Impact of basal diet on obesity phenotype of recipient mice following fecal transfer from obese or lean human donors

Daphne Rodriguez, Niklas Aardema, Abby Benninghoff, Canyon Neal, Tess Armbrust, Sumira Phatak, Michaela Brubaker, Elizabeth Park, Kimberly Campbell, Korry Hintze
OBESITY

34%

METABOLIC SYNDROME

Cluster of physiological and biochemical factors associated with the development of obesity and heart disease.

Central Obesity  High Blood Pressure  High Triglycerides  High Fasting Plasma Glucose

GUT MICROBIOTA

• Our colon is home to about 100 trillion microorganisms
• 400-500 different species
• 2/3 of those bacteria are found in everyone while 1/3 is unique to the individual

Quigley, E. Gastroenterology & hepatology 9.9 (2013): 560-69
Dysbiosis is a condition that favors pathogenic (harmful) bacteria which may precede disease, including metabolic syndrome, inflammatory bowel syndrome and colorectal cancer.
FACTORS IMPACTING MICROBIOME

- Age
- Birth
- Genetics
- Antibiotics
- Diet
- Stress
OBJECTIVE

Determine the contribution of gut microbiota from lean or obese donors on the phenotype of mice fed one of three diets, control (AIN), Western (TWD) or high-fat (DIO).
STUDY

Human Donors → Fecal Samples → Mouse Recipient → Diets

ENDPOINTS

- Body Weight
- oGTT
- Food Intake
- MRI
- Fecal Collection
- Sacrifice
FOOD AND ENERGY INTAKE

**Total food intake (g)**

<table>
<thead>
<tr>
<th>Diet</th>
<th>Ln AIN</th>
<th>Ln DIO</th>
<th>Ln TWD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ln Ob</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Total energy intake (kcal)**

<table>
<thead>
<tr>
<th>Diet</th>
<th>Ln AIN</th>
<th>Ln DIO</th>
<th>Ln TWD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ln Ob</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Mixed model main effects

<table>
<thead>
<tr>
<th></th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diet</strong></td>
<td>0.0090</td>
</tr>
<tr>
<td>Body type</td>
<td>0.0490</td>
</tr>
<tr>
<td>Diet x body type</td>
<td>0.0080</td>
</tr>
<tr>
<td>Donor ID[body type]</td>
<td>0.7502</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diet</strong></td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Body type</td>
<td>0.0490</td>
</tr>
<tr>
<td>Diet x body type</td>
<td>0.0080</td>
</tr>
<tr>
<td>Donor ID[body type]</td>
<td>0.7502</td>
</tr>
</tbody>
</table>
Mixed model main effects  

<table>
<thead>
<tr>
<th>Diet</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIN</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>DIO</td>
<td>0.5054</td>
</tr>
<tr>
<td>TWD</td>
<td>0.7077</td>
</tr>
</tbody>
</table>

Mixed model main effects  

<table>
<thead>
<tr>
<th>Diet</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIN</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>DIO</td>
<td>0.6164</td>
</tr>
<tr>
<td>TWD</td>
<td>0.7218</td>
</tr>
</tbody>
</table>
HCC and PCA for donor and mouse initial
HCC and PCA for post FMT

- PC1 (52.2%)
- PC2 (26.4%)

Diet
- AIN
- DIO
- TWD

Body type
- Lean
- Obese

Donor body type
- Lean human donor
- Lean mouse recipients
- Obese human donor
- Obese mouse recipients
HCC and PCA for Terminal
CONCLUSION

- Diet plays a larger role on the microbiota composition compared to donor microbiota, suggesting that dietary practices may be the most effective way to change the microbiome.
- Source of fecal transfer (lean vs. obese) did not impact body weight gain, body composition or glucose tolerance in recipient mice.
- As expected, mice fed high fat diet gained excess body weight and fat composition and had impaired glucose tolerance. Mice fed TWD were not statistically different from counterparts fed either AIN or DIO diets.
- The microbiome may be more of a correlative as opposed to a causative factor in the etiology of obesity.
ACKNOWLEDGEMENTS

- USTAR Applied Nutrition Research, Utah State University
- Utah Agricultural Experiment Station, Project UTA-01178
- Special thanks to:
  - Abby Benninghoff
  - Korry Hintze
  - Kerry Rood
  - Canyon Neal
  - Tess Armbrust
  - Niklas Aardema
  - Sumira Phatak
  - Ashli Hunter
  - Kevin Contreras
  - Michaela Brubaker
  - Elizabeth Park
  - Kristina Krepinski
  - Emily Speas
  - Kimberly Campbell