Comparison of Gut Microbiota in Obese, Diabetic and Healthy Control Individuals

Yalcin Basaran\textsuperscript{1}, Abdullah Taslipinar\textsuperscript{1}, Sinasi Erol Bolu\textsuperscript{1}, Mehmet Ali Saracli\textsuperscript{1}, Turker Turker\textsuperscript{1}, Coskun Meric\textsuperscript{1}, Cem Haymana\textsuperscript{1}, Kamil Baskoy\textsuperscript{1}, Mustafa Dinc\textsuperscript{1}, Ferhat Deniz\textsuperscript{2}, Mahmut Yazici\textsuperscript{1}, Aydogan Aydogdu\textsuperscript{1}, Alper Sonmez\textsuperscript{1} and Omer Azal\textsuperscript{1}

\textsuperscript{1}Gulhane Military Medical Academy School of Medicine, Ankara, Turkey
\textsuperscript{2}GATA Haydarpasha Training Hospital, Istanbul, Turkey
Worldwide epidemic of obesity and diabetes!

- Obesity and diabetes are of the greatest public health challenges.
- The prevalence continues to rise at an alarming rate.
What about Turkey?

Population age >20 years

What is the etiology of obesity and diabetes?

• Etiopathogenesis of obesity and diabetes...
  – Lifestyle changes (dietary habits and physical activity level)
  – Genetic susceptibility

• But also...
  – Changes in the gut microbiota composition

What is the gut microbiota?


- Bacteroidetes & Firmicutes: 90%
- Actinobacteria, Proteobacteria, Fusobacteria & Verrucomicrobia: 10%

100 Trillion Friends you didn't know you had
Of Mice...

- Studies in mice imply the imbalance of the gut microbiota as a potential cause of obesity and diabetes...
  
  - Mice lacking microbiota have significantly less body fat, despite eating more
  
  - Transfer of the microbiota from normal to these mice results in significant increase in adiposity and insulin resistance

...and Men

- Human studies are conflicting...
  - ↑ Firmicutes/Bacteroidetes (Ley et al., Nature, 2006.)
  - ↓ Firmicutes/Bacteroidetes (Schwiertz et al., Obesity, 2010.)
  - No difference (Arumugam et al., Nature, 2011.)
The purpose of the study...

- To examine and compare the predominant fecal microbiota 
  (Bacteroidetes, Firmicutes, Bifidobacteria and Clostridium leptum) of obese, diabetic and healthy individuals

- To demonstrate the causality between the gut microbiota and metabolic parameters
Study design...

**Obesity**
(n=27, male:20)
(BMI: 40.0±5.6 kg/m²)

**Type 2 Diabetes**
(n=26, male:18)
(BMI: 28.6±5.1 kg/m²)

**Healthy controls**
(n=28, male:22)
(BMI: 23.0±1.7 kg/m²)

**Exclusion criteria...**
- Any chronic disease
- Alcohol consumption/smoking
- Pregnancy/breastfeeding
- Antibiotics, pro-prebiotics within 3 months
- <18 years or >65 years
- History of intestinal surgery
Methods...

- Self-collected fecal samples
- qRT-PCR...
  - To quantify fecal concentrations of Bacteroidetes, Firmicutes, Bifidobacteria (Actinobacteria) and Clostridium leptum (Firmicutes)
### Bacterial counts of the study population...

<table>
<thead>
<tr>
<th>Bacteria (cfu/g)</th>
<th>Obesity group (n=27)</th>
<th>Diabetes group (n=26)</th>
<th>Control group (n=28)</th>
<th>p</th>
<th>p1</th>
<th>p2</th>
<th>p3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bacteroidetes</strong></td>
<td>9.5 (4.8-10.0)</td>
<td>9.8 (5.3-10.0)</td>
<td>8.9 (5.7-9.8)</td>
<td>0.067</td>
<td>0.279</td>
<td>0.484</td>
<td>0.084</td>
</tr>
<tr>
<td><strong>Firmicutes</strong></td>
<td>10.0 (6.9-10.0)</td>
<td>**↓**4%</td>
<td>**↓**13%</td>
<td>&lt;0.001</td>
<td>0.878</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Bifidobacteria</strong></td>
<td>8.9 (4.9-10.0)</td>
<td>**↓**14%</td>
<td>**↓**28%</td>
<td>&lt;0.001</td>
<td>0.798</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Clostridium Leptum</strong></td>
<td>10.0 (8.9-10.0)</td>
<td>**↓**14%</td>
<td>**↓**11%</td>
<td>&lt;0.001</td>
<td>0.714</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Correlations...

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Bacterial concentrations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bacteroidetes (cfu/g)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>na</td>
</tr>
<tr>
<td>Gender</td>
<td>na</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>na</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>na</td>
</tr>
<tr>
<td>LDL-C (mg/dl)</td>
<td>na</td>
</tr>
<tr>
<td>FPG (mg/dl)</td>
<td>r = -0.238, p = 0.037</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>r = -0.332, p = 0.003</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>na</td>
</tr>
<tr>
<td>LDL-C (mg/dl)</td>
<td>na</td>
</tr>
</tbody>
</table>

BMI (kg/m²)

Waist circumference (cm)

SBP (mmHg)

DBP (mmHg)

FPG (mg/dl)

İnsulin (mU/ml)

HbA1c (%)

HOMA-IR

LDL-C (mg/dl)

TG (mg/dl)

HDL-C (mg/dl)
Parameters affecting the gut microbiota...

<table>
<thead>
<tr>
<th>Bacteria (cfu/g)</th>
<th>Variables</th>
<th>$\beta$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Firmicutes</td>
<td>BMI</td>
<td>-0.394</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>HbA1c</td>
<td>-0.285</td>
<td>0.011</td>
</tr>
<tr>
<td>Bifidobacteria</td>
<td>Waist circumference</td>
<td>-0.476</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>HbA1c</td>
<td>-0.321</td>
<td>0.003</td>
</tr>
<tr>
<td>Clostridium Leptum</td>
<td>Weight</td>
<td>-0.509</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>FBG</td>
<td>-0.306</td>
<td>0.005</td>
</tr>
</tbody>
</table>
Altered gut microbiota in obesity and type 2 diabetes

Parameters of adiposity (weight, BMI, waist circumference) and glucose control (FPG and HbA1c) determine the altered composition
Perspective...

• Further studies should be carried out to answer the following questions...

  – Are the gut microbiota changes a cause or effect of obesity and diabetes?

  – May manipulation of the gut microbiota – using pro-prebiotics or fecal microbiota transplantation – prevent/treat obesity and diabetes?
Thank you for your attention...