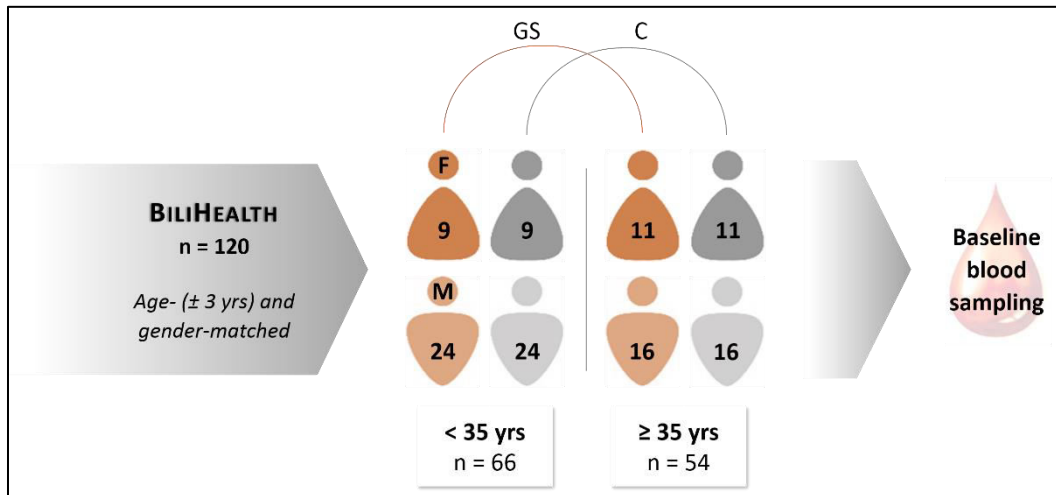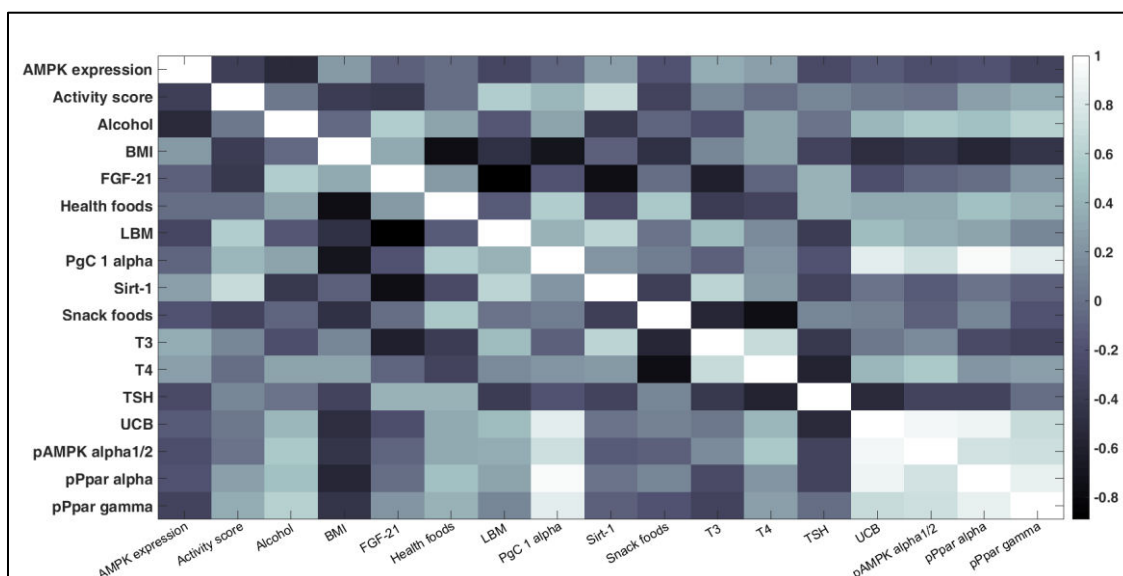**"Features of an altered AMPK metabolic pathway in Gilbert's Syndrome, and its role in energy turnover and metabolic health."**

Christine Mölzer, Marlies Wallner, Carina Kern, Anela Tosevska, Ursula Schwarz, Rene Zadnikar, Daniel Doberer, Rodrig Marculescu, Karl-Heinz Wagner
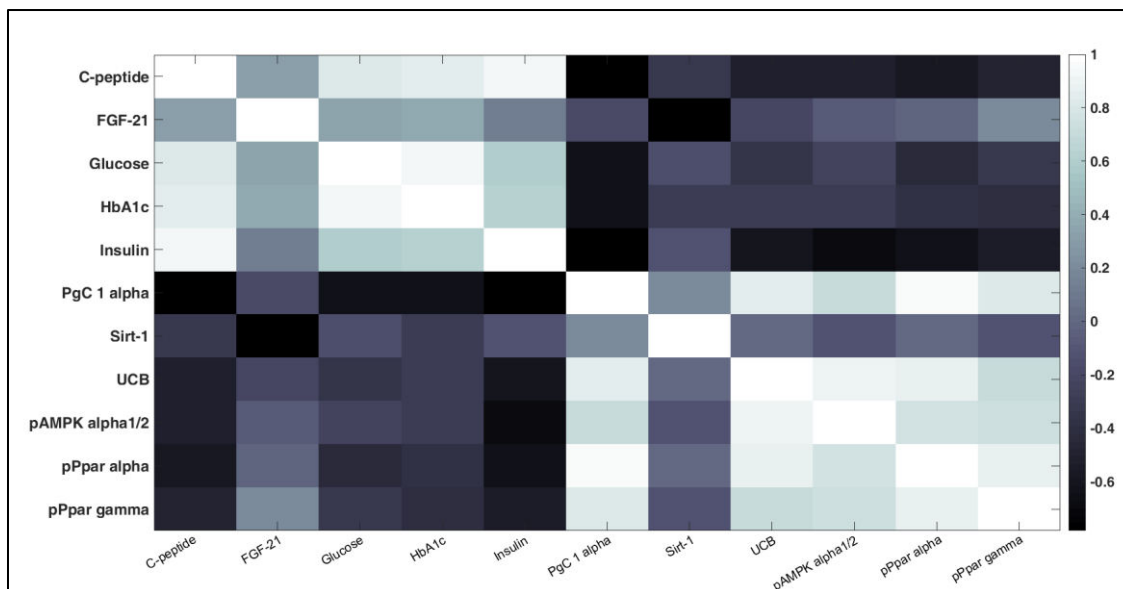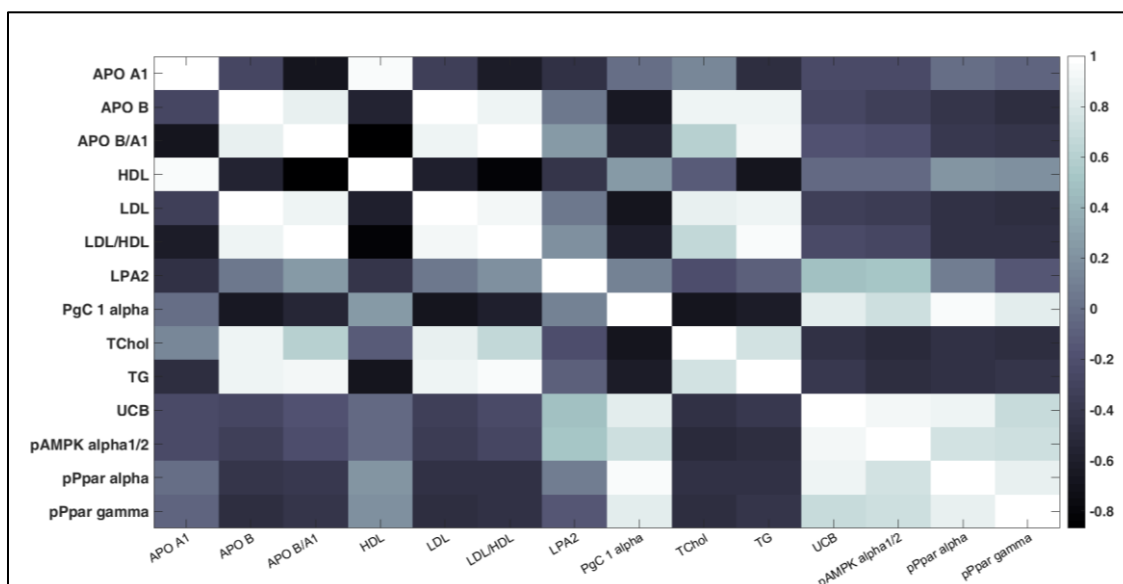
SUPPLEMENTARY FIGURES:

Supplementary figure S1. BiliHealth study design. A total of 80 males and 40 females (n = 120) completed the study. Subjects were age- and gender-matched. Study group allocation (Gilbert's Syndrome, GS; controls, C) was based on the subjects' respective serum UCB concentrations (unconjugated bilirubin </≥ 17.1 μM). Participants were furthermore allocated to age groups (</≥ 35 years of age). All subjects underwent a baseline blood sampling.

Supplementary figure S2 a. Heat map showing inter-variable connection for markers of energy-metabolism.

Supplementary figure S2 b. Heat map showing inter-variable connection for markers of glucose-metabolism.

Supplementary figure S2 c. Heat map showing inter-variable connection for markers of lipid-metabolism.

Supplementary figures S2 a – c. Heat maps showing inter-variable connection with respect to energy- (a), glucose- (b) and lipid metabolism (c). Heat maps were generated using the COVAIN toolbox for MATLAB [MATLAB and Statistics Toolbox Release 2015a, The MathWorks, Inc., Natick, Massachusetts, United States.], and including the entire dataset (all subjects).

Abbreviations: UCB: unconjugated bilirubin; UGT1A1: UGT1A1 genotype; pAMPK α1/α2: Phosphorylated 5'-AMP activated kinase; pPpar α: Phosphorylated peroxisome proliferator activated receptor alpha; pPpar γ: Phosphorylated peroxisome proliferator activated receptor gamma; PgC 1α: Peroxisome proliferator-activated receptor c coactivator 1; AMPK1a expr.: AMPK gene expression as relative quantification, RQ to cDNA pool; Sirt-1: Sirtuin-1; FGF-21: Fibroblast growth factor 21; TSH: Thyroid stimulating hormone; T3: Free triiodothyronine; T4: Free thyroxine; BMI: Body mass index; LBM: Lean body mass; HbA1c: Glycated haemoglobin A1c; TChol: Total cholesterol; HDL: High density lipoprotein cholesterol; LDL: Low density lipoprotein cholesterol; TG: Triglyceride; LPA2: Lipoprotein A2; ApoA1: Apolipoprotein A1; ApoB: Apolipoprotein B; Activity score: self-reported daily activity (walking, climbing stairs, physical exercise); Alcohol/Health foods/Snack foods: self-reported weekly consumption.