exacerbated liver fibrosis without changes in total liver lipid amount and composition. GDF11 mRNA levels showed significant positive correlation with Kleiner score (NAFLD activity score) in all patients but correlations between GDF11 expression levels and those of genes CPT1, PPAR-gamma, SREBP1 and Col1A1 were significant only in morbidly obese patients with NASH (not in the NAFLD subgroup).

Conclusion: The use of GDF11 is harmful in the context of obesity dependent NAFLD as its supplementation leads to the promotion of liver fibrosis in both in vitro and in vivo. Taking into the account the high prevalence of NAFLD in the developed countries (up to 30% of the general population), caution should be taken when considering therapies based on GDF11 regulation or supplementation.

SAT025
The influence of TRPM8 variant on brown adipose tissue activity and contribution to increased susceptibility to non-alcoholic fatty liver disease among South Asians
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Background and Aims: South Asians are at risk of developing non-alcoholic fatty liver disease (NAFLD) and diabetes at a lower BMI than Caucasians. Brown adipose tissue (BAT) activity is linked to whole-body energy expenditure, body fat and it’s associated metabolic complications. We recently demonstrated that native Indians have lower BAT activity than Caucasians. The single nucleotide polymorphism encodes a cold receptor with a putative role in physiological thermoregulation and adaption to cold environments. We hypothesise that presence of the TRPM8 variant influences BAT activity and may contribute to the susceptibility of South Asians to the metabolic syndrome including NAFLD.

Method: BAT activity was assessed in 24 native Indian (10 NAFLD, 14 control), 32 UK South Asian (17 NAFLD, 15 control) and 51 UK Caucasian (21 NAFLD, 30 control) male participants using a thermal imaging method measuring the change in temperature within the supraclavicular fossa relative to a reference point (Tref), following cold stimulus. TRPM8 rs10166942 genotyping was performed using real-time PCR.

Results: T allele frequency among Caucasians and South Asians was 0.8 and 0.48 respectively. Presence of T allele was strongly associated with increased BAT activity (0.49+/−0.22 vs 0.33+/−0.21 p = 0.006). On univariate analysis, T allele was associated with higher BMI (27.2 vs 24.7 p = 0.017), prevalent diabetes (41.6% vs 16.7% p = 0.046), but lower likelihood of NAFLD (39.3% vs 72.2% p = 0.01). Through multiple logistic regression modelling, adjusting for BMI, presence of diabetes and BAT activity, T allele was negatively associated with NAFLD (odds ratio 0.06 (0.008, 0.43; p = 0.005)).

Conclusion: Possession of the TRPM8 T allele variant is associated with increased BAT activity. Environmental factors interacting with a lower prevalence of T allele may result in reduced BAT activity among South Asians and hence, account for increased risk of NAFLD and other metabolic consequences observed in this community.

SAT026
Combinatorial effect of ezetimibe and empagliflozin in non-alcoholic fatty liver disease in a mouse model and a liver organoid for disease modeling of hepatic steatosis
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Background and Aims: Sodium-glucose cotransporter 2 inhibitor (SGLT2i) and ezetimibe, a cholesterol-lowering drug by targeting NPC1L1, have shown therapeutic potential for non-alcoholic fatty liver disease (NAFLD). SGLT2i and ezetimibe have different pharmacological mechanism, we hypothesized the combination of empagliflozin (selective SGLT2i) and ezetimibe could improve NAFLD.

Method: We used the choline-deficient high fat diet (CD-HFD)-induced murine model of NAFLD that has key features of human metabolic syndrome. 6-week-old C57BL/6J mice were fed a CD-HFD for 8 weeks. Then these mice were divided into four groups: vehicle, ezetimibe (10 mg/kg), empagliflozin (10 mg/kg), and ezetimibe