The gut and the heart

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Layout

- The microbiome- a brief introduction
- Relevant for cardiovascular disease?
- Can we target the gut microbiome in personalized medicine and nutrition?
  - Is a banana always a banana?

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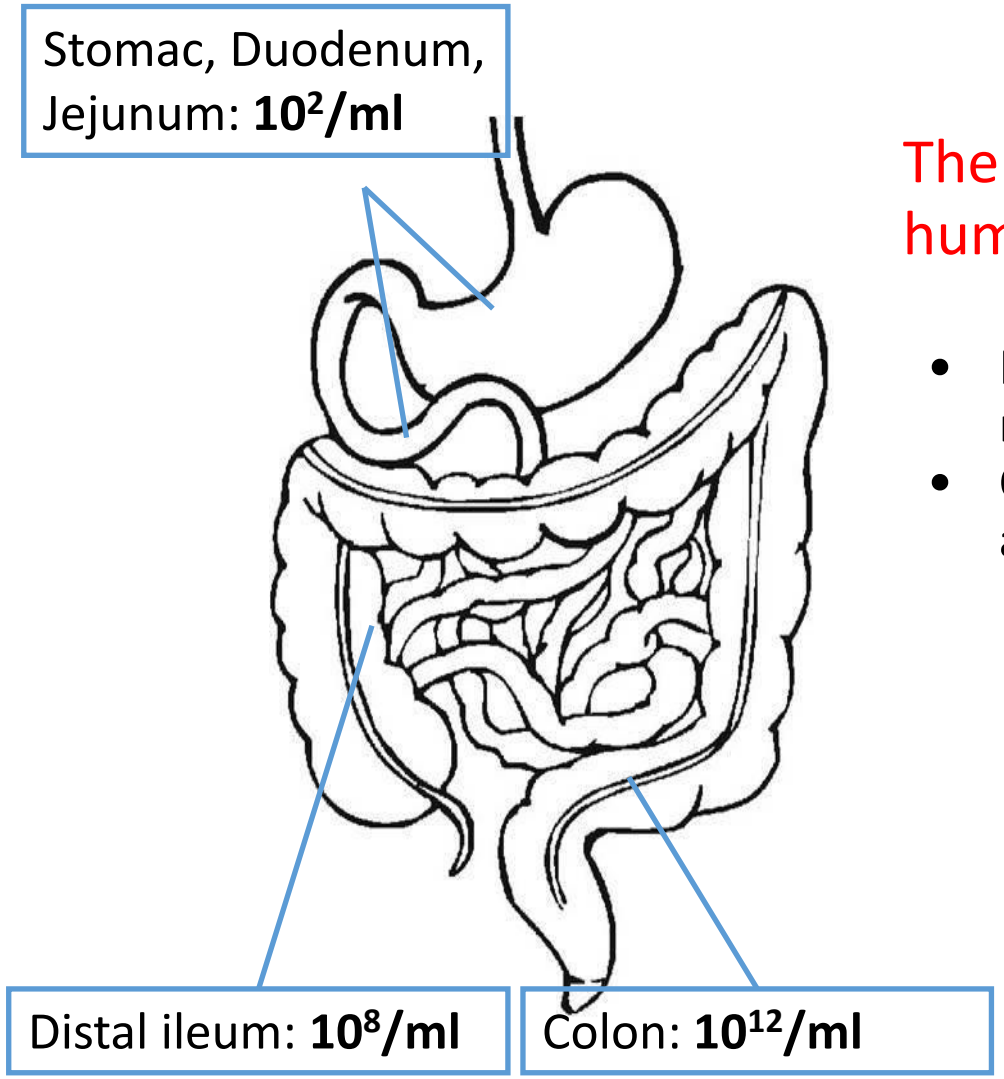
What is the microbiome?

- Microbiota = the sum of microbes in a specific location
- Microbiome = the total genes of these microbes

Young, BMJ 2017

Trillions of microbes and their genes



The gut flora outnumbers the human body

- Microbiome: 500 times the number of human genes?
- Comparable number of bacteria and human cells?

Sonnenburg, Nature 2016
Sender, Cell 2016

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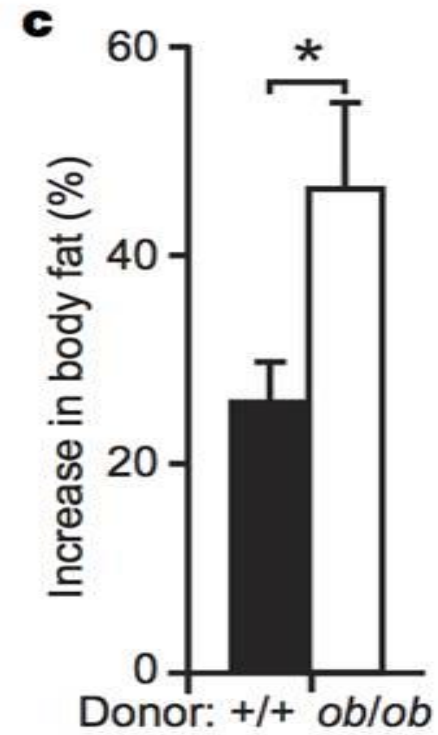
The power of the gut flora: contagious obesity



Lean mice became obese when living in the same cage as obese mice

- Diet did not change
- Change in microbiota

Turnbaugh, Nature 2006

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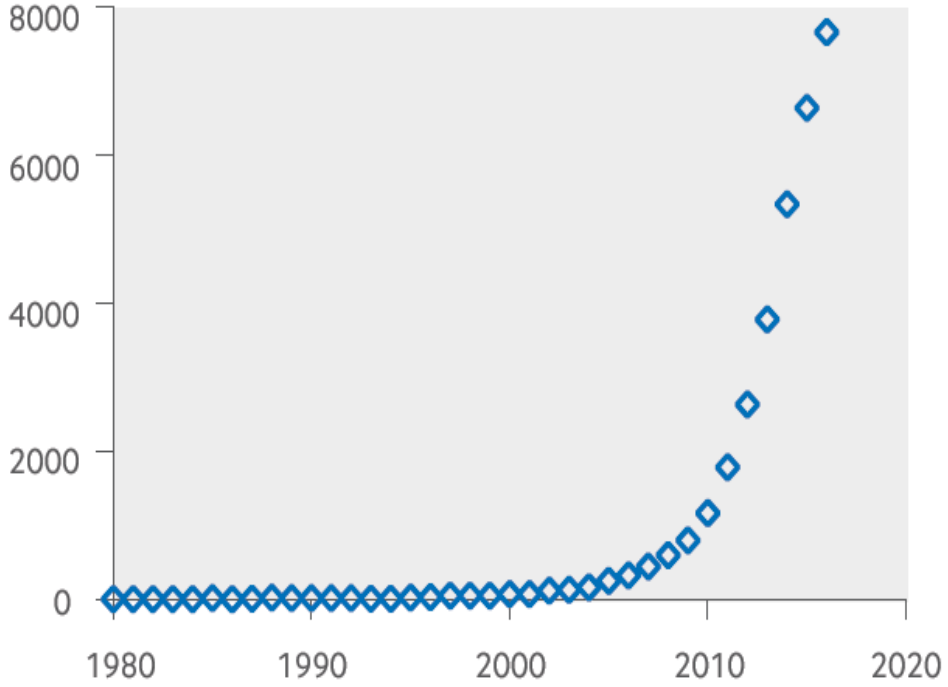
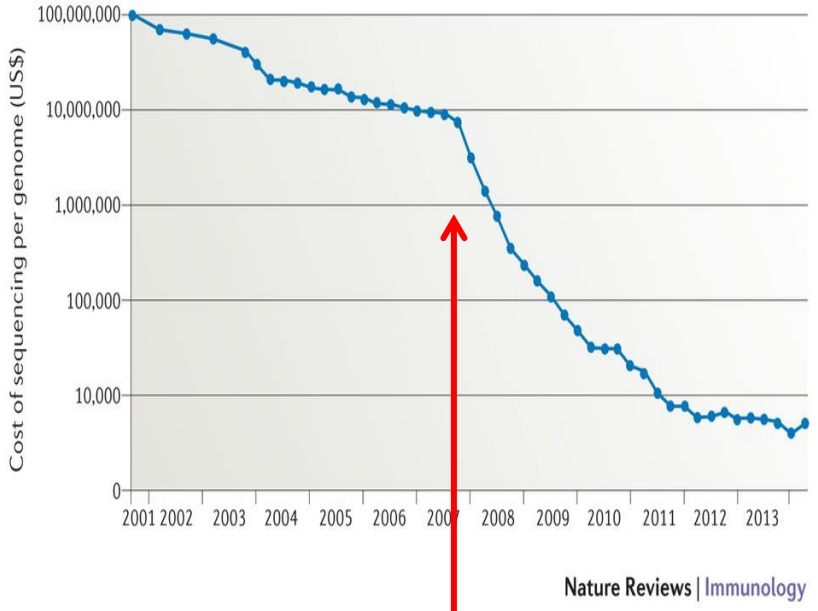
Technology-driven frontier

Hits on ”microbiome” in PubMed



Sequencing costs per genome



Illumina

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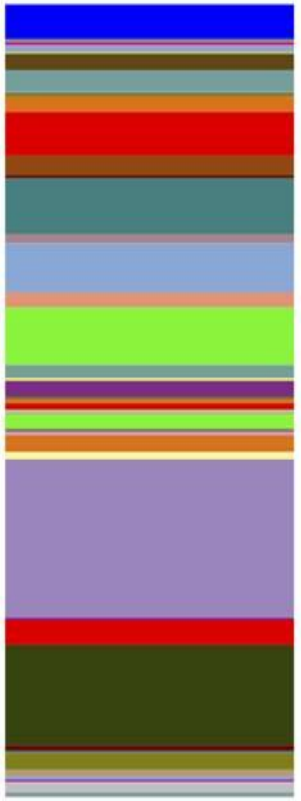
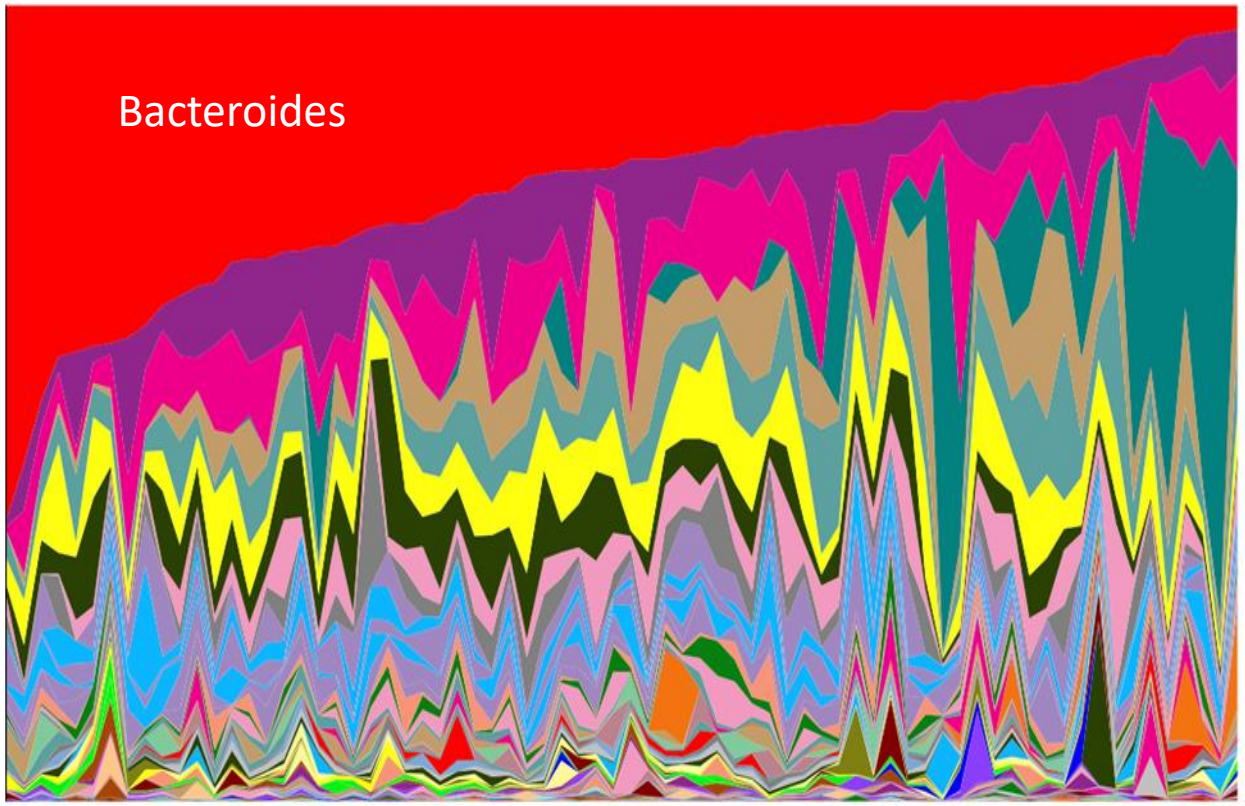
Role in personalized diet and medicine?



1 individual



117 healthy Norwegians

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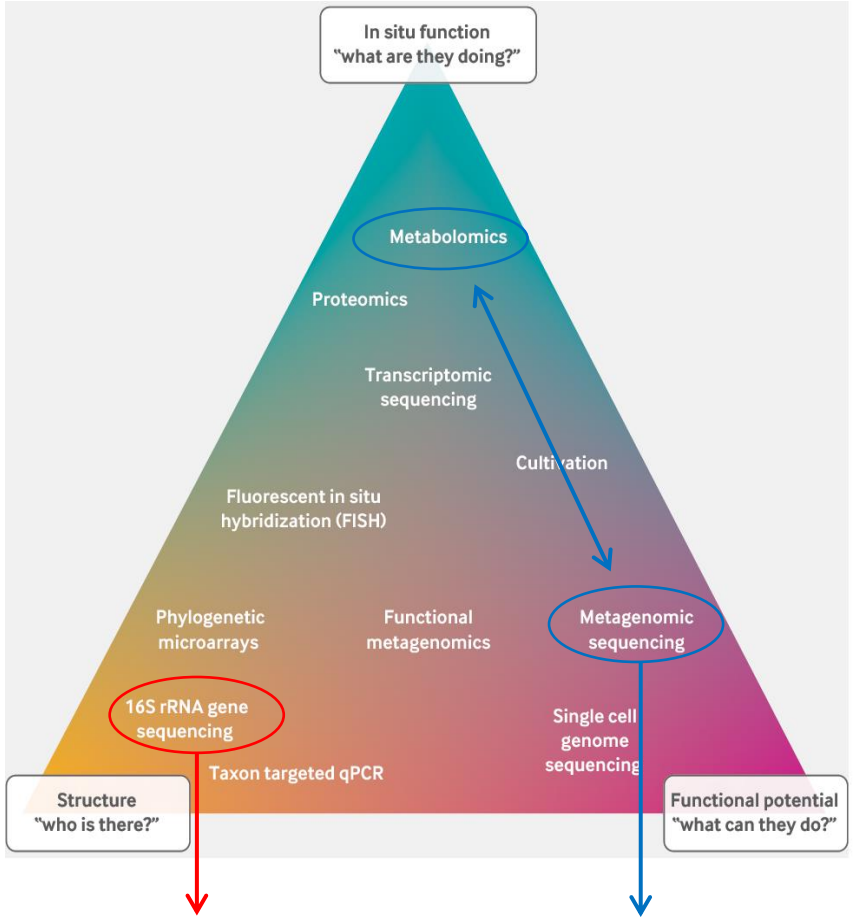
Microbiota is just one piece of the puzzle



Integration of big data

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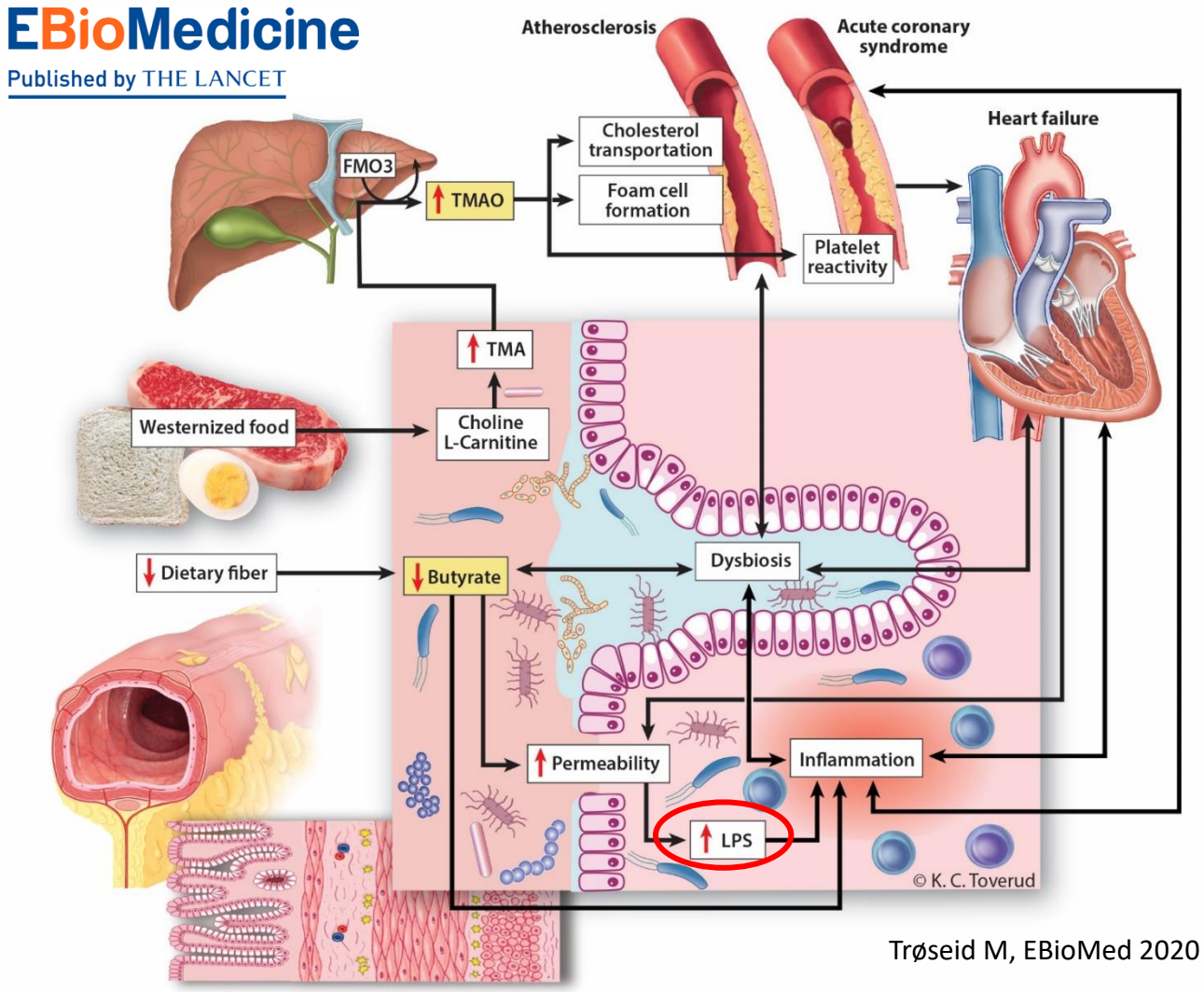
Diet, microbiome and cardiovascular risk



Trøseid M, EBioMed 2020

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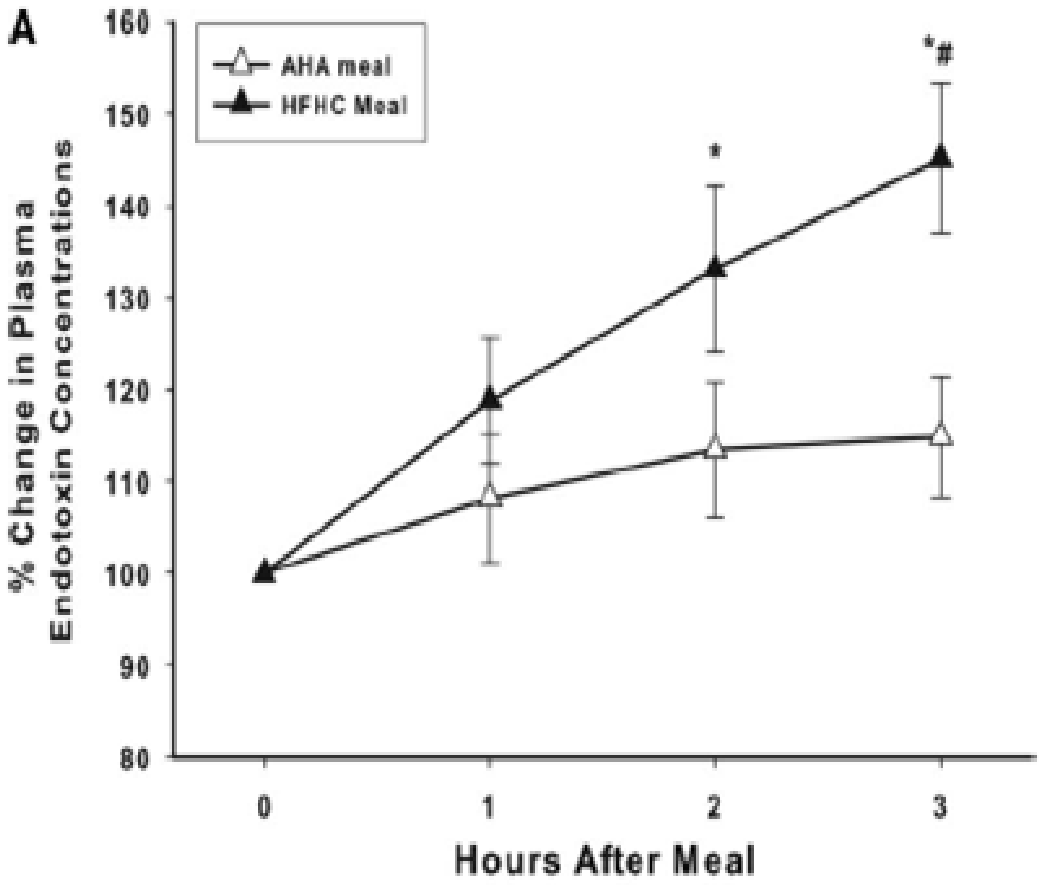
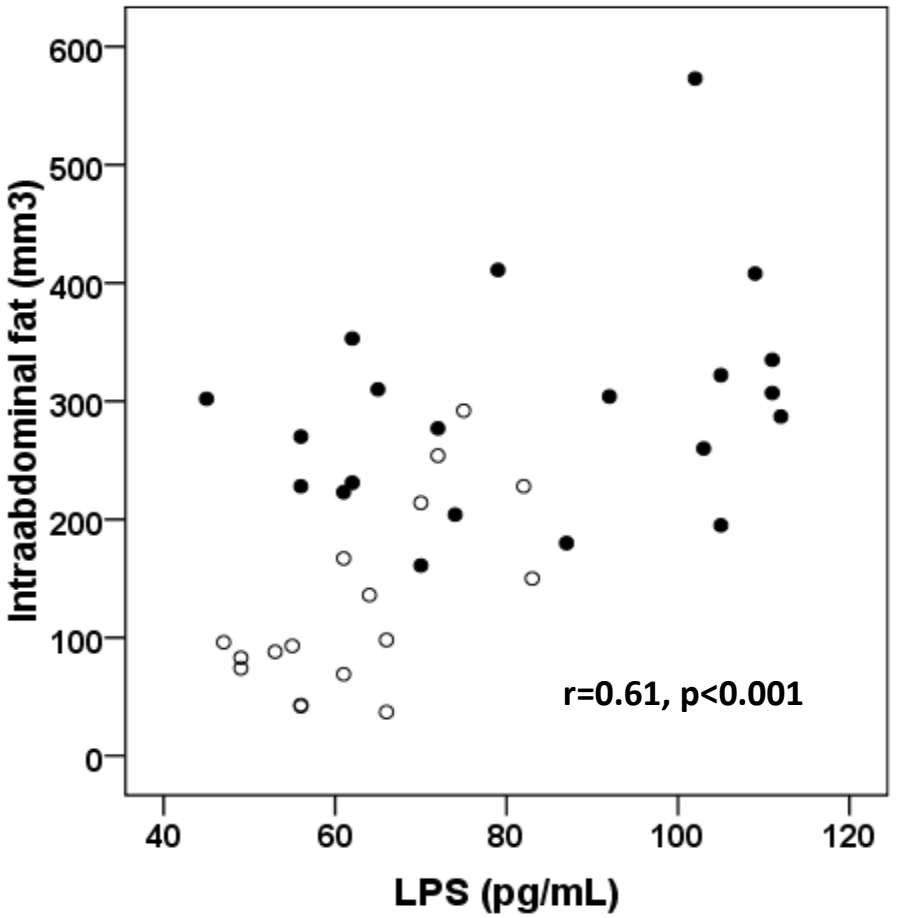
LPS increases after high fat high carb meal

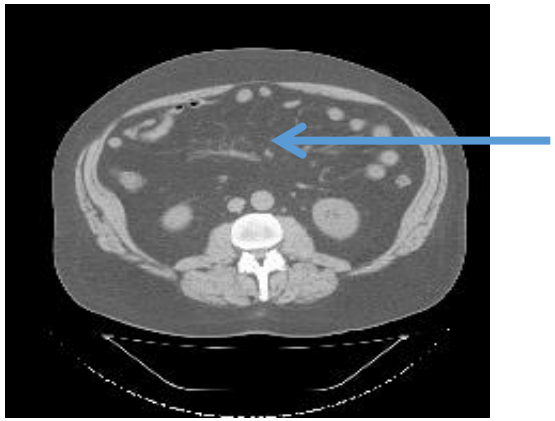


Ghanim, Diabetes Care 2009

Higher LPS: more abdominal fat



Obese
Controls



Trøseid, Diabetes Care 2013

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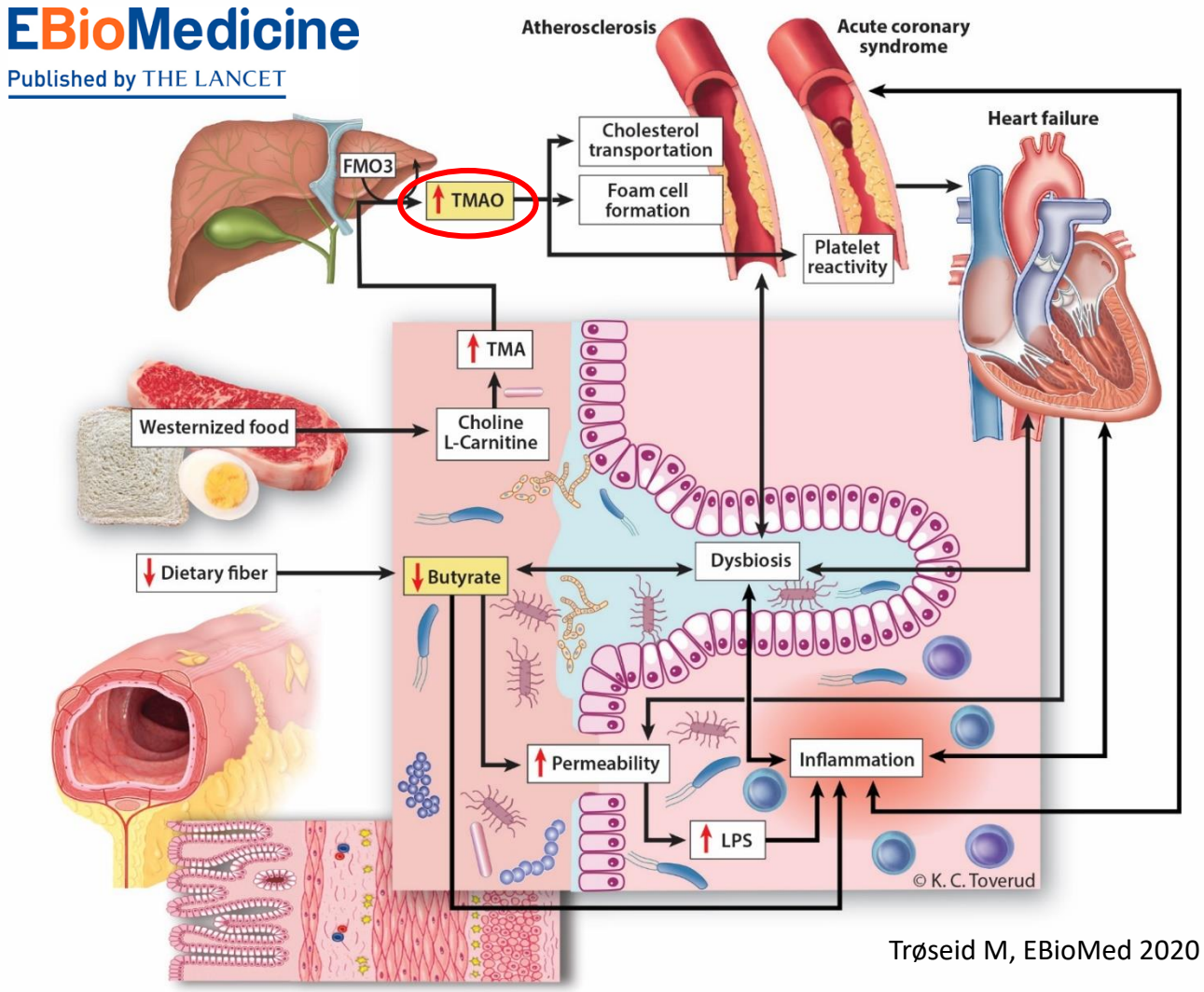

Trøseid M, EBioMed 2020

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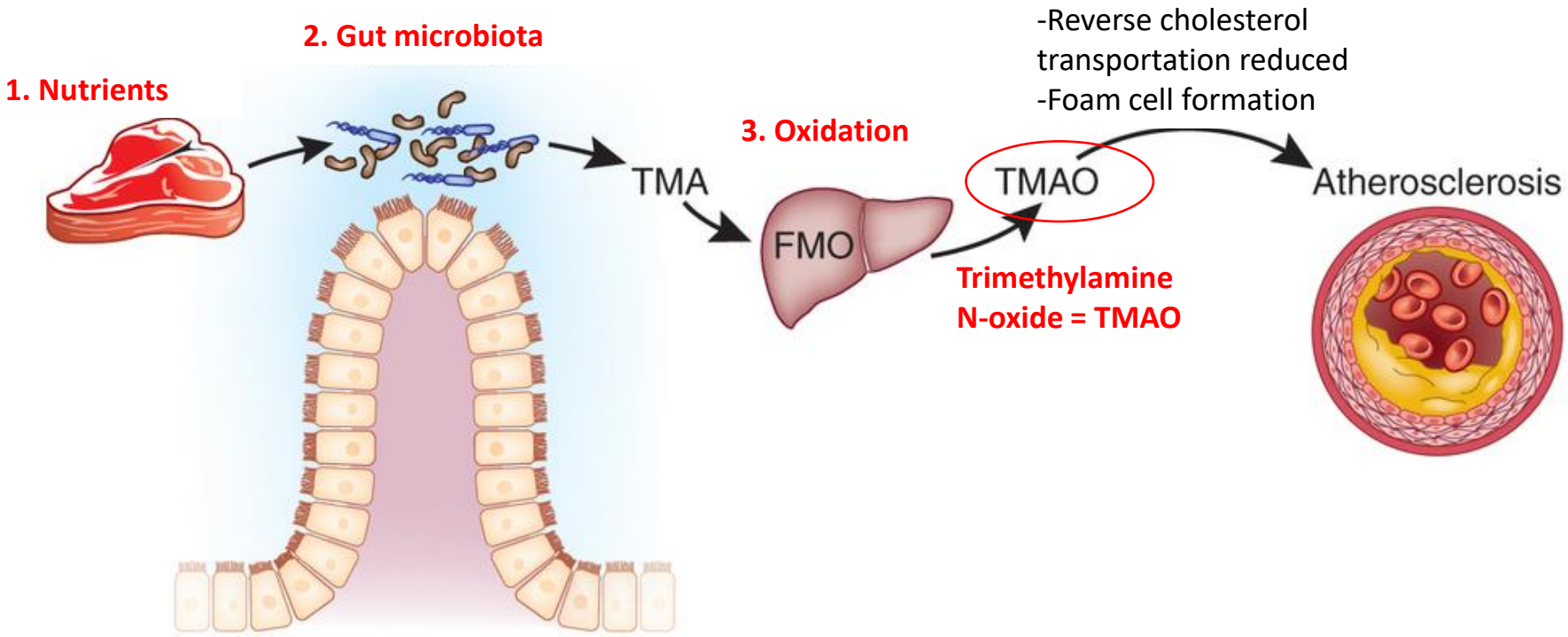
Meat metabolizing microbes and heart disease



Backhed, Nat Med 2013

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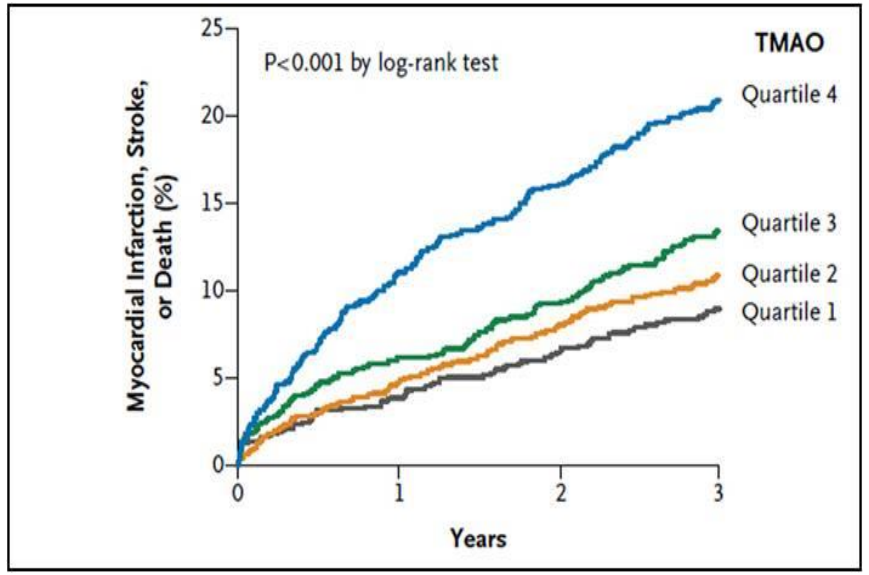
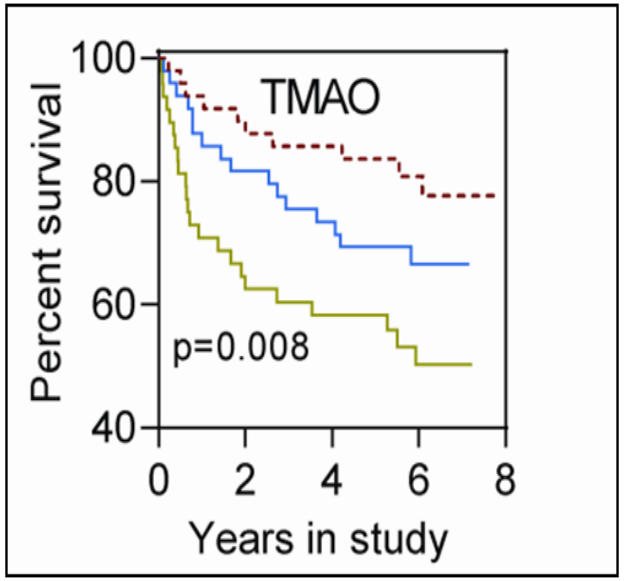
TMAO as a biomarker of cardiovascular disease

Atherosclerotic heart disease



Tang, NEJM 2013

Heart failure



Trøseid, J Int Med 2014

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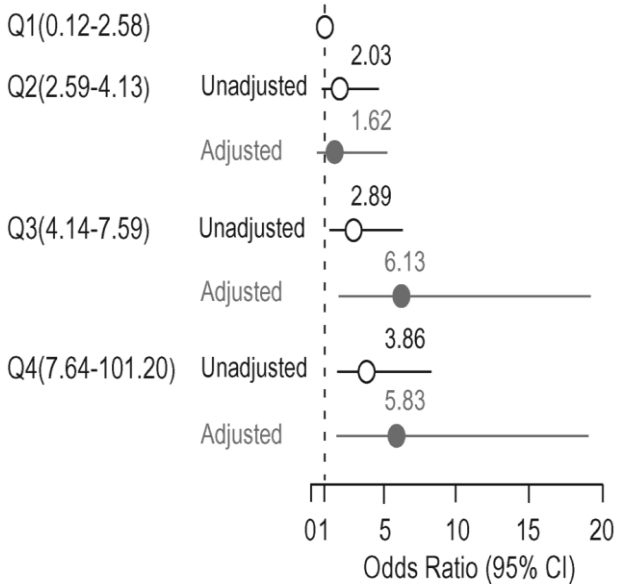
TMAO as a biomarker of cardiovascular disease

Predicts acute events 30 days after myocardial infarction



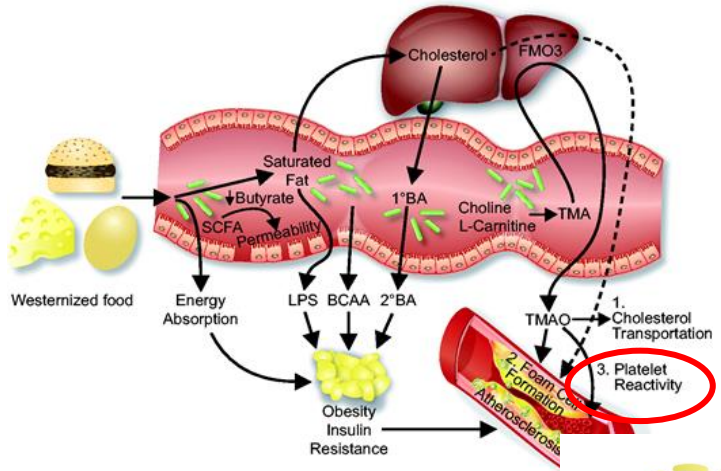
Li, Eur Heart J, 2017

European Heart Journal (2017) 0, 1–3
doi:10.1093/eurheartj/ehx005

EDITORIAL

Gut microbiota and acute coronary syndromes: ready for use in the emergency room?

Marius Trøseid[1,2,3,4]*



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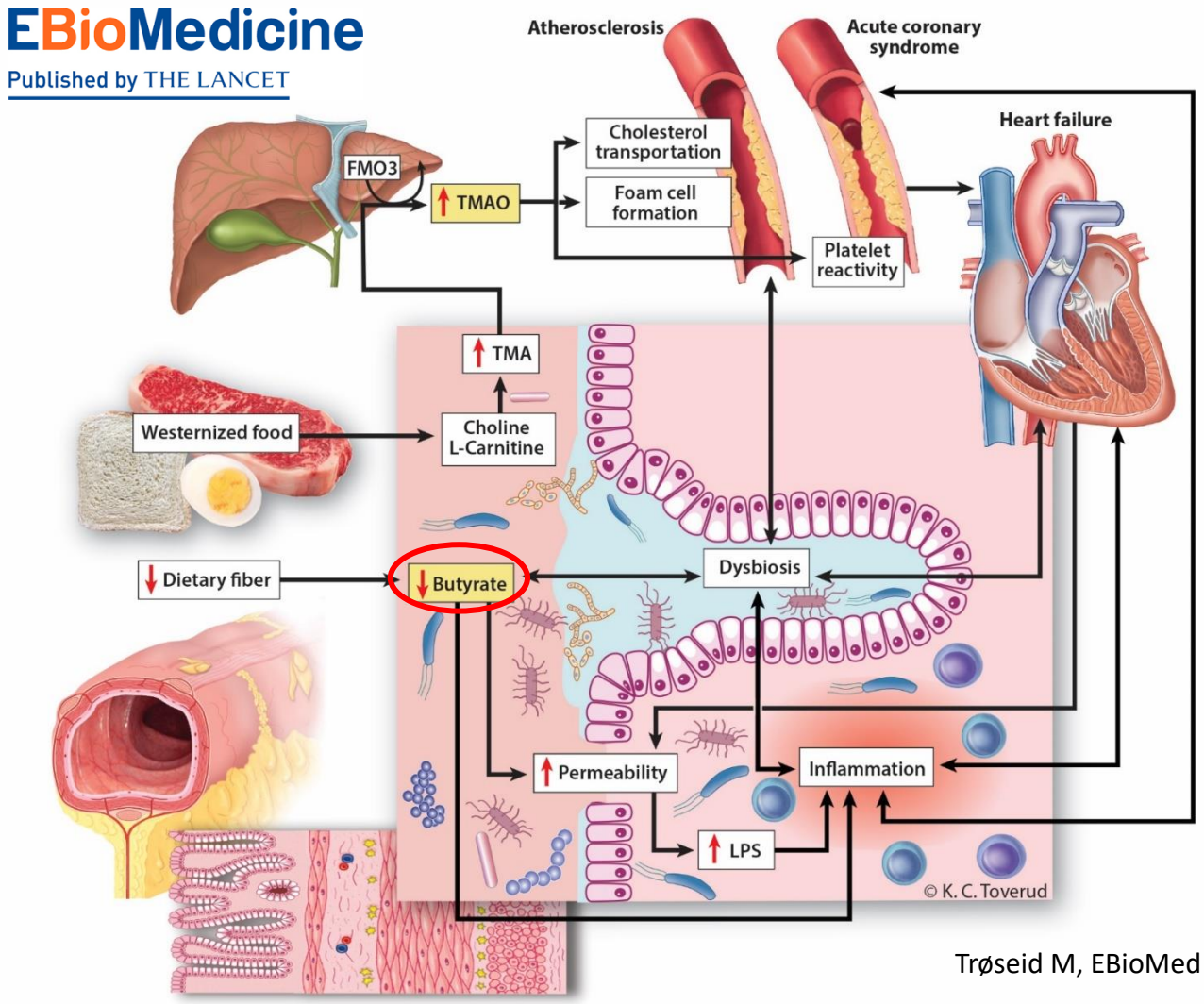
Diet, microbiome and cardiovascular risk



Trøseid M, EBioMed 2020

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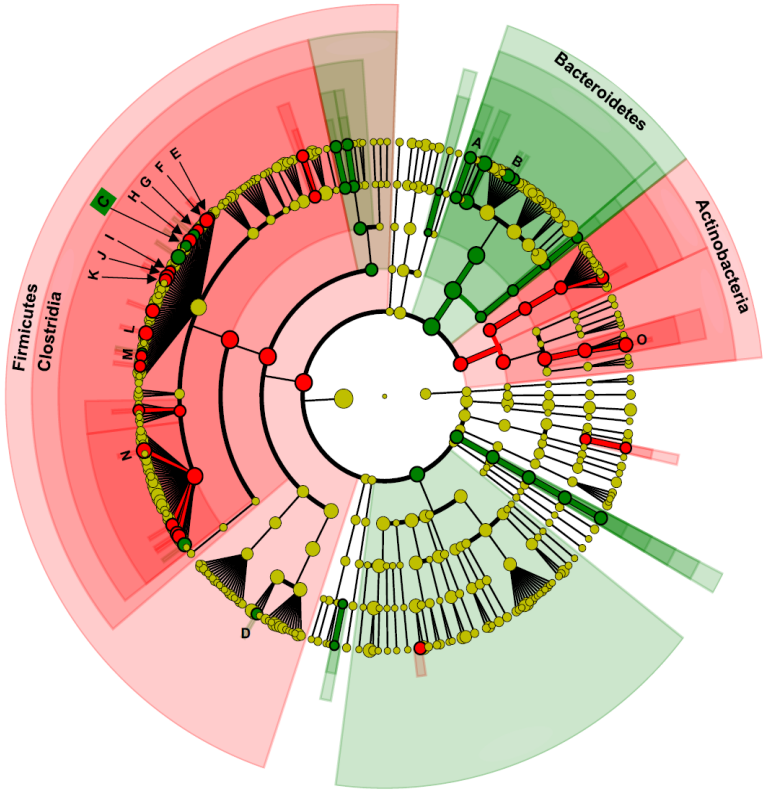
Gut microbiota in heart failure



↑ in Heart Failure

↓ in Heart Failure

	Order	Family	Genus
A	Bacteroidales	Uncultured	Uncultured bacterium
B	Bacteroidales	Prevotellaceae	Prevotella (7)
C	Clostridiales	Lachnospiraceae	Hungatella
D	Selenomonadales	Acidaminococcaceae	Succiniclasticum
E	Clostridiales	Lachnospiraceae	Anaerostipes
F	Clostridiales	Lachnospiraceae	Blautia
G	Clostridiales	Lachnospiraceae	Coprococcus (3)
H	Clostridiales	Lachnospiraceae	Fusicatenibacter
I	Clostridiales	Lachnospiraceae	Lachnospiraceae FCS020
J	Clostridiales	Lachnospiraceae	Lachnospiraceae NC2004
K	Clostridiales	Lachnospiraceae	Lachnospiraceae ND3007
L	Clostridiales	Lachnospiraceae	Pseudobutyrivibrio
M	Clostridiales	Lachnospiraceae	Eubacterium hallii group
N	Clostridiales	Ruminococcaceae	Faecalibacterium
O	Bifidobacteriales	Bifidobacteriaceae	Bifidobacterium

Kummen&Mayerhofer,
JACC 2018

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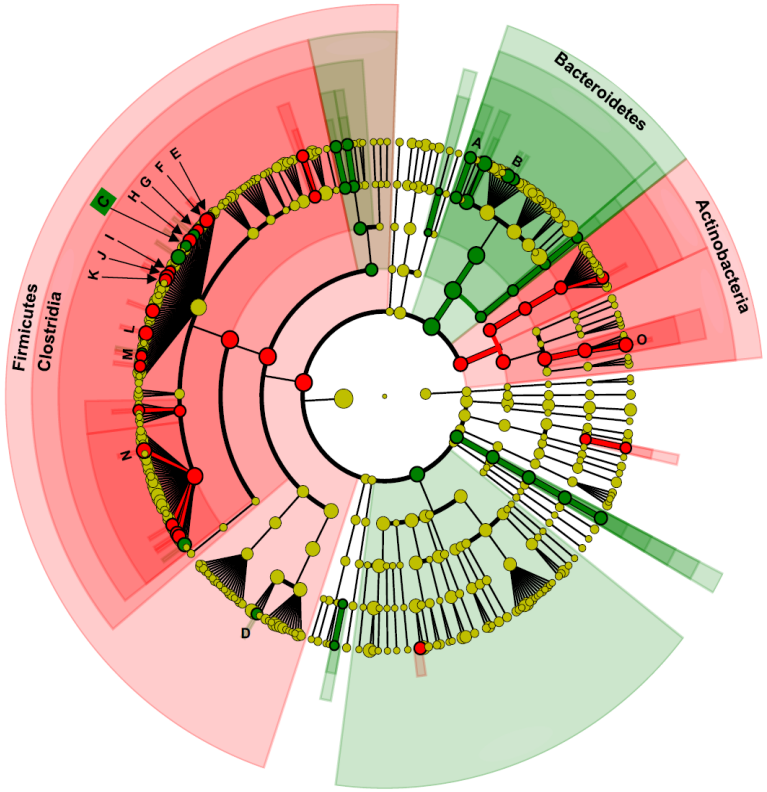
Gut microbiota in heart failure



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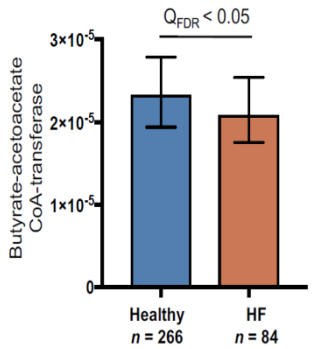
Butyrat-producing bacteria reduced

Butyrate producing genes



Kummen&Mayerhofer, JACC 2018

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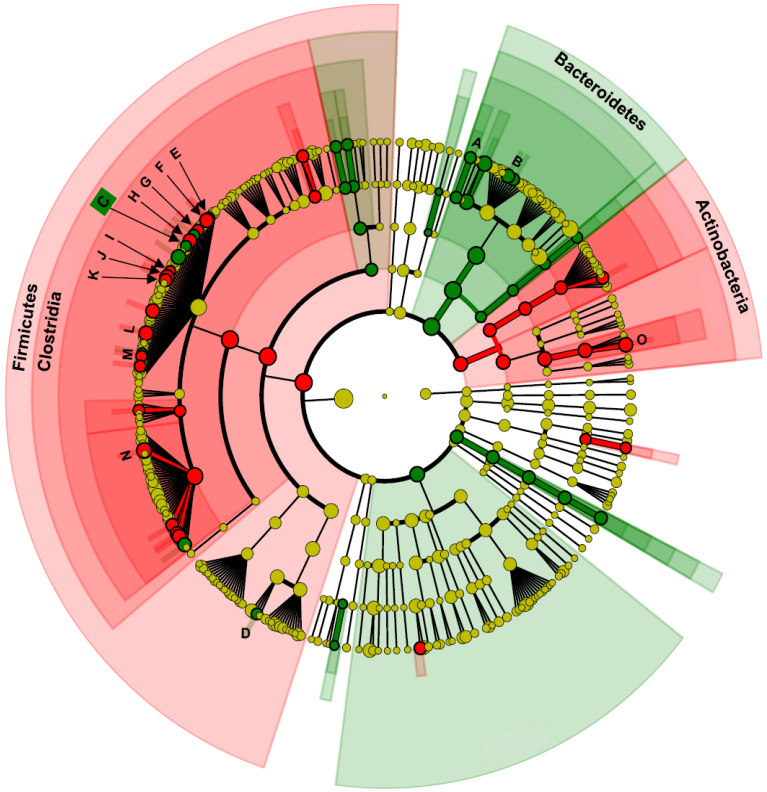
Related to clinical progression?



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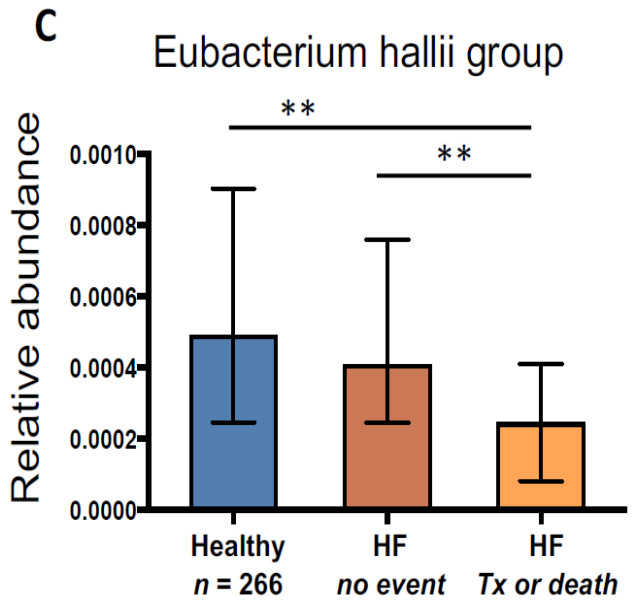

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How about interaction with diet?

	Fiber Intake (g) $n = 37$	
	rho	***P* value**
Chao1	**0.386***	**0.018**
Observed OTUs	**0.341***	**0.039**
FB-ratio	0.186	0.271
Bifidobacterium	0.324	0.050
Fusicatenibacter	**0.413***	**0.011**
Lachnospiraceae NC2004	0.322	0.052
Lachnospiraceae FCS020	**0.373***	**0.023**
Pseudobutyrivibrio	0.058	0.732
Lachnospiraceae ND3007	**0.393***	**0.016**
Blautia	-0.074	0.662
Anaerostipes	**0.473****	**0.003**
Eubacterium hallii group	0.037	0.829
Coprococcus (3)	0.125	0.461
Faecalibacterium	-0.208	0.216

Low fibre intake correlated with much of the dysbiosis in heart failure

Mayerhofer C, ESC HF 2019

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How about interaction with diet?

- TMAO correlated with intake of red meat, but not with dysbiosis of heart failure
- Is TMAO a diet-dependent biomarker?

Mayerhofer C, ESC HF 2019

Layout

- The microbiome- a brief introduction
- Relevant for cardiovascular disease?
- Can we target the gut microbiome in personalized medicine and nutrition?
  - Is a banana always a banana?

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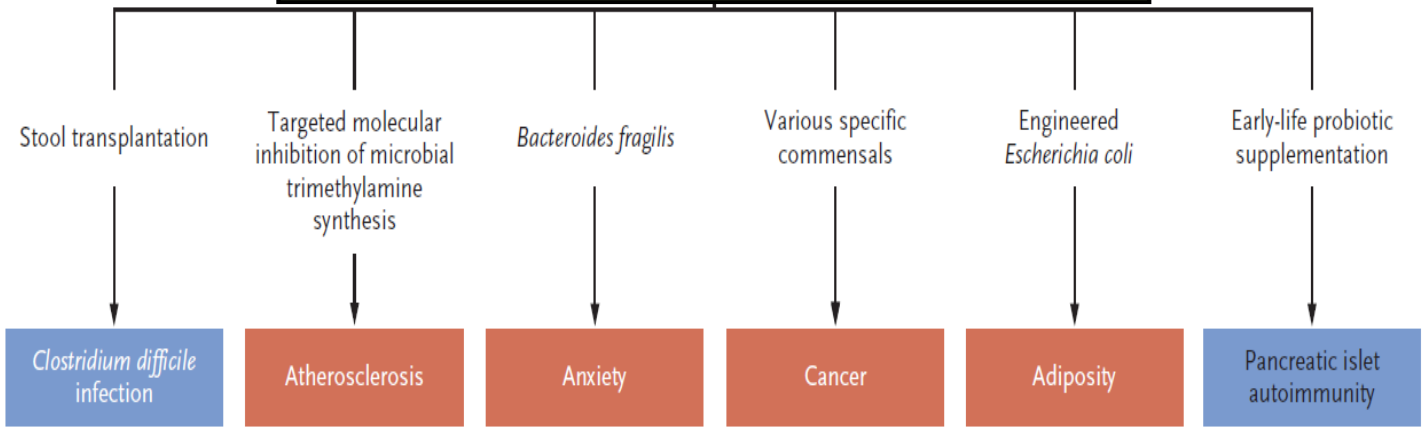
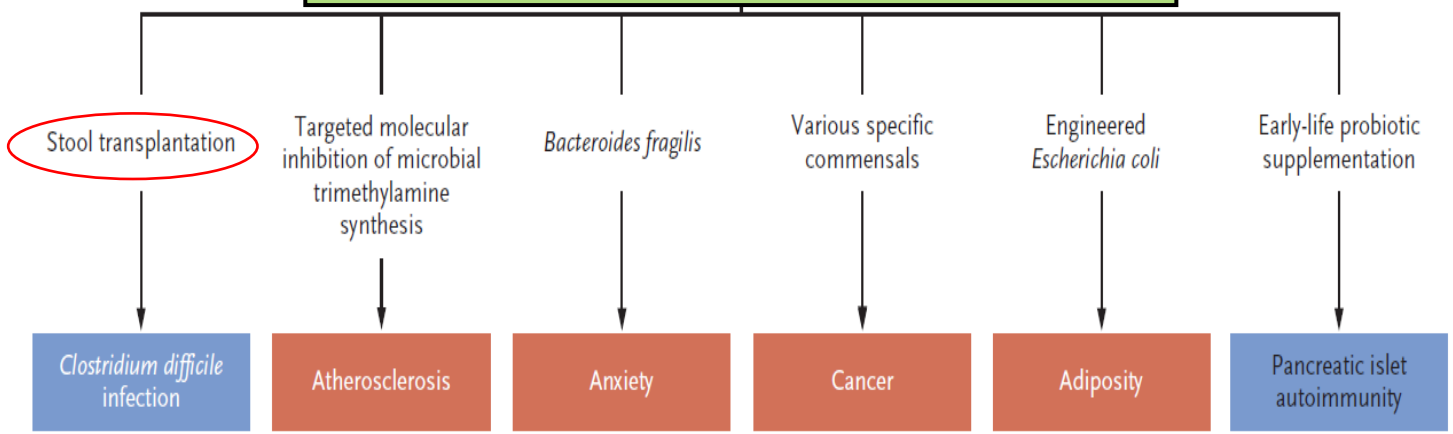
Strategies to target the gut microbiome

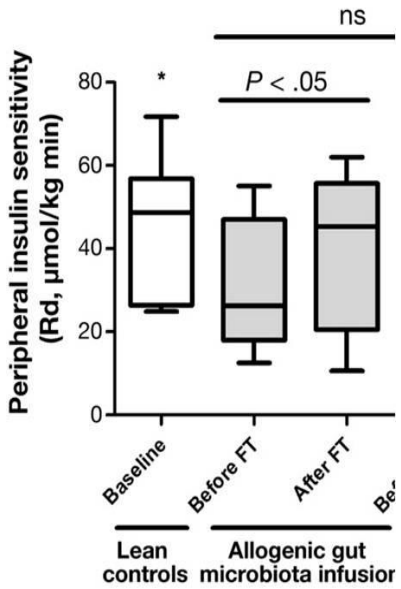


Lynch SM, NEJM 2016

Strategies to target the gut microbiome



Lynch SM, NEJM 2016



FATLOSE: Fecal transplantation to lose metabolic syndrome

Gut microbiota from lean donors normalized insulin sensitivity – but only for a few weeks

Vrieze, Gastroenterology 2012

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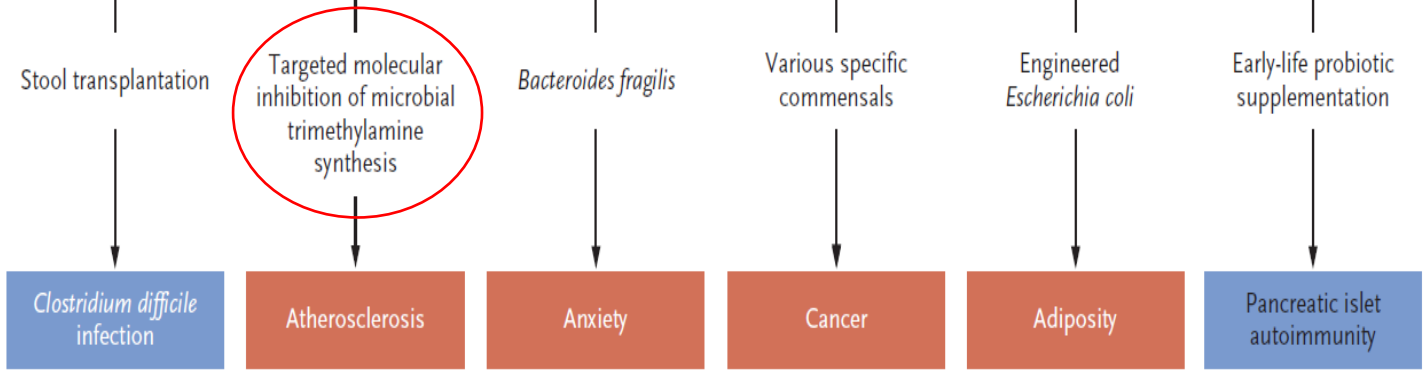
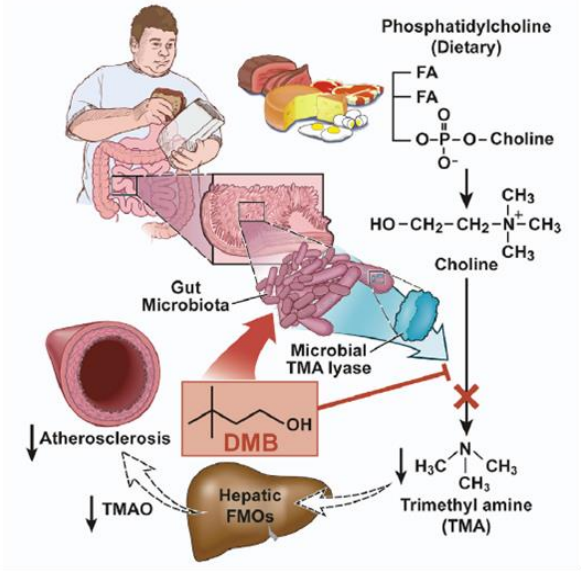
Strategies to target the gut microbiome



Lynch SM, NEJM 2016



Drug the bug!

By targeting the microbes with a TMA-inhibitor, TMAO-levels were reduced and atherosclerosis reversed

Wang, Cell 2015

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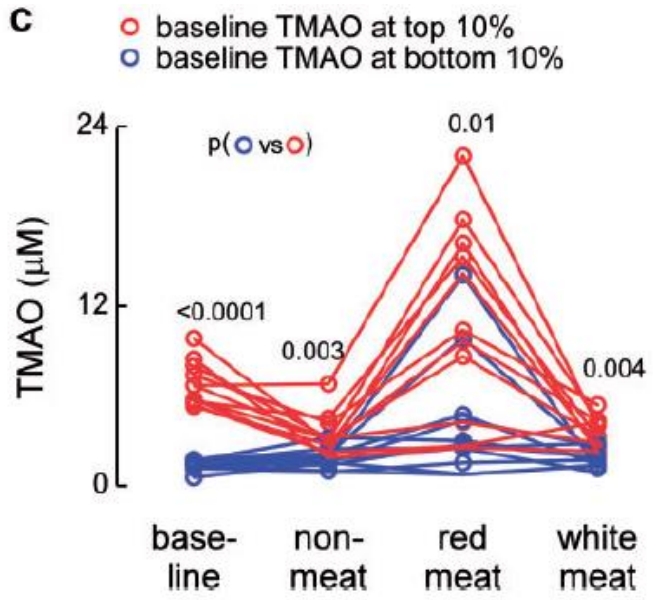
Perhaps easier to change your diet?

Impact of chronic dietary red meat, white meat, or non-meat protein on trimethylamine



Wang Z, Eur Heart J 2019

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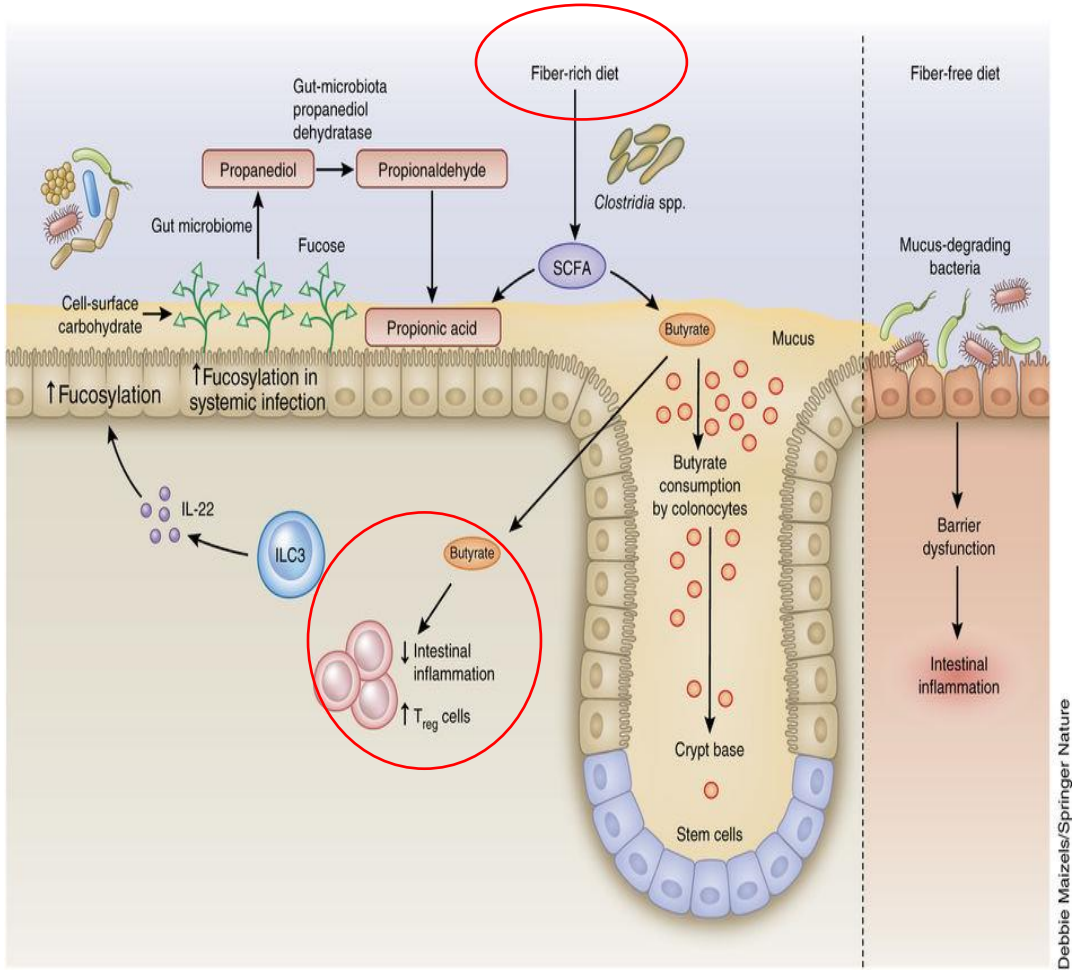
High fibre diet to increase butyrate?



- Soluble fibres increased butyrate producing microbes
- Improved glycemic control in type 2 diabetes

Dall Àlba V, Br J Nutr 2013

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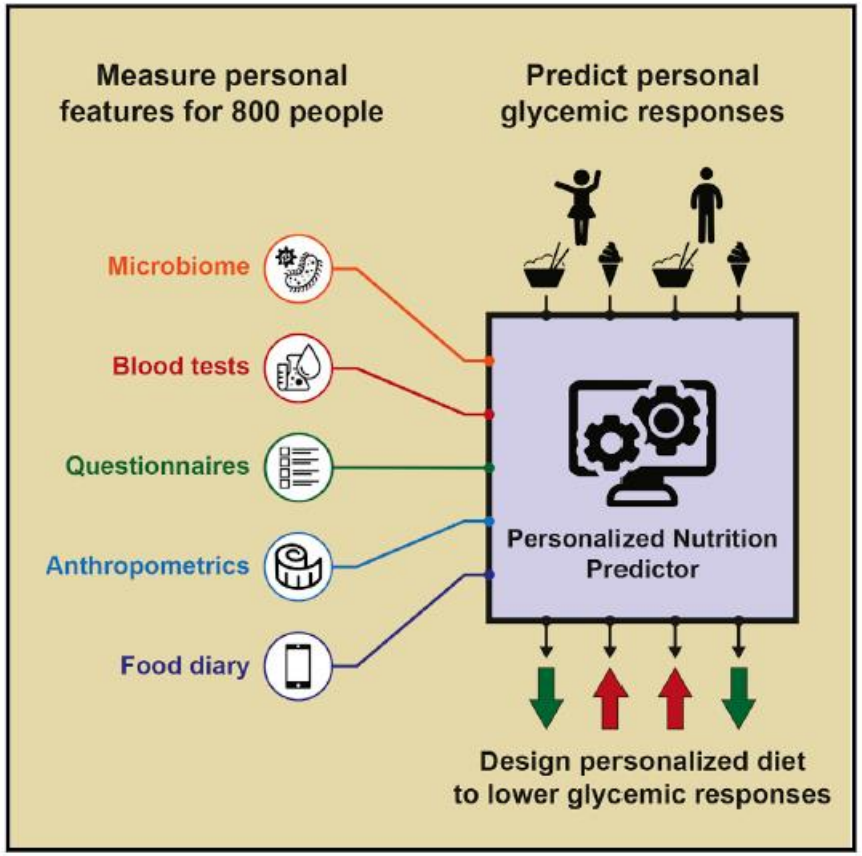
Article

Cell

Personalized Nutrition by Prediction of Glycemic Responses

- Personalized nutrition: What is healthy for <u>you</u>?



Zeevi, Cell 2015

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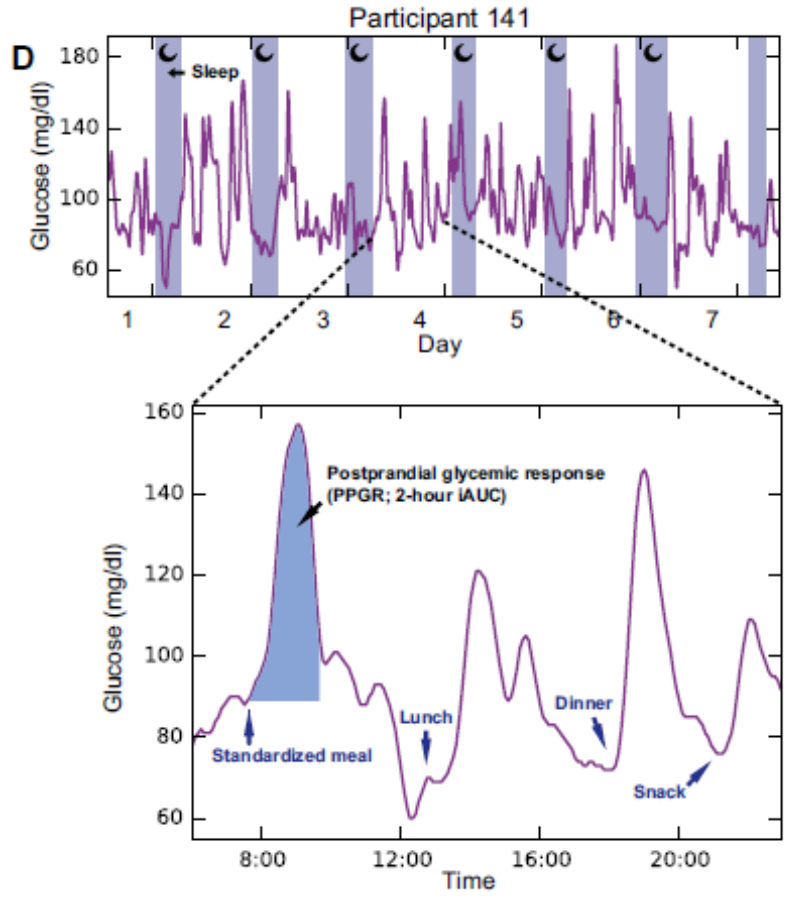
Continous blood glucose monitoring



N=800 individuals received a subcutaneous blood glucose sensor and registered all meals ”real time” by a smart phone

Zeevi, Cell 2015

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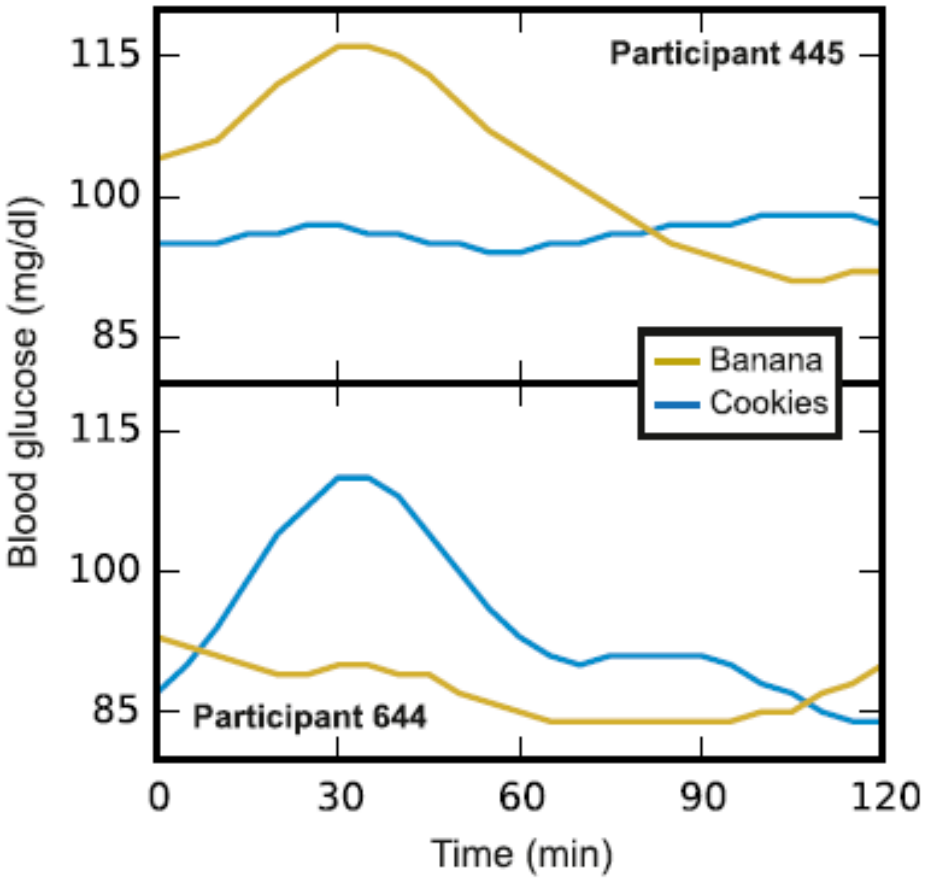
A banana is not always a banana!

Extreme individual blood glucose after intake of different nutrients



Zeevi, Cell 2015

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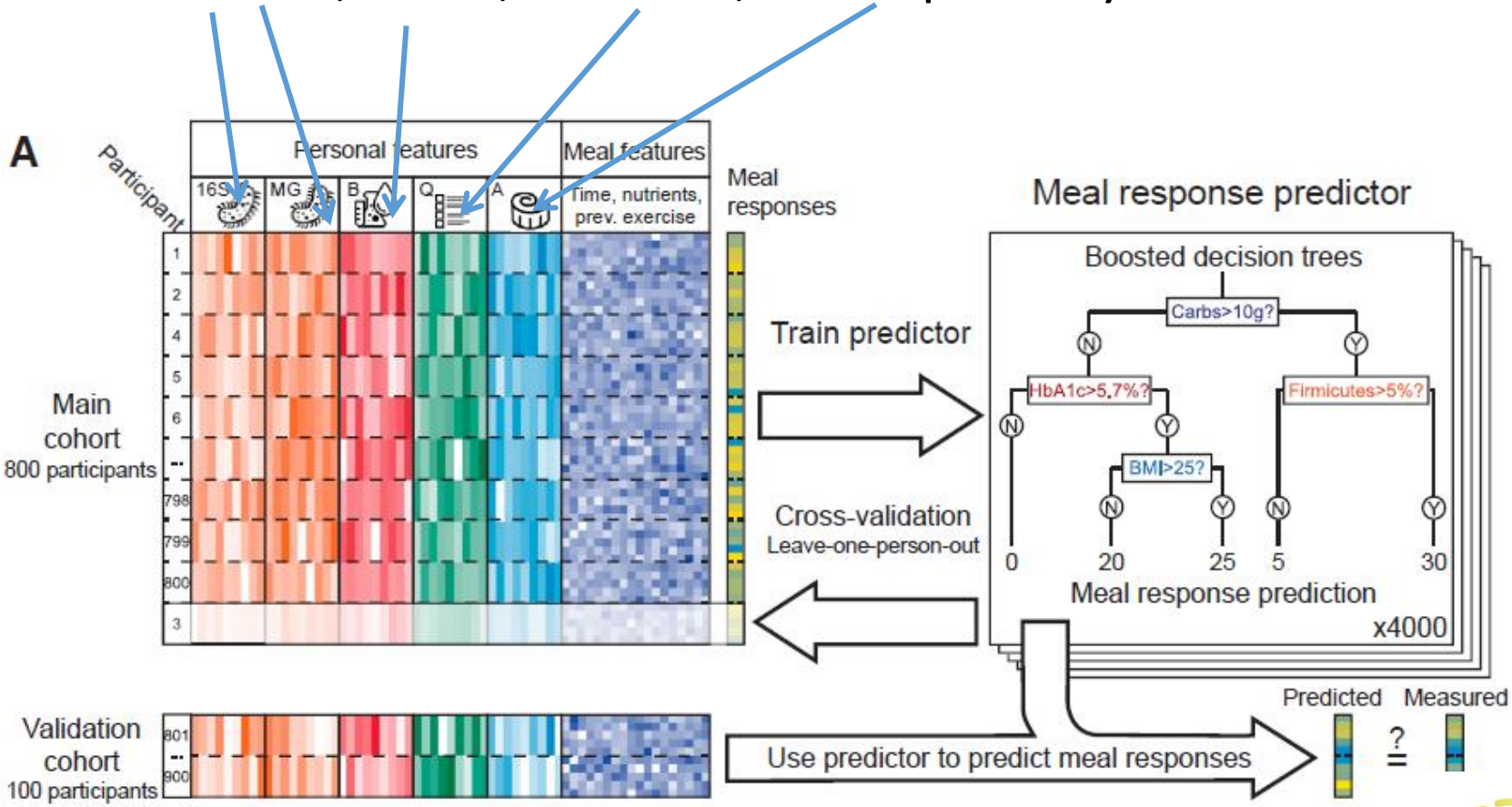
Caused by variable gut microbiota?

Microbiota, blood, nutrition, anthropometry



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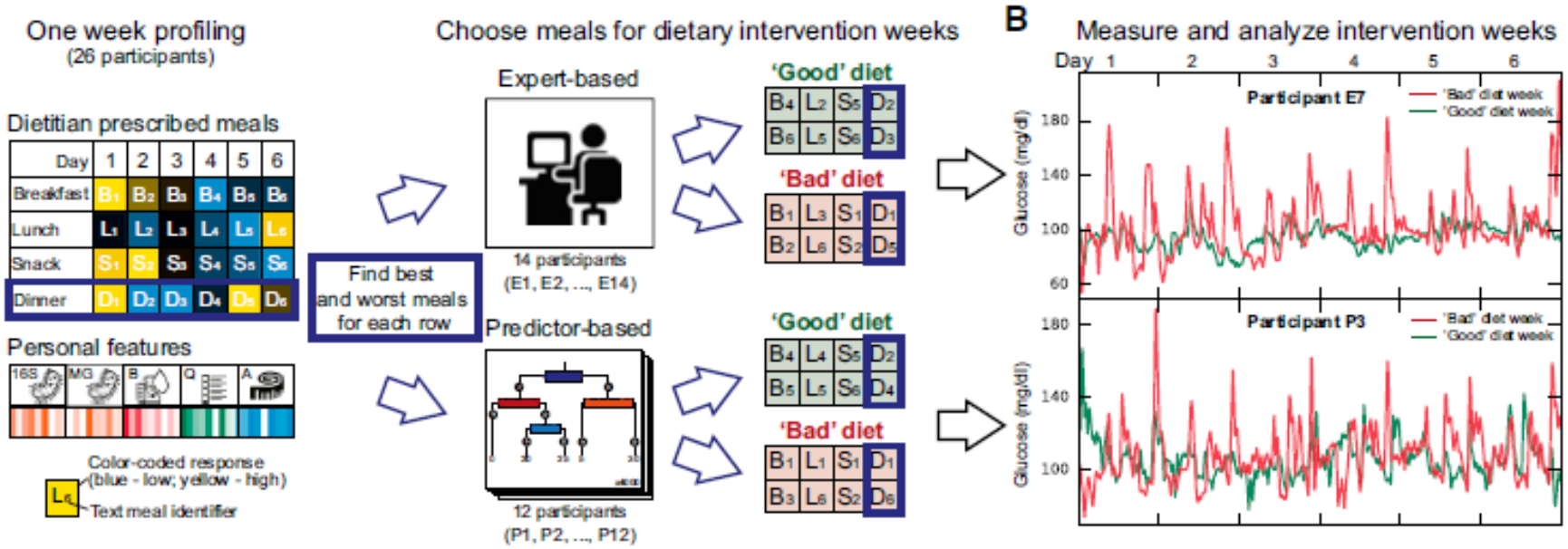
Personalized nutrition



Individualized nutritional advice. Some recommended potatoes, other pizza, to stabilize blood glucose

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Conclusion

- The gut microbiome is altered in cardiovascular disease
- Inflammatory and metabolic pathways could be targets for interventions
- However, the individual variation is substantial
- If the gut microbiome should be clinically relevant, a personalized approach is probably necessary

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- Rolf Berge
- Hedda Hoel
- Beate Vestad
- Kaspar Broch

Forskningsrådet

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Oslo universitetssykehus

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