SESSION VIII

ENDOCRINE REGULATIONS
CONTROL OF BODY WEIGHT

Thursday (September 16, 2021; 9:00 – 10:10)
Thursday (September 16, 2021; 11:30 – 12:15)

Chair:

Prof. Magdalena Olszanecka-Glinianowicz
Health Promotion and Obesity Management Unit, Department of Pathophysiology Medical Faculty in Katowice, Medical University of Silesia, Katowice, Poland

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DETAILED SESSION VIII SCHEDULE

Oral presentations (Thursday; September 16, 2021; 9:00 – 10:10; *virtual stream A*)

S8.L1 THE POSITIVE IMPACT OF VITAMIN D SUPPLEMENTATION ON GLUCOCORTICOSTEROID-DEPENDENT NEUROIMMUNOLOGICAL CHANGES. **D. Korewo [1], M.J. Karnia[1], D. Myslinska [2], P. Berezka, Z.M. Ciepielewski[2], J.J. Kaczor[1]** ([1]Gdansk University of Physical Education and Sport, Gdansk, Poland, [2]Faculty of Biology, University of Gdansk, Gdansk, Poland).

S8.L2 MOTS-C A NEW QUAINT ENDOCRINE PLAYER. **J. Bien, P. Kolodziejski, E. Pruszynska-Oszmalek, N. Leciejewska, D. Szczepankiewicz, K.W. Nowak, L. Nogowski, M. Sassek** ([1]Poznan University of Life Sciences, Department of Animal Physiology, Biochemistry and Biostructure, Poznan, Poland).

S8.L3 METABOLIC PARAMETERS IN OVARIECTOMIZED, ESTRADIOL-IMPLANTED SHEEP RESULTING FROM A LONG-TERM CHANGES IN BODY WEIGHT AND RESISTIN. **W. Biernat, M. Szczesna, K. Kirsz, D.A. Zieba** (Department of Animal Nutrition and Biotechnology, and Fisheries, Faculty of Animal Sciences, University of Agriculture in Krakow, Krakow, Poland).

S8.L4 EFFECT OF WHOLE BODY VIBRATION ON BONE NANOCOMPOSITES ORGANISATION AND PREVENTION OF BONE MINERAL DENSITY LOSS IN RATS WITH OBESITY AND LIMITED MOBILITY **N. Kostyshyn, M. Gzhegotskyi M.** (Danylo Halytsky Lviv National Medical University, Lviv, Ukraine).

Session summary

Poster session (Thursday, September 16, 2021; 11:30 – 12:15; *virtual stream C*)

S8.P1 LEPTIN, OMENTIN-1, MELATONIN AND VITAMIN D IN PATIENTS WITH CANCER OF LIP, ORAL CAVITY AND PHARYNX. **J. Nuszkiewicz, M. Budek, K. Szewczyk-Golec** (Department of Medical Biology and Biochemistry, Faculty of Medicine, Ludwik Rydygier Collegium Medicum in Bydgoszcz Nicolaus Copernicus University in Torun, Bydgoszcz, Poland).

S8.P2 CROSS-TALK BETWEEN THYROID HORMONES AND VITAMIN D. **E. Smolinska-Fijolek[1], J. Wierzbicka[2], M. Zmijewski[2]** ([1]Department of Physiology, Medical University of Gdansk, Gdansk, Poland; [2]Department of Histology, Medical University of Gdansk, Gdansk, Poland).

S8.P3 THE IMPORTANCE OF LEPTIN AND LIPIDS IN SHEEP'S MILK FOR HUMAN HEALTH. **E. Molik[1], Z. Flis[1], E. Marciniak[3], H. Pustkowiak[2]** ([1]Department of Animal Nutrition and Biotechnology, and Fisheries, University of Agriculture in Krakow, Poland, [2]Department of Genetics and Animal Breeding, and Ethology, University of Agriculture in Krakow, Krakow, Poland, [3]The Kielanowski Institute of Animal Physiology and Nutrition, Polish Academy of Sciences, Jablonna, Poland).

S8.P4 SINGLE NUCLEOTIDE POLYMORPHISM OF THE PROMOTER OF TNFRSF1A GENE (-610T>G, RS4149570) AS A USEFUL PREDICTOR OF MALNUTRITION IN PATIENTS TREATED WITH INTENSITY-MODULATED RADIATION THERAPY DUE TO HEAD AND NECK CANCER. **I. Homa-Mlak[1], R. Mlak[1], M. Mazurek[1], A. Brzozowska[2], T. Powrozek[1], T. Malecka-Massalska[1]** ([1]Department of Human Physiology, Medical University of Lublin, Lublin, Poland, [2]Department of Oncology, Medical University of Lublin, Lublin, Poland).

S8.P5 REGULATORY EFFECT OF IRISIN ON CARDIAC FIBROBLASTS PROLIFERATION IS DEPENDENT ON GLUCOSE CONCENTRATION. **M. Drobnik[1], M. Galdyszynska[1], J. Szymanski[2], P. Radwanska[1]** ([1]Laboratory of Connective Tissue Metabolism, Department of Pathophysiology, Medical University of Lodz, Lodz, Poland, [2]Central Scientific Laboratory, Medical University of Lodz, Lodz, Poland).

S8.P6 EFFECT OF N-ACETYLCYSTEINE SUPPLEMENTATION ON FATTY ACID TRANSPORTERS IN ADIPOSE TISSUE. **M. Wolosowicz[1], M. Maciejczyk[2], E. Zebrowska[1], B. Lukaszuk[1], A. Chabowski[1]** ([1]Department of Physiology, Medical University of Bialystok, Bialystok, Poland, [2]Department of Hygiene, Epidemiology and Ergonomics, Medical University of Bialystok, Bialystok, Poland).

S8.L1

THE POSITIVE IMPACT OF VITAMIN D SUPPLEMENTATION ON GLUCOCORTICOSTEROID-DEPENDENT NEUROIMMUNOLOGICAL CHANGES

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Dexamethasone (DEX) is used in treating a wide range of conditions. However, long-term exposure to its action affects immune system homeostasis disorders, memory, anxiety, and stress impairment response to the activation of inflammatory mediators in the brain. The study aimed to investigate whether vitamin D_3 supplementation would positively affect DEX-induced neuroimmunological changes measured by hippocampus and thymus total mass in long-term DEX administration. The research lasted 28 days and was carried out on 21 male Wistar rats randomly divided into three groups. These included two groups treated by abdominal injection of DEX at a dose of 2 mg/kg/day supplemented with vegetable oil (DEX PL; *n*=7) or with vitamin D_3 600 IU/kg/day (DEX SUP; *n*=8), respectively, and a control group treated with an abdominal injection of saline (CON; *n*=6). Blood, hippocampus, and thymus were collected and weighed immediately after sacrifice. The vitamin D metabolites concentration were measured. We found decreased serum $25(OH)D_3$ level and a lower hippocampus and thymus mass in both DEX-treated groups; however, vitamin D_3 attenuates this adverse effect in a statistically significant manner.

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S8.L2

MOTS-C - A NEW QUAINT ENDOCRINE PLAYER

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D. SZCZEPANKIEWICZ, K.W. NOWAK, L. NOGOWSKI, M. SASSEK

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MOTS-c is a recently discovered mitochondrial-derived peptide. Its coding sequence was found *in silico* in mitochondrial genome, exactly in 12S rRNA part of it. It has very conservative amino acid sequence in different animal species such as mouse, rat, bonobo and human. Moreover this newly discovered peptide proved to be biologically active. There are studies that show its attenuating effect in insulin resistance and diet induced obesity in mice. It this study we examined the influence of MOTS-c peptide on secretion of two main pancreatic hormones: glucagon and insulin. We used two types of models to test this: laboratory cell lines INS-1E and αTC-1 and isolated rat pancreatic islets. Insulin secretion increases significantly from both pancreatic islets and INS-1E cells, when the glucagon secretion lowers significantly from αTC-1 cells and isolated rat pancreatic islets. These results are promising since MOTS-c is still not well examined and someday it may play a significant role in curing type 2 diabetes and obesity.

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S8.L3

METABOLIC PARAMETERS IN OVARIECTOMIZED, ESTRADIOL-IMPLANTED SHEEP RESULTING FROM A LONG-TERM CHANGES IN BODY WEIGHT AND RESISTIN

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Both long-term undernutrition and overnutrition disturb metabolic balance, which is mediated partially by the action of two adipokines, leptin and resistin (RSTN). In this study, we manipulated the diet of ewes to produce either a thin (lean) or fat (fat) body condition and investigated how RSTN affects endocrine and metabolic status under different leptin concentrations. In the current study, we manipulated the diet of ewes over 4 months to produce either a thin (Lean) or fat (Fat) body condition and investigated how resistin affects metabolic status under low (thin sheep) or high (fat sheep) circulating levels of leptin (fat sheep). Twenty ovariectomized ewes with estrogen replacement were assigned to one of four groups. Plasma was assayed for RSTN, leptin, GH, glucose, insulin, total cholesterol, nonesterified fatty acid (NEFA), high-density lipoprotein (HDL)-cholesterol, low-density lipoprotein (LDL)-cholesterol and triglycerides. The results indicate that long-term alterations in body weight affect RSTN-mediated effects on metabolic parameters. Body weights of Lean and Fat groups were 41.2 ± 0.92, and 78.1 ± 1.78 kg, respectively ($P < 0.01$). Abdominal fat weight was 0.2 ± 0.02 kg in Lean and 5.3 ± 0.4 kg in Fat animals ($P < 0.01$) postmortem. Jugular blood samples (5 ml) were collected at 10-min intervals over 4 h *via* indwelling catheters to establish metabolic hormone status before and after resistin challenge. Within nutrition groups, mean (± SEM) pretreatment plasma concentrations of leptin were over 5-fold lower ($P < 0.01$) in Lean compared to Fat group, plasma NEFA was greater ($P < 0.05$) in Lean compared to Fat sheep. Resistin treatment increased ($P < 0.01$) plasma concentrations of leptin in both Lean and Fat groups. RSNT enhanced ($P < 0.05$) plasma total cholesterol in Fat group compared to Lean one, and decreased ($P < 0.05$) HDL fractions in Lean relative to Fat group. Mean GH concentrations were increased ($P < 0.05$) by resistin in Lean ewes, whereas insulin concentrations were increased ($P < 0.001$) by resistin treatment in Fat ewes. In conclusion, we have shown that alterations in BW influence the effects of RSTN on metabolic parameters in sheep. RSTN appears to be another adipokine, in addition to leptin, that is strongly involved in the regulation of body conditions in female sheep.

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S8.L4

EFFECT OF WHOLE BODY VIBRATION ON BONE NANOCOMPOSITES ORGANISATION AND PREVENTION OF BONE MINERAL DENSITY LOSS IN RATS WITH OBESITY AND LIMITED MOBILITY

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Several studies indicate that obesity is associated with increased bone mass due to excessive mechanical stress. However, these data are controversial, and the risk of fractures in this group is high. This study aimed to investigate the influence of high-frequency whole body vibration on metabolic and structural responses of rats' bone tissue with limited mobility and obesity. Obesity combined with a sedentary lifestyle can present the potential for negative health effects. However, whole body vibration can be used as a means of non-pharmacological correction of bone mineral density. For characterization of bone nanocomposites organisation and prevention of mineral density loss X-ray diffraction method was used. Markers of bone remodeling in the rats' blood: leptin, osteocalcin, tartrate resistant acid phosphatase 5b, alkaline phosphatase. Using a high-calorie diet and low-mobility model, we proved that bone mineral mass had been decreasing since 8th week. It should be noted that the decrease in the relative amount of crystalline phase - hydroxyapatite, continued throughout the experiment, up to 24 weeks ($p < 0.05$). These structural changes were accompanied by changes in quantitative indicators of the bone remodeling markers. Rats had lower bone mineral density compared to the animals that were on the normal diet and were further affected by whole body vibration. We observed the increase of the crystalline phase volume fraction from 84% to 93% ($p < 0.05$) in group with additional whole body vibration and the decrease of the mineral component in rats with limited mobility condition and high-calorie diet. Therefore, vibration could improve structural conditions of bone and prevent fat accumulation and obesity-associated biochemical markers in obese rats. This can be an effective method to improve the structural and functional state of the bones while preventing the loss of bone mineral density.

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S8.P1

LEPTIN, OMENTIN-1, MELATONIN AND VITAMIN D IN PATIENTS WITH CANCER OF LIP, ORAL CAVITY AND PHARYNX

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Tumors of the lip, oral cavity and pharynx (LOCP) are classified as cancers of the head and neck. LOCP neoplasms have been determined to account for approximately 6% of all tumors. In the course of LOCP neoplasms, the organism homeostasis is disturbed, leading to endocrine and metabolic changes. Adipose tissue hormones, known as adipokines, regulate metabolism, food intake and modulate inflammation. Melatonin and calcitriol, an active form of vitamin D, are hormones found to influence the synthesis and secretion of adipokines. They are also compounds with antioxidant activity. Clinicians point to the deficiency of both melatonin and vitamin D worldwide. The aim of the study is to determine the concentration of melatonin, vitamin D and two adipokines, namely leptin and omentin-1, in patients diagnosed with LOCP cancer. The study group consisted of 25 patients with LOCP neoplasm (10 female and 15 male, mean age 58.24) and the control group consisted of 25 healthy subjects (14 female and 11 male, mean age 55.36). Blood serum samples were obtained after collecting venous blood. $P < 0.05$ was considered as statistically significant. A significantly lower concentration of vitamin D was observed in the LOCP cancer patients. Similar results were observed for leptin level. There were no statistically significant differences in the level of omentin-1 and melatonin. The obtained results indicate the occurrence of vitamin D deficiency in patients with LOCP cancer. Lower levels of leptin in cancer patients may indicate the body depletion accompanying the disease.

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S8.P2

CROSS-TALK BETWEEN THYROID HORMONES AND VITAMIN D

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Vitamin D is actively produced in the skin subjected to UV radiation. Its biological faction is complex and multidimensional, resulting from its pleiotropic properties. In addition to its well established impact on calcium-phosphate homeostasis vitamin D is known modulator of cell proliferation and differentiation, including keratinocytes. The long-recognized “thyroid-skin conection” encompasses many layers of complexity and it has become a hot frontier in dermatoendocrinology. Thyroid disorders are known to involve all organ systems of the body and the skin is no exception. Cutaneous manifestations generally appear subsequent to the development of thyroid disease, but may be the first presenting sign or even precede the diagnosis by many years. However, the relationship between vitamin D and “thyroid-skin connection” has not been well elucidated. The aim of the research was to analyze the *in vivo* effect of vitamin D on the keratinocytes and thyrocytes cells lines. Cytotoxic and anti-proliferative activities of $1,25(OH)_2D_3$ against thyrocyte were tested. Gene expression profiling was performed by real-time qPCR on keratinocytes or thyrocytes treated with vitamin D. No remarkable cytotoxicity activity of vitamin D was observed in the range of tested conditions in HaCaT keratinocytes, while inhibition of proliferation of thyrocytes in a dose-dependent manner was shown. Testing the effects of vitamin D on human keratinocyte and thyrocyte transcriptional pattern, we found that this compound modulated of expression of receptors and enzymes responsible for thyroid hormone synthesis and activity. Our results suggest that expression of genes involving in metabolism and intracellular activities of the thyroid hormones in skin and in thyroid follicular cell can be modulate by the vitamin D. Our results suggest that expression of genes involving in metabolism and intracellular activities of the thyroid hormones in skin and in thyroid follicular cell can be modulate by the vitamin D.

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S8.P3

THE IMPORTANCE OF LEPTIN AND LIPIDS IN SHEEP'S MILK FOR HUMAN HEALTH

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Chronic metabolic disorders, referred to as „civilization diseases", such as diabetes, obesity or cancer are major public health problems. In recent years, people are becoming more aware that the cause of these diseases is an inappropriate lifestyle and diet. In the conditions of epidemiological threats and living in a polluted environment, the consumption of natural products, such as sheep's milk and its products, may support the functioning of the body. A measure of the high pro-health value of sheep's milk is i.a. lower cholesterol content, more favorable fatty acid composition, such as conjugated linoleic acid (CLA) and higher polar lipid content. CLA is one of the most important antioxidants of milk fat and has anti-carcinogenic and antimutagenic properties. Metabolic hormones, in particular leptin, are also crucial bioactive factor in sheep's milk. Leptin is involved in the control of the reproductive and endocrine systems, blood pressure, hematopoiesis and angiogenesis. The aim of the research was to determine the content of CLA and leptin in sheep's milk. The conducted research shows, that with the progress of lactation and the shortening of the day, the content of leptin in milk increases. Leptin content in the first two months of milking was (May 36.7 ± 6.2 ng/ml; June 36.7 ± 5.3 ng/ml), while in the last month it increased significantly ($P \leq 0.01$) and was (September 47.7 ± 6.2 ng/ml). Additionally, the content of CLA in the tested milk changed. In May, the content of CLA was (2.529 ± 0.01%), and in September (2.674 ± 0.01%). The obtained research results may allow the production of medicinal food from sheep's milk, which can be used in the prevention of many human diseases, including civilization diseases.

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S8.P4

SINGLE NUCLEOTIDE POLYMORPHISM OF THE PROMOTER OF *TNFRSF1A* GENE (-610T<G, RS4149570) AS A USEFUL PREDICTOR OF MALNUTRITION IN PATIENTS TREATED WITH INTENSITY-MODULATED RADIATION THERAPY DUE TO HEAD AND NECK CANCER

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Head and neck cancers (HNCs) are 7th for the prevalence among malignancies in the world. In this group of patients malnutrition, at the moment of diagnosis, is observed even in 52%. Malnutrition in patients with cancer is associated with a higher risk of morbidity and mortality. It is usually related to a higher rate of toxicities associated with treatment (chemotherapy or radiotherapy) and decreased quality of life. Defining risk factors of developing moderate and severe malnutrition would enable the introduction of greater individualization of treatment of HNC patients. Available studies suggest that inflammation caused by abnormalities levels of pro-inflammatory cytokines, e.g. tumor necrosis factor-α or alterations in their receptors, e.g. tumor necrosis factor receptor superfamily member 1A (TNFRSF1A) may promote the development of malnutrition. The study included 74 patients with advanced HNC (III and IV stage according to VII edition of TNM) treated with intensity modulated radiation therapy (IMRT). Nutritional status was determined using BMI, subjective global assessment (SGA), and nutritional risk score (NRS-2002) scales and laboratory tests. Single nucleotide polymorphism (SNP) (-610T>G; rs4149570) in the *TNFRSF1A* gene was determined by mini-sequencing. The occurrence of the GG genotype of TNFRSF1A gene significantly increased (over 5.5 times) the risk of severe (C) malnutrition according to the SGA scale (53.12% vs.16.67%; OR = 5.67; p=0.0015). On the other hand, GT heterozygote carriers had a significantly lower (more than 4-fold) risk of severe (C) malnutrition according to the SGA scale (17.14% vs. 46.15%; OR=0.24; p=0.0100). Based on the multivariate analysis, it was found that M1 feature (HR=9.46; p=0.0308), stage IV according to TNM classification (HR=3.76; p=0.0168) and the GG genotype of the *TNFRSF1A* gene (HR=2.18; p=0.0419) were independent, unfavorable prognostic factors. Conclusion: assessment of the *TNFRSF1A* SNP could be a useful tool in assessing the risk of disturbances in nutritional status and body composition in patients treated with IMRT due to HNC. Moreover, studied SNP in this group of patients may serve as an independent prognostic factor.

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S8.P5

REGULATORY EFFECT OF IRISIN ON CARDIAC FIBROBLASTS PROLIFERATION IS DEPENDENT ON GLUCOSE CONCENTRATION

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Irisin, (the myokine derived from precursor of fibronectin III) is secreted by skeletal muscle, heart and adipose cells. The myokine increases glucose uptake by muscle cells. Irisin upregulates expression of glucose transporters genes in adipose and muscle cells. Irisin involvement in induction of heart fibrosis in diabetics is supposed. The study is aimed at: 1) Verification of hypothesis suggesting that irisin may be involved in regulation of cardiac fibroblast proliferation, 2) Explanation, whether concentration of glucose in medium may influence on the final effect of the myokine, 3) Clarification, whether irisin may influence on the glucose transporter (GLUT) density on cardiac fibroblast membrane. The experiments were performed on cardiac fibroblasts, cultured in different concentrations of glucose: 1 M (hypoglycemia), 5 M (normoglycemia) and 25 M (hyperglycemia). Proliferation of fibroblasts was evaluated by BrdU method. Expression of GLUT was confirmed by flow cytometry. Different concentration of glucose did not influence on cardiac fibroblasts proliferation. Irisin treatment in hypoglycemic conditions was ineffective. The myokine applied at concentration 10^{-8} M, in normoglycemic as well as 10^{-8} M and 10^{-9} M in hyperglycemic conditions, increased proliferation of cardiac fibroblasts. Moreover, the expression of GLUT1, GLUT3 and GLUT4 on cardiac fibroblasts membrane was proved. The blockade of all three glucose transporters by application of WZB 117 markedly decreased proliferation of tested fibroblasts. However, irisin did not modified density of glucose transporters on fibroblasts membrane. We conclude that irisin stimulates the cardiac fibroblasts proliferation. The effect is dependent on glucose concentration in medium. Irisin did not modify density of glucose transporters (GLUT1, 3 and 4) on cellular membrane of cardiac fibroblasts.

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S8.P6

EFFECT OF N-ACETYLCYSTEINE SUPPLEMENTATION ON FATTY ACID TRANSPORTERS IN ADIPOSE TISSUE

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Obesity is a systemic, multifactorial, and largely preventable disease, affecting, along with overweight, over a third of the world's population in the XXI century. Chronically elevated body mass index (BMI) is linked to the occurrence of a broad range of diseases, namely cardiovascular diseases, diabetes, musculoskeletal disorders, and cancers. The adipose tissue is a critical regulator of systemic energy homeostasis by acting as a caloric reservoir. Augmented oxidative stress in adipose tissue of obese subjects leads to insulin resistance, dysregulated adipokines secretion, inflammation, and increased protein carbonylation. Based on this, we aimed to check whether anti-oxidative agent - N-acetylcysteine (NAC) impacts fatty acid transporters expression in adipose tissue using a rodent model of a high-fat diet (HFD). Four-weeks old Wistar rats were randomly divided into four groups (n=10): normal diet, normal diet + NAC, HFD, and HFD + NAC. The mRNA levels and protein expression of FAT/CD36, FABPpm, FATP1, and FATP4 were assessed using real-time PCR and Western Blot analyses. The level of lipids abundance (FFA, DAG, TAG, and PL) was estimated by GLC. In visceral and subcutaneous adipose tissues statistically significant differences in the mRNA and protein levels of the long-chain fatty acid transporters have been found. Eight weeks of NAC treatment during the HFD regime resulted in a significant increase ($p > 0.05$) in FATP1, FATP4, and FABPpm proteins expression in visceral and subcutaneous adipose tissue compared to the respective HFD. On the other hand there were observed a significant decrease ($p > 0.05$) in FATP1, FATP4, FABPpm, and also in FAT/CD36 mRNA expressions in both adipose tissues. Interestingly, there were observed decrease in FFA, DAG, TAG and PL content in NAC+HFD groups compared to HFD, in visceral and subcutaneous adipose tissue. Our results revealed that NAC supplementation during the HFD regime promotes a decrease in the lipids pool in adipose tissue compared to HFD. Currently, studies are underway to identify the mechanisms involved in the observed phenomena.

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