

Obesitas, microbiota en inflammatie

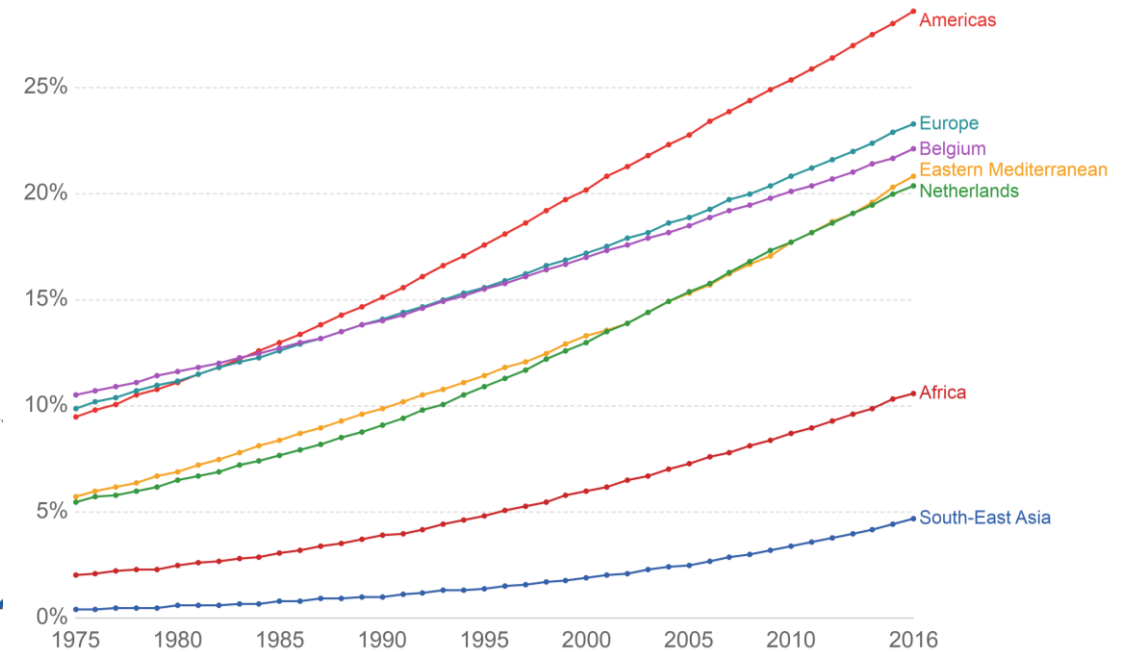
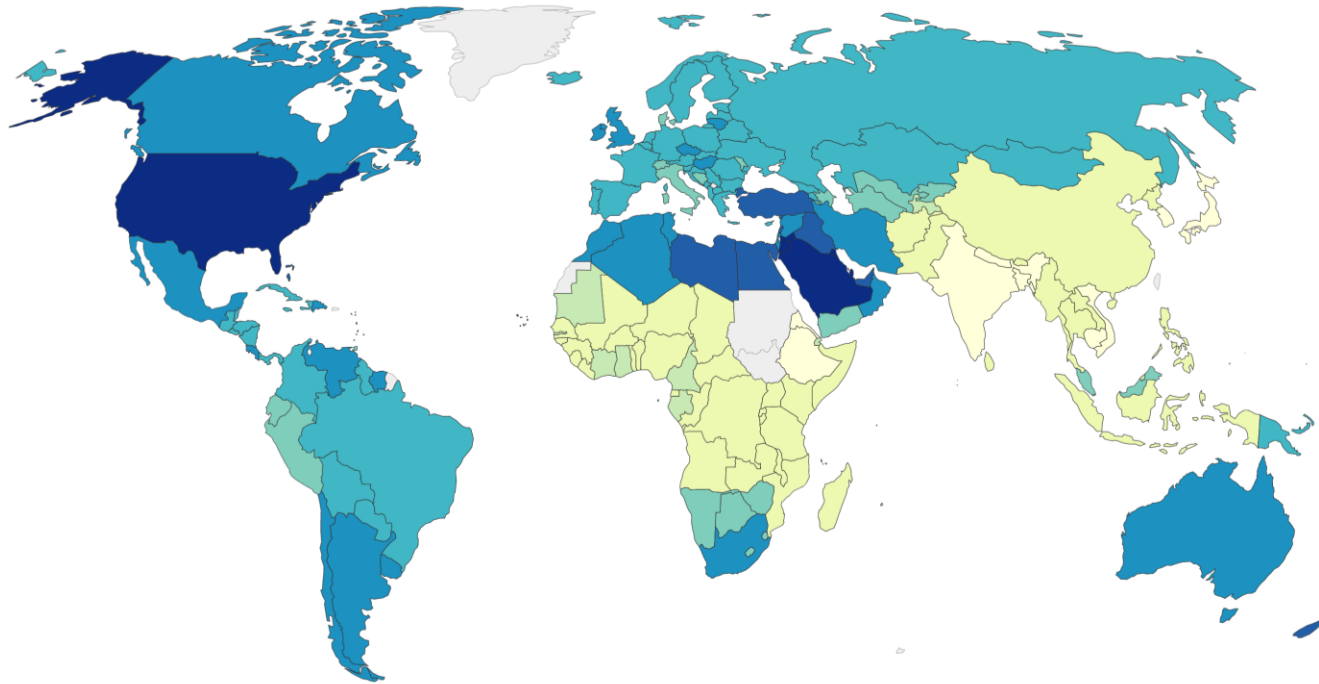
Kristin Verbeke

Translational Research in Gastrointestinal Disorders

KU Leuven, Leuven, België



The obesity epidemic



Source: WHO, Global Health Observatory

OurWorldInData.org/obesity • CC BY



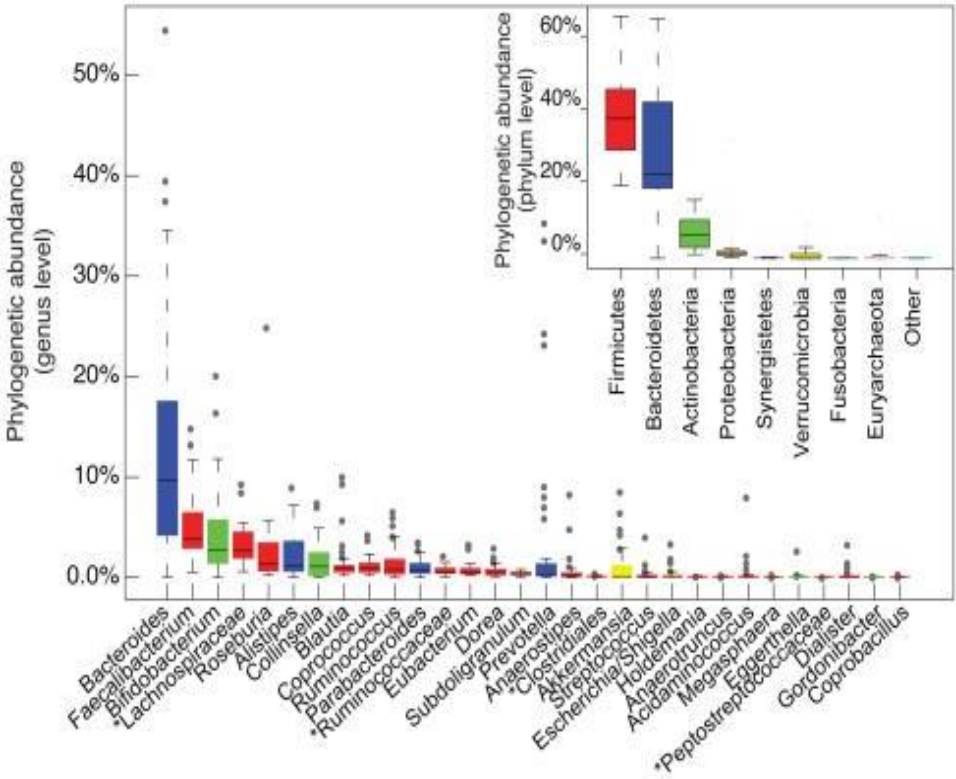
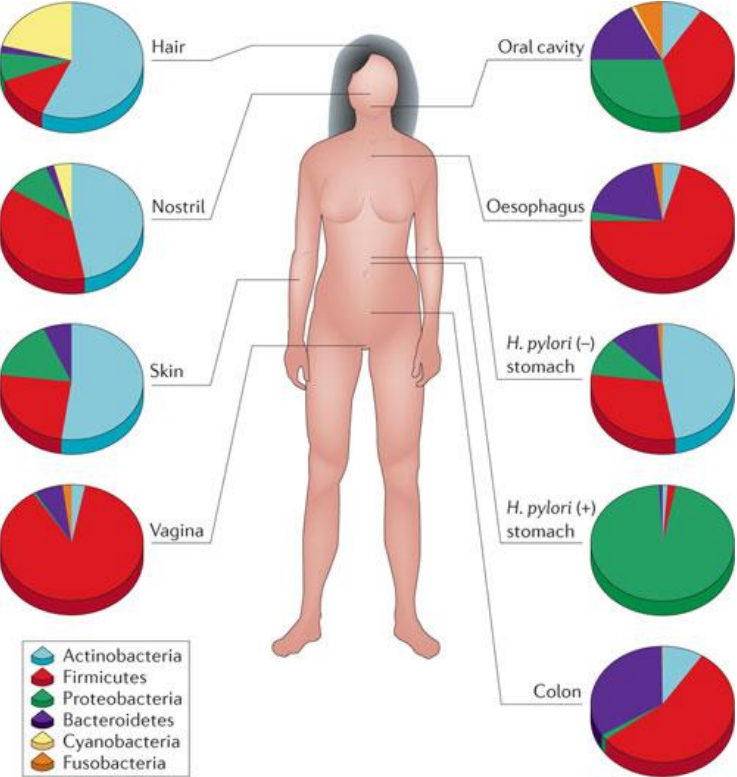
Source: WHO, Global Health Observatory

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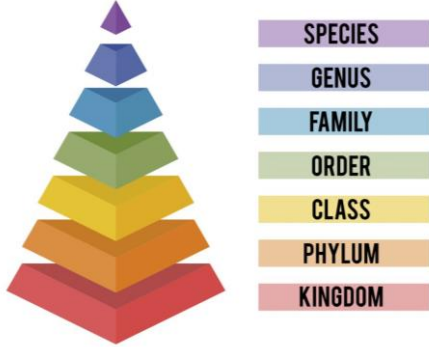
Oorzaken van obesitas



De mens is een superorganisme

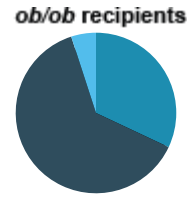
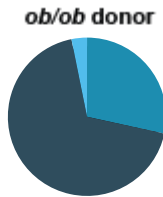
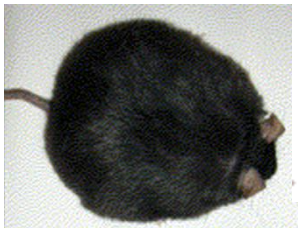


HIERARCHY OF BIOLOGICAL CLASSIFICATION

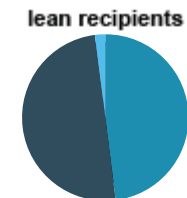
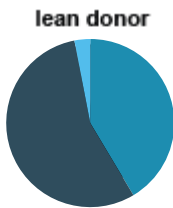


Obese muizen

obese donor (*ob/ob*)

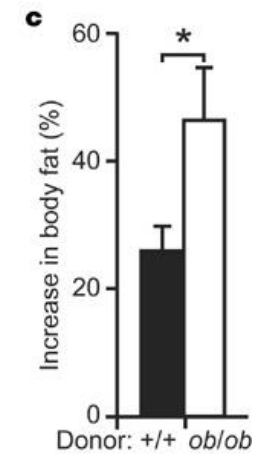


lean donor

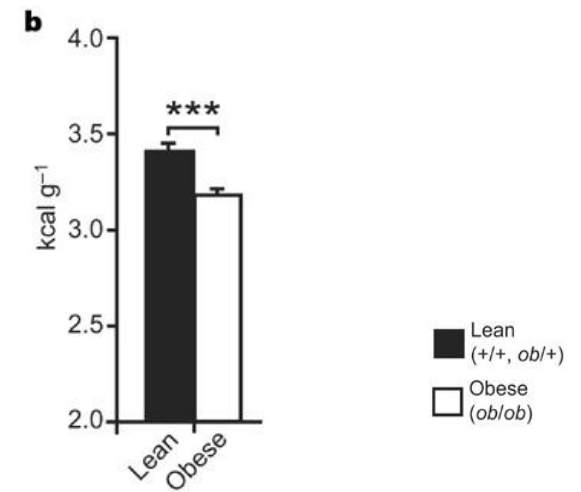


■ Firmicutes ■ Bacteroidetes ■ Other

Increase in body weight



Energy in feces



obese microbiome possesses metabolic pathways that are highly efficient at extracting energy from food

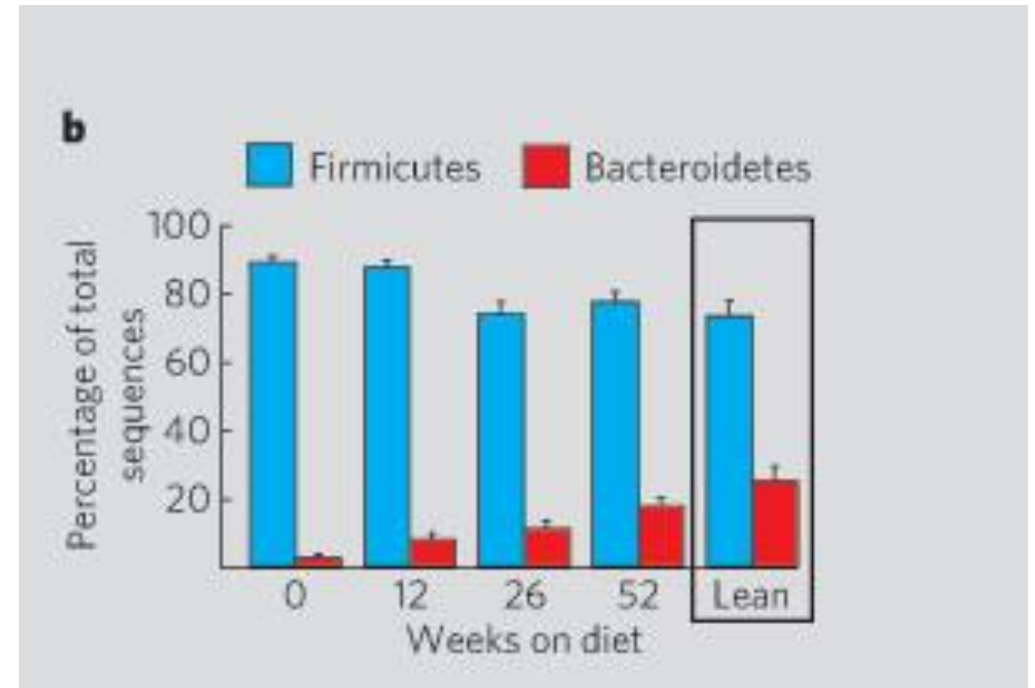
Microbiota samenstelling in obese personen



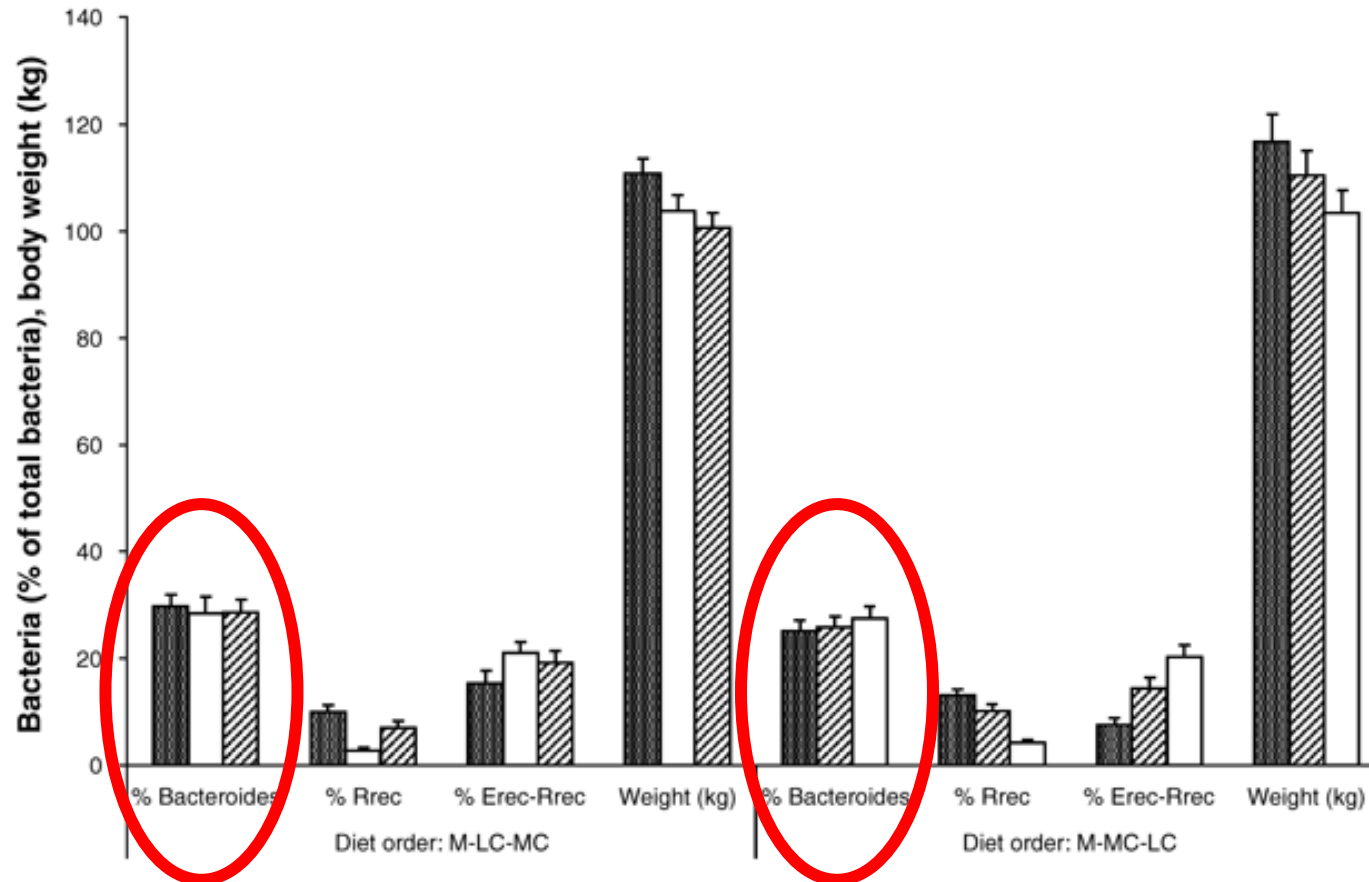
12 obese personen



Laag calorie dieet



Others do not confirm



No effect on % Bacteroides after weight loss

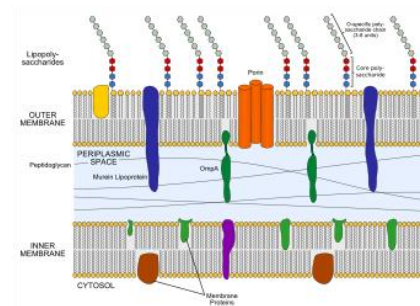
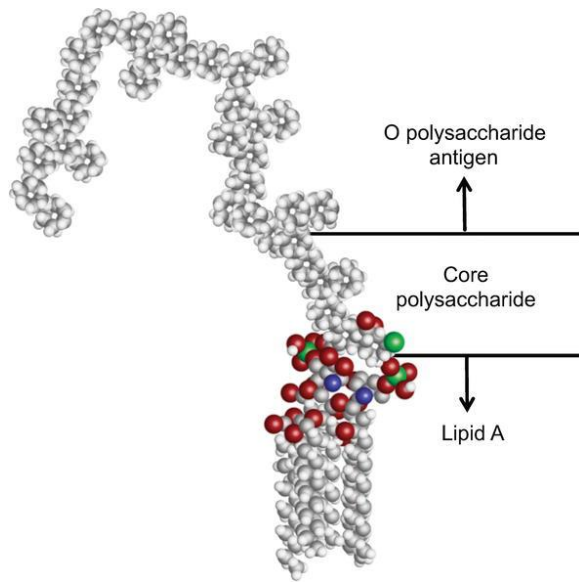
Gut microbiota and obesity

- Phylumwide changes currently not considered as biomarker for obesity
- Changes at lower taxonomic level may better define dysbiosis
- Several genera increased or decreased in obesity – species may follow opposite trend
 - Lactobacilli ↗
 - Bifidobacteria ↘
 - Faecalibacterium prausnitzii ↘
 - Akkermansia muciniphila ↘
- Mainly association studies -> cause or consequence?

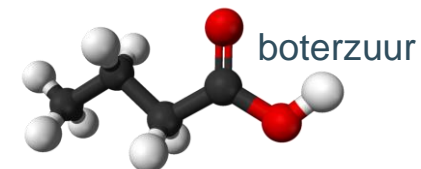
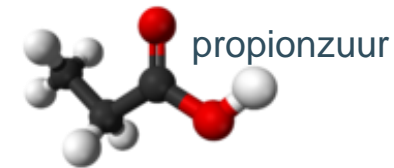
It is still impossible to define an obese microbiome

Microbial signals linked to obesity

Lipopolysaccharide (LPS)

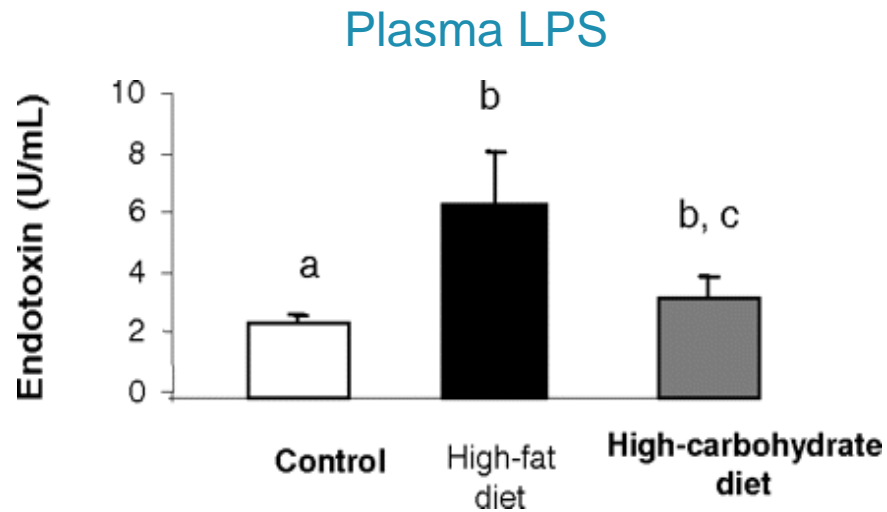


SCFA

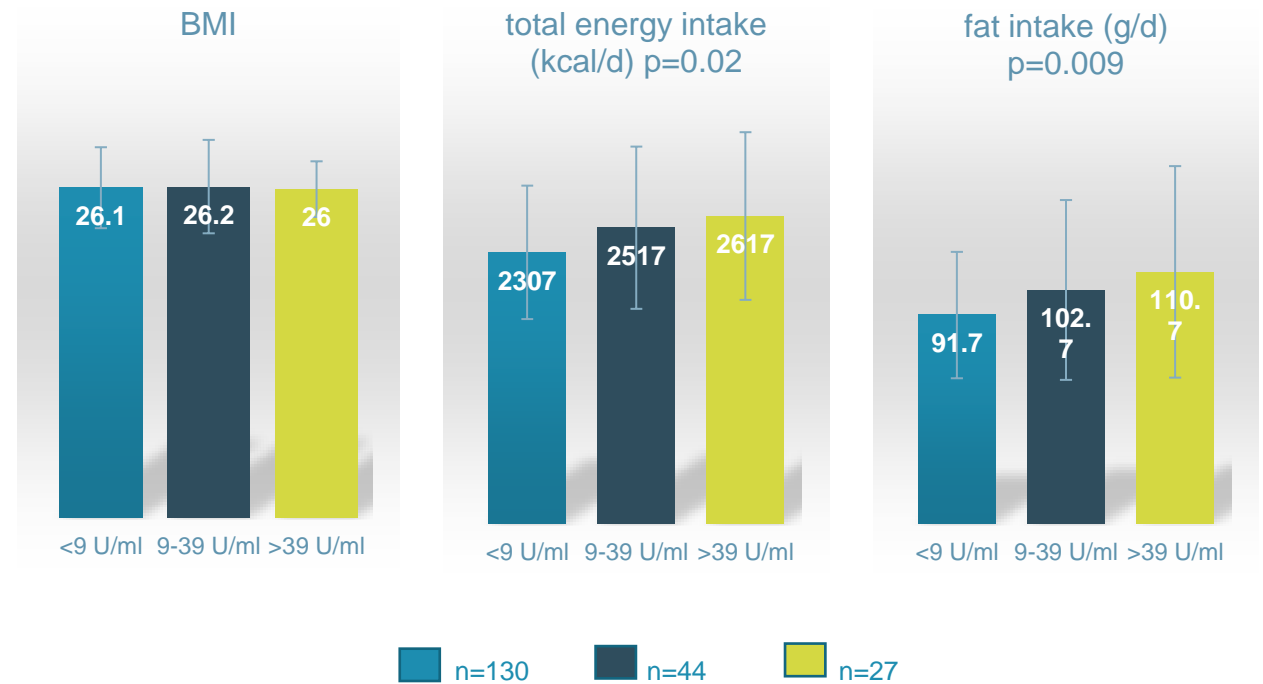


High fat intake increases plasma LPS

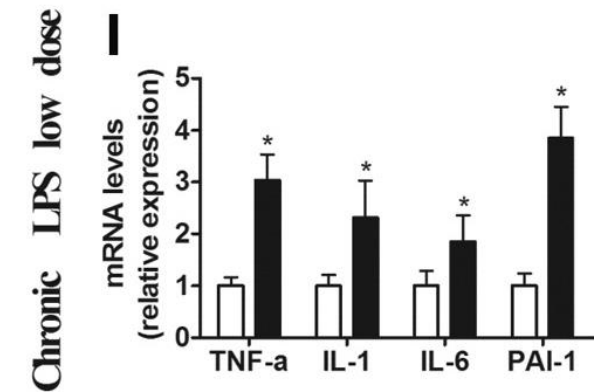
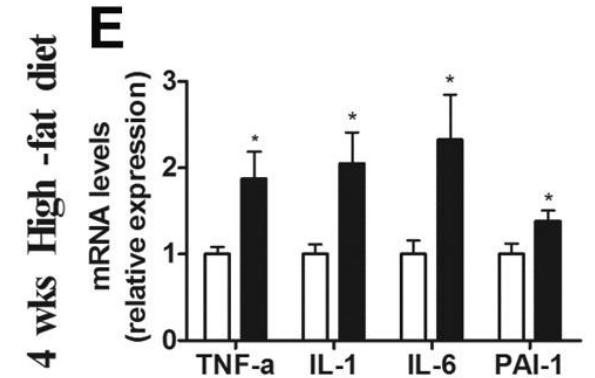
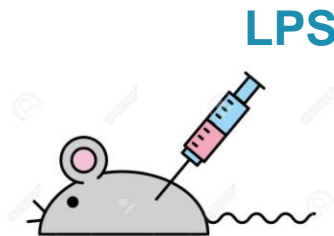
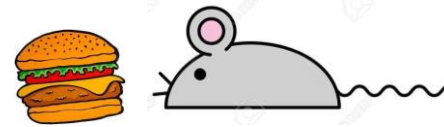
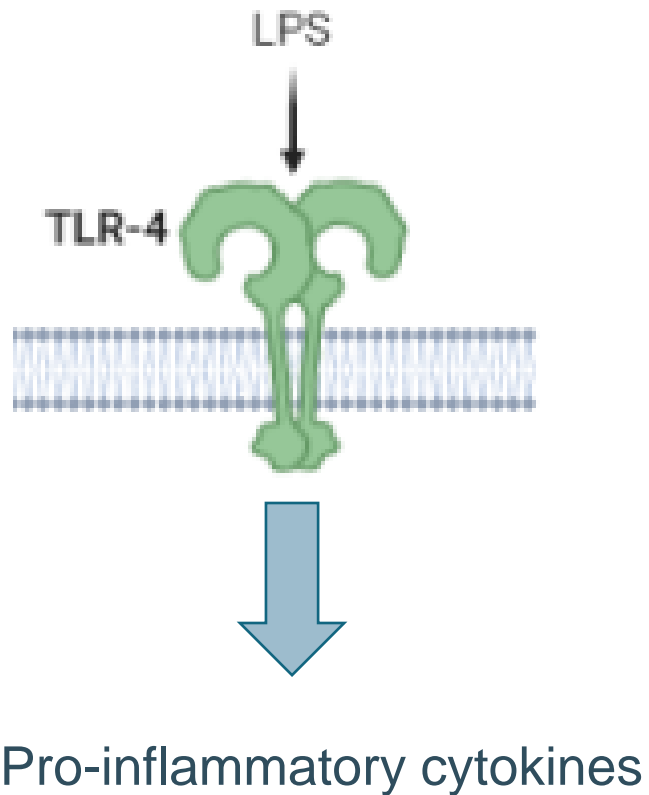
Mice
Intervention for 4 wks



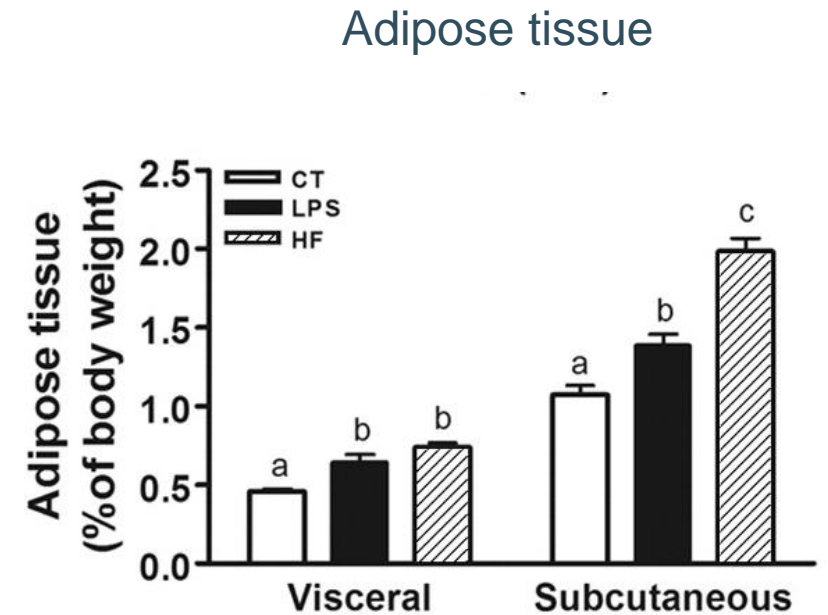
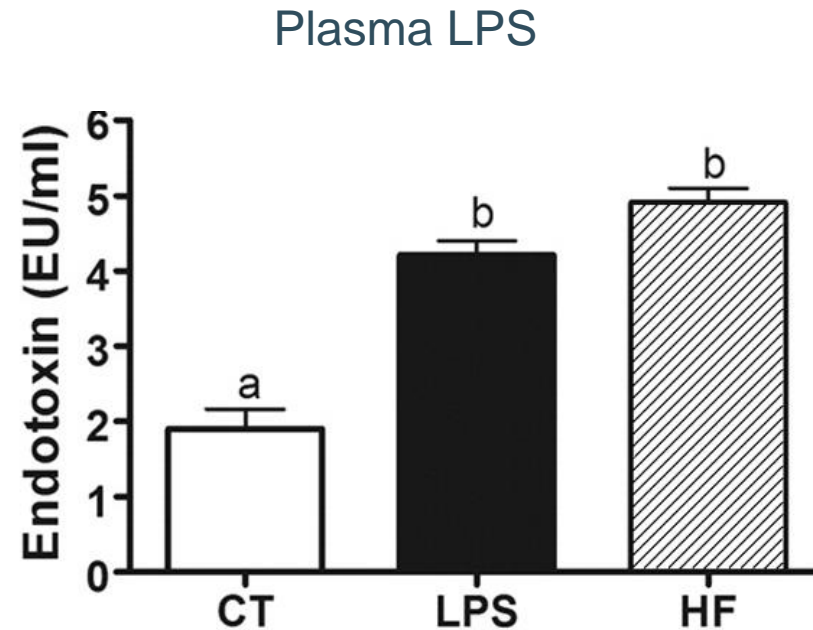
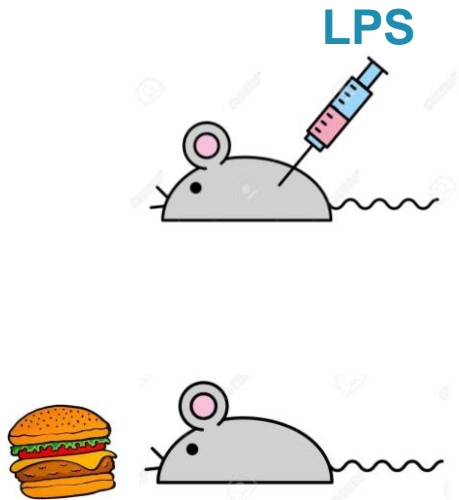
Humans
Cross-sectional analysis, n=201



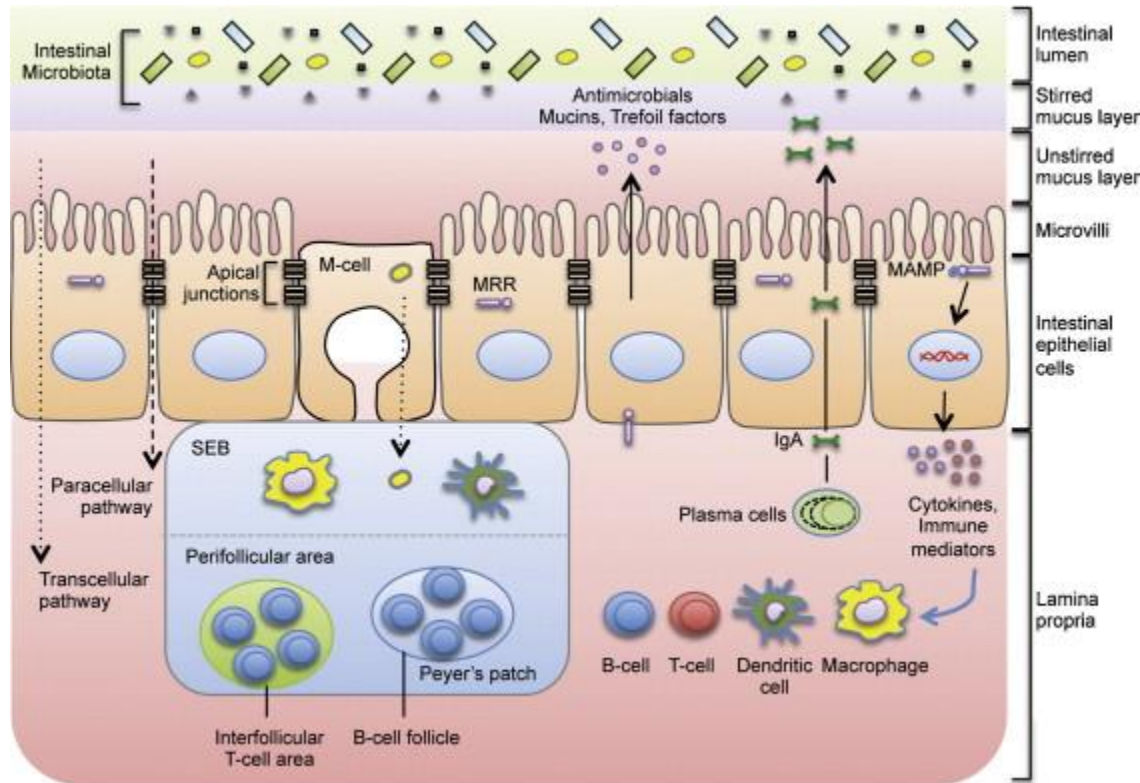
Increased plasma LPS induces inflammation



Increased plasma LPS induces obesity

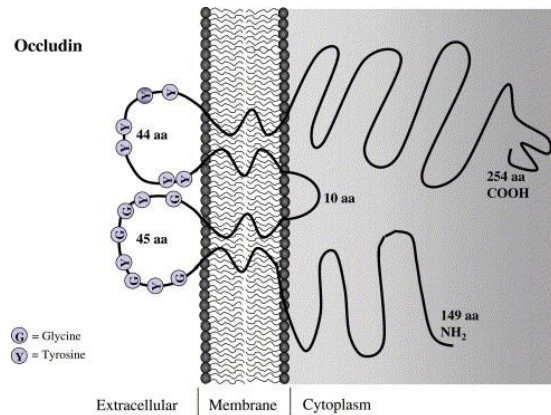
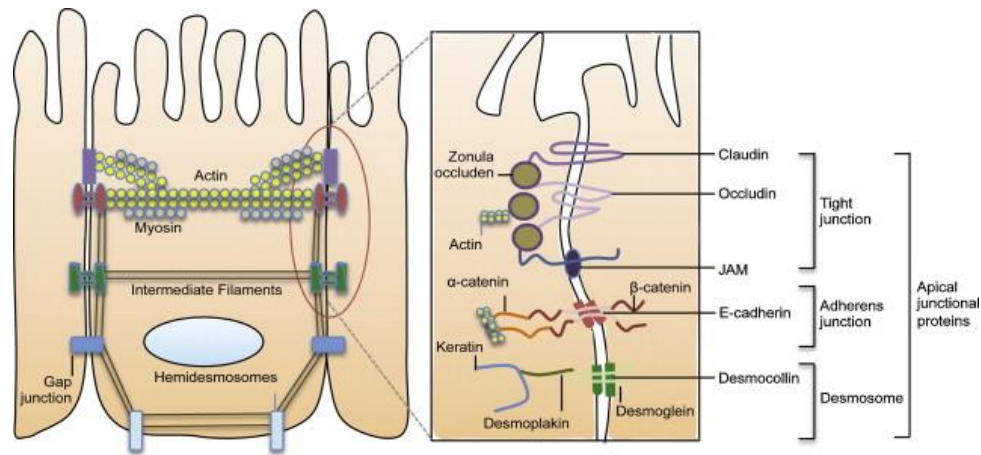


SCFA protect against inflammation

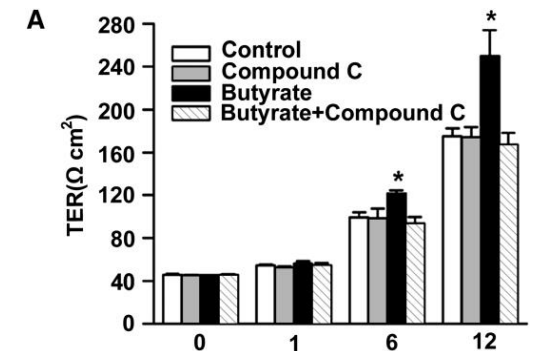
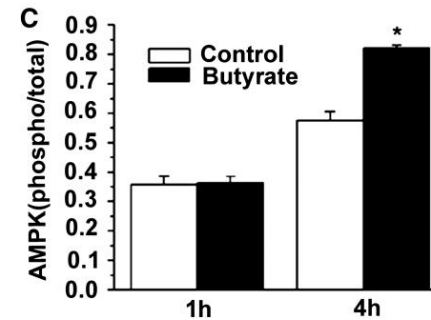


- Epithelial cells
- Mucus
- Immune system
- antimicrobials

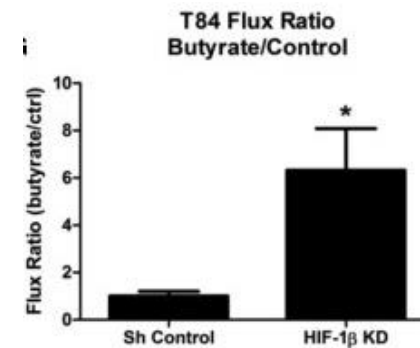
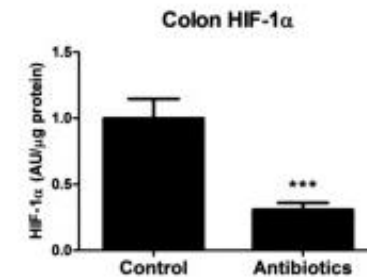
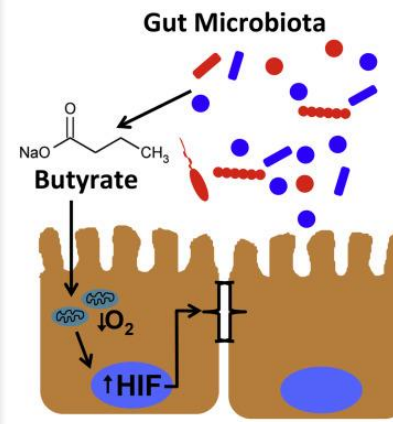
SCFA versterken de tight junctions



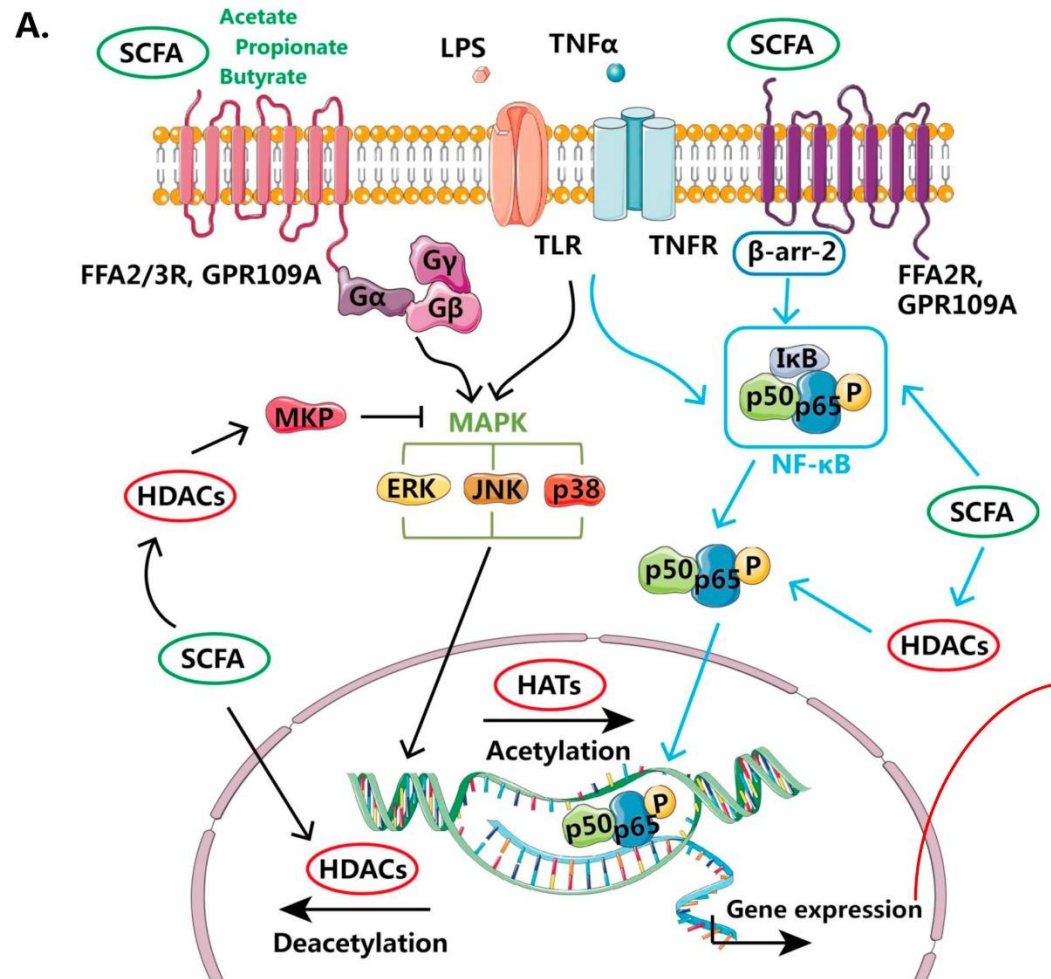
Activatie van AMPK



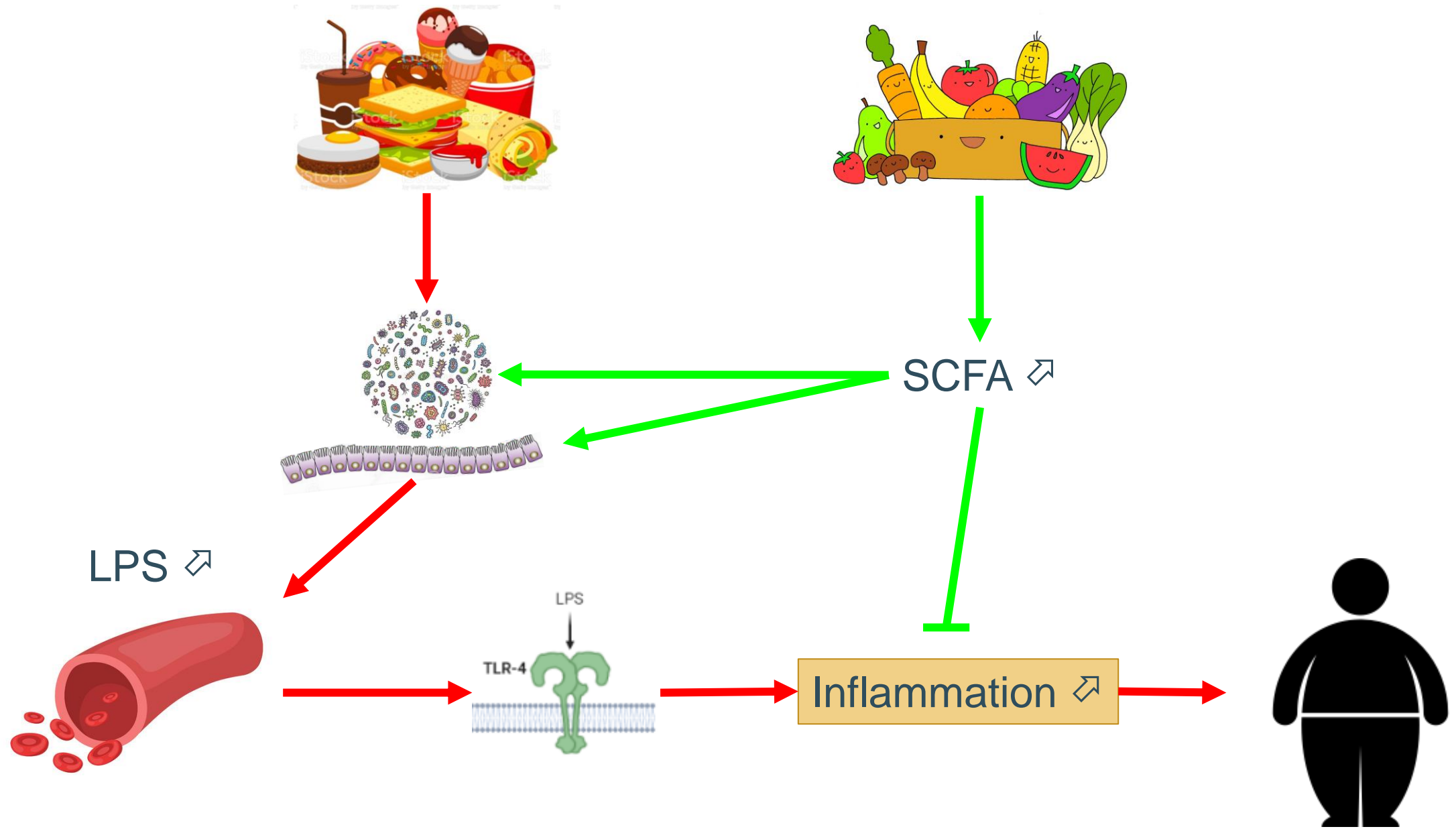
Stabilisatie van HIF



SCFA interfereren met het immuunsysteem

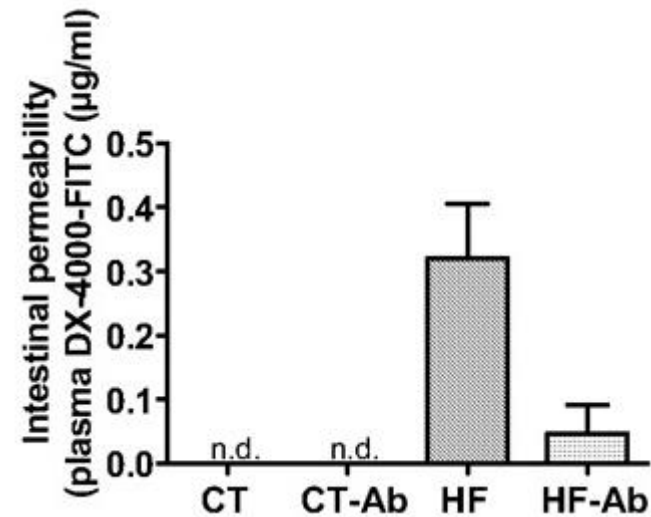


- Stimulatie van MAPK
- Inhibitie van NF-κ-B
- Inhibitie van HDACs

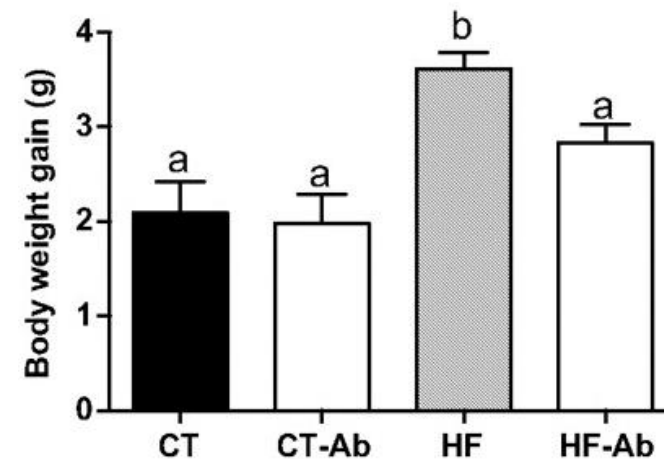


Obese mice have increased gut permeability

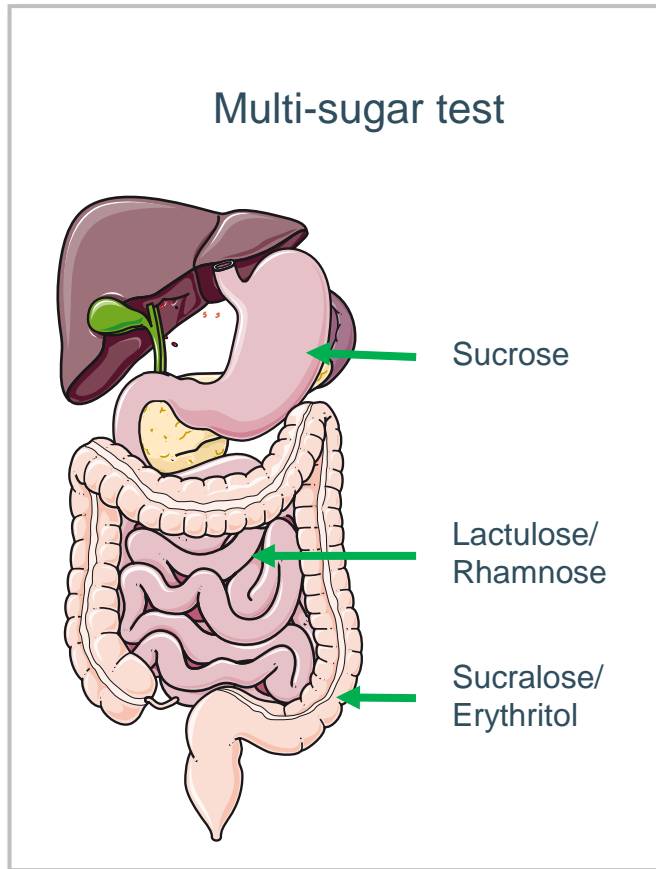
In vivo permeability



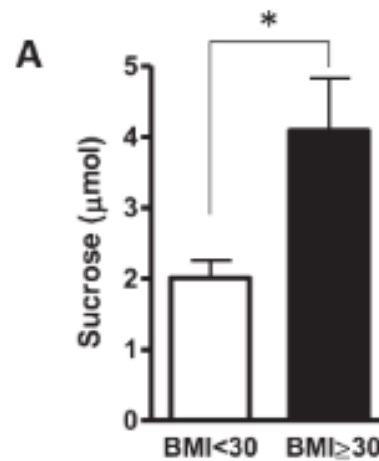
Body weight



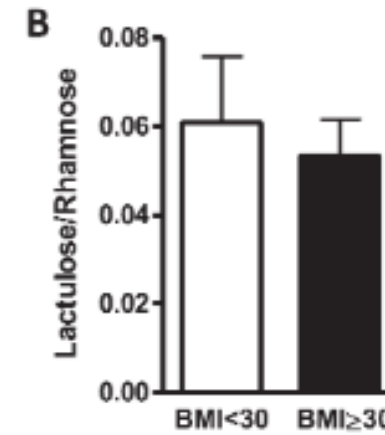
Gut permeability in humans



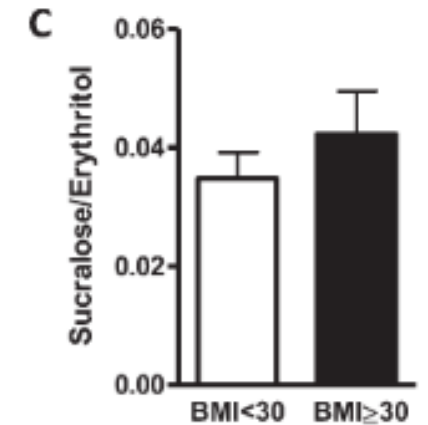
stomach



small intestine



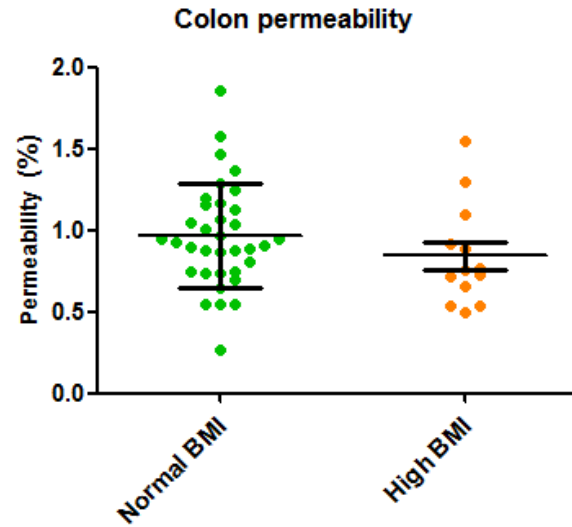
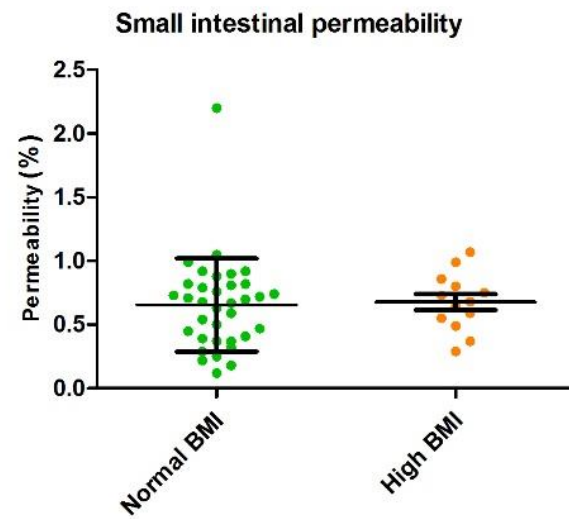
colon



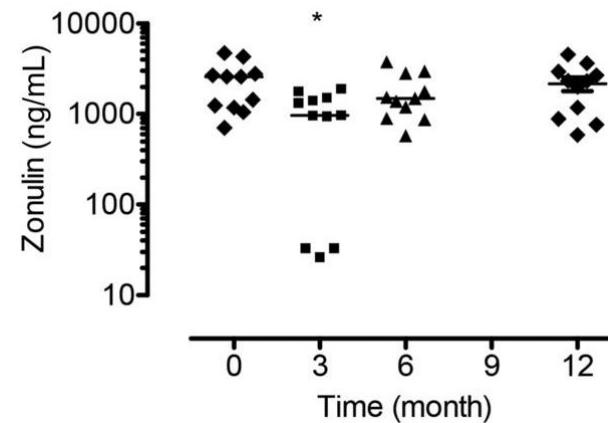
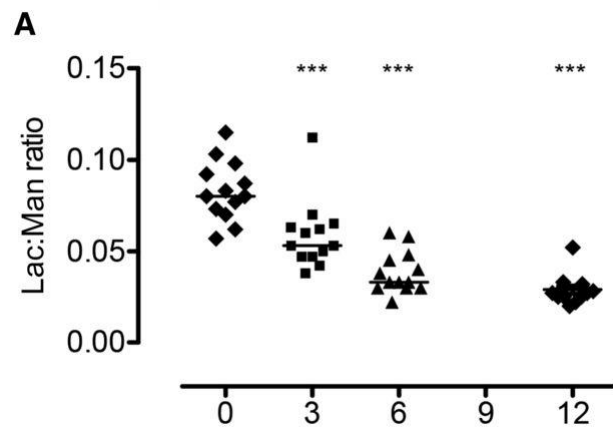
28 subjects

- 13 non-obese
- 15 obese

Gut permeability in humans



Obese subjects BMI: 32 (IQR 31-34)

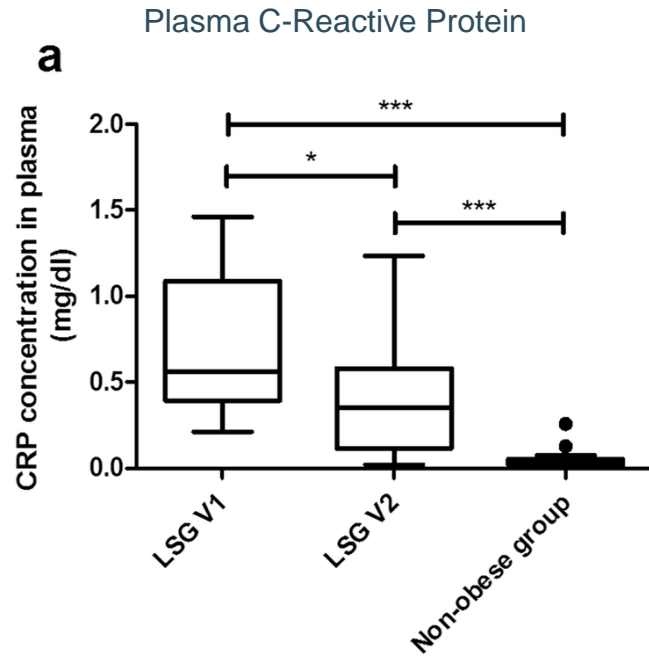


Obese subjects BMI:

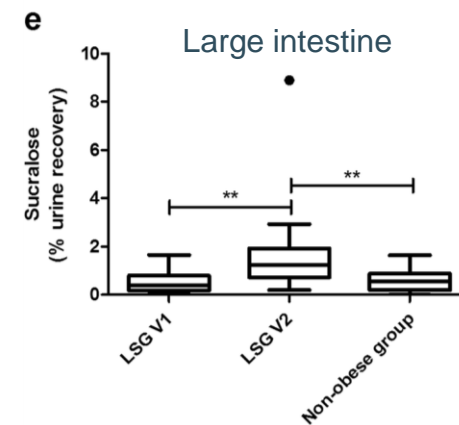
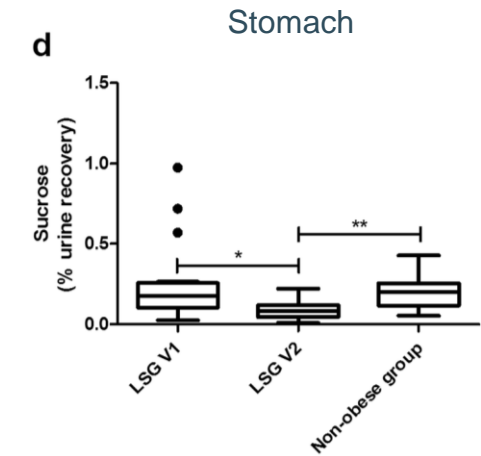
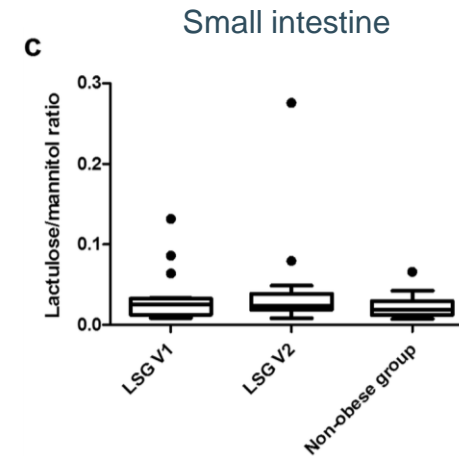
t_{0m} : 43.7 ± 5.2

t_{12m} : 36.4 ± 5.1

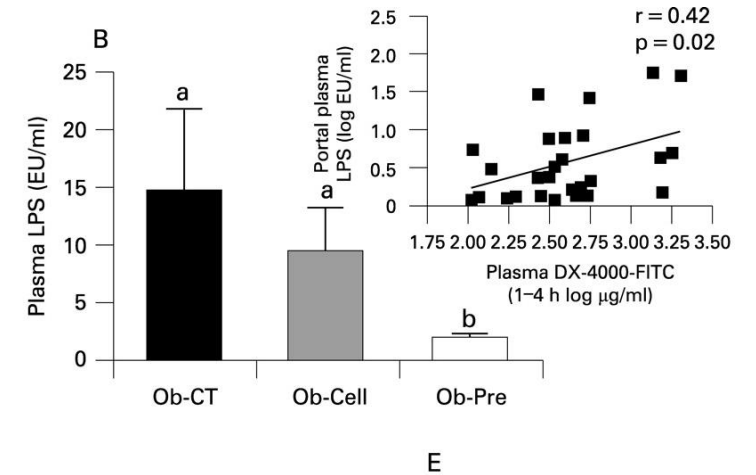
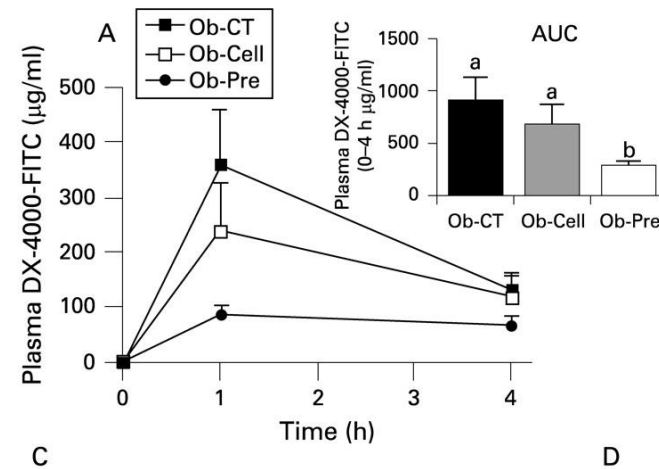
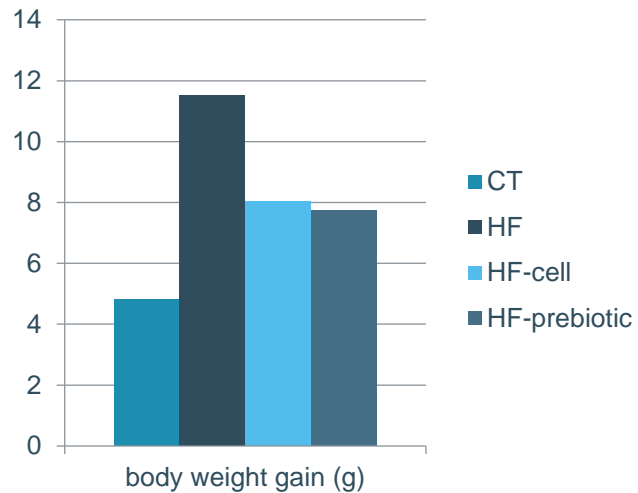
Gut permeability in humans



	BMI (median; IQR)
Before surgery (LSG V1)	52.5 (47.0; 56.8)
After surgery (LSG V2)	39.1 (32.6; 44.0)
Control group	21.5 (19.6; 23.3)

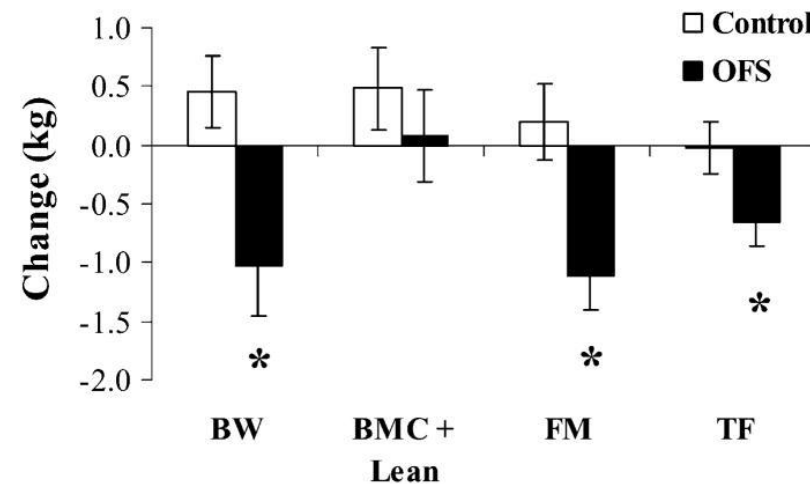
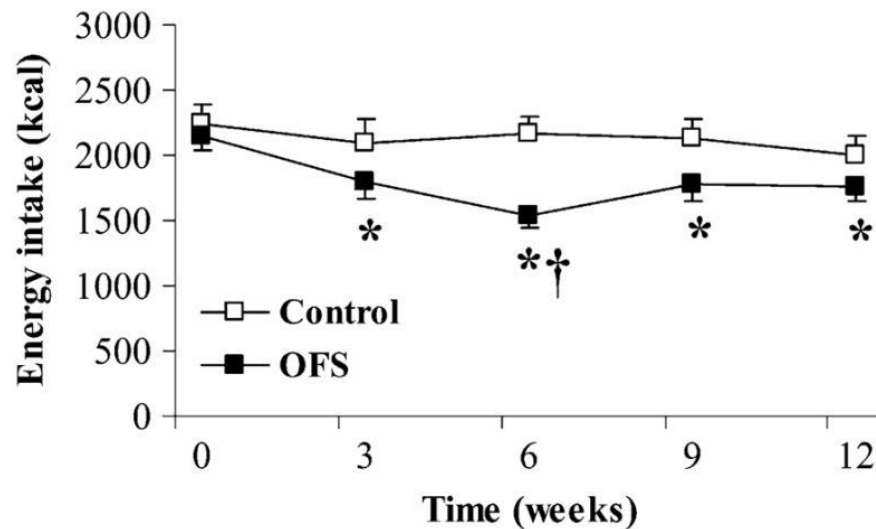


Prebiotics to treat obesity: mice studies



Prebiotics in humans

- 48 healthy adults with BMI > 25 kg/m²
- 21 g oligofructose or placebo for 12 weeks

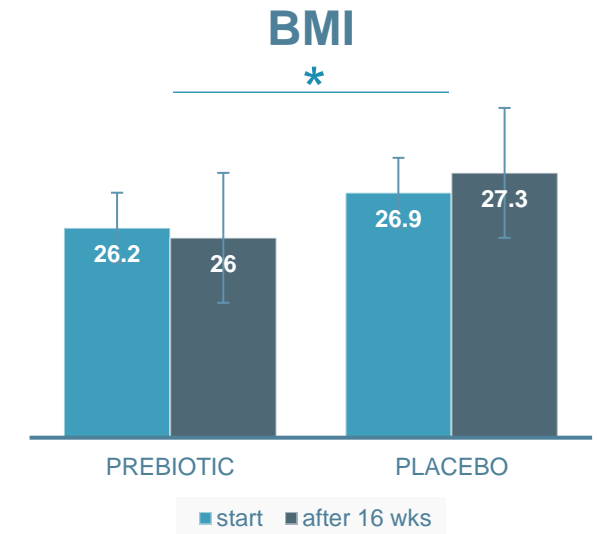
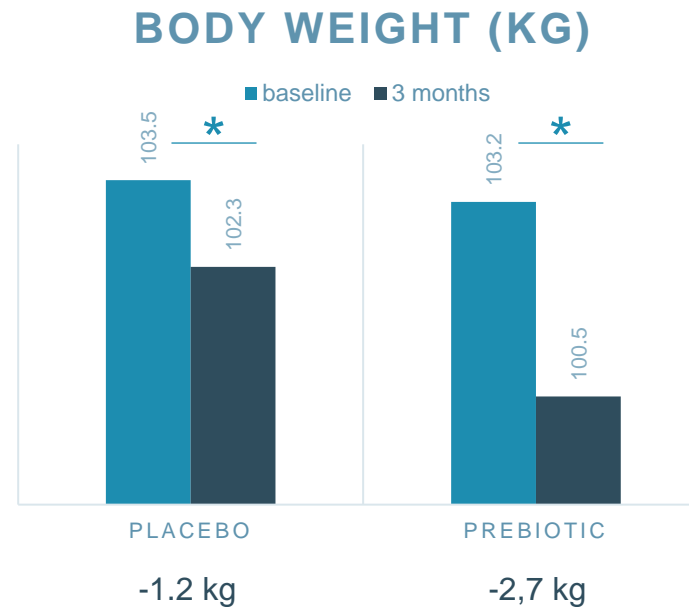
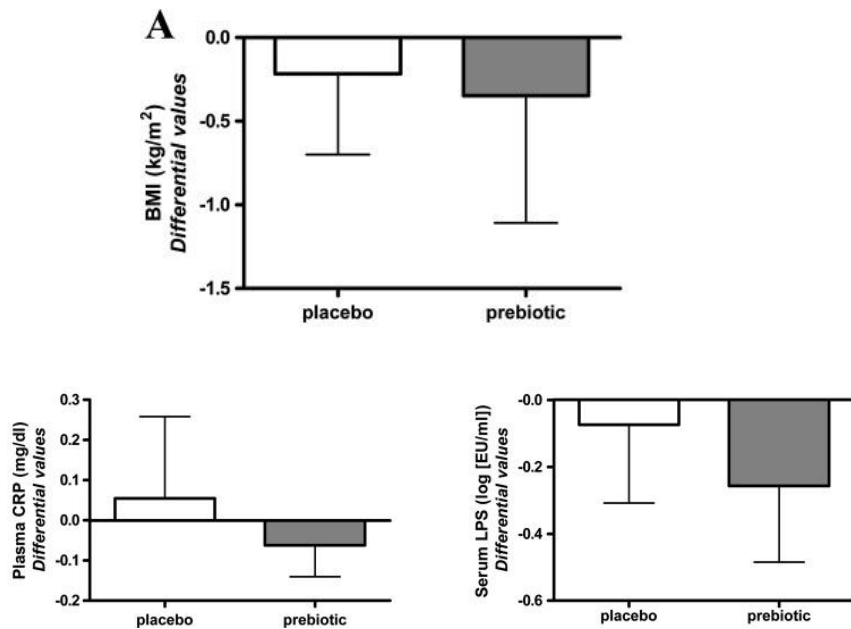


Prebiotics in humans

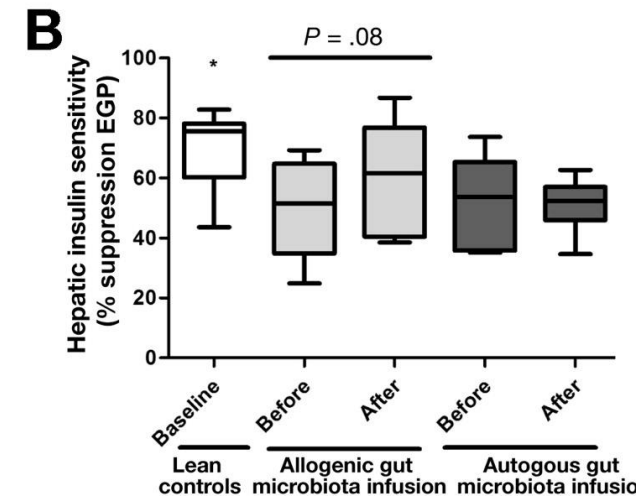
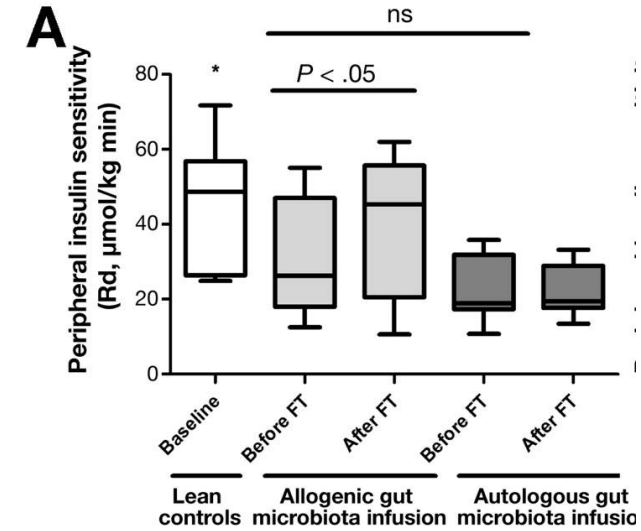
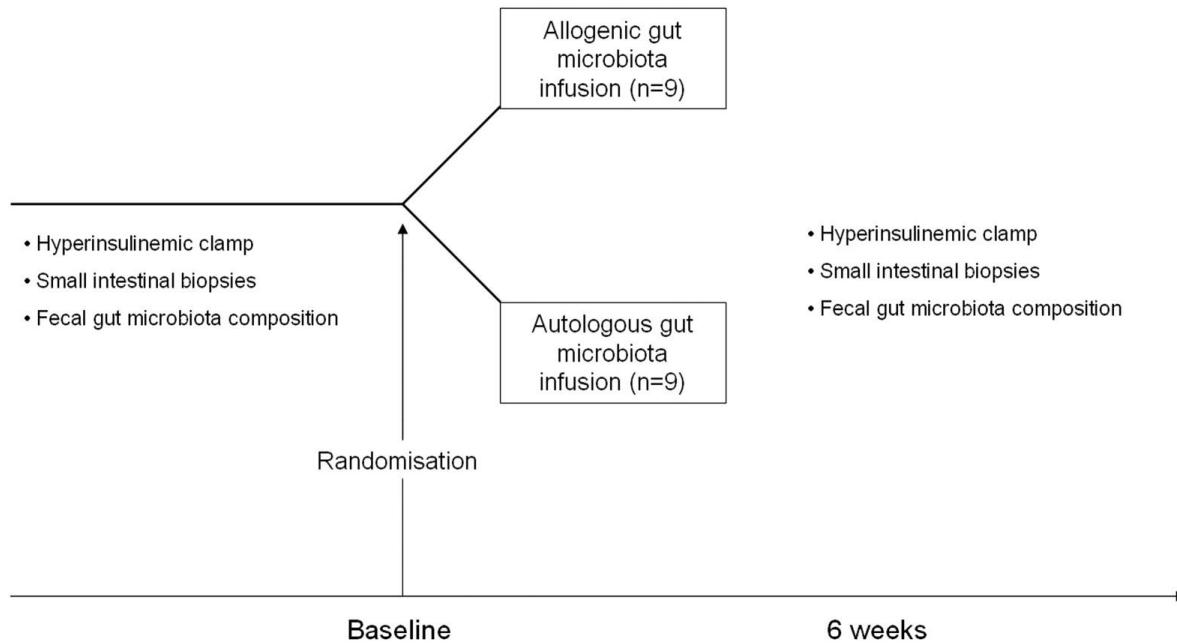
- 30 obese women
- 16 g oligofructose/inulin (50/50) or placebo for 3 months

- 106 obese people (m/f)
- caloric restriction with 30% of energy intake
- 16 g inulin or placebo for 3 months

- 42 obese children 7-12y
- 8 g oligofructose/inulin (50/50) or placebo for 16 wks



Fecal microbiota transplantation



Take home messages

- Er zijn meer en meer aanwijzingen dat de microbiota betrokken is in het ontstaan van obesitas
- Microbiële componenten/metabolieten kunnen fungeren als signaalmoleculen
 - In combinatie met een hoog-vet dieet wordt meer LPS opgenomen dat obesitas en inflammatie induceert
 - SCFA verhinderen inflammatie
- De rol van darmpermeabiliteit bij de mens is niet duidelijk
- Interventies bij proefdieren die de microbiota moduleren leveren veelbelovende resultaten
- De effecten van dergelijke interventies bij de mens zijn eerder bescheiden

Bedankt voor uw aandacht!

