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# Obesity-induced alterations in the gut microbiome in female mice fed a high-fat diet are antagonized by dietary supplementation with a novel, wax ester-rich, marine oil

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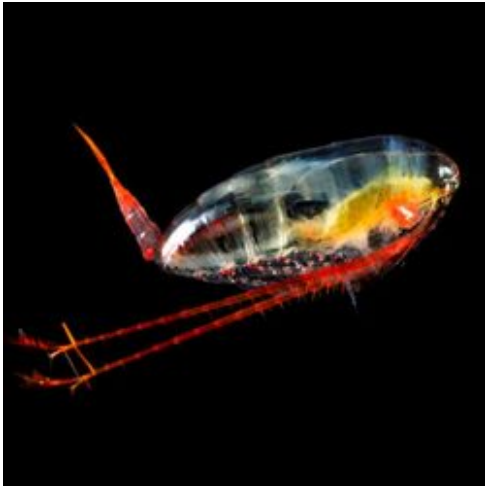
Potential Health Effects from Marine Ingredients on Gut Microbiota









11.12.2020



# Background on Calanus<sup>®</sup> Oil

- *Calanus finmarchicus*



	Phospholipid	
	Triglyceride	
	Ethyl ester	
	Wax ester	

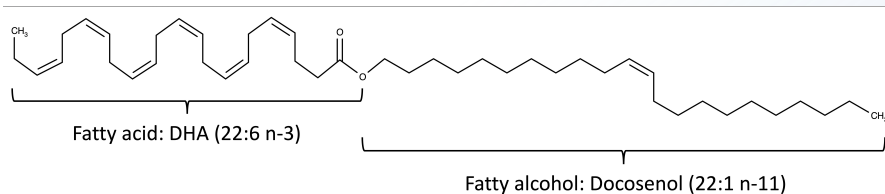
# Background on Calanus<sup>®</sup> Oil

Lipid class composition (mg/g lipid) of Calanus<sup>®</sup> oil

Calanus oil	
<b>WE/CE<sup>a)</sup></b>	<b>857.70</b>
TAG	16.96
FAOH	nd
C	41.91
FFA	16.59
CL	nd
PC	nd
$\Sigma$ lipid class	933.16

nd, not detected; WE, wax ester; CE, cholesteryl ester; TAG, triacylglycerol; FAOH, fatty alcohol; C, cholesterol; FFA, free fatty acid; CL, cardiolipin; PC, phosphatidylcholin.

a)WE and CE coelute.



Fatty acids	Calanus oil
14:0	64.42
16:0	45.05
18:0	2.42
20:0	0.40
$\Sigma$ SFA	112.29
16:1n-7	17.17
18:1n-7	1.53
<b>18:1n-9</b>	<b>15.54</b>
<b>20:1n-9</b>	<b>24.01</b>
20:1n-11	3.90
22:1n-9	2.63
<b>22:1n-11</b>	<b>43.33</b>
24:1n-9	2.81
$\Sigma$ MUFA	110.92
18:2n-6	6.64
18:3n-3	13.72
<b>18:4n-3</b>	<b>69.58</b>
20:2n-6	0.71
20:4n-6	1.39
<b>20:5n-3</b>	<b>54.73</b>
<b>22:5n-3</b>	<b>2.96</b>
<b>22:6n-3</b>	<b>39.35</b>
$\Sigma$ PUFA	189.08
$\Sigma$ n-6	8.74
$\Sigma$ n-3	180.34
$\Sigma$ n-6/n-3	0.05
$\Sigma$ Fatty acids	412.29

Oleic acid  
Gondoic acid

Fatty acid and fatty alcohol content (mg/g lipid) of Calanus<sup>®</sup> oil

Cetoleic acid

SDA

EPA

DHA

1 portion Mølles Tran (1 tablespoon/5ml):  
600 mg DHA + 400 mg EPA

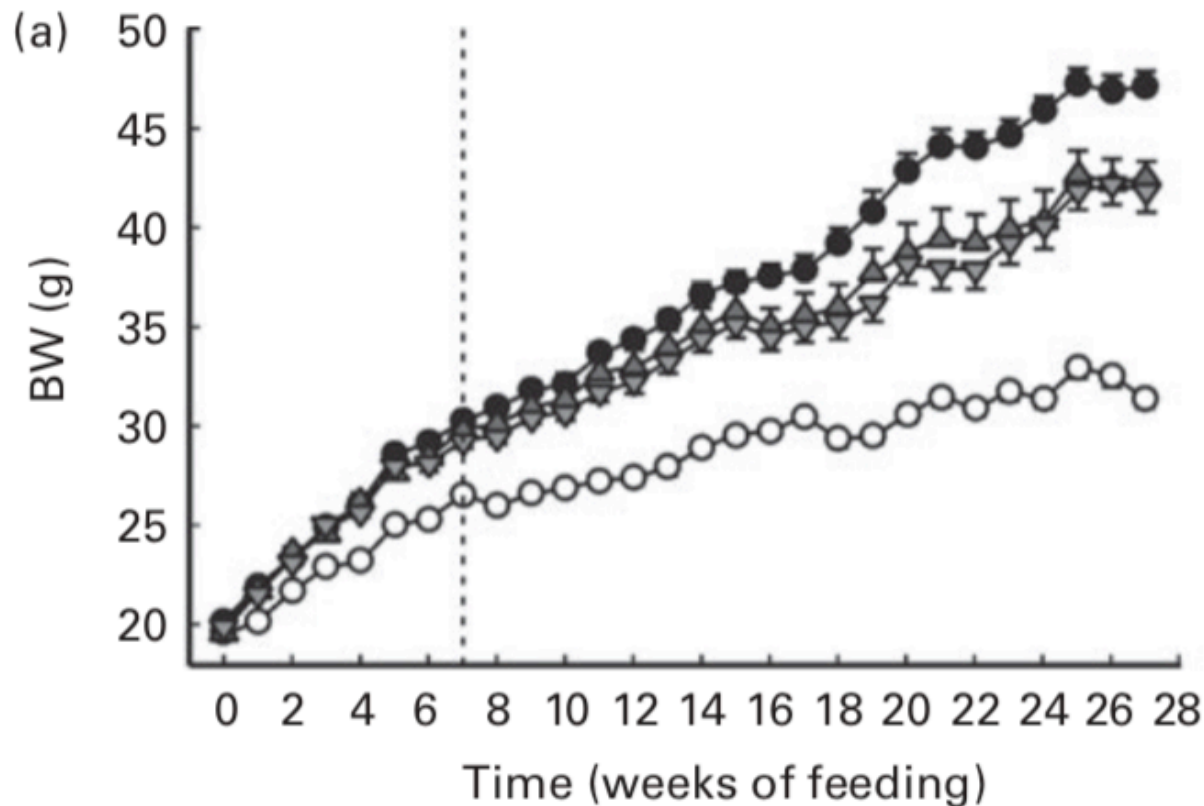
1 portion Calanus<sup>®</sup> Oil (2 capsules):  
58mg DHA + 68 mg EPA

Fatty alcohols	Calanus oil
14:0	4.50
16:1n-7	5.80
18:1n-9	10.40
<b>20:1n-9</b>	<b>128.80</b>
22:1n-9	10.40
<b>22:1n-11</b>	<b>188.10</b>
$\Sigma$ Fatty alcohols	348.00

eicosenol

docosenol

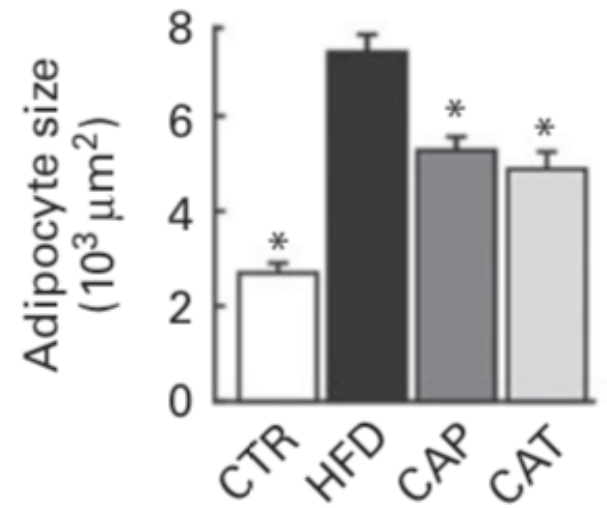
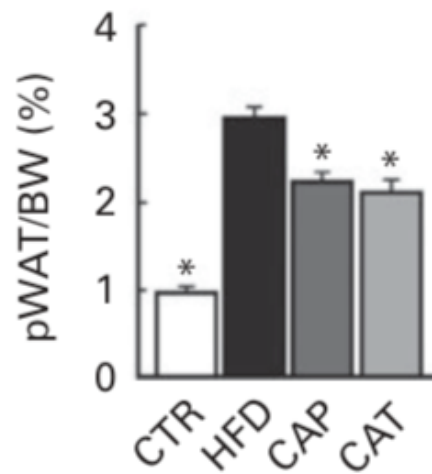
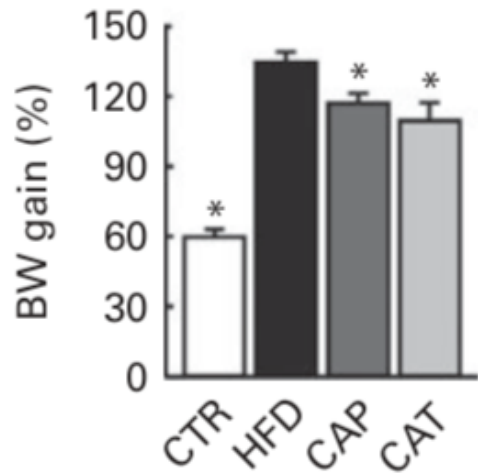
# Background on Calanus<sup>®</sup> Oil and obesity



- High-fat diet (HFD): 46% energy from fat
- ▲ CAP: HFD supplemented with 1,5% Calanus oil from start (**Preventative**)
- ▼ CAP: HFD supplemented with 1,5% Calanus oil from week 7 (**Treatment**)
- Control: 10% energy from fat

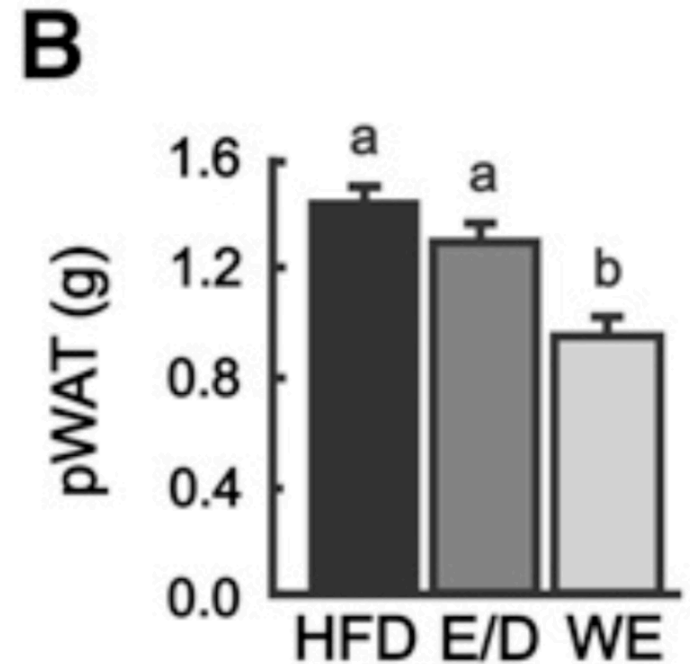
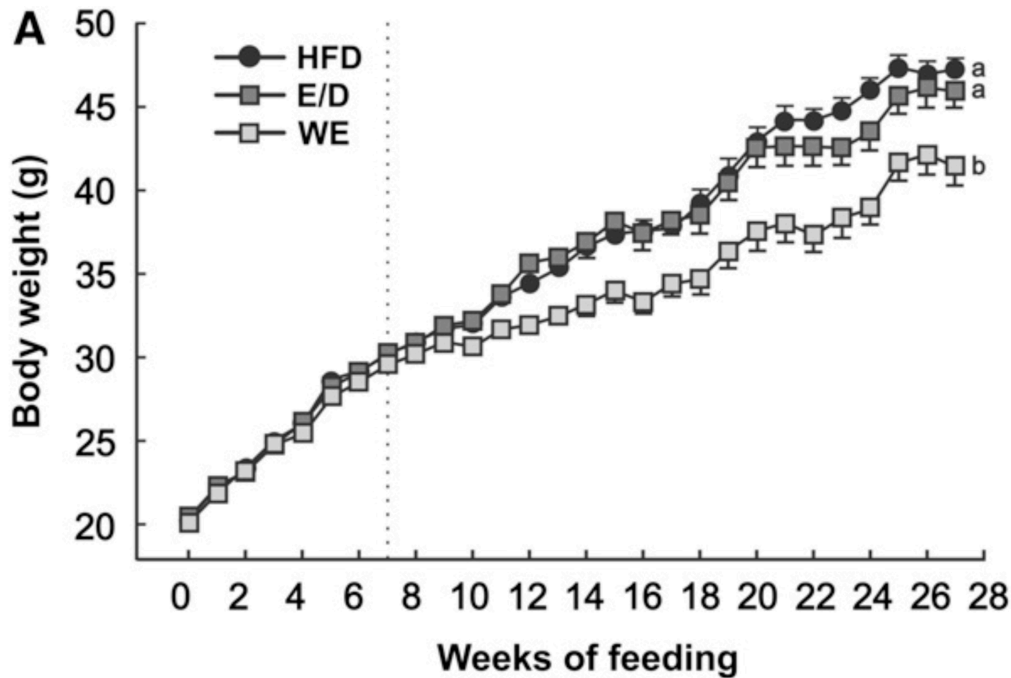


# Background on Calanus<sup>®</sup> Oil and obesity



CTR: Control diet  
HFD: High fat diet  
CAP: Calanus oil preventative  
CAT: Calanus oil treatment

# Background on Calanus<sup>®</sup> Oil and obesity



HFD: High-fat diet

E/D: HFD supplemented with 0.2% purified EPA + DHA ethyl esters

WE: HFD supplemented with 1% Calanus oil derived wax esters\*

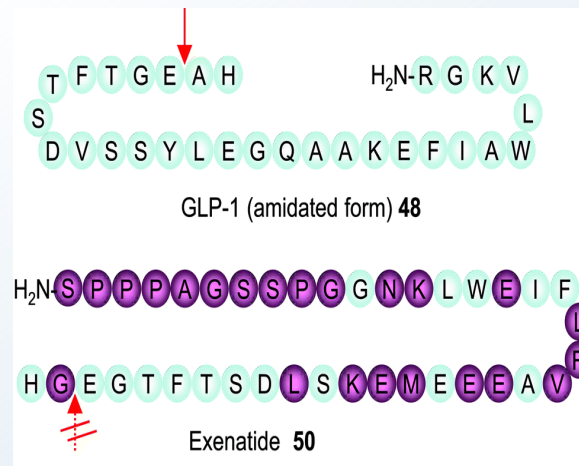
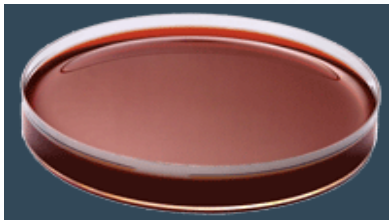
\*The content of EPA and DHA in the E/D-supplement diet was equivalent to the total content of n-3 PUFAs in the WE-supplemented diet.

# Introduction + Aim

Alterations in the composition of the gut microbiome have been linked to several pathologies, including obesity-related metabolic disorders

Aims:

1. Does diet-induced obesity have an impact on the composition of the gut microflora?
2. Does dietary **Calanus oil** modify any obesity-induced alterations in the microbiome? Comparison to infusion of the GLP-1 receptor agonist, **exenatide**.



# Methods

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Seven-week old female C57bl/6J mice were fed a high-fat diet (HFD) for 12 weeks in order to induce obesity. During the following 8 weeks they received:

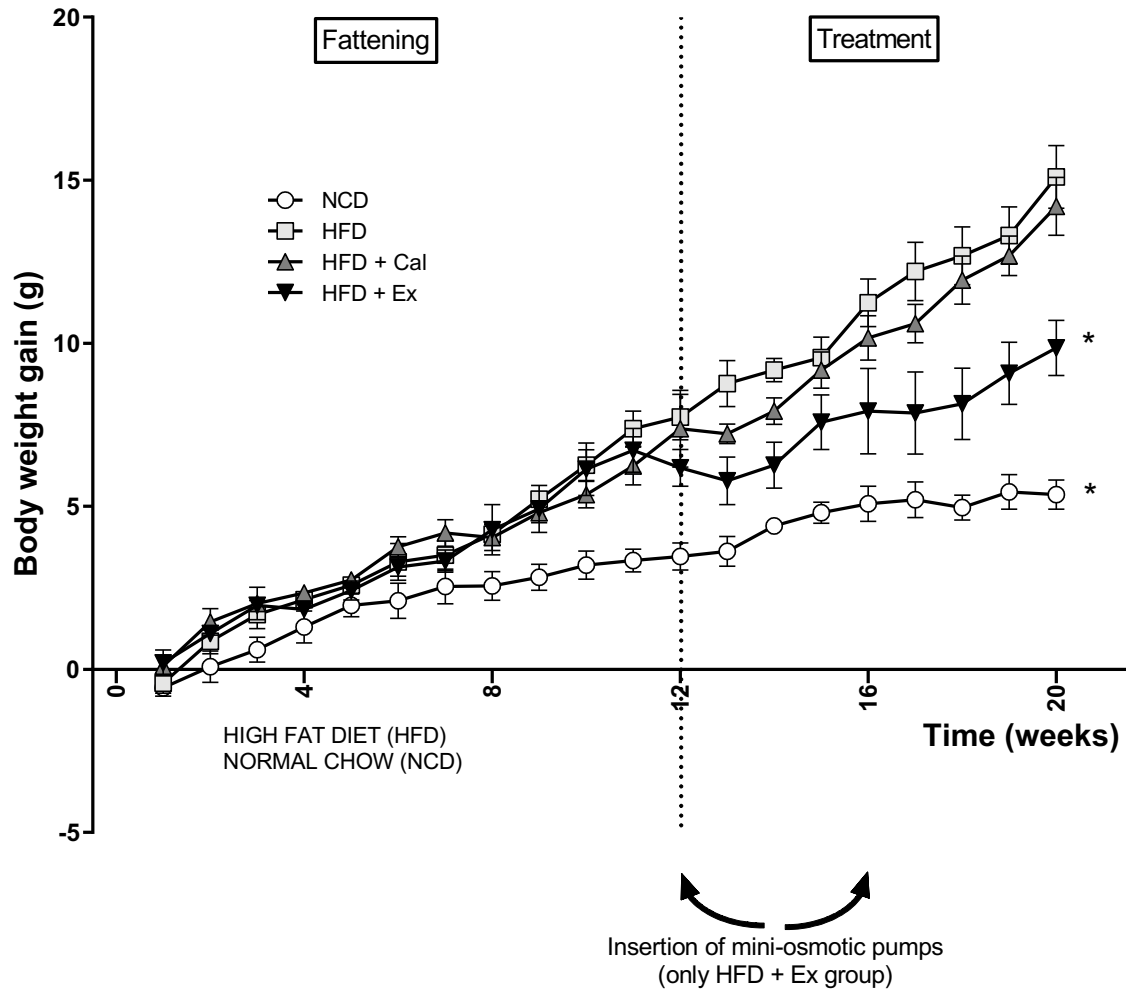
1. HFD supplemented with **2% Calanus oil (Cal)**
2. HFD plus sub-cutaneous administration of **10  $\mu\text{g}/\text{kg}/\text{day}$  exenatide (Ex)**

Mice fed normal chow (NCD) or non-supplemented HFD served as lean and obese controls, respectively.

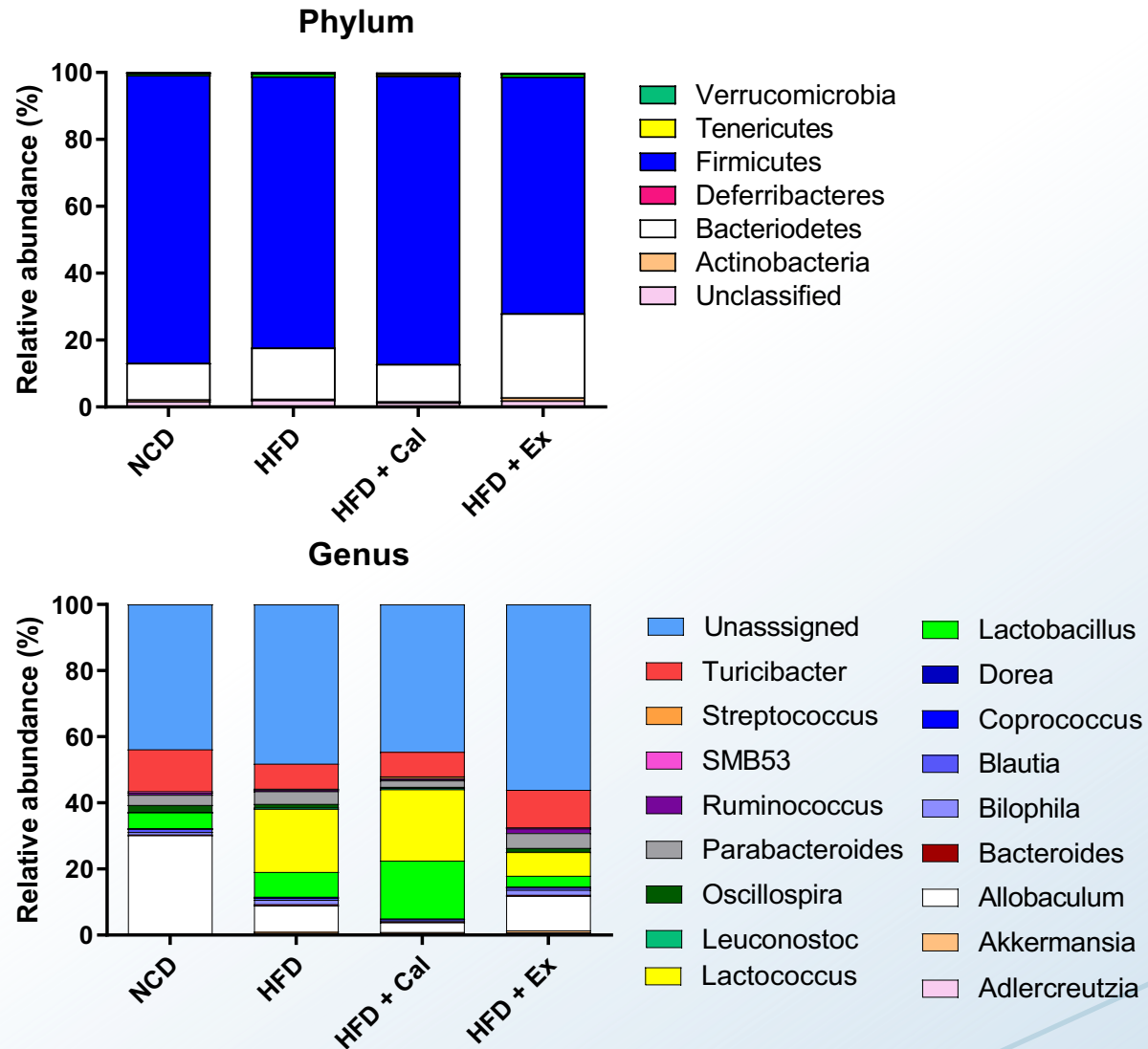
At the end of the treatment period, colonic feces was collected, and the microbiota was analyzed using 16S sequencing.



# Weight gain



# Relative abundance of the microbiota at phylum and genus level

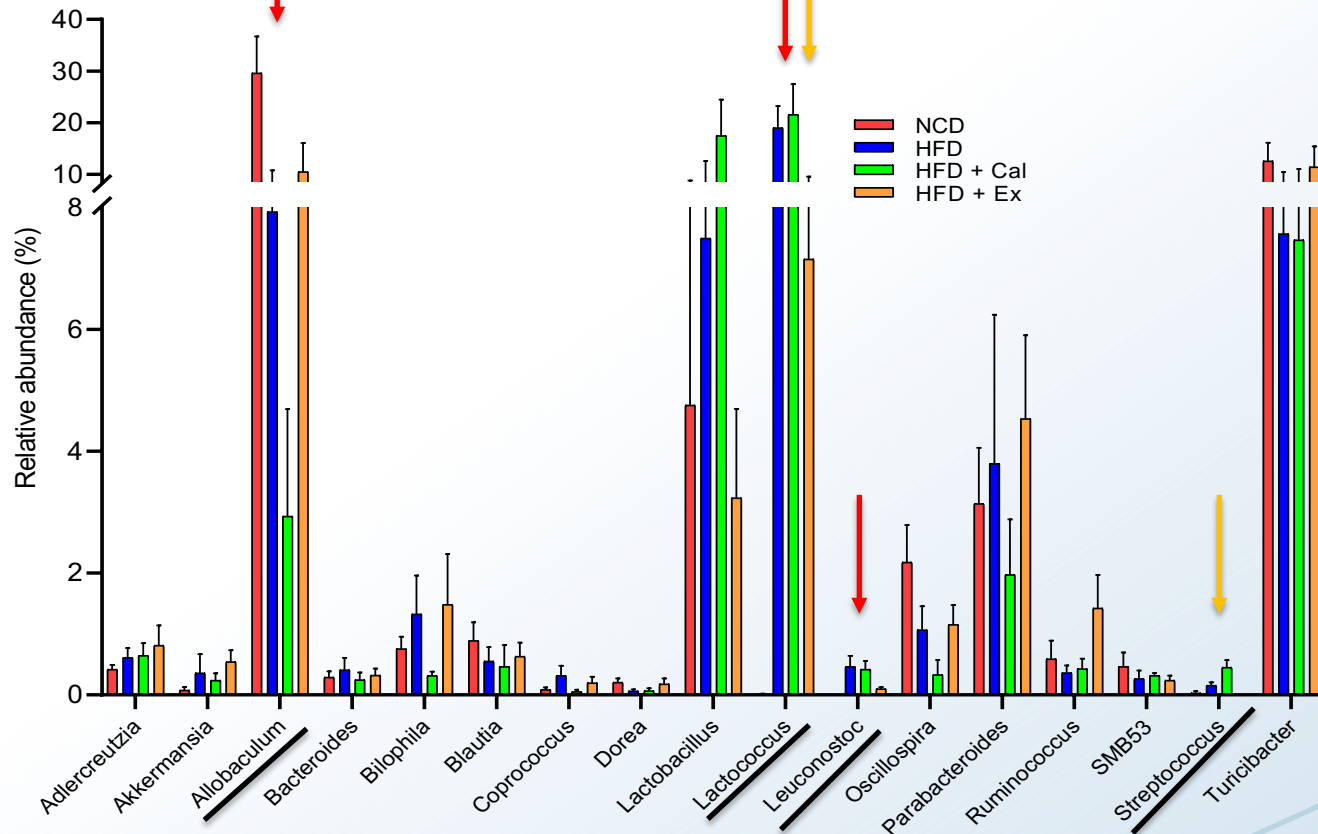




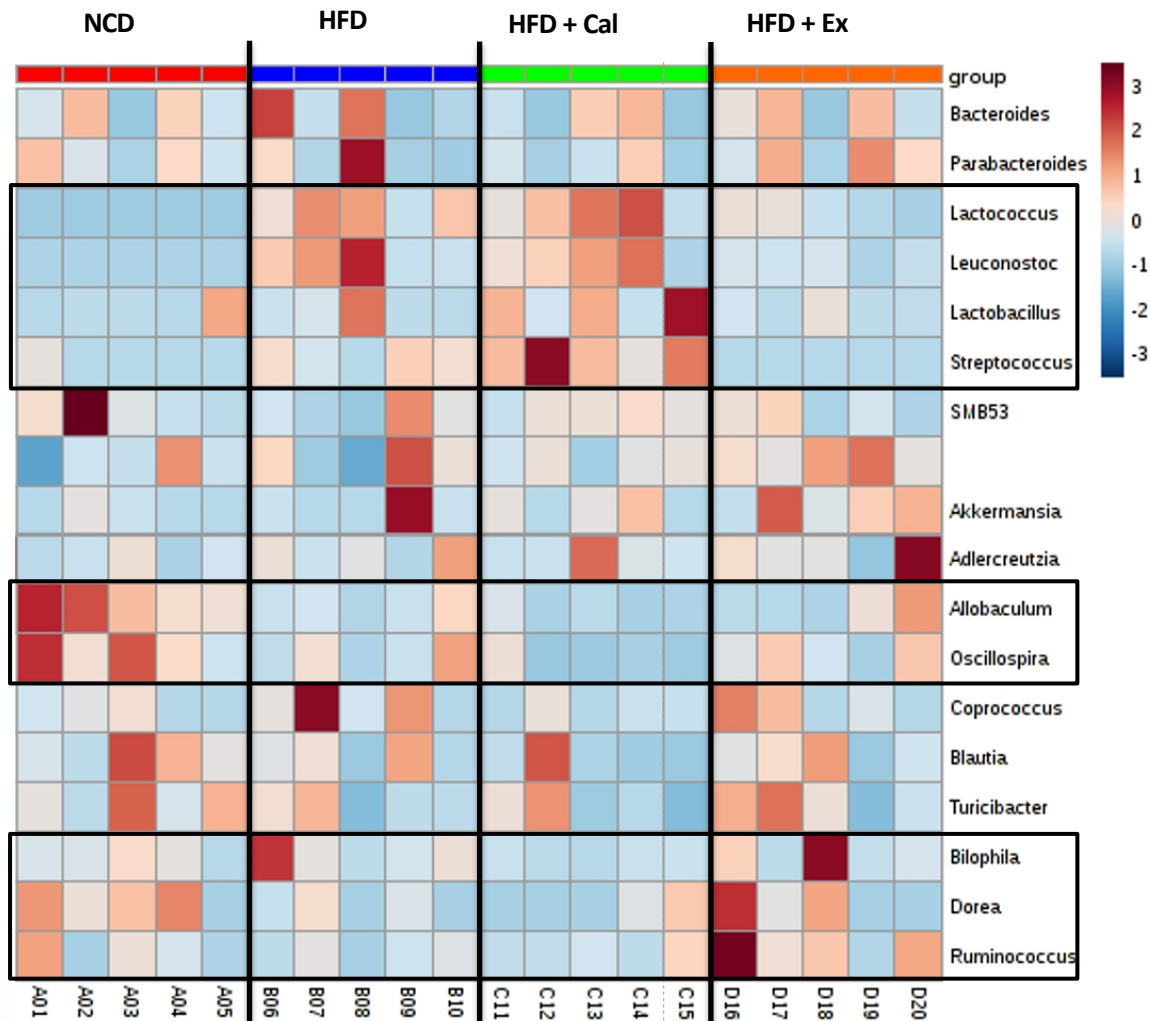
# Relative abundance of the microbiota on genus level

Differences in relative abundance between:

- ↓ HFD vs NCD
- ↓ HFD vs HFD + Ex



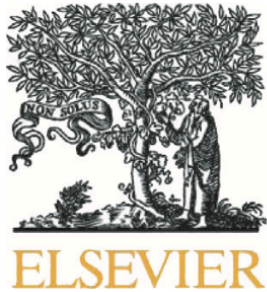
# Relative abundance of the microbiota on genus level



# Conclusions

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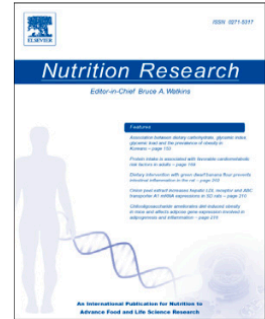
1. Does diet-induced obesity has an impact on the composition of the gut microflora?
  - HFD changed the microbiota composition in an **unhealthy direction**
  - **Enrichment of the pro-inflammatory *Lactococcus* and depletion of the anti-inflammatory and health promoting *Allobaculum* and *Oscillospira***
2. Does dietary Calanus oil or infusion of Exenatide modify any obesity-induced alterations in the microbiome?
  - Dietary Calanus oil was not able to restore the microbiota composition to that of the NCD group. It did show a relatively **high abundance** of *Lactobacillus*, a **health promoting genus** which is often related to weight loss. As well as a **decreased abundance in the pathogenic** considered genus *Bilophila*
  - Treatment with exenatide partly restored the bacterial profile found in the NCD group and seemed to **reduce** the abundance of *Streptococcus* and *Lactococcus*, which are considered **pathogenic**



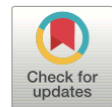
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