ASSESSMENT OF FECAL MICROBIOTA AND Fecal Metabolome IN Symptomatic UNComplicated Diverticular Disease OF THE Colon

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1st PCR: phyla Firmicutes, Bacteroidetes, Actinobacteria, Fusobacteria, and Verrucomicrobia (Akkermansia)

2nd PCR: phylum Proteobacteria
**Aims**

**Background:** Data on intestinal microbiota and metabolome in symptomatic uncomplicated diverticular disease (SUDD) of the colon are lacking.

**Aims:** To assess the intestinal microbiota and metabolome in SUDD, comparing them with patients with asymptomatic diverticulosis (AD) and with healthy people (HC).
Subjects having the following characteristics were enrolled:

- Female
- Middle-aged

<table>
<thead>
<tr>
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<th>Age (mean ± SD) [range]</th>
<th>BMI (mean ± SD) (Kg/m²)</th>
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</thead>
<tbody>
<tr>
<td><strong>HC (n=16)</strong></td>
<td>60.5 ± 5.0 [56-69]</td>
<td>26.2 ± 1.8</td>
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<td>(Healthy control)</td>
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<tr>
<td><strong>AD (n=16)</strong></td>
<td>61.7 ± 3.8 [56-68]</td>
<td>26.5 ± 2.1</td>
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<tr>
<td>(Asymptomatic Diverticulosis)</td>
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<tr>
<td><strong>SUDD (n=17)</strong></td>
<td>62.7 ± 4.5 [52-70]</td>
<td>26.8 ± 3.3</td>
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<tr>
<td>(Symptomatic Uncomplicated Diverticular Disease)</td>
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- Living in the same district
- No use of antibiotics in the three months before enrollment
- No bacterial and/or parasitic intestinal diseases (by stool cultures)
- No lactose malabsorption (breath test)

Stool samples were collected at least 4 weeks after colonoscopy
Fecal Microbiota -> REAL-TIME PCR

- Total bacteria

**Firmicutes**

**Bacteroidetes**

**Actinobacteria**

**Proteobacteria**

**Verrucomicrobia**
## Study design

**Metabolome** → **$^1$H NMR Spectroscopy**

<table>
<thead>
<tr>
<th>Category</th>
<th>Compounds</th>
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<tbody>
<tr>
<td><strong>Short-chain fatty acids</strong></td>
<td>Valerate, isovalerate, acetate, butyrate</td>
</tr>
<tr>
<td><strong>Organic acids</strong></td>
<td>Formate, 3-(3-hydroxyphenol) propionic acid, fumaric acid, 3-phenyl acetic</td>
</tr>
<tr>
<td><strong>Alcohols</strong></td>
<td>Ethanol, methanol</td>
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<tr>
<td><strong>Amino acids</strong></td>
<td>Valine, alanine, glycine, methionine, glutamate</td>
</tr>
<tr>
<td><strong>Amines</strong></td>
<td>Methylamine, trimethylamine, niacinamide</td>
</tr>
<tr>
<td><strong>Miscellaneous</strong></td>
<td>Uracil, choline</td>
</tr>
<tr>
<td><strong>Carbohydrates</strong></td>
<td>Glucose, N-Acetyl-derivatives</td>
</tr>
</tbody>
</table>
Quantification of fecal **MICROBIOTA** in healthy control (HC), Asymptomatic Diverticulosis (AD) and Symptomatic Uncomplicated Diverticular Disease (SUDD)

The overall bacterial quantity did not differ between the three groups.

The amount of each bacterial group was normalized for each subject and calculated as the log number of targeted bacteria minus the log number of all bacteria.
Quantification of fecal **microbiota** in healthy control (HC), Asymptomatic Diverticulosis (AD) and Symptomatic Uncomplicated Diverticular Disease (SUDD)

The amount of **Akkermansia** was significantly higher in SUDD in comparison to HC.

**Firmicutes/Bacteroidetes** ratio and **Proteobacteria** load were comparable among patients and controls ($p=\text{ns}$).
Treatment with a Monoclonal Anti-IL-12p40 Antibody Induces Substantial Gut Microbiota Changes in an Experimental Colitis Model

Josué Castro-Mejia, Maja Jaksevec, Łukasz Krych, Dennis S. Nielsen, Lars H. Hansen, Bodil C. Sondergaard, Peter H. Kvist, Axel K. Hansen, and Thomas L. Holm

markers were found. The relative abundances of the RF32 order (Alphaproteobacteria) and Akkermansia muciniphila were positively correlated with damaged histopathology and colonic inflammation. Conclusions. Shifts in GM distribution were observed with

Akkermansia muciniphila and improved metabolic health during a dietary intervention in obesity: relationship with gut microbiome richness and ecology

Maria Carlota Dao, Amandine Everard, Judith Aron-Wisnewsky, Nataliya Sokolovska, Edi Pritti, Eric O Verger, Brandon D Kayser, Florence Levenez, Julien Chiloux, Lesley Hoyles, MICRO-Obes Consortium, Marc-Emmanuel Dumas, Salwa W Rizkalla, Joel Doré, Patrice D Cani and Karine Clément

Gut 2016 65: 426-436 originally published online June 22, 2015
PLS-DA showed a good discrimination between AD and SUDD

The SUDD patients were characterized by low levels of valerate, butyrate and choline, and by high levels of N-Acetyl derivatives and unassigned resonance (U1)

<table>
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<tbody>
<tr>
<td>Valerate</td>
<td>0.009</td>
<td>-0.015</td>
</tr>
<tr>
<td>Butyrate</td>
<td>0.047</td>
<td>-0.048</td>
</tr>
<tr>
<td>N-Acetyl derivatives</td>
<td>&lt; 0.001</td>
<td>0.077</td>
</tr>
<tr>
<td>Isovalerate</td>
<td>ns</td>
<td>0.050</td>
</tr>
<tr>
<td>U1 [2.11-2.12]</td>
<td>0.003</td>
<td>0.065</td>
</tr>
<tr>
<td>Choline</td>
<td>0.009</td>
<td>-0.033</td>
</tr>
</tbody>
</table>
Quantification of fecal METABOLITES in healthy control (HC), Asymptomatic Diverticulosis (AD) and Symptomatic Uncomplicated Diverticular Disease (SUDD)

- Valerate
- Butyrate
- N-Acetyl-derivatives
- Isovalerate
- U1[2.11–2.12]
- Choline

`p<0.05`
Correlation between NAc-derivatives and the predictive model obtained by PLS

LVs Score plot

Weighted regression coefficients

NAc-derivatives positively correlate with bifidobacteria and Escherichia and negatively with clostridia and lactobacilli
Correlation between fecal microorganisms and N-Acetyl-derivatives

No correlation was found in the HC group

- **Lactobacillus**
  - AD: \( r = -0.776, p = 0.005 \)

- **Akkermansia**
  - SUDD: \( r = 0.704, p = 0.015 \)

- **N-Acetyl-derivatives**
  - No correlation was found in the HC group

- **Δ log\(_{10}\)/g**
  - AD
  - SUDD

- **Δ log\(_{10}\)/g**
  - Lactobacillus
  - N-Acetyl-derivatives

- **Δ log\(_{10}\)/g**
  - Akkermansia

- **HC**, **AD**, **SUDD**

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- **Box plots**
  - HC, AD, SUDD
N-acetylglucosamine is preferentially utilized as a carbon and energy source by *Escherichia coli* and *Bifidobacterium* species.

*Akkermansia muciniphila*—grow in medium containing mucin as the sole carbon and nitrogen source—stimulate mucin synthesis—has the capacity to degrade mucins releasing N-acetylglucosamine, N-acetyl-galactosamine, and other saccharides that can be further metabolized by the resident microbiota.

NAc-derivatives positively correlate with *Akkermansia*, bifidobacteria and *Escherichia* and negatively with clostridia and lactobacilli.
Conclusions

It needs to be determined whether changes in the gut microbiome and metabolome indeed are a cause or just a consequence of DD.

Thank you for your attention.