



Faculty of Science



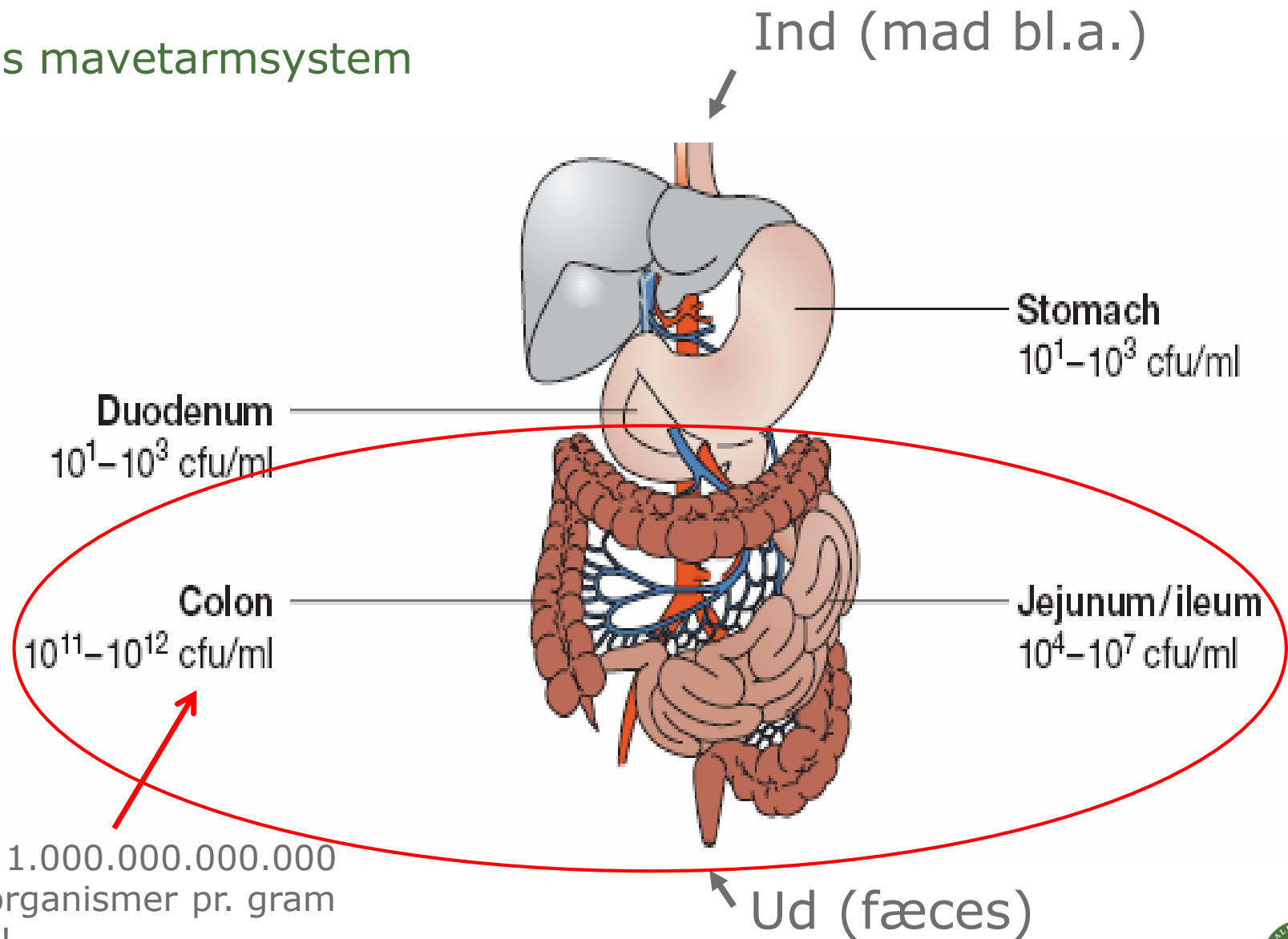
# Du bliver hvad du spiser – og det gør dine tarmbakterier også

Dennis S. Nielsen

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## Vores mavetarmsystem



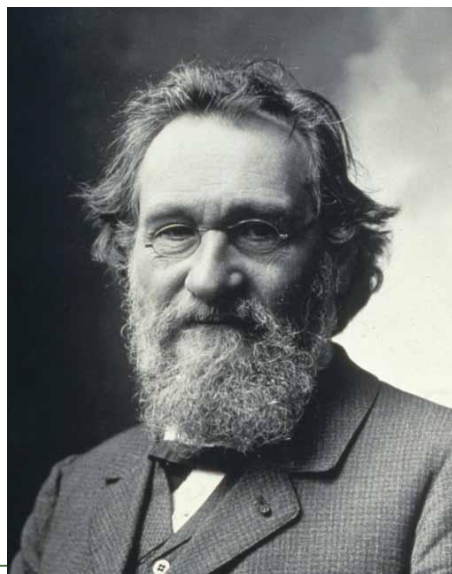
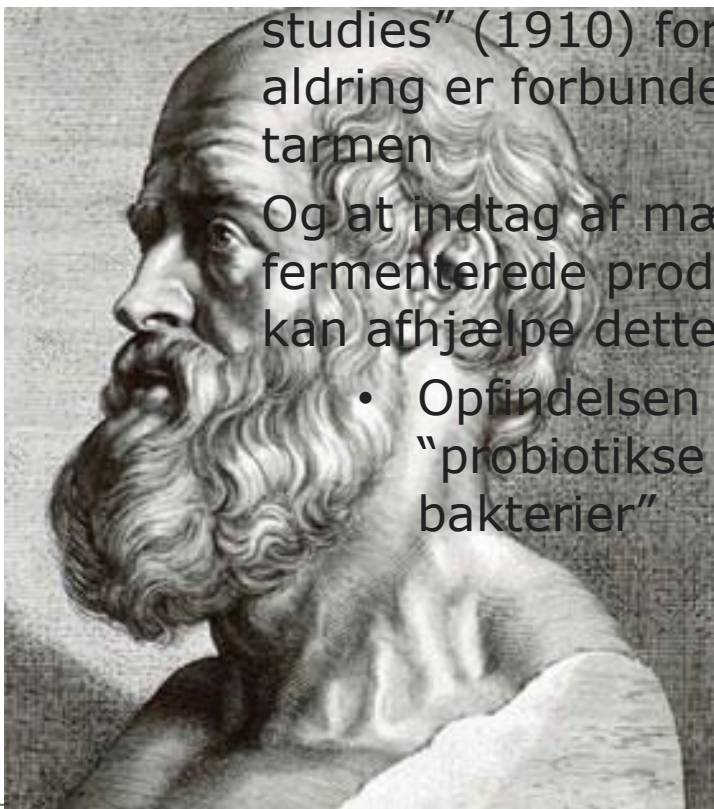
Det er 1.000.000.000.000  
mikroorganismer pr. gram  
fæces!!

## Tarmmikrobiomet, sundhed og sygdom

- "Al sygdom begynder i tarmene"  
(Hippocrates 460-370 BC)
- "Mange sygdomme begynder i tarmene"  
(Dennis S. Nielsen, 1977-? AD...)
- I bogen "The prolongation of life. Optimistic studies" (1910) foreslår Metchnikoff at aldrig er forbundet med "dårlige" bakterier i tarmen

Og at indtag af mælkesyrebakterier fra fermenterede produkter kan afhjælpe dette

- Opfindelsen af "probiotiske bakterier"



## Tarmmikrobiomet, sundhed og sygdom

- Vi har faktisk gjort som Metchnikoff sagde vi skulle gøre i meget lang tid uden at vide det.



Something rotten in Scandinavia: The world's earliest evidence of fermentation

Adam Boethius

9200 år gamle spor af strukturer til fermentering af fisk fish fermentation



### Probiotics History

*Giovanni Gasbarrini, MD, PhD,\* Fiorenza Bonvicini, MD,† and Annagiulia Gramenzi, MD†*

DMS 2019 Bulletin

*J Clin Gastroenterol* • Volume 50, Supp. 2, November/December 2016

**TABLE 1. History and Origin of Some Fermented Foods**

#### History of Some Fermented Foods

Food Origin	Approximate Year of Introduction	Region
Mushrooms	4000 BC	China
Soy sauce	3000 BC	China, Korea, Japan
Wine	3000 BC	North Africa, Europe, Middle East
Fermented milk	10,000 BC	Middle East
Fermented milk products	7000-5000 BC	Egypt, Greece, Italy
Fermented rice	2000 BC	China, Asia
Fermented honey (mead)	2000 BC	North Africa, Middle East
Cheese	2000 BC	Middle East, China
Fermented malted cereals: beer	2000 BC	North Africa, China, Middle East
Bread	1500 BC	Egypt, Europe
Fermented meats	1500 BC	Middle East
Sourdough bread	1000 BC	Europe
Fish sauce	1000 BC	Southeast Asia, North Africa
Garum (from fish guts)	400 BC	Greece, Italy (Rome)
Pickled vegetables	1000 BC	China, Europe
Tea	200 BC	China

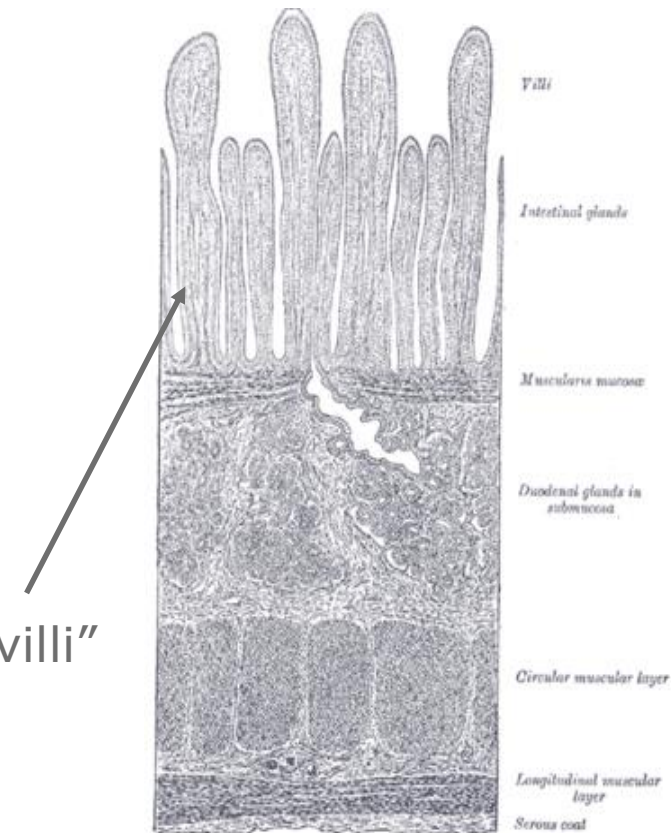
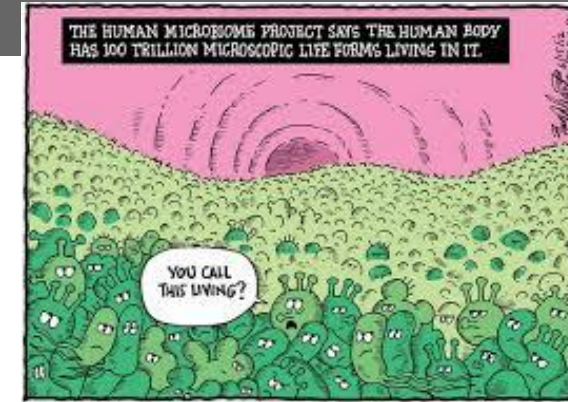


## Min mavefønemmelse siger mig...

- En voksen bærer rundt på ca. 1 kg mikroorganismer
- Et menneske indeholder lidt flere bakterieceller end menneskeceller i vores krop
- Vores tarm-system
  - Cirka 5 (-9) m langt
  - Overfladeareal 250-400 m<sup>2</sup>



- Dette enorme overfladeareal er muligt pga. "villi" på overfladen



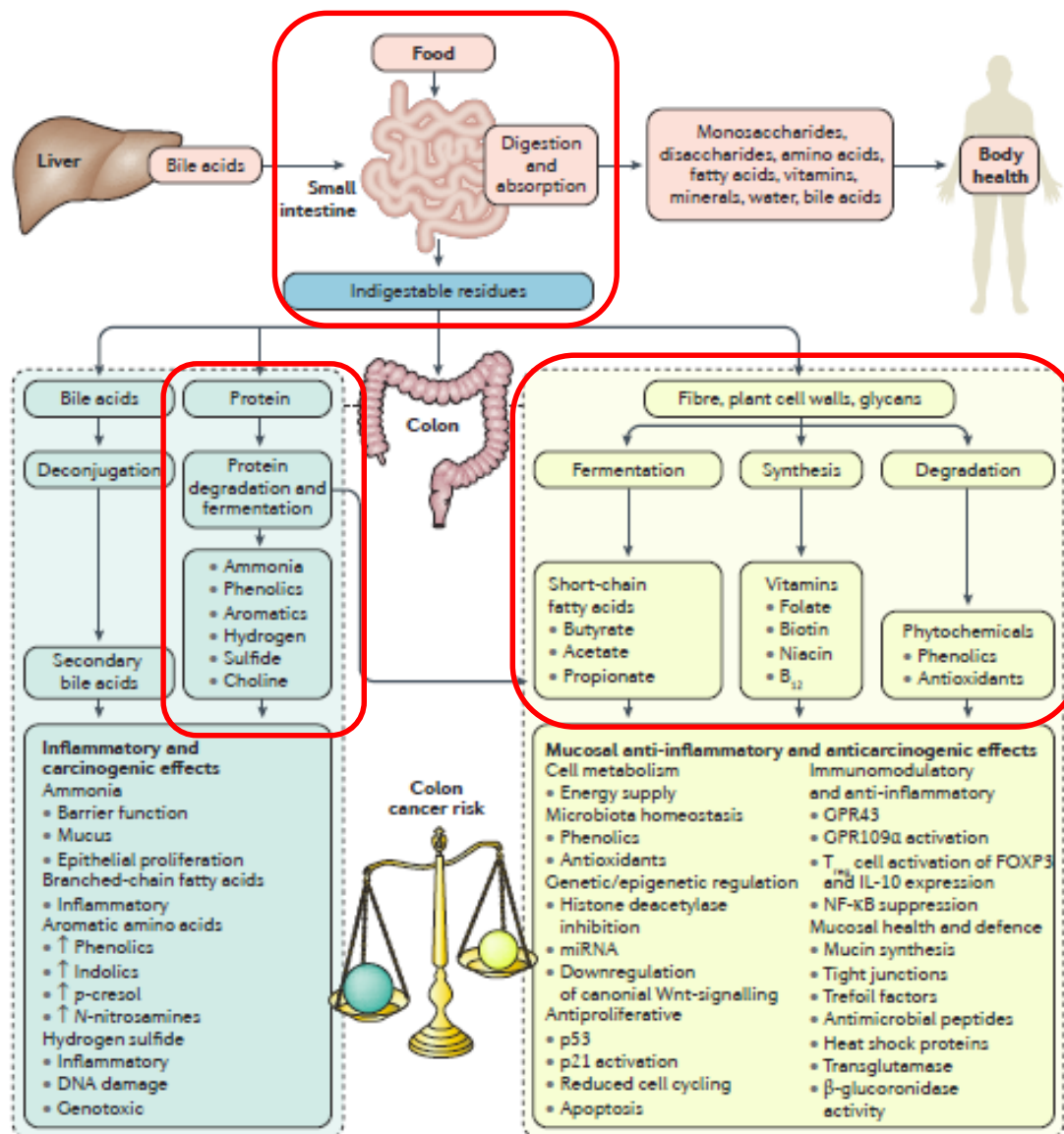
Duodenum (sektion)

## Hvad ved vi i dag?

- Vi ved at en lang liste af sygdomme er forbundet med tarmmikrobiom-ubalance
- Overvægt, metabolisk syndrom, type 2 diabetes
  - Og giver en forklaring på, hvorfor det kan være svært at tabe sig.
- Type 1 diabetes
- Andre autoimmune sygdomme (asthma, eksem...)
- Inflammatorisk tarmsygdom (IBD)
- Irritabel tyktarm (IBS)
- Kolon-cancer
- Hjertekar-sygdomme
- Skrøbelighed ("frailty") hos ældre
- Mentale tilstande/opførsel (i hvert fald i mus...)
- Osv. osv. osv.



## Hvad ved vi?



- Vi ved også, at det er ret kompliceret. Her tarm-mikrobiom-ubalance og kolon-cancer som eksempel

## Diet, microorganisms and their metabolites, and colon cancer

Stephen J. D. O'Keefe

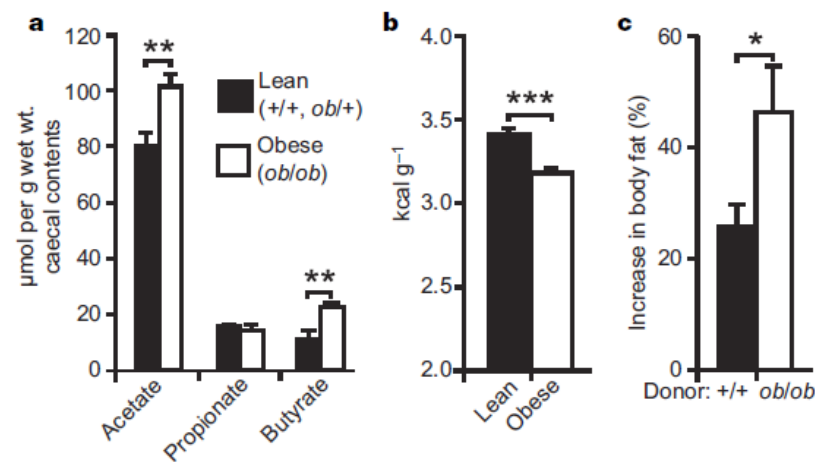
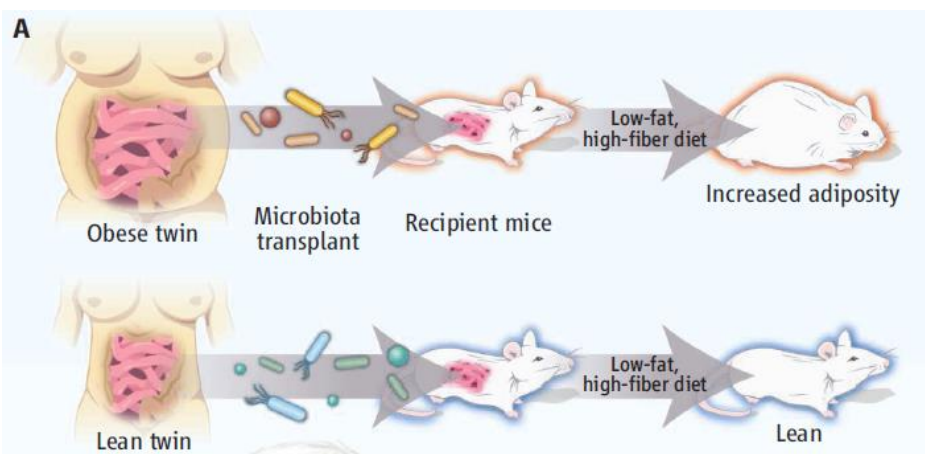
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VOLUME 13 | DECEMBER 2016 | 691



## Gut microbiota and obesity

- For 15 år siden var tarmmikrobiomet et perifært forskningsfelt
- Obesity alters gut microbial ecology** PNAS | August 2, 2005 | vol. 102
- Ruth E. Ley<sup>†</sup>, Fredrik Bäckhed<sup>†</sup>, Peter Turnbaugh<sup>†</sup>, Catherine A. Lozupone<sup>‡</sup>, Robin D. Knight<sup>§</sup>, and Jeffrey I. Gordon<sup>†¶</sup>
- Dernæst blev det vist, at overvægtiges mikrobiom har en øget kapacitet til at høste energi
  - Og at overvægt kan overføres tarmmikrobiomet



### Gut Microbiota from Twins Discordant for Obesity Modulate Metabolism in Mice

Vanessa K. Ridaura,<sup>1</sup> Jeremiah J. Faith,<sup>1</sup> Federico E. Rey,<sup>1</sup> Jiye Cheng,<sup>1</sup> Alexis E. Duncan,<sup>2,3</sup> Andrew L. Kau,<sup>2</sup> Nicholas W. Griffin,<sup>1</sup> Vincent Lombard,<sup>4</sup> Bernard Henricsson,<sup>4,5</sup> James R. Bain,<sup>6,7,8</sup> Michael J. Muehlbauer,<sup>6</sup> Olga Ilkayeva,<sup>6</sup> Clay F. Semenkovich,<sup>9</sup> Katsuhiko Funai,<sup>9</sup> David K. Hayashi,<sup>10</sup> Barbara J. Lyle,<sup>11</sup> Margaret C. Martin,<sup>11</sup> Luke K. Ursell,<sup>12</sup> Jose C. Clemente,<sup>12</sup> William Van Treuren,<sup>12</sup> William A. Walters,<sup>13</sup> Rob Knight,<sup>12,14,15</sup> Christopher B. Newgard,<sup>6,7,8</sup> Andrew C. Heath,<sup>2</sup> Jeffrey I. Gordon<sup>1\*</sup>

### An obesity-associated gut microbiome with increased capacity for energy harvest

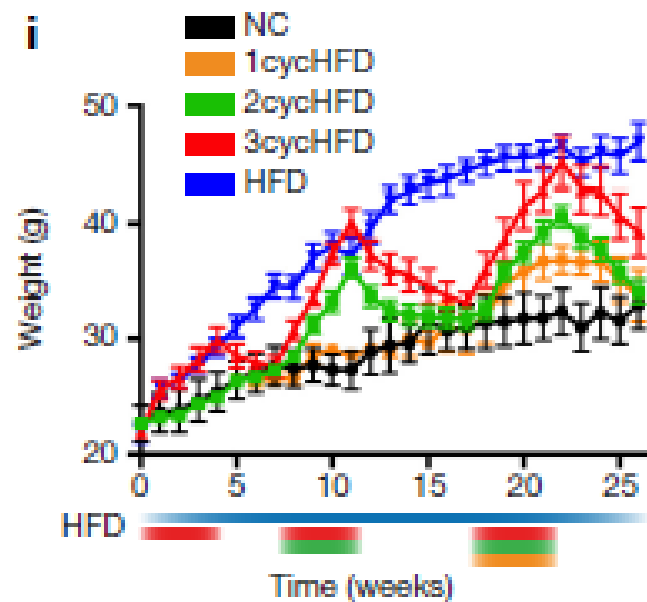
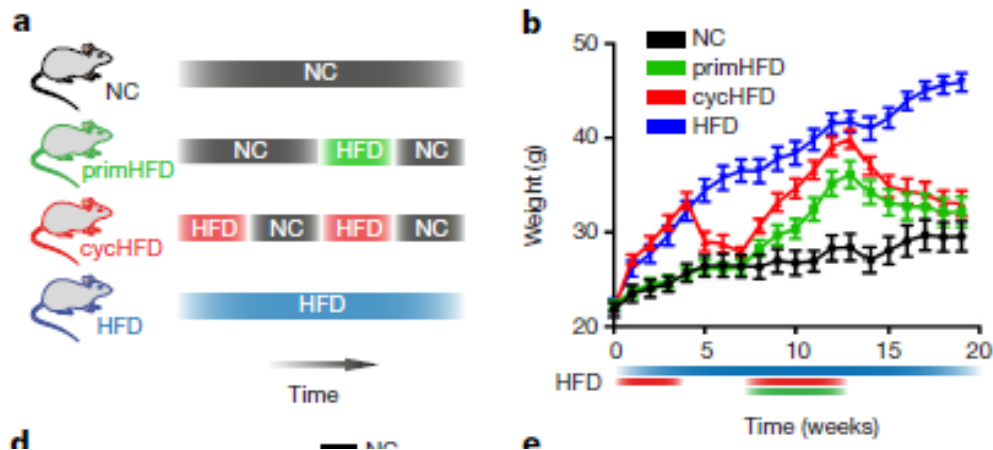
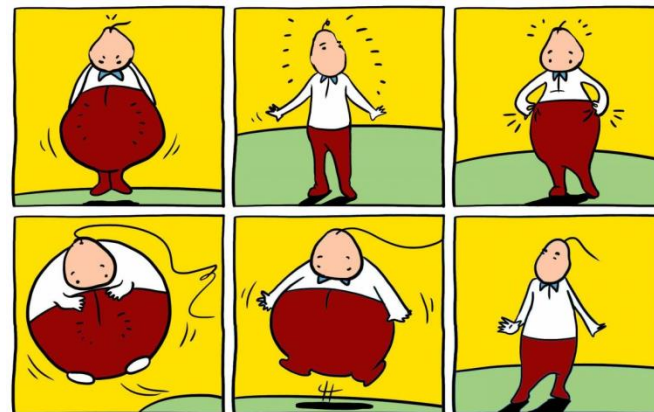
Peter J. Turnbaugh<sup>1</sup>, Ruth E. Ley<sup>1</sup>, Michael A. Mahowald<sup>1</sup>, Vincent Magrini<sup>2</sup>, Elaine R. Mardis<sup>1,2</sup> & Jeffrey I. Gordon<sup>1\*</sup>





## Har du svært ved at tabe de par ekstra kilo du "vandt" henover sommerferien?

- Tarmmikrobiom-ubalance spiller både en rolle i udvikling af overvægt – og gør det sværere at tabe sig
  - Den såkaldte "yoyo" effekt

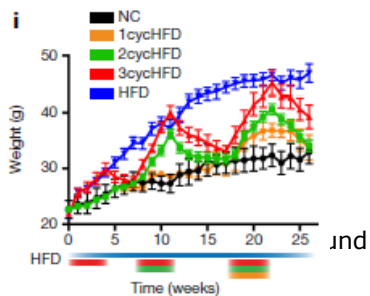
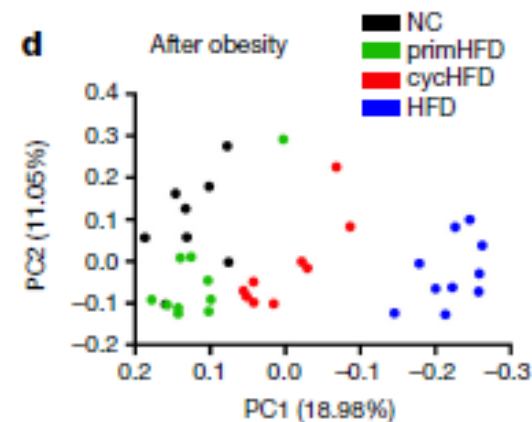
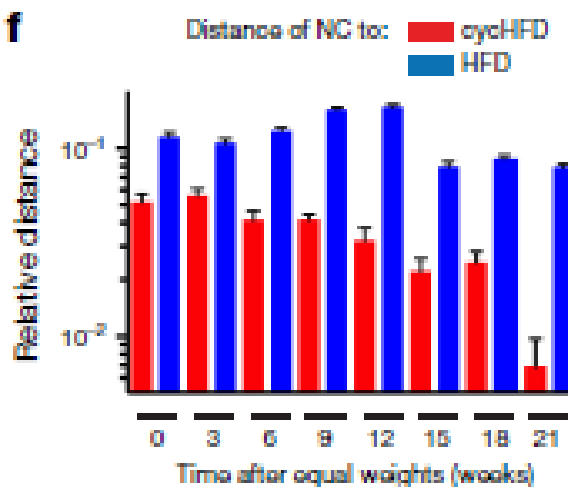
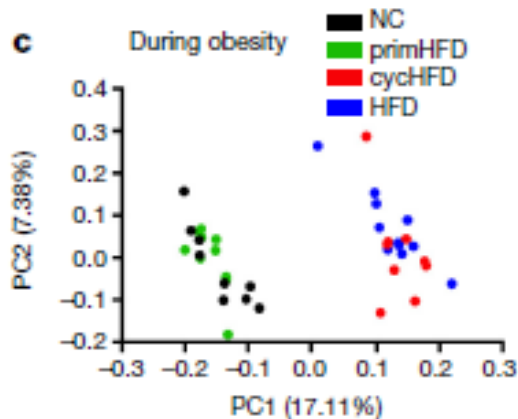
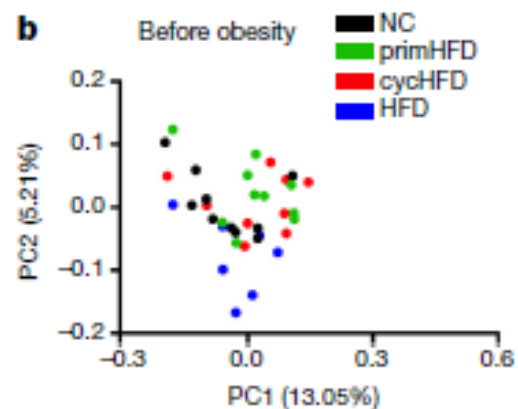


### Persistent microbiome alterations modulate the rate of post-dieting weight regain

Christoph A. Thaiss<sup>1\*</sup>, Shlomik Itav<sup>1\*</sup>, Daphna Rothschild<sup>2,3\*</sup>, Mariska T. Meijer<sup>2</sup>, Maayan Levy<sup>2</sup>, Claudia Moresi<sup>1</sup>, Lenka Dohnalová<sup>1</sup>, Sofia Braverman<sup>1</sup>, Shachar Rozin<sup>1</sup>, Sergey Malitsky<sup>4</sup>, Mally Dori-Bachash<sup>1</sup>, Yael Kuperman<sup>5</sup>, Inbal Biton<sup>5</sup>, Arieh Gertler<sup>6</sup>, Alon Harmelin<sup>5</sup>, Hagit Shapiro<sup>1</sup>, Zamir Halpern<sup>7,8</sup>, Asaph Aharoni<sup>1</sup>, Eran Segal<sup>2,3,9</sup> & Eran Elinav<sup>1,9</sup>

# Har du svært ved at tabe de par ekstra kilo du "vandt" henover sommerferien?

- "Yo yo" effekt – et kendt fænomen i forbindelse med vægttab
- Det er ikke din skyld, det er din tarmfloras...(den har i hvert fald meget af skylden)



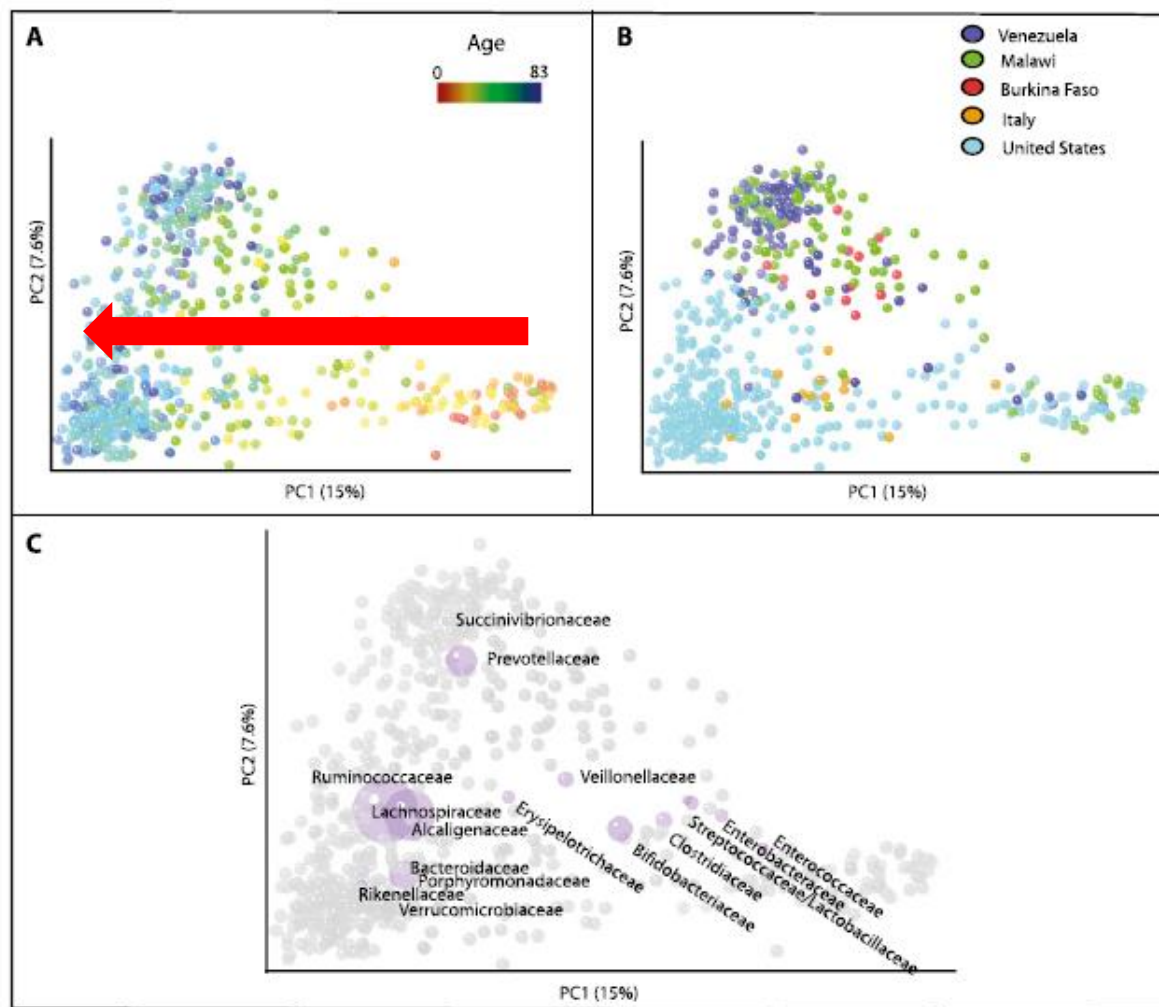
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Hvad er de primære faktorer, der påvirker vores tarmmikrobioms sammensætning?



“Alder”

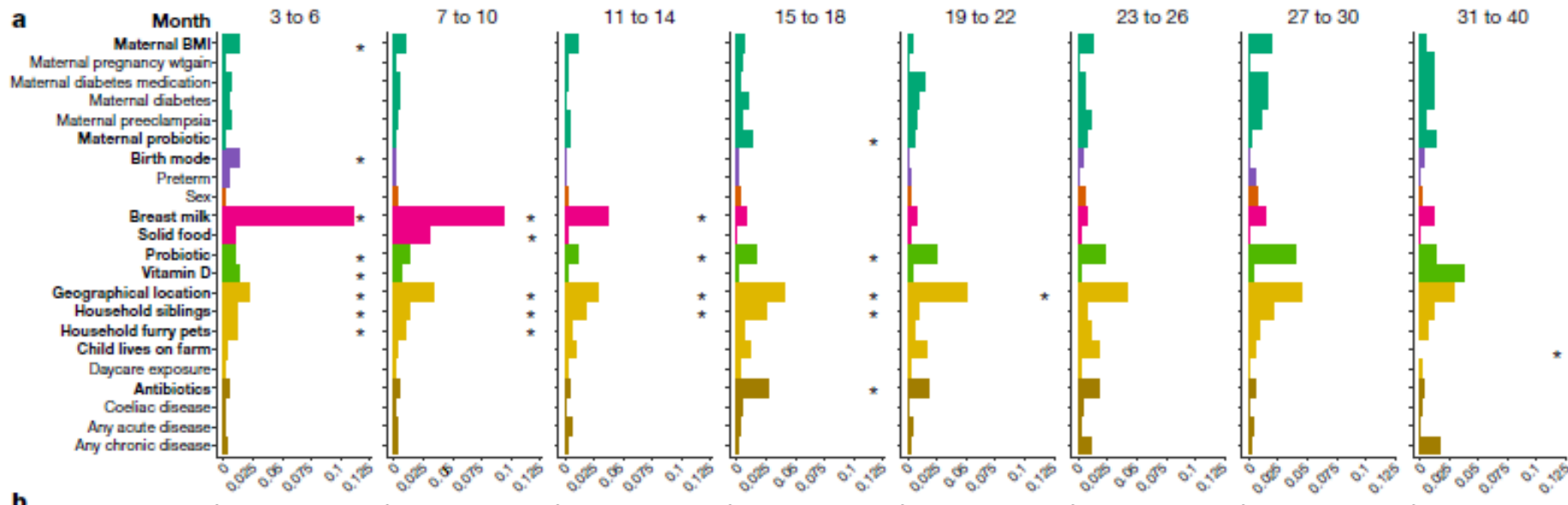
Kolonisering og eksponering tidligt i livet

Kost - både tidligt og senere i livet

Andre miljøfaktorer.  
F.eks. parasitter

## Hvad påvirker mikrobiomets udvikling de første år?

- 12500 fæcesprøver fra 903 børn fulgt fra 3-40 mdr.
- England, Sverige, Finland, USA

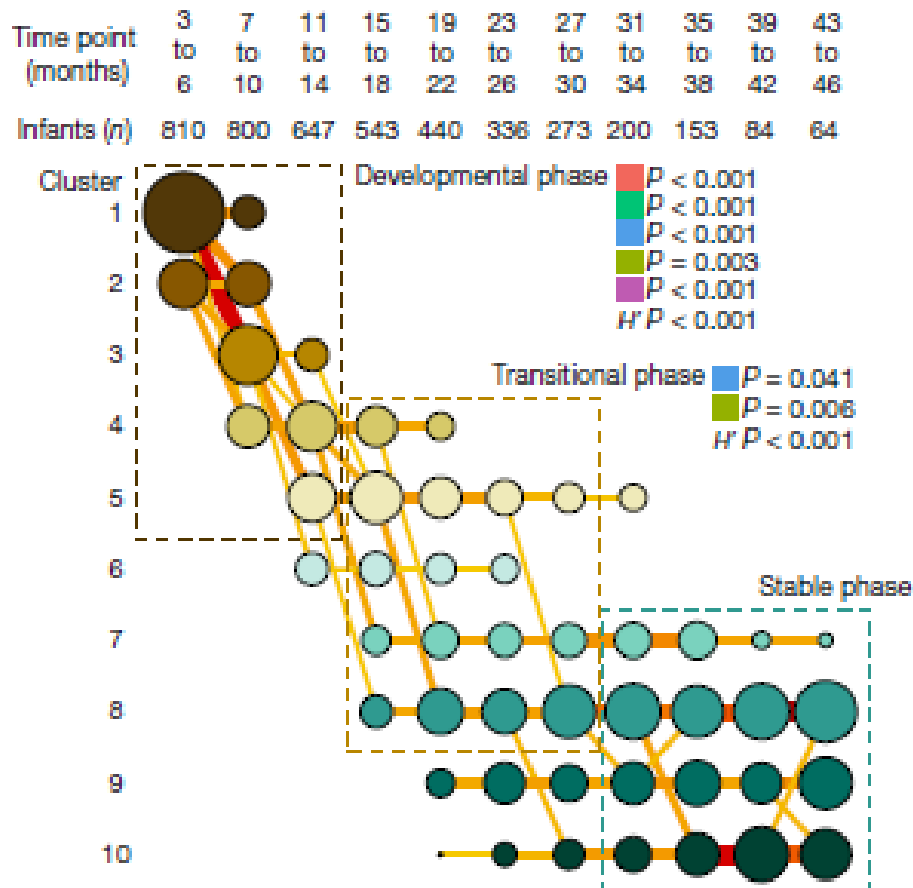


### Temporal development of the gut microbiome in early childhood from the TEDDY study

Christopher J. Stewart<sup>1,2,18\*</sup>, Nadim I. Ajami<sup>1,18</sup>, Jacqueline L. O'Brien<sup>1</sup>, Diane S. Hutchinson<sup>1</sup>, Daniel P. Smith<sup>1</sup>, Matthew C. Wong<sup>1</sup>, Matthew C. Ross<sup>1</sup>, Richard E. Lloyd<sup>1</sup>, HarshaVardhan Doddapaneni<sup>1</sup>, Ginger A. Metcalf<sup>1</sup>, Donna Muzny<sup>1</sup>, Richard A. Gibbs<sup>1</sup>, Tommi Vatanen<sup>4</sup>, Curtis Huttenhower<sup>4</sup>, Ramnik J. Xavier<sup>4</sup>, Marian Rewers<sup>5</sup>, William Hagopian<sup>6</sup>, Jorma Toppari<sup>7,8</sup>, Anette-G. Ziegler<sup>9,10,11</sup>, Jin-Xiong She<sup>12</sup>, Beena Akolkar<sup>13</sup>, Ake Lernmark<sup>14</sup>, Heikki Hyöty<sup>15,16</sup>, Kendra Vehik<sup>17</sup>, Jeffrey P. Krischer<sup>17</sup> & Joseph F. Petrosino<sup>18</sup>

# Hvad påvirker mikrobiomets udvikling de første år?

- 12500 fæcesprøver fra 903 børn fulgt fra 3-40 mdr.
- England, Sverige, Finland, USA
- 3 faser (tidlig, transition, stabil)



## Temporal development of the gut microbiome in early childhood from the TEDDY study

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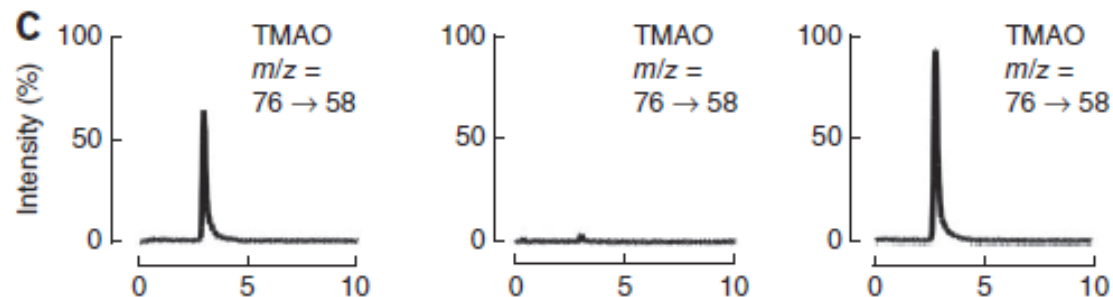
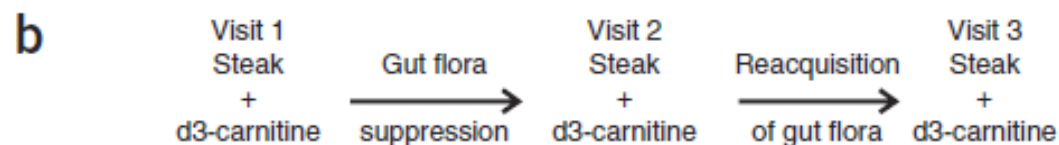
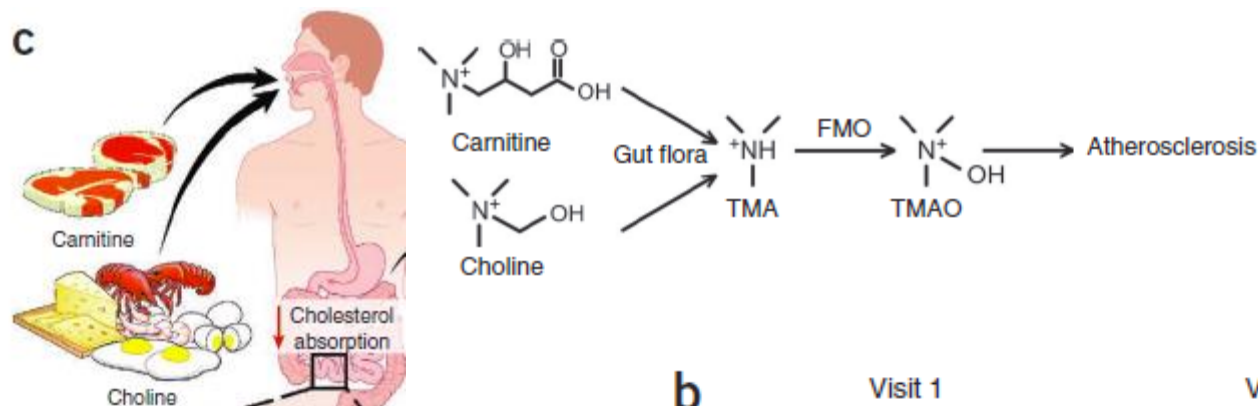


## Du bliver, hvad du spiser

Et eksempel:

Høje niveauer af TMAO (trimethylamine-N-oxide) i blodet er forbundet med øget risiko for hjerte-kar-sygdomme

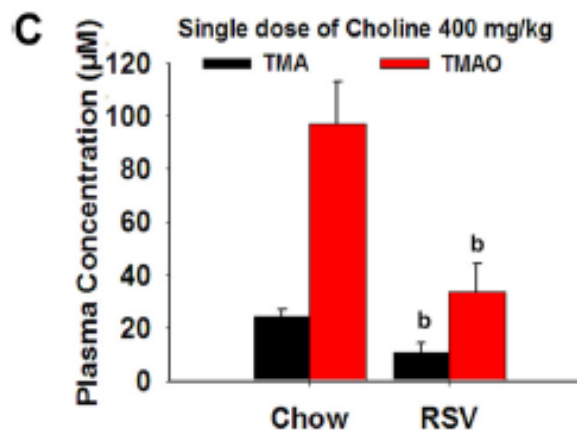
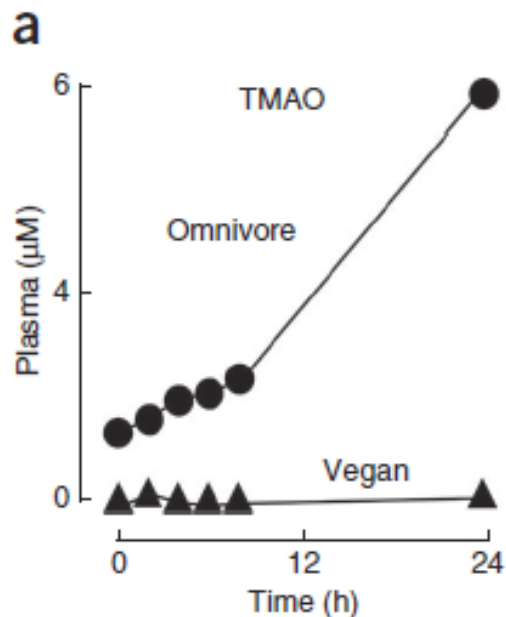
- Drevet af kost og tarm-mikrobiom i fællesskab



## Du bliver, hvad du spiser

Høje niveauer af TMAO I blodet (trimethylamine-N-oxide) er forbundet med øget risiko for hjerte-kar-sygdomme

- Drevet af kost og tarm-mikrobiom i fællesskab
- Veganere danner ikke TMAO, da deres tarm-mikrobiom ikke har været eksponeret for substraterne i lang tid
- Men andre kostkomponenter kan modvirke TMAO-dannelse, f.eks. resveratrol



RESEARCH ARTICLE



Resveratrol Attenuates Trimethylamine-N-Oxide (TMAO)-Induced Atherosclerosis by Regulating TMAO Synthesis and Bile Acid Metabolism via Remodeling of the Gut Microbiota

Ming-Iang Chen, Long Yi, Yong Zhang, Xi Zhou, Li Ran, Jining Yang, Jun-dong Zhu, Qian-yong Zhang, Man-tian Mi  
Research Center for Nutrition and Food Safety, Institute of Military Preventive Medicine, Third Military Medical University, Chongqing, People's Republic of China

nature  
medicine

Intestinal microbiota metabolism of L-carnitine, a nutrient in red meat, promotes atherosclerosis

Robert A Koeth<sup>1,2</sup>, Zeneng Wang<sup>1,2</sup>, Bruce S Levison<sup>1,2</sup>, Jennifer A Buffa<sup>1,2</sup>, Elin Org<sup>3</sup>, Brendan T Sheehy<sup>4</sup>, Earl B Britt<sup>1,2</sup>, Xiaoming Fu<sup>1,2</sup>, Yaping Wu<sup>1</sup>, Lin Li<sup>1,2</sup>, Jonathan D Smith<sup>1,2,5</sup>, Joseph A DiDonato<sup>1,2</sup>, Jun Chen<sup>6</sup>, Hongzhe Li<sup>6</sup>, Gary D Wu<sup>7</sup>, James D Lewis<sup>6,8</sup>, Manya Warrier<sup>9</sup>, J Mark Brown<sup>9</sup>, Ronald M Krauss<sup>10</sup>, W H Wilson Tang<sup>1,2,5</sup>, Frederic D Bushman<sup>5</sup>, Aidons J Lusis<sup>3</sup> & Stanley L Hazen<sup>1,2,5</sup>



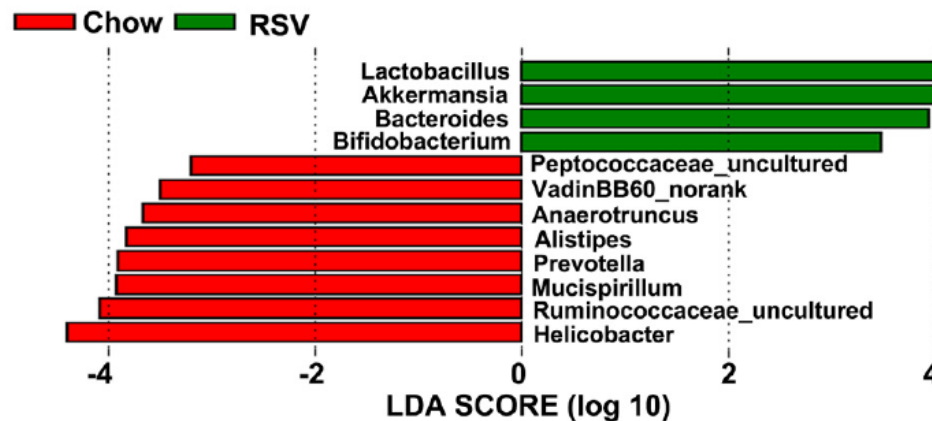
## Resveratrol Attenuates Trimethylamine-N-Oxide (TMAO)-Induced Atherosclerosis by Regulating TMAO Synthesis and Bile Acid Metabolism via Remodeling of the Gut Microbiota

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Research Center for Nutrition and Food Safety, Institute of Military Preventive Medicine, Third Military Medical University, Chongqing, People's Republic of China

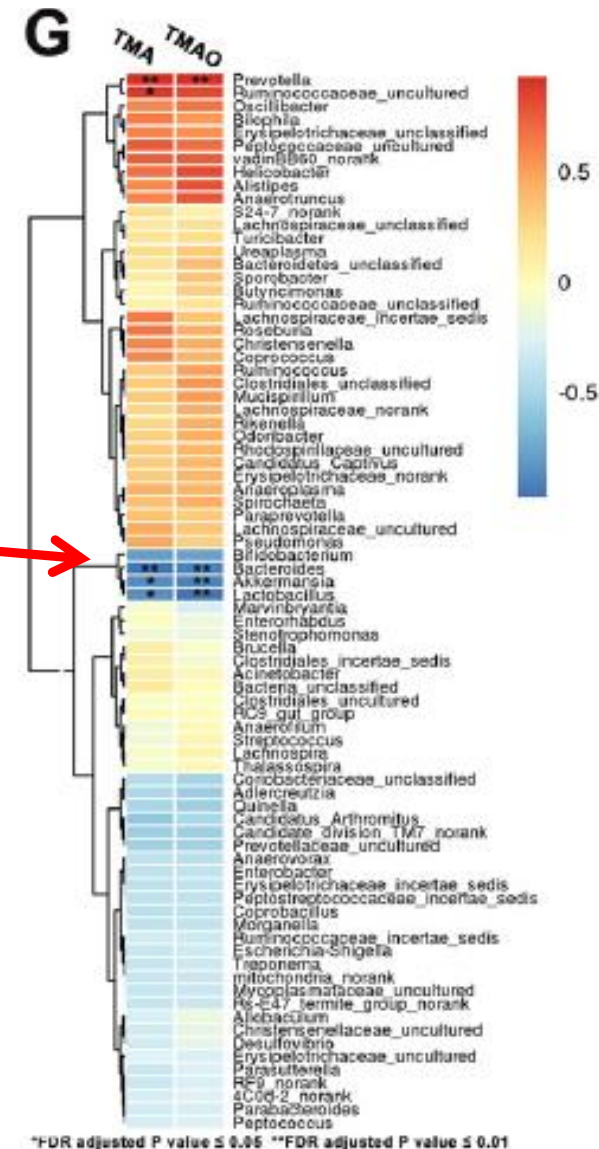
## Du bliver, hvad du spiser

Resveratrols beskyttende evne mod TMAO-dannelse er forbundet med ændringer i tarmmikrobiomet

- Resveratrol i kosten ændrer tarmmikrobiomet

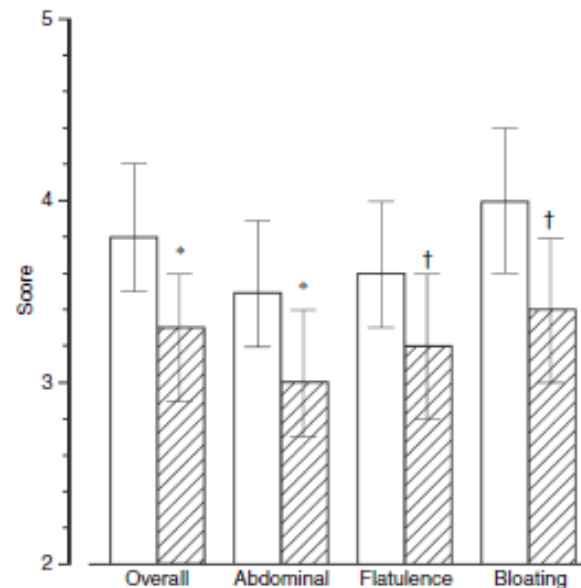
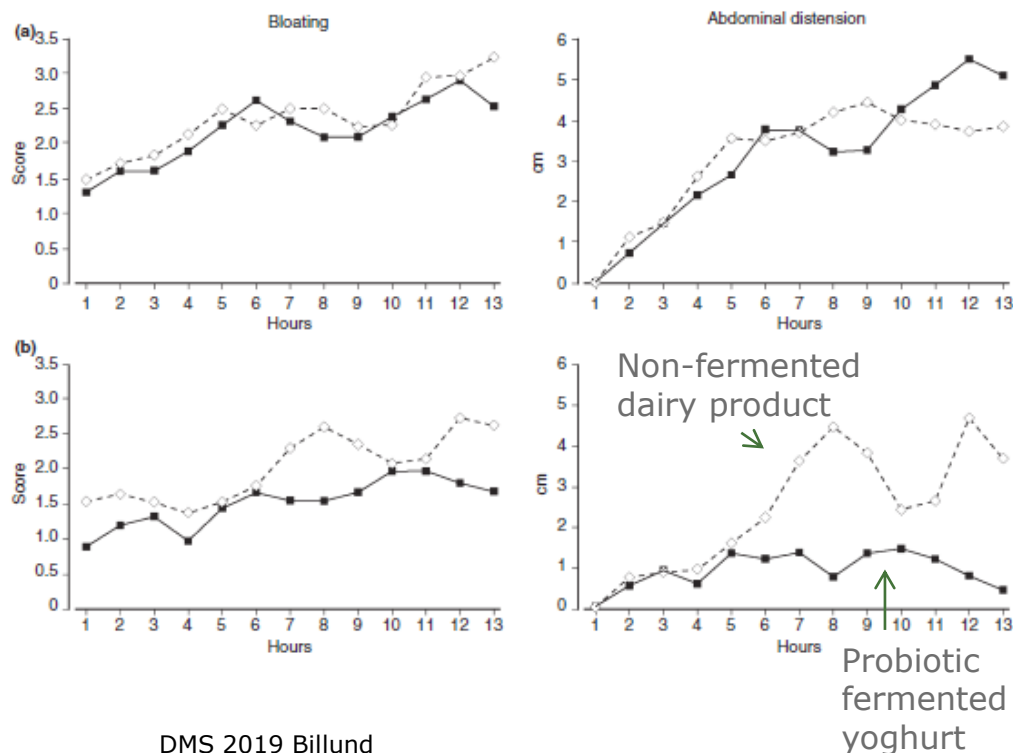


- Som igen påvirker dannelsen af TMAO



# Irritabel tyktarm (irritable bowel syndrome, IBS) og fermenterede mælkeprodukter

- IBS er en non-inflammatorisk, "funktionel" sygdom, der leder til mavesmerter, oppustethed og forstoppelse
  - Formodentlig forbundet med tarmmikrobiom ubalance

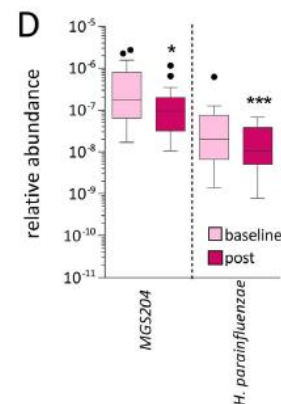
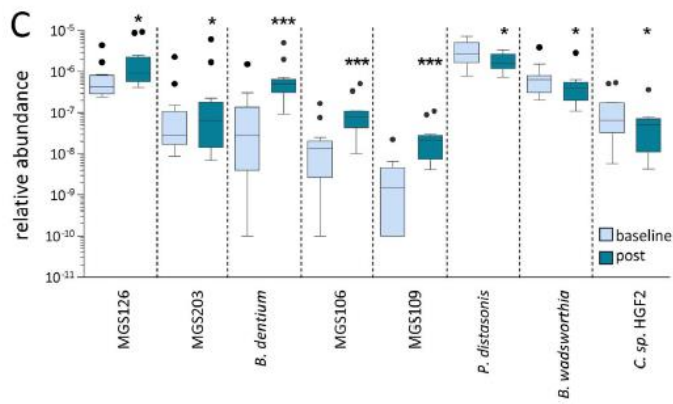
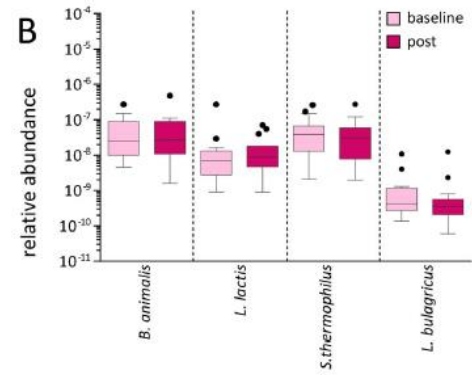
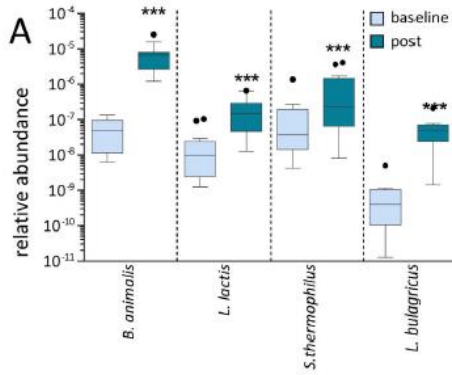
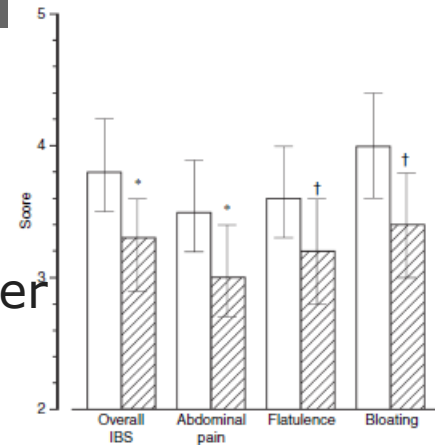


Clinical trial: the effects of a fermented milk product containing *Bifidobacterium lactis* DN-173 010 on abdominal distension and gastrointestinal transit in irritable bowel syndrome with constipation

A. AGRAWAL\*, L. A. HOUGHTON\*, J. MORRIST†, B. REILLY  
 N. GOUPIL FEULLERATS, A. SCHLUMBERGERS, S. JAKOB  
*Aliment Pharmacol Ther* 29, 104–114

# IBS, fermenterede mælkeprodukter og tarmmikrobiom modulering

- Fermenteret mælkeprodukt lindrer IBS symptomer
- Er det pga. Tarmmikrobiom-modulering?
  - (Formodentlig) Ja



Changes of the human gut microbiome induced by a fermented milk product

Patrick Veiga<sup>1</sup>, Nicolas Pons<sup>2</sup>, Anurag Agrawal<sup>3</sup>, Raish Oozeer<sup>1</sup>, Denis Guyonnet<sup>1</sup>, Rémi Brozelles<sup>5</sup>, Jean-Michel Faurie<sup>1</sup>, John E. T. van Hylckama Vlieg<sup>1</sup>, Lesley A. Houghton<sup>4,5</sup>, Peter J. Whorwell<sup>1</sup>, S. Dusko Ehrlich<sup>2,7</sup> & Sean P. Kennedy<sup>2</sup>

SCIENTIFIC REPORTS | 4 : 6328 |



## Hvad med andre fermenterede fødevarer?

- Fermenterede fødevarer indeholder mange "gode" mikroorganismer, men det er ofte svært at adskille effekt af råvare, fermentering og indtag af f.eks. mælkesyrebakterier

ELSEVIER

Nutrition Research 31 (2011) 436–443

www.njournal.com

1004

DOI 10.1002/mnfr.201400780

Mol. Nutr. Food Res. 2015, 59, 1004–1008

Fermented kimchi reduces body weight and improves metabolic parameters in overweight and obese patients

Eun Kyoung Kim<sup>a,1</sup>, So-Yeon An<sup>a,1</sup>, Min-Seok Lee<sup>a,1</sup>, Tae Ho Kim<sup>b</sup>, Hye-Kyoung Lee<sup>c</sup>,  
Won Sun Hwang<sup>c</sup>, Sun Jung Choe<sup>c</sup>, Tae-Young Kim<sup>d</sup>, Seung Jin Han<sup>a</sup>, Hae Jin Kim<sup>a</sup>,  
Dae Jung Kim<sup>a</sup>, Kwan-Woo Lee<sup>a,\*</sup>

Table 4

Changes in clinical and anthropometric parameters

	Baseline <sup>a</sup> (n = 22)	Fresh kimchi (n = 22)		Fermented kimchi (n = 22)	
		Initial <sup>b</sup>	Final <sup>c</sup>	Initial <sup>d</sup>	Final <sup>e</sup>
Body weight (kg)	73.6 ± 9.9	72.9 ± 9.6	71.7 ± 9.4 *	73 ± 10.1	71.5 ± 9.7 *
BMI (kg/m <sup>2</sup> )	27.7 ± 2.0	27.4 ± 2.2	27.0 ± 2.2 *	27.5 ± 2.2	26.9 ± 2.2 *
WHR	0.87 ± 0.53	0.86 ± 0.05	0.85 ± 0.06	0.86 ± 0.06	0.84 ± 0.06 *
Body fat (%)	32.7 ± 3.8	31.9 ± 4.0	31.6 ± 4.0 *	32.1 ± 4.3	31.4 ± 4.4 * <sup>***</sup>
Systolic BP (mm Hg)	128.7 ± 11.7	125.8 ± 10.7	122.1 ± 7.9	126.1 ± 12.1	121.3 ± 6.9 **
Diastolic BP (mm Hg)	78.6 ± 10.4	76.1 ± 9.9	74.7 ± 8.5	76.9 ± 9.7	72.7 ± 7.4 **
Total cholesterol (mg/dL)	177 ± 25.7	176 ± 29.5	172 ± 31.6	171 ± 25.7	161 ± 29.9 * <sup>***</sup>

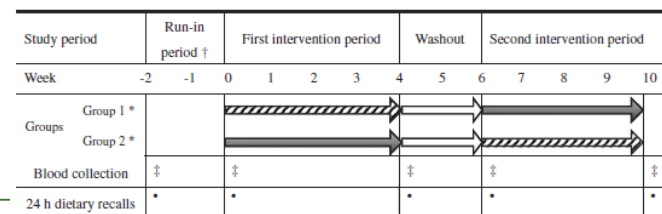
FOOD &amp; FUNCTION

**Contrasting effects of fresh and fermented kimchi consumption on gut microbiota composition and gene expression related to metabolic syndrome in obese Korean women**

Kyungsun Han<sup>1</sup>, Shambhunath Bose<sup>2</sup>, Jing-hua Wang<sup>1</sup>, Bong-Soo Kim<sup>3</sup>, Mi Jeong Kim<sup>4</sup>,  
Eun-Jung Kim<sup>5</sup> and Hojun Kim<sup>1</sup>

- Konklusion: Det er godt at spise kimchii. Det er endnu bedre at spise fermenteret kimchii*

DMS 2019 Billund



## Hvad med de fermenterede fødevarer?

- I andre tilfælde er det produktet (inkl. metaboliter produceret via fermentering) og ikke indtaget af levende "gode" mikroorganismer, der har positiv effekt
- Interventionsstudie i Oslo udført af KU-studerende
  - 6 uger på enten pasteuriseret eller "levende" sauerkraut (surkål), 75 g/dag (60 IBS patients)

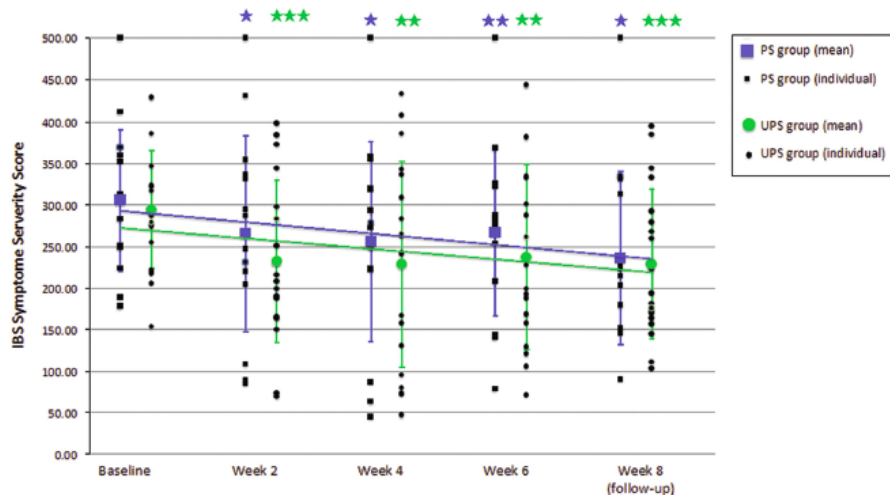


Salt,  
fermentation



Pasteurised

Not  
pasteurised



Food &  
Function

PAPER

Check for updates

Cite this: *Food Funct.*, 2018, 9, 5323

**Lacto-fermented sauerkraut improves symptoms in IBS patients independent of product pasteurisation – a pilot study†**

Elsa Sandberg Nielsen,<sup>a</sup> Eirik Garnås,<sup>a</sup> Kathrine Juul Jensen,<sup>b</sup> Lars Hestbjerg Hansen,<sup>b</sup> Peder Sandvold Olsen,<sup>c</sup> Christian Ritz,<sup>d</sup> Lukasz Krych,<sup>e</sup> and Dennis Sandris Nielsen<sup>b</sup>



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## Smarte bakterier!

- Der er en stigende forståelse af, at tarmmikrobiomet interagerer med hjernen og den vej påvirker humør og opførsel (inkl. Depression, formodentlig også appetit)
- F.eks. direkte link til serotonin produktion (i mus)

### Indigenous Bacteria from the Gut Microbiota Regulate Host Serotonin Biosynthesis

Jessica M. Yano,<sup>1</sup> Kristie Yu,<sup>1</sup> Gregory P. Donaldson,<sup>1</sup> Gauri G. Shastri,<sup>1</sup> Phoebe Ann,<sup>1</sup> Liang Ma,<sup>2</sup> Cathryn R. N. Rustem F. Ismagilov,<sup>2</sup> Sarkis K. Mazmanian,<sup>1</sup> and Elaine Y. Hsiao<sup>1,\*</sup>

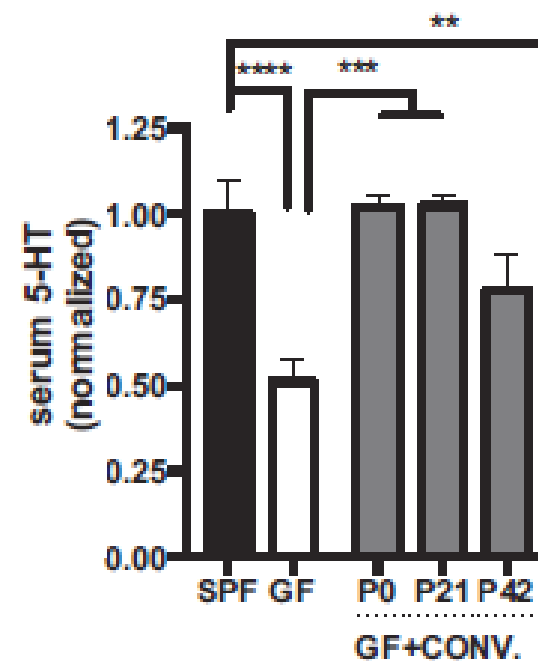
<sup>1</sup>Division of Biology and Biological Engineering, California Institute of Technology, Pasadena, CA 91125, USA

<sup>2</sup>Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, CA 91125, USA

<sup>3</sup>Department of Pathology and Department of Medicine, University of Chicago, Chicago, IL 60637, USA

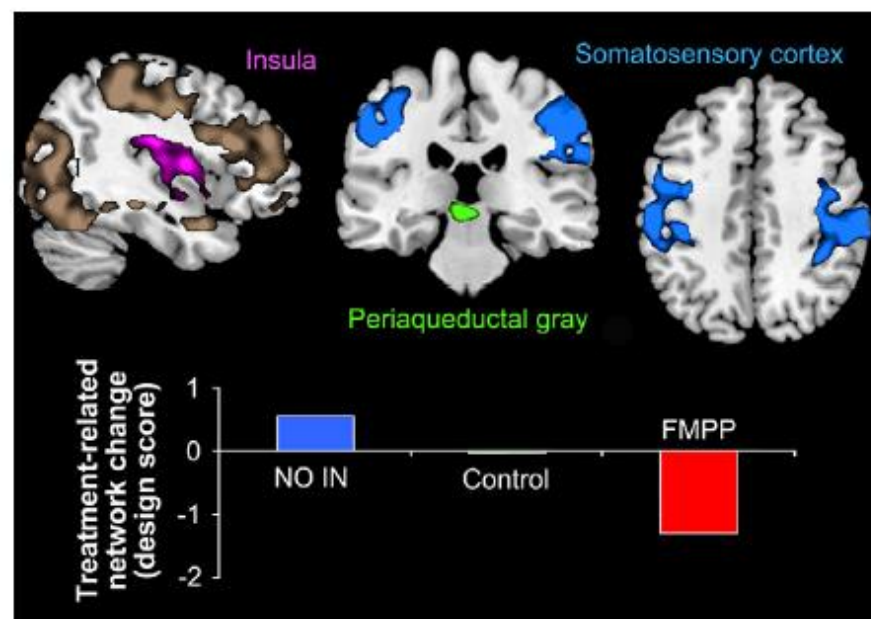
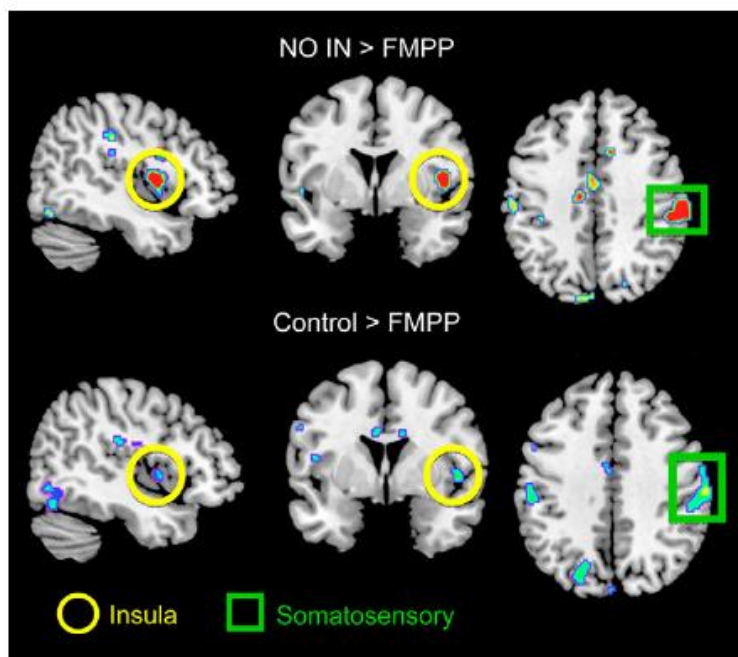
\*Correspondence: [ehsiao@caltech.edu](mailto:ehsiao@caltech.edu)

<http://dx.doi.org/10.1016/j.cell.2015.02.047>



## Meget smarte bakterier

- Dette synes også at være tilfældet i mennesker, og vise fermenterede produkter synes at have en effekt (måske)  
=>I dette studie viser kvinder mindsket hjerneaktivitet som respons på "emotionelt" stimuli efter intervention med et fermenteret, bifidobacteria-holdigt mælkeprodukt





# Et alternativt take på den historie i Ekstrabladet

ekstrabladet.dk/kup/sundhed/article4243491.ece

Iden | Nyheder | Sport | flash! | TV | EKSTRA | Side 9 | flere | Dennis

Sundhed 31. aug. 2011 - kl. 11:03

3 Kommentarer 0 f Del Del Mail

## Yoghurt kan blive den nye lykkepille

Forskere mener, at bakterier fra yoghurt kan hjælpe mod depression og stress. Men ikke hvilken som helst yoghurt har de lykkebringende egenskaber

At: **Asser Bøggild Christensen**

**ER DU SIKKER PÅ AT DU VED HVAD DU BETALER FOR, NÅR DU LADER EN BANK HÅNDTERE DINE INVESTERINGER?**

Investerer du for mere end 2,5 mio. kr.? Find ud af, hvorfor en bank ikke nødvendigvis er det bedste valg for dig

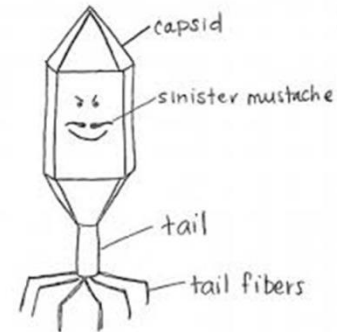
**DOWNLOAD**





## Pokkers! Min tarmflora har fået virus ☹️

- Vores tarmmikrobiom er mere end "kun" bakterier
  - Parasitter, archaea, svampe
- Og vira! Bl.a. bakteriofager, der er vira som angriber bakterier
- Ikke særligt velstuderede i tarmen
  - Ratio bakterier:phager  $\approx$  1:1 i tarmen hos voksne
- De spiller (formodentlig) vigtige roller i:
  - Forme/vedligeholde GMs sammensætning
  - Tarmmikrobiom ubalance, der leder til visse sygdomme

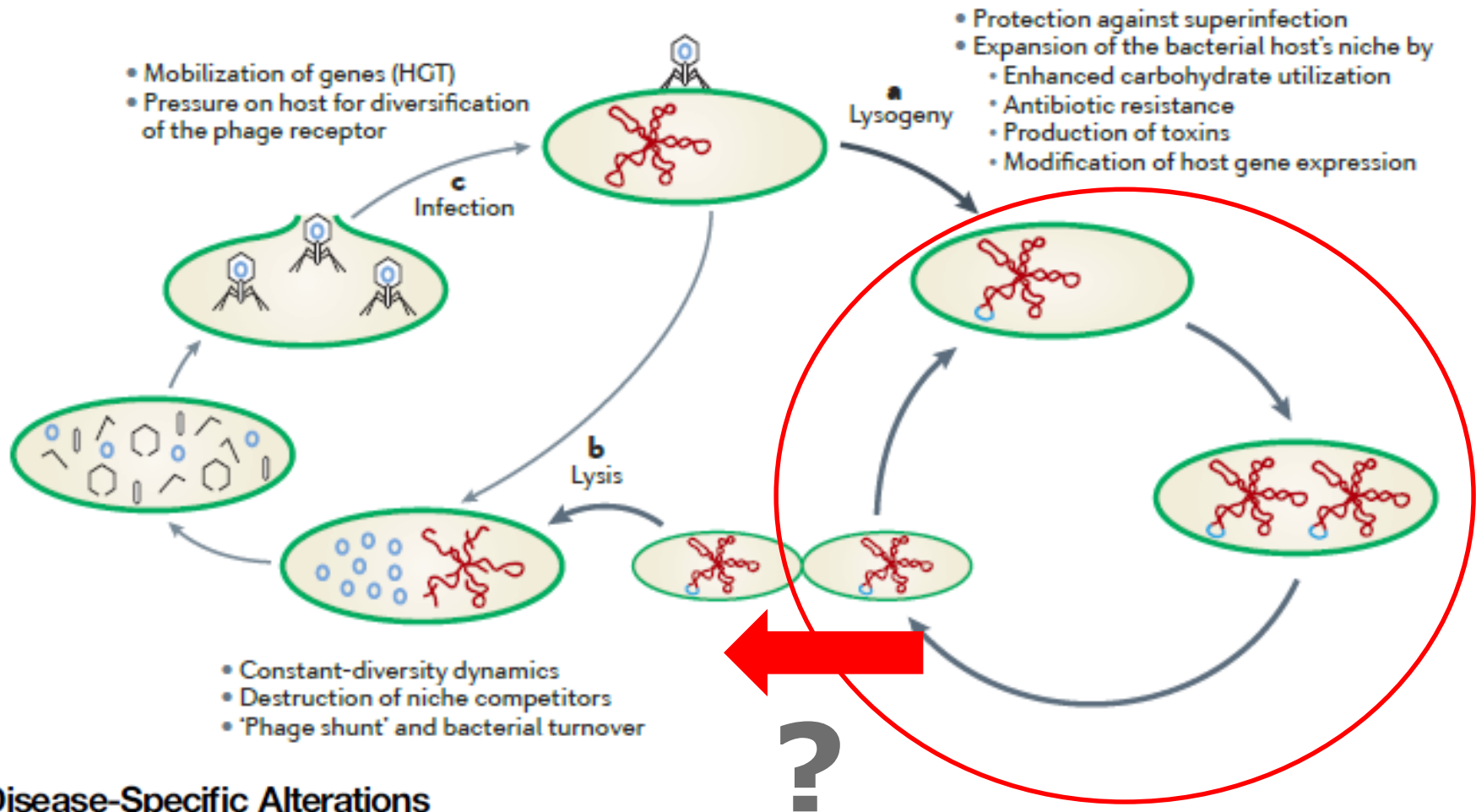


### Disease-Specific Alterations in the Enteric Virome in Inflammatory Bowel Disease

Jason M. Norman,<sup>1,10</sup> Scott A. Handley,<sup>1,10</sup> Megan T. Baldrige,<sup>1</sup> Lindsay Droit,<sup>1</sup> Catherine Y. Liu,<sup>1</sup> Brian C. Keller,<sup>1,2</sup> Amal Kambal,<sup>1</sup> Cynthia L. Monaco,<sup>1,2</sup> Guoyan Zhao,<sup>1,2</sup> Phillip Fleshner,<sup>4</sup> Thaddeus S. Stappenbeck,<sup>1</sup> Dermot P.B. McGovern,<sup>5</sup> Ali Keshavarzian,<sup>6</sup> Ece A. Mutlu,<sup>6</sup> Jenny Sauk,<sup>7</sup> Dirk Gevers,<sup>8</sup> Ramnik J. Xavier,<sup>7,8</sup> David Wang,<sup>1,3</sup> Miles Parkes,<sup>9</sup> and Herbert W. Virgin<sup>1,\*</sup>

Reyes et al. (2012). Nat. Rev. Microbiol.

## Bakteriofager og deres livscyklus



### Disease-Specific Alterations in the Enteric Virome in Inflammatory Bowel Disease

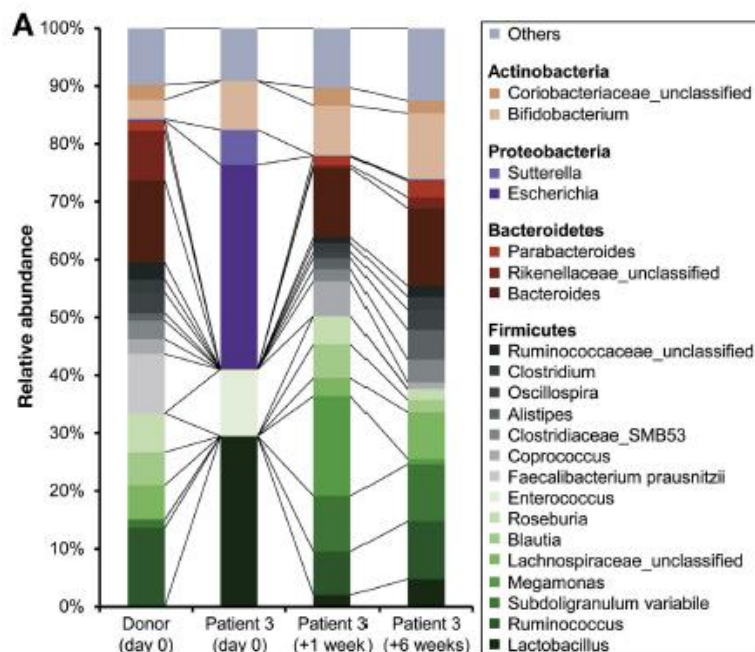
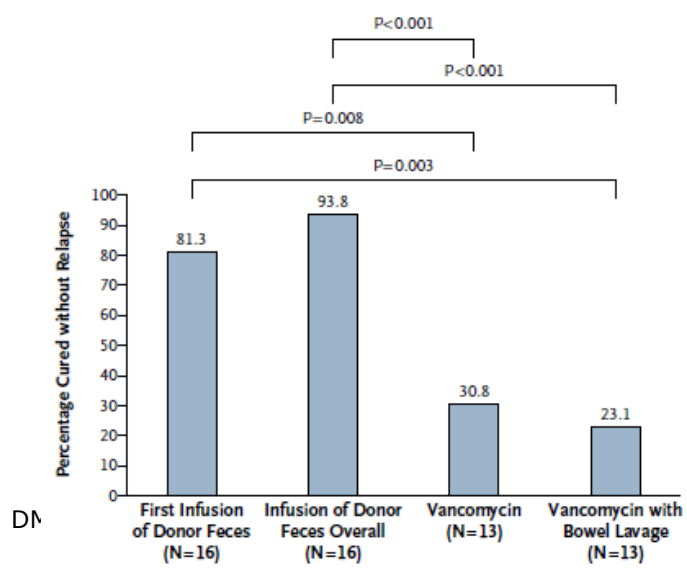
Jason M. Norman,<sup>1,10</sup> Scott A. Handley,<sup>1,10</sup> Megan T. Baldrige,<sup>1</sup> Lindsay Droit,<sup>1</sup> Catherine Y. Liu,<sup>1</sup> Brian C. Keller,<sup>1,2</sup> Amal Kambal,<sup>1</sup> Cynthia L. Monaco,<sup>1,2</sup> Guoyan Zhao,<sup>1,3</sup> Phillip Fleshner,<sup>4</sup> Thaddeus S. Stappenbeck,<sup>1</sup> Dermot P.B. McGovern,<sup>5</sup> Ali Keshavarzian,<sup>6</sup> Ece A. Mutlu,<sup>6</sup> Jenny Sauk,<sup>7</sup> Dirk Gevers,<sup>8</sup> Ramnik J. Xavier,<sup>7,8</sup> David Wang,<sup>1,3</sup> Miles Parkes,<sup>9</sup> and Herbert W. Virgin<sup>1,\*</sup>



## Fækal transplantation – nu uden bakterier!

Fækal transplantation nu standardbehandling af *Clostridium difficile* infektion, hvis antibiotika ikke virker

- Den positive effekt af FMT kan tilsyneladende opnås ved blot at overføre fækalt filtrat
  - Dvs. med alle bakterierne filtreret fra
  - Indeholder primært bakteriofager
  - Men (i principet) også metaboliter, bacteriociner osv.



Efficacy of Sterile Fecal Filtrate Transfer for Treating Patients With *Clostridium difficile* Infection

Stephan J. Ott,<sup>1\*</sup> Georg H. Waetzig,<sup>2\*</sup> Ateequr Rehman,<sup>3\*</sup> Jacqueline Moltzau-Andersen,<sup>3,4</sup> Richa Bharti,<sup>3</sup> Juns A. Grass,<sup>5</sup> Liam Cassidy,<sup>6</sup> Andreas Tholey,<sup>6</sup> Helmut Fickenscher,<sup>7</sup> Dirk Seegert,<sup>2</sup> Phillip Rosenstiel,<sup>1,3,8</sup> and Stefan Schreiber<sup>1,3,8</sup>

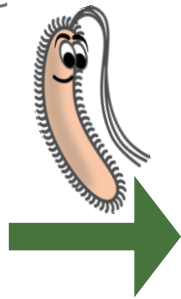
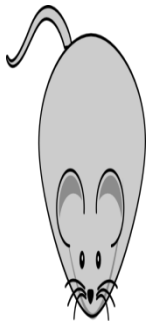
Duodenal Infusion of Donor Feces for Recurrent *Clostridium difficile*

Eisvan Noord, M.D., Anne Vriente, M.D., Max Nieuwendorp, M.D., Ph.D., Susana Fuentes, Ph.D., Erwin G. Zoetendal, Ph.D., Willem M. de Vos, Ph.D., Caroline E. Visser, M.D., Ph.D., Edj. Kluijper, M.D., Ph.D., Joep F.W.M. Barelsmann, M.D., Jan G.P. Tijssen, Ph.D., Peter Speelman, M.D., Ph.D., Marcel G.W. Dijkgraaf, Ph.D., and J. Osbert, J. Keller, M.D., Ph.D.

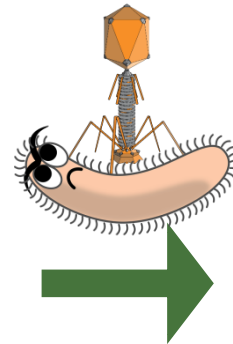
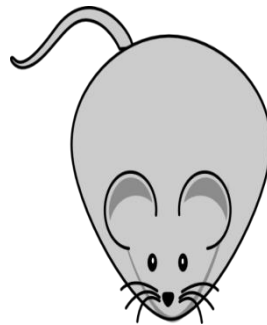
## PhageGut – vi redder mus fra at blive tykke!

- Overvægt er forbundet med tarm-mikrobiom-ubalance
- Kan vi bruge bakteriofager til forhindre/modvirke overvægt og udvikling af metabolisk syndrom?

Tynd fænotype

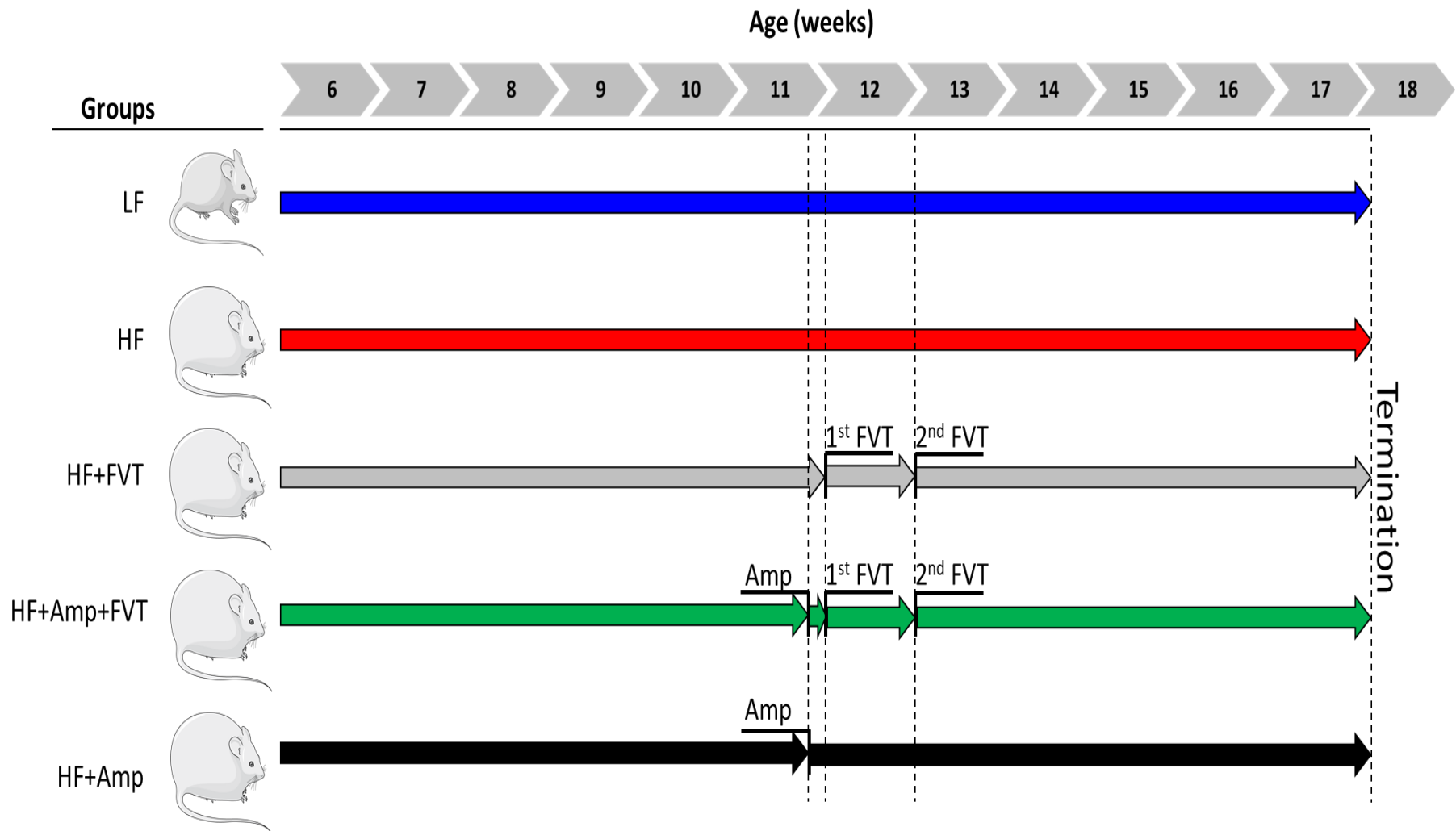


Tyk fænotype



Tynd fænotype



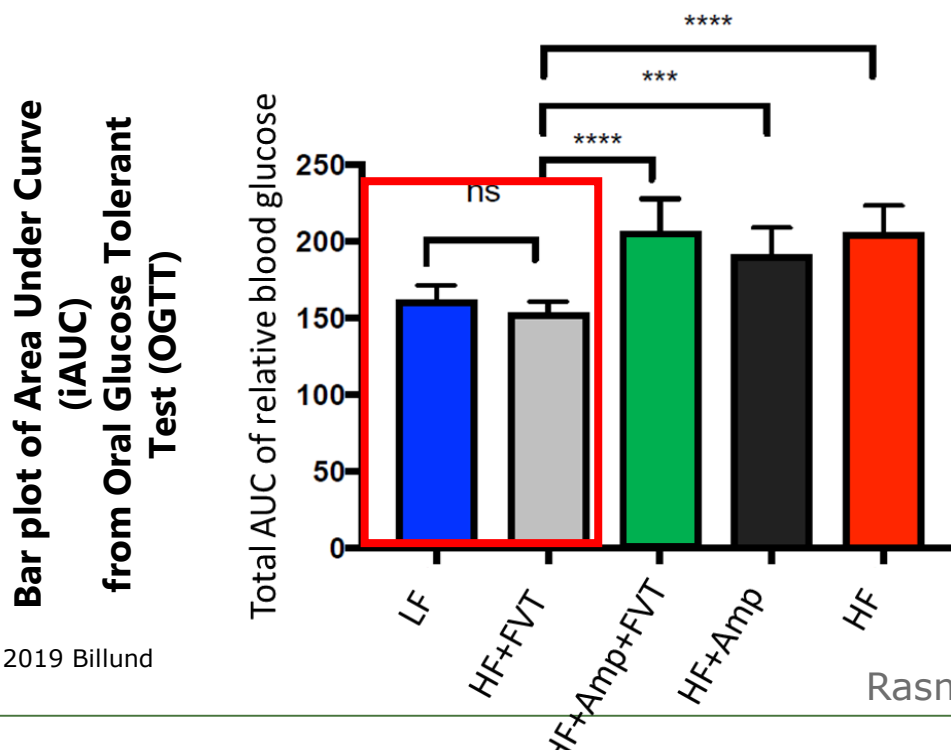


**FVT = Fækal Virom Transplant fra mus på mindst 13 ugers lav-fedt diet**



## Effekt af FVT 6 uger efter behandling

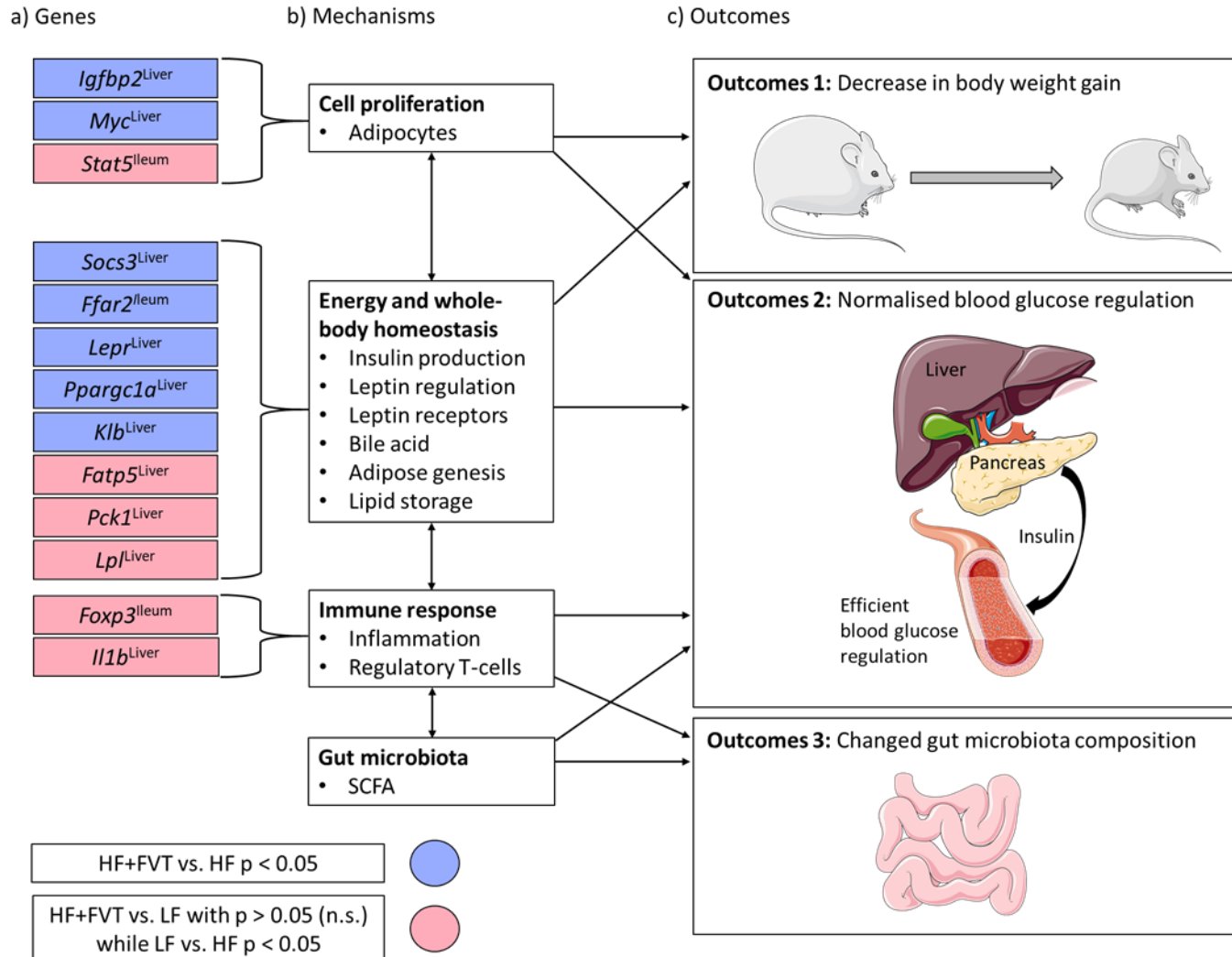
- FVT-behandlede, høj-fedt (HF+FVT) diet mus tog  $\approx 15\%$  mindre på end HF-mus (HF)
- Og deres sukkermetabolisme normaliseres
- For tarm-bakterie, tarm-virom, blod metabolome, genekspression i lever og tyndtarm: HF+FVT mus bliver  $\approx$  LF (control) mice



At 6 weeks post-treatment:  
HF-FVT vs. LF:  
**adj. p-value = 0.9648**



# Virom-transfer – en slags overblik



## Alt i alt

- Din tarmflora er din ven
  - Men venner kan også komme i dårligt selskab
- Tarmfloraubalance ("dysbiosis") kan lede til en lang række autoimmune og livsstilssygdomme
  - Og påvirke effekten af (nogle typer) medicin
- Kosten er den største enkeltfaktor ift. sammensætningen af vores tarmmikrobiom
  - Så du kan faktisk i meget høj grad påvirke dit tarmmikrobioms sammensætning og funktion
- Målrettet tarmmikrobiom-manipulering er på vej!

