Dietary and weight loss effects on human gut microbiome diversity and metabolism

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INTRODUCTION:
Recently an association of the gut microbiome and the human energy homeostasis has been shown, suggesting the gut microbiome as a possible target in obesity therapy. Additionally, host metabolism is influenced by the gut microbiome, as the transfer of intestinal microbiota from lean donors to type 2 diabetes patients resulted in improved insulin sensitivity of the recipients. Further, it has been shown, that nutritional load influences the overall microbial comminuty in the gut. Therefore the impact of a multimodal obesity program including a VLCD (approx. 800 kcal/d) on gut microbiome an metabolism was examined.

METHODS:
18 obese subjects underwent 3 months VLCD followed by 3 months of weight maintenance. A lean and an obese control group were included. The microbiome was characterized by performing high-throughput dual-indexed 16S rRNA amplicon sequencing.

RESULTS:
Body weight and insulin sensitivity of the intervention group

<table>
<thead>
<tr>
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<th>0 months</th>
<th>3 months (end of VLCD)</th>
<th>6 months (end of weight maintenance)</th>
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<tbody>
<tr>
<td>weight (kg)</td>
<td>123.75**</td>
<td>102.30**</td>
<td>99.37**</td>
</tr>
<tr>
<td>(114.08-102.25)</td>
<td>(90.73-110.25)</td>
<td>(87.73-110.00)</td>
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<tr>
<td>HOMA-IR index</td>
<td>3.09*</td>
<td>1.73*</td>
<td>2.11</td>
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<tr>
<td>(1.64-5.14)</td>
<td>(1.03-3.70)</td>
<td>(1.51-3.87)</td>
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Gut microbiome diversity
At baseline a significant difference in the Firmicutes/Bacteroidetes ratio between the lean control group and the obese intervention group could be observed (p=0.047).
The VLCD resulted in significant alterations in α-diversity from baseline to 3 months. The changes in diversity diminished during the weight maintenance phase, despite sustained reductions in body weight and sustained improvements of insulin sensitivity.

The first coordinate of the GAP explained 62.22% (p=0.046) of the variance in the microbiota due to the VLCD intervention.

Constrained analysis of principal coordinates (CAP) of the dietary intervention group explaining variance in the microbiota. Baseline (0 months)=0, VLCD intervention (3 months)=3, weight maintenance period (6 months)=6

Unconstrained Principal Component Analysis of the intervention group and both control groups at the end of the study period.

Defined species of the gut microbiome
Acinetobacter represented an indicator species for the observed effect in microbiome diversity (IndVal=0.998; p=0.006).

Bacterial metabolic changes
Metabolic analyses revealed nominal statistically significant alterations of the bacterial riboflavin pathway from baseline to 3 months (pnom=0.0078). During weight maintenance phase the changes diminished.

Relative abundance of the riboflavin pathway during the dietary intervention. Baseline (0 months)=0, VLCD intervention (3 months)=3, weight maintenance period (6 months)=6

CONCLUSION:
The present data show that in obese humans a VLCD is able to beneficially alter both gut microbiome diversity and metabolism, but also that these changes are not sustained during weight maintenance. This finding might suggest additional measures to target the microbiome during obesity programs.