enriched diets on non-alcoholic steatohepatitis (NASH) model assessed in T2DM Wistar rats. Degree of evolution of NAFLD to NASH was histopathological evaluated according to a NAFLD-activity score (NAS, maximum punctuation of 8). Rats were randomly divided into three groups: lateT2DM-control (D) group, CFE as preventive of late T2DM (ED) group, and CFE as therapeutic treatment of late T2DM (DE). D group revealed panlobular steatosis with macrovesicular and microvesicular intracellular lipid droplets, predominantly in portal area (NAS, 7.25±0.89). ED rats displayed lower steatosis and lobular inflammation, (NAS, 5.50±0.76; $p<0.01$ vs. D group); and DE group revealed a reduction in lobular inflammation and a lower NAS (NAS, 6.25±0.71; $p<0.05$ vs. D group). ED and DE rats showed a better distribution according to 7-8 punctuation NAS prevalence (75%, 12.5%, and 37.5% in D, ED, and DE groups, respectively; X2= 0.009). Present results indicate that CFE-RM consumption effectively protects against NASH development by reducing steatosis degree and lobular inflammation suggesting its potentiality as an appropriate meat-product functional ingredient in managing NAFLD associated to T2DM.

Keywords: Type 2 Diabetes Mellitus; functional meat; carob fruit; NASH

Abbreviations: NAFLD, Non-alcoholic Fatty Liver Disease; NASH, Non-alcoholic Steatohepatitis; CFE, Carob Fruit Extract; RM, restructured meat; T2DM, Type 2 Diabetes Mellitus.

Funding and Conflicts of Interest: This work was supported by Spanish Project PID2019- 103872RB-I00. Macho-González A received a predoctoral fellowship award from the Spanish Ministry of Education, Culture and Sports (FPU15/02759).
The authors declare no conflict of interest.

doi:10.1016/j.metabol.2020.154620

0154
Deletion Of Thimet Oligopeptidase Attenuates Nash Trough Microrna MIR-34a

Bruna A.C. Santos, Lucas A.F. da Rocha, Emer S. Ferro, Alice C. Rodrigues

Department of Pharmacology, Institute of Biomedical Sciences, University of São Paulo, Sao Paulo, Brazil

Abstract
Background: In metabolic disorders, thimet oligopeptidase (THOP1) deletion protects mice from developing obesity-related diabetes and consequently, nonalcoholic fatty liver disease (NAFLD). Recently, it has been shown peptides processed by THOP1 can prevent the maturation of the microRNAs. Objectives: Herein, we aimed to clarify if microRNAs are enrolled in the mechanism by which THOP1 protects mice from progression of NAFLD. Methods: 8-week-old male mice knockout for THOP1 (KO) and its background (WT) were fed a control (C) or high-fat, choline deficient diet (CD) for 8, 15 or 24 weeks. Mouse liver was harvested for histopathological analyses, miRNA global expression using microarray, RNAm expression by qPCR and protein expression by western blot. Results: KO mice were resistant to obesity and insulin resistant after 15 and 24 weeks of diet. CD diet induced NAFLD in both KO and WT mice after 8 weeks of diet. Surprisingly, from 15 weeks of diet, THOP1 deletion reduced steatosis and fibrosis scores measured from histological sections stained with hematoxylin-eosin and Mason´s trichrome, respectively, in mouse liver. Improvements of NAFLD was correlated with the downregulation of microRNA miR-34a in the liver, as well as, reduced expression of PPARg, CD36, Col1a1 and Timp1. Conclusion: Our data suggest that the deletion of thimet oligopeptidase seems to counteract fibrosis and steatosis associated to obesity/diabetes by affecting miR-34a.

Keywords: THOP1, steatohepatitis, obesity, diabetes, microRNA.

Abbreviations: Control diet (C); Choline deficient diet (CD)

Funding and Conflicts of Interest: This work was supported from grants and scholarship by Fundação de Amparo à Pesquisa do Estado de São Paulo [grants number 15/24789-8; 16/04000-3; 19/15965-8] and CNPQ.

doi:10.1016/j.metabol.2020.154621

0155
The Study of Association Between BGLAP HindIII-Polymorphic Variant And Type 2 Diabetes Mellitus Development Among Ukrainians With Arterial Hypertension

Yaroslav Chumachenko[a], Aliona Kolnoguz[a], Viktoriia Harbuzova[a], Alexander Ataman[b]

[a]*Scientific Laboratory of Molecular Genetic Studies, Medical Institute of the Sumy State University, 40004, Ukraine*
[b]*Department of Physiology and Pathophysiology with Medical Biology Course, Medical Institute of the Sumy State University, 40018, Ukraine*

Abstract
Background: Nowadays, the attention of scientists is focused on the systemic energy metabolism regulation by skeleton. Bone tissue affects the glucose turnover through the production of undercarboxylated osteocalcin (ucOCN), which in turn stimulates insulin expression and secretion as well as increases sensitivity of adipocytes, muscle cells and hepatocytes for this hormone. Current evidence showed an inverse association between serum OCN concentration and adverse metabolic outcomes, assuming the crucial role of OCN in type 2 diabetes mellitus (T2DM) pathogenesis. Objective: To analyze the link between OCN gene (BGLAP) HindIII-polymorphism and T2DM occurrence among Ukrainians with arterial hypertension (AH). Methods: The study included 153 patients with T2DM (mean age ± SD 64.67±8.2 years) and 311 relatively healthy individuals (mean age 65.65±12.58 years). Polymerase chain reaction- restriction fragments length polymorphism analysis (PCR-RFLP) was performed for genotyping. Logistic regression with interaction term "genotype × AH" was used for the association analysis under four models of inheritance. Bonferroni correction was applied for accurate results. P ˂ 0.05 was considered as significant. Results: There was no statistically significant association between BGLAP HindIII-polymorphic variant under dominant, recessive, over-dominant and additive models of inheritance (Pab > 0.05; Paint b > 0.05). Conclusion: No association was found between BGLAP HindIII-polymorphic variant and T2DM development among Ukrainians with AH. Further studies are necessary to confirm the results.

Keywords: type 2 diabetes mellitus, osteocalcin, single nucleotide polymorphism

Funding and Conflicts of Interest: This study was performed under scientific project "Molecular-genetic and morphological features of lower limb tissues regeneration under conditions of chronic hyperglycemia" (0117U003926). There is no conflict of interests.

doi:10.1016/j.metabol.2020.154622