.59±2.92a. Alfa-linolenic(ALA) B: 0.29±0.12c BF:0.30±0.10b BCh:0.73±0.23a C:0.94±0.28a. EPA B:0.95±0.21a BF: 2.23±1.06b BCh: 2.74±0.45b C: 0.93±0.33a. DHA: B:1.90±0.30a BF:3.67±1.11b BCh:3.44±0.73 b C:1.33±0.19a .
THYMUS: OLEIC B:22.32±5.21 BF:25.58±2.66 BCh:22.38±4.79 C:18.42±2.82. LA B:3.95±0.58b BF:3.60±0.87b BCh:4.83±0.45b C:10.86±2.23a. ALA B:0.33±0.05b BF:0.26±0.06b BCh:0.54±0.06a C:0.57±0.13a. EPA B:0.49±0.17a BF:0.51±0.15a BCh:0.89±0.29b C:0.50±0.10a. DHA: B:0.62±0.14a BF:0.66±0.17a BCh:0.85±0.17b C:0.58±0.17a. Media that didn't present a letter(a,b) in common, were different(p<0.01).
In sera, B, BF and BCh groups showed lower LA levels and higher oleic acid levels, compared to C. Only B and BF present low values of ALA. BF and BCh groups presented high levels of EPA and DHA. In thymus, B, BF and BCh groups showed lower levels of LA than C. ALA present the same behavior than sera. Only BCh group increased EPA and DHA.
The results suggest that dietary lipids provoked changes in serum and thymus fatty acids profiles and the supplementation with omega 3 fatty acid provided by chía oil is better than that provided by fish oil.

56. (273) **TRANS FATTY ACIDS INTAKE, INCORPORATION INTO CIRCULATING LIPIDS AND LIPID PROFILE MODIFICATION IN UNIVERSITY STUDENTS**

Emilse Negro, Carolina Gerstner, Ainelén Radosevich, María Rosa Williner
Facultad de Bioquimica y Ciencias Biologicas-UNL

The effects of high intake of industrial trans fatty acids (t-FAs) can have a high long-term impact on human health. These t-FAs produce among others, alterations in lipid profile: increase of triglycerides (TG), total cholesterol (TC), LDL-cholesterol and Lip-a in plasma, and decrease levels of HDL-cholesterol. These isomers can be measured by gas chromatography in serum or plasma, erythrocytes and adipose tissue (AT) as biomarkers of t-FAs intake. However, the availability of AT limits their use in epidemiological studies. Therefore blood samples, that are most available, are widely used. This study describes the correlation between recent t-FAs intake calculated by a 24 hours recall (R- 24 hours) and their incorporation into circulating lipids, as well as the association between t-FAs intake and lipid profile modification in 116 university students of Santa Fe, Argentina. It was observed that 72.2% of students exceeded 1% total daily caloric value (TDCV) recommended by World Health Organization (WHO) for t-FAs intake and there is a significant correlation ($p < 0.05$) between "total t-FAs intake" vs "total t-FAs in serum". In relation with lipid profile, the effect which showed the strongest association with t-FAs intake was the decreased levels of HDL-cholesterol, with an OR of 2.26 ($p = 0.23$), followed by increased TG (OR 2.01, $p = 0.53$), increased LDL-cholesterol (OR 1.80, $p = 0.27$) and finally, the increased CT (OR 1.34, $p = 0.67$). The incorporation of t-FAs into circulating lipids was confirmed. Regarding the deleterious effect of them on the lipid profile, a certain association could be observed although it was not significant. Therefore, chronic t-FAs intake should be evaluated. Although the results were not conclusive, it is very important to avoid the consumption of t-FAs from the first stages of life.

57. (282) **CDK4 INHIBITION IMPAIRS BROWNING OF INGUINAL ADIPOSE TISSUE**

Andrea Estefanía Portales, Sabrina Gambaro, Ignacio Miguel, Alejandro Ezequiel Harnichar, Andrés Giovambattista
Instituto Multidisciplinario de Biología Celular (CICPBA-CONICET-UNLP)

Browning of adipose tissue (AT) is the appearance of thermogenically competent adipocytes in white AT depots upon cold exposure. Here, we aimed to assess if browning is regulated by cyclin-dependent kinase 4 (CDK4) activity. To this end, CDK4 was inhibited with simultaneous browning stimulation. C57BL/6J male mice were gavaged CDK4 inhibitor (Palbociclib (PAL), 50mg/Kg) or vehicle for 10 days. At day 3, groups were subdivided: half remained at 22°C (PAL and CTR) and the others were housed at 4°C (PAL-C and CTR-C). Body weight and caloric intake were daily recorded. At day 10, mice were euthanized and inguinal AT (IAT) was collected. Besides, stroma vascular fraction of IAT from CTR and PAL groups was differentiated to adipocytes. At day 8 post-differentiation, a subgroup of CTR and PAL differentiated adipocytes was treated with Forskolin for thermogenesis stimulation (CTR-F and PAL-F). qPCR was used in all experiments for analysis of thermogenic markers (Ucp1, Pgc1a, Prdm16). Results showed no differences in body weight between groups, whereas cold induced a rise in caloric intake (CTR-C vs CTR and PAL-C vs PAL). In IAT, PAL reduced expression of Ucp1, Pgc1a and Prdm16 in both basal and browning stimulated conditions ($p<0,05$, PAL vs CTR and PAL-C vs CTR-C). Similarly, Ucp1 and Pgc1a were downregulated in differentiated adipocytes of PAL group in basal conditions ($p<0,05$ PAL vs CTR). Thermogenic stimulation of Pgc1a was also reduced by PAL ($p<0,05$ PAL-F vs CTR-F). To assess the direct effect of CDK4 inhibition in AT, matures and differentiated adipocytes from IAT of CTR animals were treated in vitro with PAL or DMSO for 48 hs. qPCR analysis showed a decreased expression of Ucp1 in PAL matures and differentiated adipocytes ($p<0,05$ PAL vs CTR). Overall, these results show that CDK4 inhi-