EX527 induces an increase in acetylation of H3K9 but decrease overall methylation.

Conclusions: The results of our work indicate for the first time that PFD can regulate epigenetic marks possibly through modulation of the PPARγ-SIRT1-DNMT1 axis. Acetylation in H3K9 decreases with PFD treatment, however overall methylation increases. The perspectives of this work will be to analyze the methylation of specific genes (PPARalpha, IL-6, TNFalpha) involved in the development of liver diseases.

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Molecular, histological and biochemical changes in a NASH murine model whit a diet high in fats and sugars

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Background and aim: The increase in NASH prevalence coincides with the current obesity pandemic. Obesity is characterized by a state of chronic inflammation with oxidative stress in adipose tissue and liver. A high fat/sugar diet can induce non-alcoholic steatohepatitis, which is characterized by inflammation, hepatocyte swelling, and steatosis. To assess molecular, histological, and biochemical changes in a murine NASH model subjected to a high-fat diet for 16 weeks.

Material and methods: Male mice 4-5 weeks old, C57BL / 6J were fed a high-fat diet (HF, 60% fat, 42gr / L sugars in water) for 16 weeks. Every 4 weeks 4 mice were sacrificed for a follow-up of the model at 4, 8, 12 and 16 weeks. Serum glucose was measured after 4 hours of fasting, animal weight and caloric intake. The liver was removed and weighed, as was the epididymal adipose tissue. AST, ALT, TAG, Chol and VLDL were measured. Immunohistochemistry was performed for α-SMA and hematoxylin-eosin staining, Masson's trichrome and Syrian red. The hepatic expression of IL-6, TNFα, COL1A1 and TGF-β mRNAs was determined by qRT-PCR. Quantitative variables were analyzed with ANOVA, Tukey for parametric data and Kruskal-Wallis for non-parametric data. Opinion CI00518 of ethics and investigation committee.

Results: Animals at week 16 showed high body weight compared to animals with standard diet, presence of steatosis and liver inflammation ($p < 0.05$). Serum glucose increased at week 12 and 16 ($p < 0.05$). The weight of the liver and epididymal fat increases as the model is established, without achieving statistical significance. The histological parameters coincide with the establishment of a steatohepatitis, while the values of the biochemical parameters increase remarkably compared to the control group. Inflammatory and fibrotic genes increase at 16 weeks compared to the control group.

Conclusions: Exposure to a diet high in fat and simple sugars induced increased body weight, steatohepatitis, inflammation, hyperglycemia, and increased expression of liver enzymes and genes involved in inflammation and fibrosis.

Conflicts of interest: The authors have no conflicts of interest to declare.

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Development of a defatting strategy to reduce lipid accumulation and improve the viability of steatotic grafts in liver transplantation

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Background and aim: In order to reduce mortality on waiting list, therapeutic strategies are required to increase the use of steatotic liver grafts in transplantation. However, steatotic grafts tolerate poorly ischemia-reperfusion (I/R) injury, and therefore they show a very high risk to early allograft dysfunction or primary nonfunction after transplantation. The aim of the present research was to evaluate the potential of 3 pharmacological modulators of lipid metabolism to induce defatting and protection against hepatic damage during cold preservation period in steatotic liver grafts.

Material and methods: Wistar rats were fed with a high-fat diet to induce steatosis. Then, steatotic livers were preserved at 4° C for 6 hours, either in Custodiol preservation solution, or in Custodiol solution enriched with caffeine, choline, or L-carnitine. At the end of this period, grafts were washed-out and transaminases and triglycerides in liver tissue were determined. This study was approved by the institutional Research Ethics Committee.

Results: Addition of caffeine to Custodiol solution decreased hepatic triglycerides content by 56% in steatotic grafts when compared with grafts preserved only in Custodiol. Triglycerides content was similar in steatotic grafts preserved in Custodiol enriched with choline or L-carnitine, and in those grafts preserved in Custodiol without additives. Regarding liver injury, preservation in Custodiol supplemented with caffeine, choline or L-carnitine resulted in a decrease in transaminases, compared to the levels observed in preservation with solely Custodiol.

Conclusions: Addition of caffeine to preservation solution trigger defatting in steatotic liver grafts, which is associated with protection against I/R injury. The enrichment of preservation solution with choline or L-carnitine decrease I/R injury in steatotic grafts, but this effect was not related to reduction in triglyceride content.