Modulations in bilirubin metabolism are phenotypically shown as moderately increased unconjugated bilirubin (UCB) levels. This has been identified as a health promoting condition by showing protection from cardiovascular diseases and type 2 diabetes as well as BMI-lowering effects. Increased UCB above the defined threshold of 17.1 µM is the characteristic trait for Gilbert’s syndrome (GS). Furthermore, it is well established that the gut microbiota and its composition is linked to the health as well as anthropometric status. The connection however, between bilirubin metabolism and the gut microbiota has not been evaluated so far. The aim of this project was therefore to discover links between UCB, microbiota diversity and possible consequences on body composition.

Methods

DNA from feces of participants of the BILIHEALTH study pool, split by a plasma UCB threshold of 17.1 µM with age/gender-matched controls (n = 45/45), was extracted (Fig. 1) and 16S rRNA gene sequence amplified using a multiplex barcoding-approach. Sequences were analyzed by an Illumina paired-end MiSeq run and microbiota identified by comparative sequence analysis.

Results

Results showed effects of mildly increased UCB-levels (≥ 17.1 µM) on microbiota, mainly in individuals above 35 years of age (p = 0.008). Age itself seems to contribute to a higher diversity (p = 0.007). Indicator species (Table 1) identified in this project correlating with subjects of the increased UCB group are associated with beneficial impacts on health and body composition.

Conclusions

Treated as “detrimental agent” in the last decades, bilirubin was investigated in the BILIHEALTH project from a different angle: our working group had already shown that a mildly increased serum level of unconjugated bilirubin is associated with a leaner and healthier phenotype. The given results add the idea of a slightly, beneficially shifted and more diversified gut microbiota profile, which may result from increased levels of unconjugated bilirubin, which are representative for Gilbert’s syndrome, a benign condition which affects about 10 percent of the Caucasian population.

Table 1: Indicator species analysis identified Operational Taxonomic Units (OTU) associated with the two groups, but these were very less abundant. Assigned family: Christensenellaceae and especially Christensenella minuta is known as beneficial for health and body composition.

References

a = Mölzer et al., Scientific Reports, 2016
b = Herbold et al., Frontiers in Microbiology, 2015
c = Goodrich et al., Cell, 2014