

Microbiote intestinal et son hôte humain: une relation complexe à dévoiler

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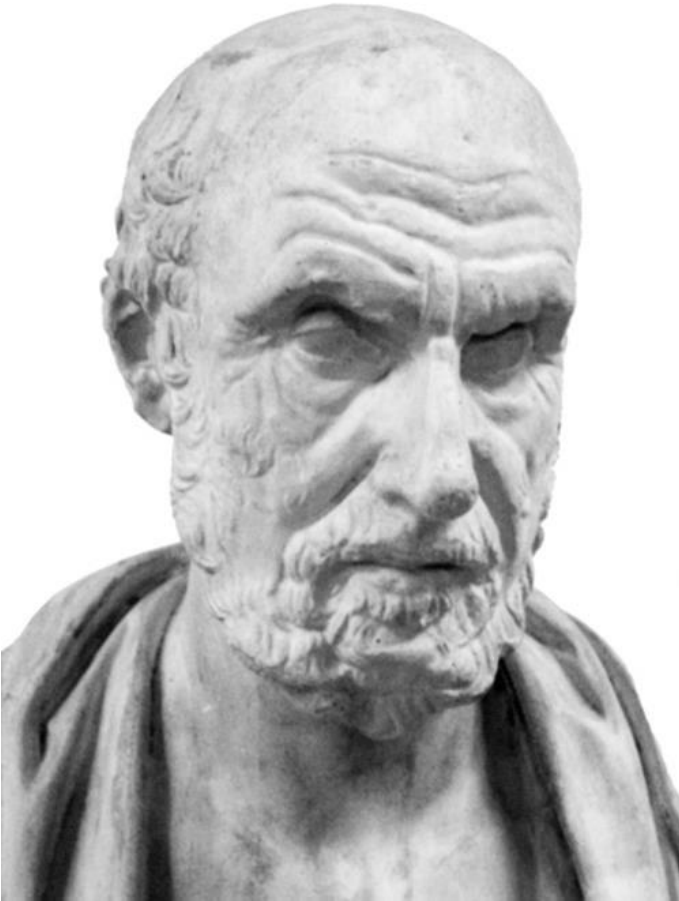
Agenda

- Gut microbiota (GM) what are we talking about?
- How can we measure and interpret GM?
- GM and human host a complex relationship: diet or genetic?
- GM and aging
- Take home messages

Back to the origine

“Death resides in the gut”

“Poor digestion is the source of all
ills”



In the modern times

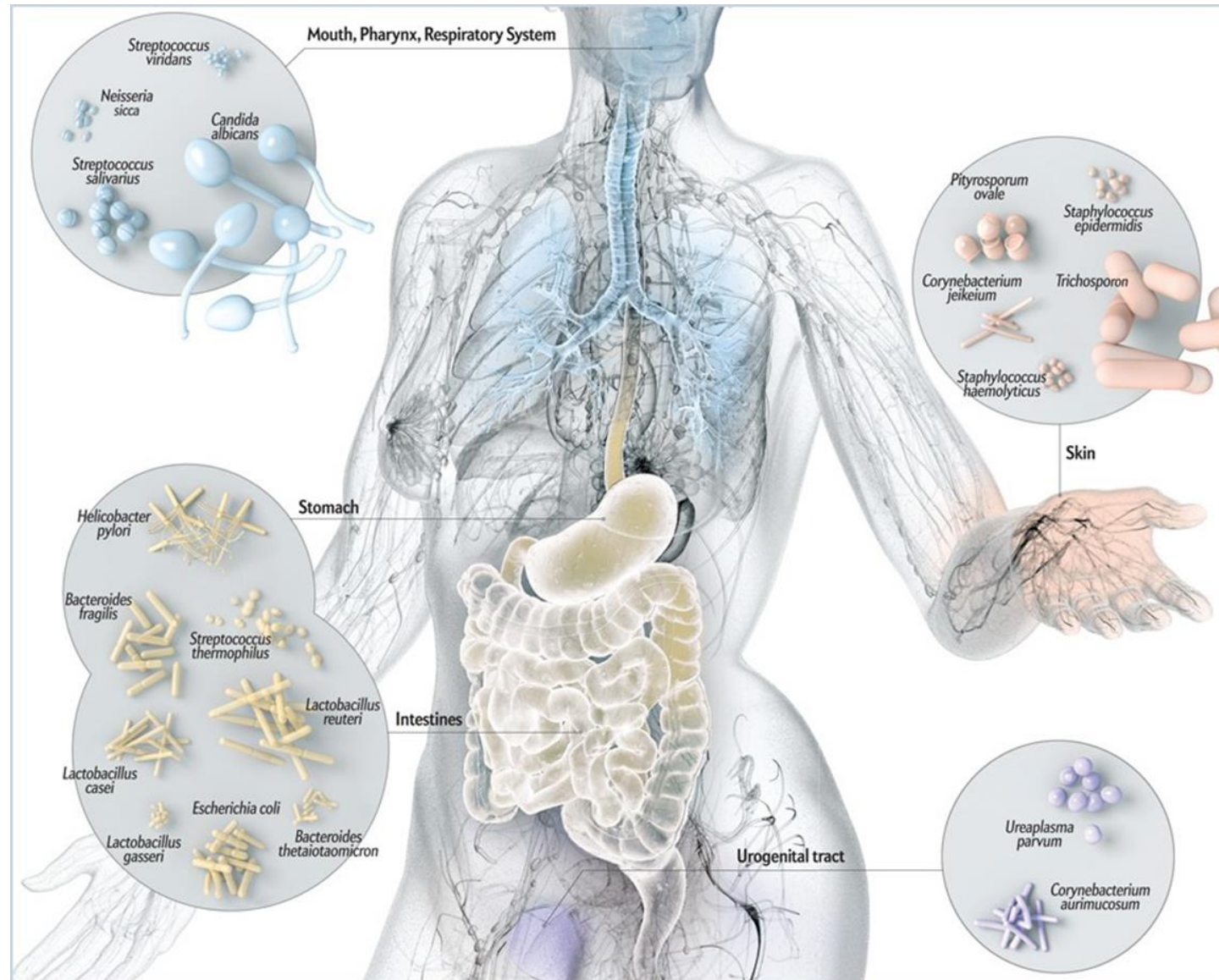
The term “microbiome” signifies the genome of the ecological community of commensal, symbiotic, and pathogenic microorganisms that literally share our body space

The term “microbiota” signifies the whole of the ecological community of commensal, symbiotic, and pathogenic microorganisms that literally share our body space

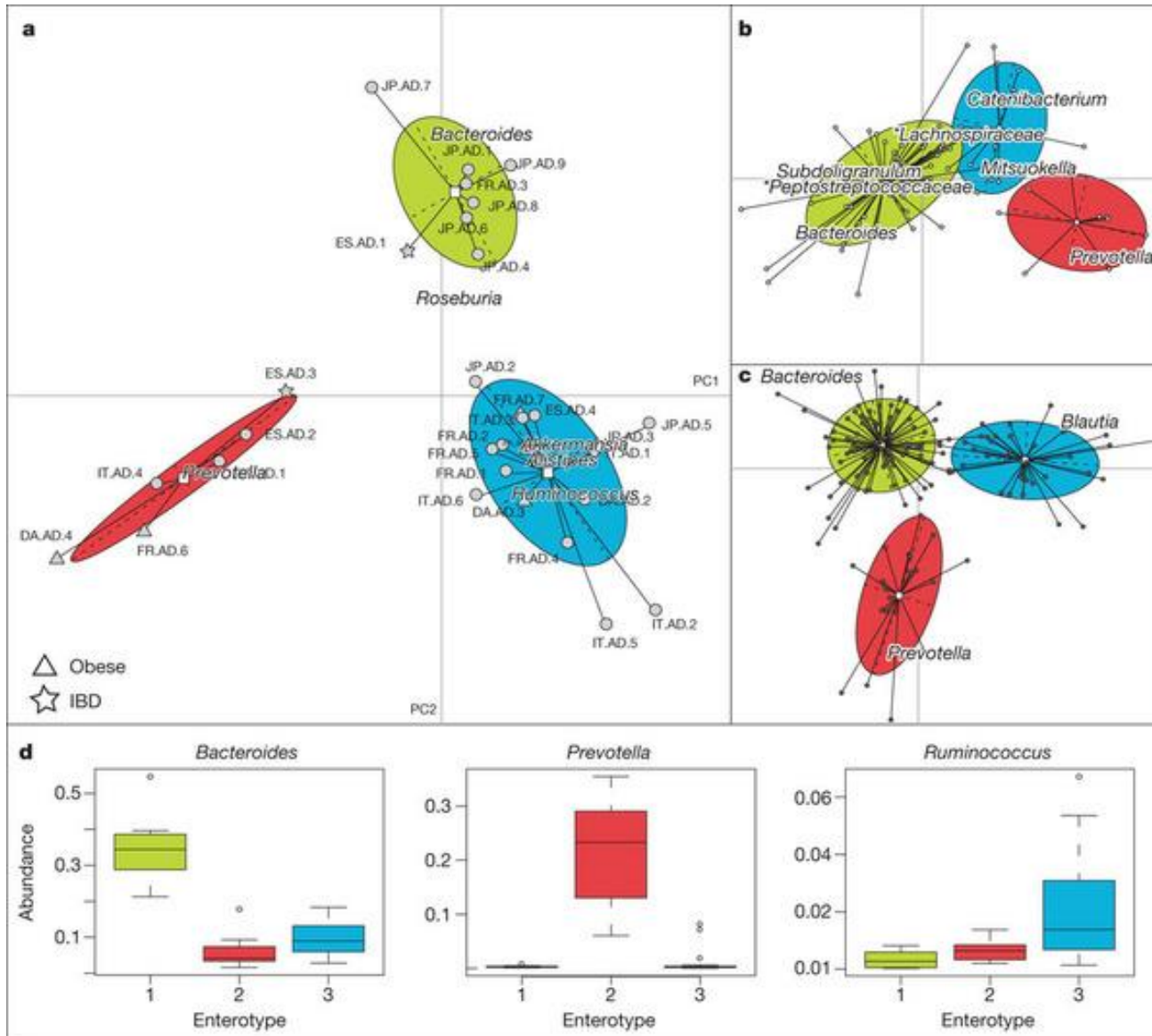
Humans as Holobionts



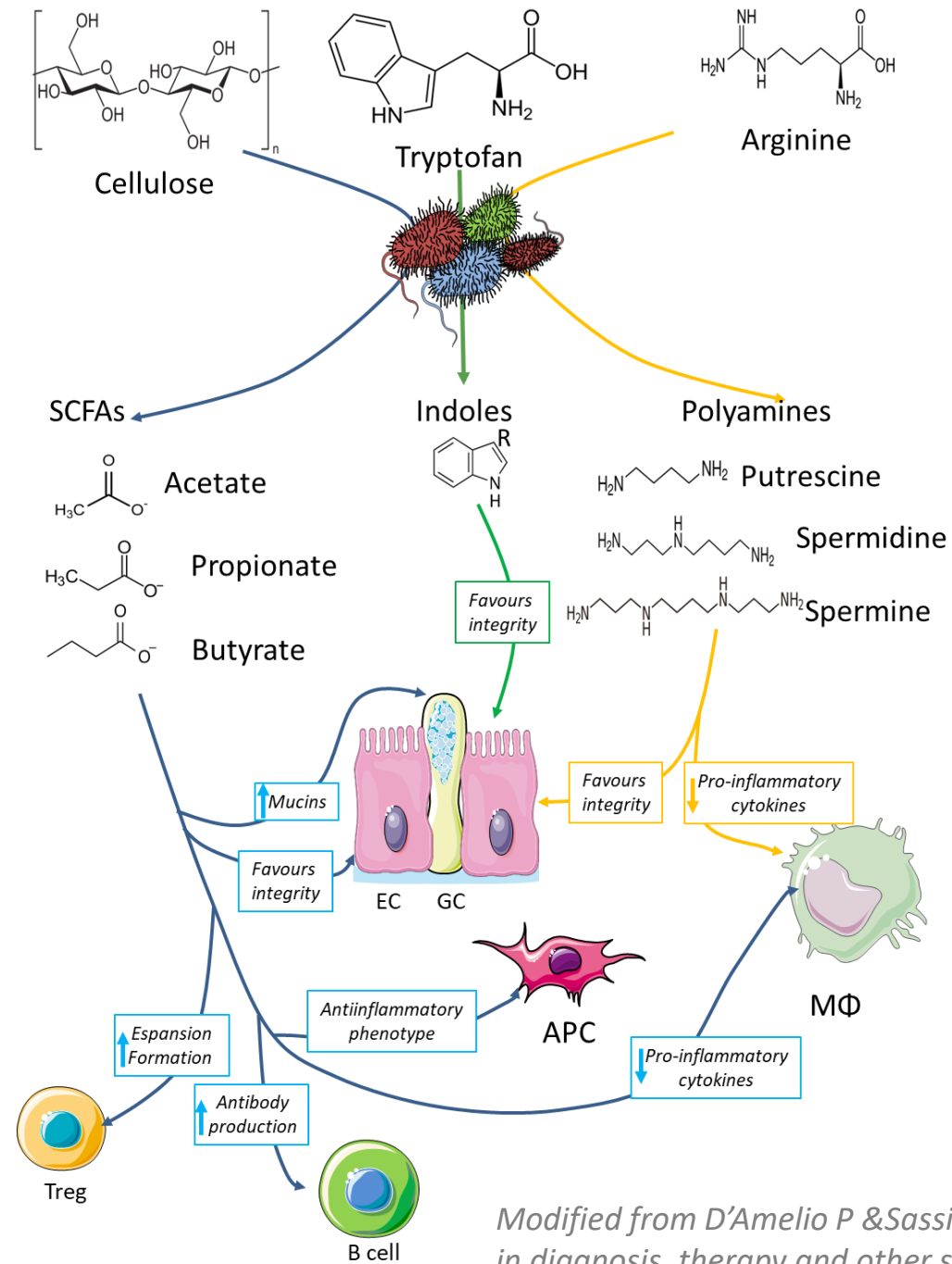
Different microbiota in different body sites



Enterotypes



GM and host interaction



Modified from D'Amelio P & Sassi F. In microbiome and metabolome in diagnosis, therapy and other strategic applications. 2018

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Comparison metagenomics VS. 16SrRNA

METAGENOMICS

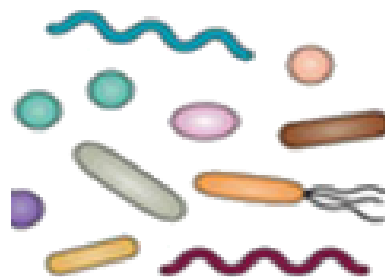


Genome fragments



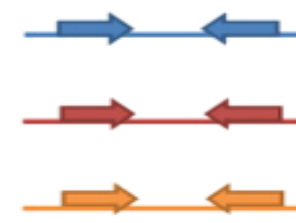
Alignments of sequences

- Entire communities (viruses and fungi)
- Relatively expensive
- Highly variability, higher resolution
- Direct assessment of genes and pathways



Bacterial Genome

16SrRNA SEQUENCING



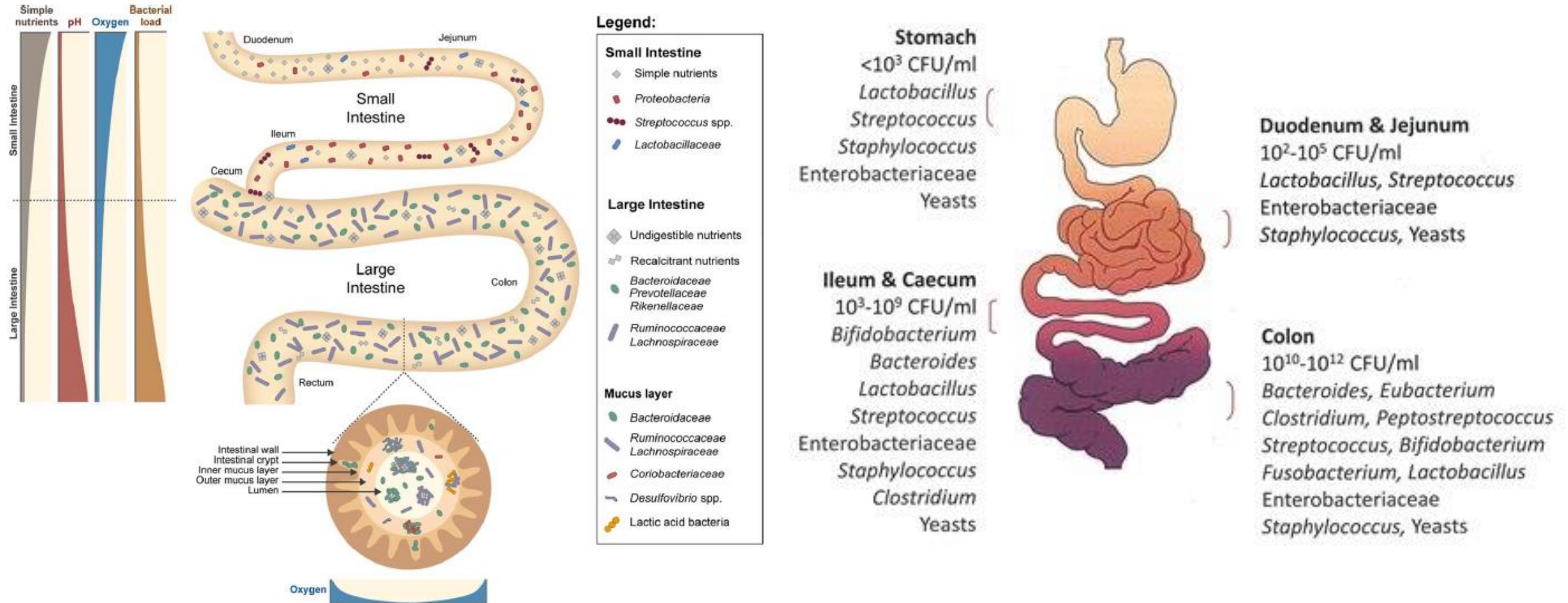
PCR marker gene



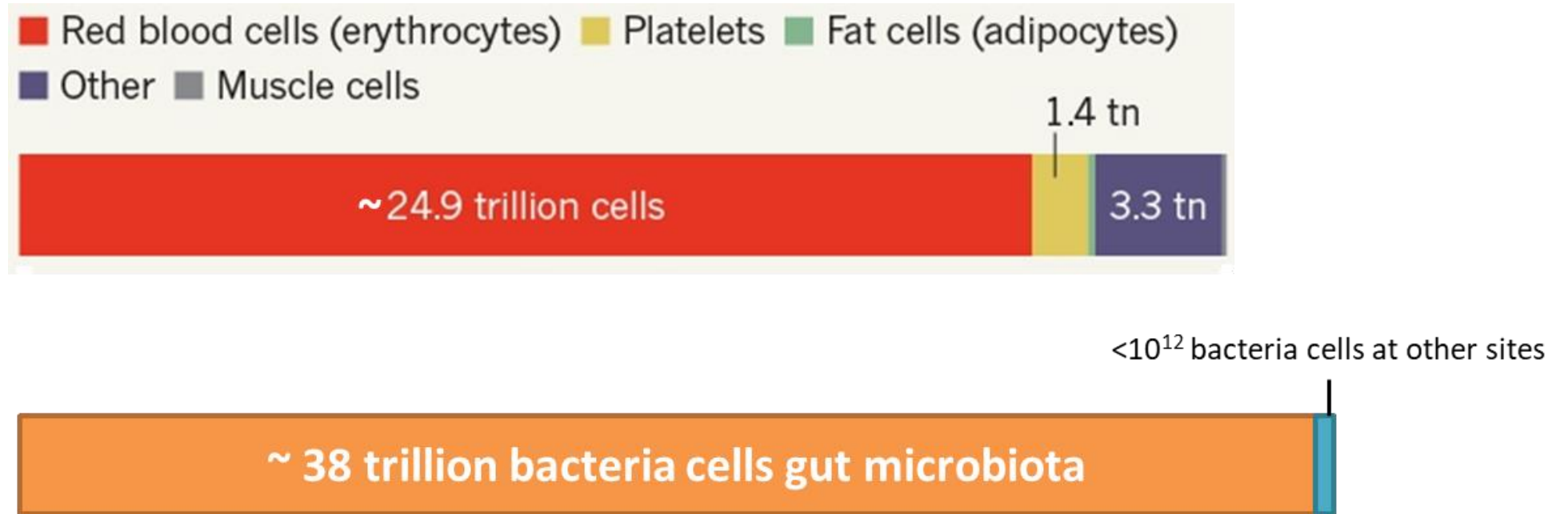
Amplicon library

- Only bacteria and Archaea
- Relatively cheap – large sample sizes
- Taxonomic classification to Genus level?
- Genes and pathways based on classification

Biogeography of the intestine



Humans as Holobionts



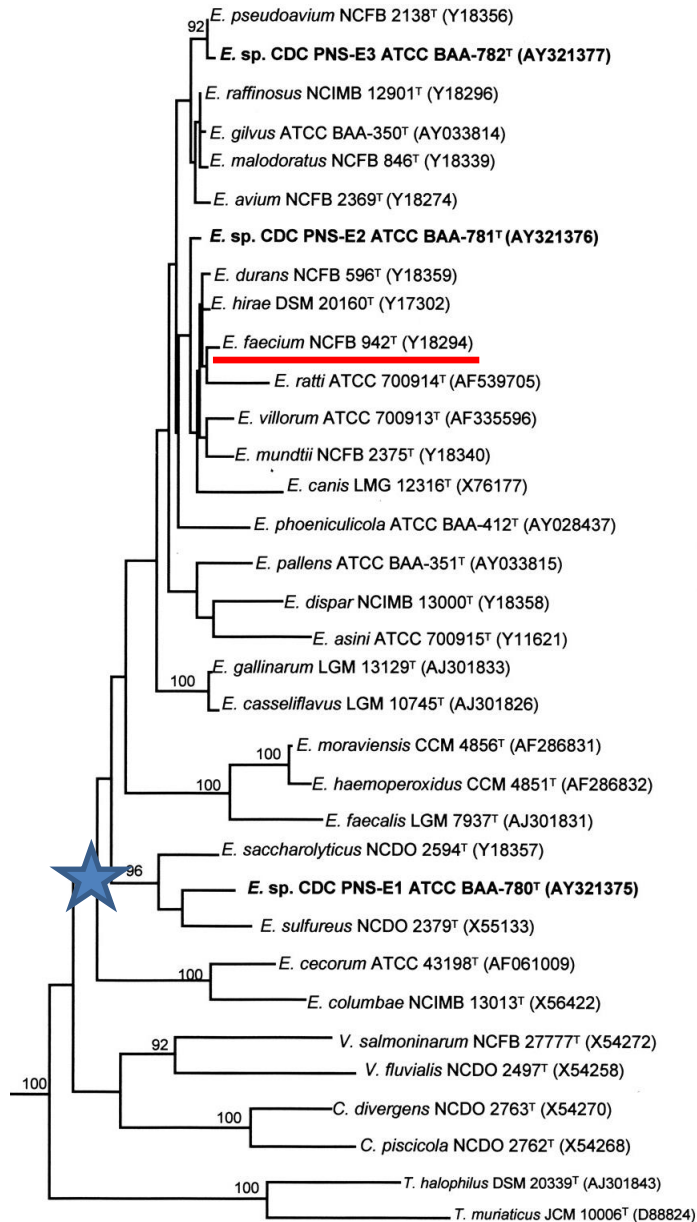
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Stool samples: adequate representation of gut content

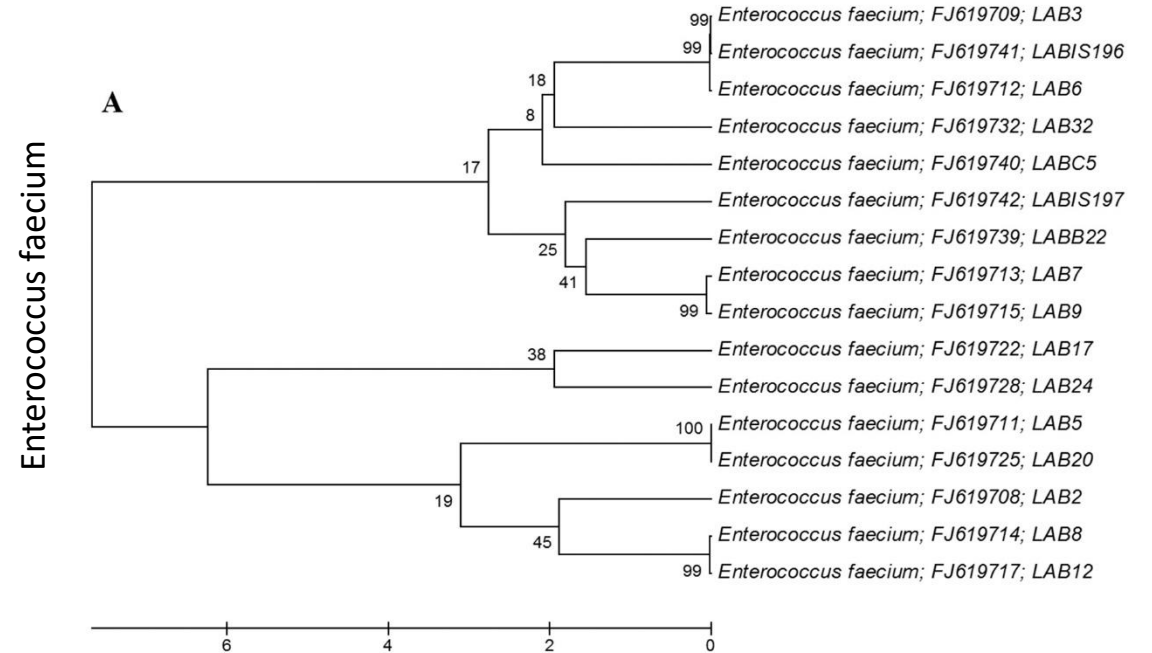
Operational Taxonomic Unit (OUT) is used to classify bacteria based on sequence similarity of the 16S marker gene. An OTU consists of a group of bacteria whose 16S marker gene shows a sequence identity of 97 percent and above. It is used to classify bacteria at the genus

OTU	N.not.0	Direction	<u>No BMI adjustment</u>		<u>BMI adjustment</u>	
			P.value	Q.value	P.value	Q.value
Bacilli class	2003	positive	6.93E-04	0.014	0.058	>0.1
Lactobacillales order	2003	positive	6.93E-04	0.014	0.307	>0.1
Enterococcaceae family	261	positive	1.53E-05	0.001	4.14E-04	0.032
Enterococcus genus	261	positive	1.60E-05	0.001	4.41E-04	0.032
Rikenellaceae family	2081	negative	1.43E-04	0.004	0.037	>0.1
Alistipes genus	2079	negative	1.32E-04	0.004	0.033	>0.1
Porphyromonadaceae family	2102	negative	0.001	0.024	0.122	>0.1
Odoribacter genus	1935	negative	1.93E-05	0.001	0.021	>0.1
Ruminococcaceae UCG002 group	2071	negative	1.28E-04	0.004	0.083	>0.1
rectalegroup	2098	positive	6.17E-04	0.014	0.083	0.045
Hungatella genus	1030	negative	0.002	0.035	0.083	0.035
ErysipelotrichaceaeUCG003 genus	1902	positive	0.061	>0.1	5.2E-04	0.032
ventriosumgroup	1980	positive	0.008	0.071	0.001	0.045

Enterococcus sp. Phylogenetic tree



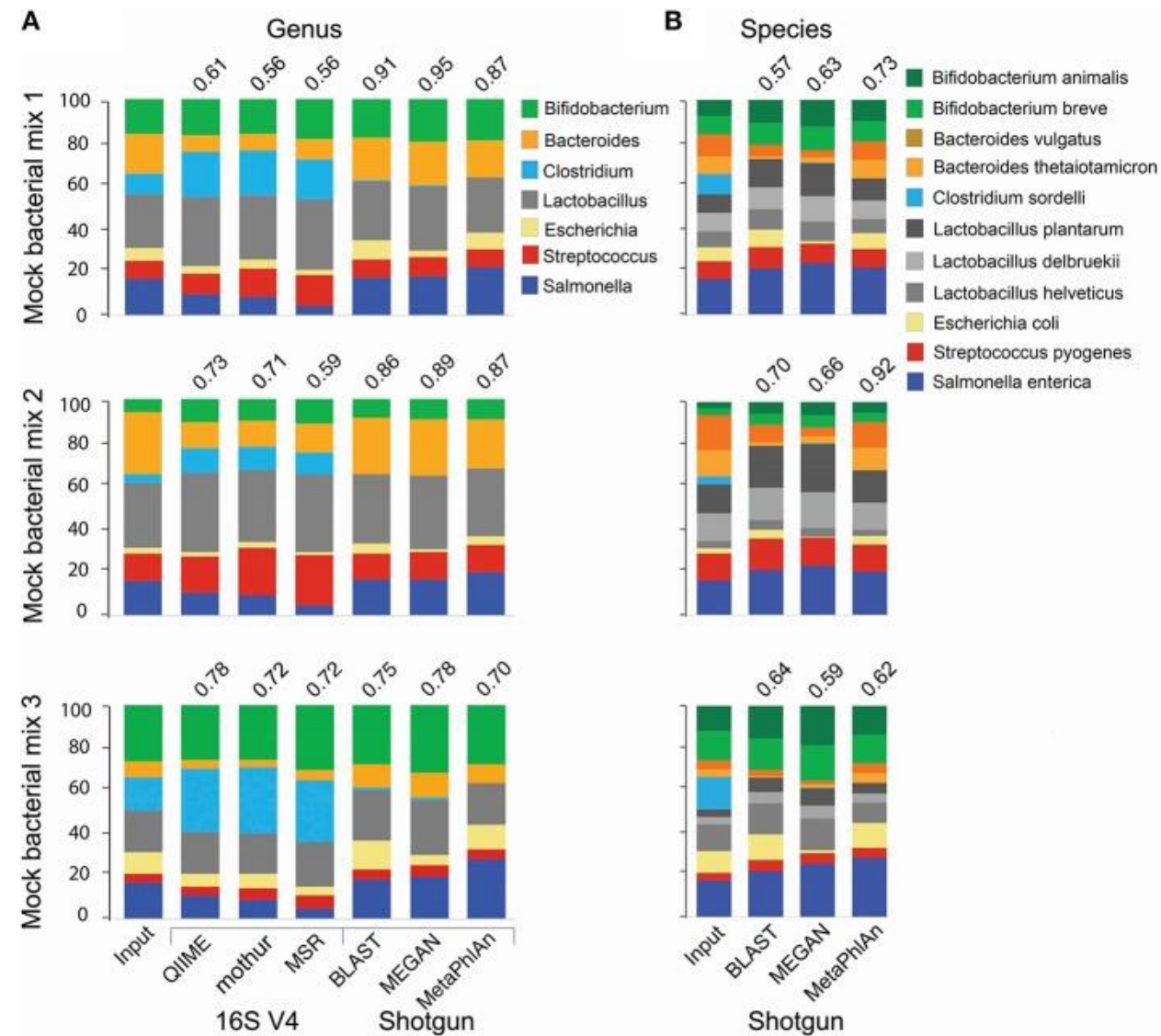
2004: 28 sp
2018: 52 sp.

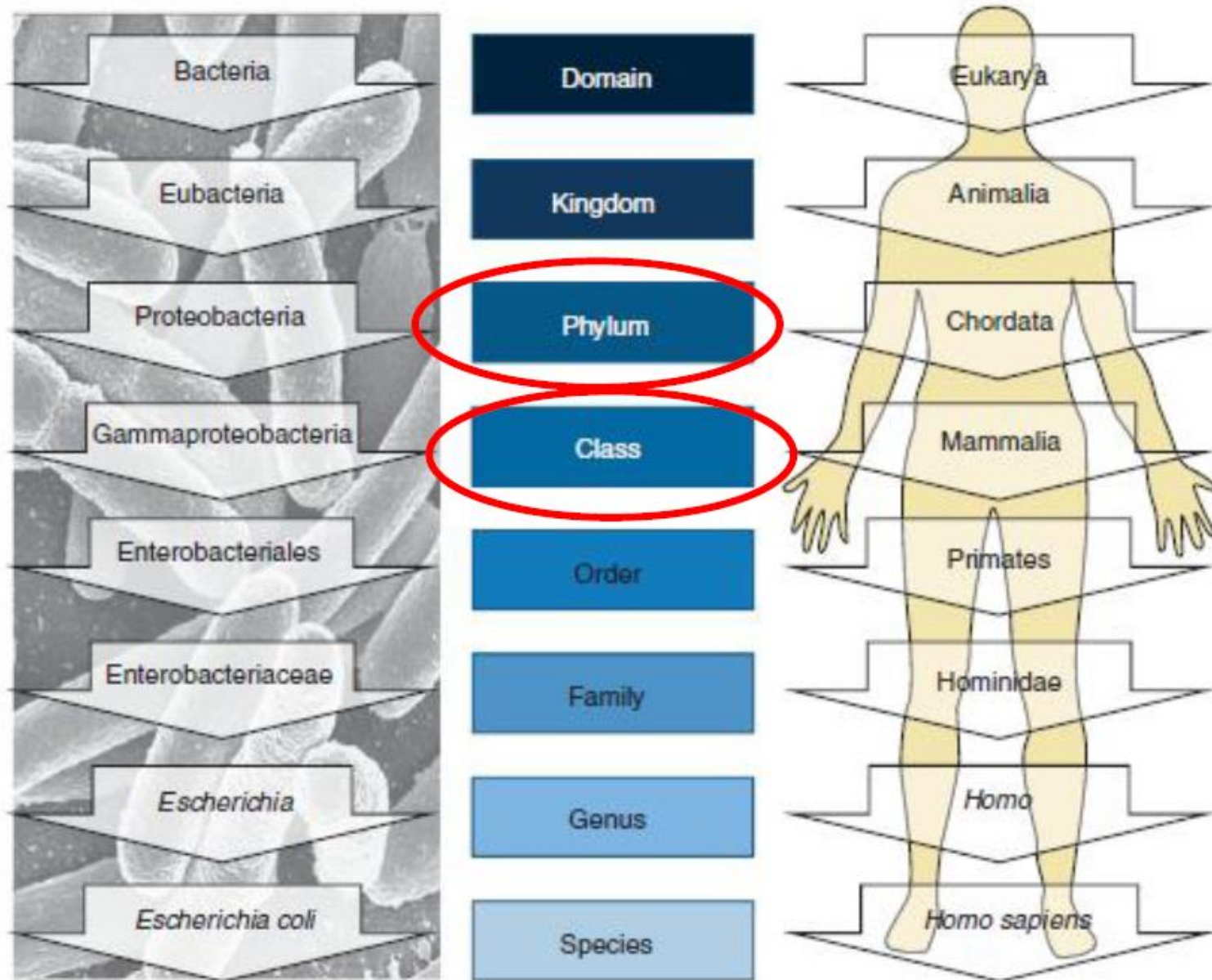


J. Clin. Microbiol. 2004. 42 (3): 1192-1198
Braz. J. Biol. 2015. 75 (4)

Taxonomic Classification of Bacterial Sequences

NEXTflex V4 16S amplicon
Nextera XT

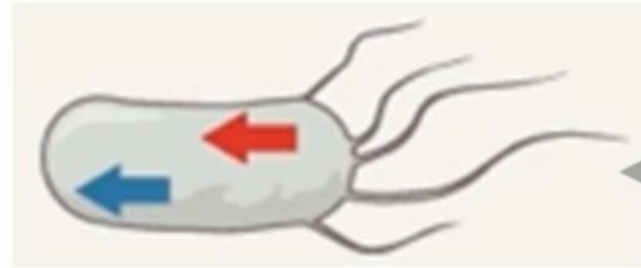
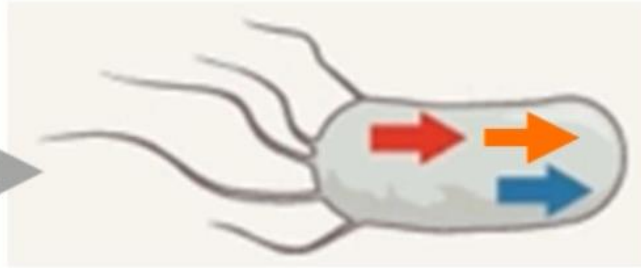




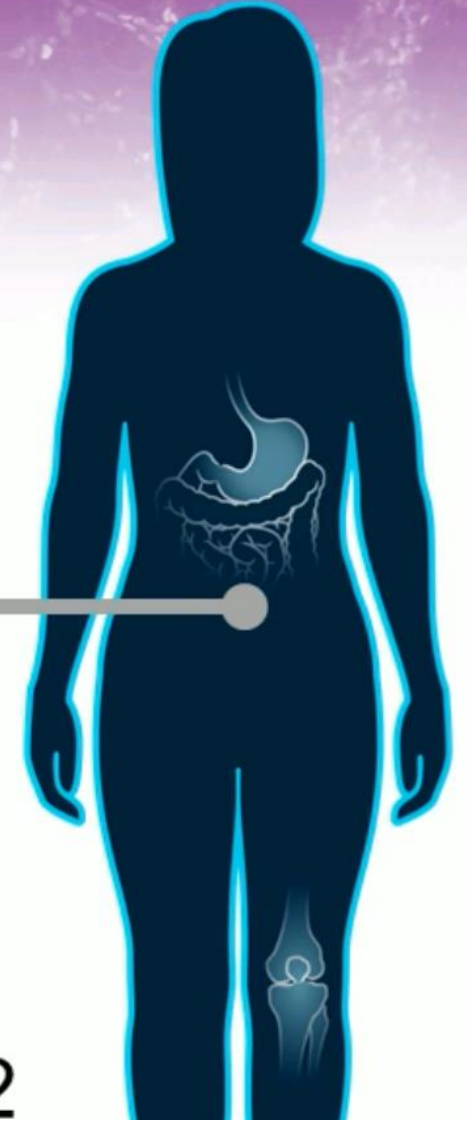
Genes gains and losses at subspecies level



Person 1



Person 2

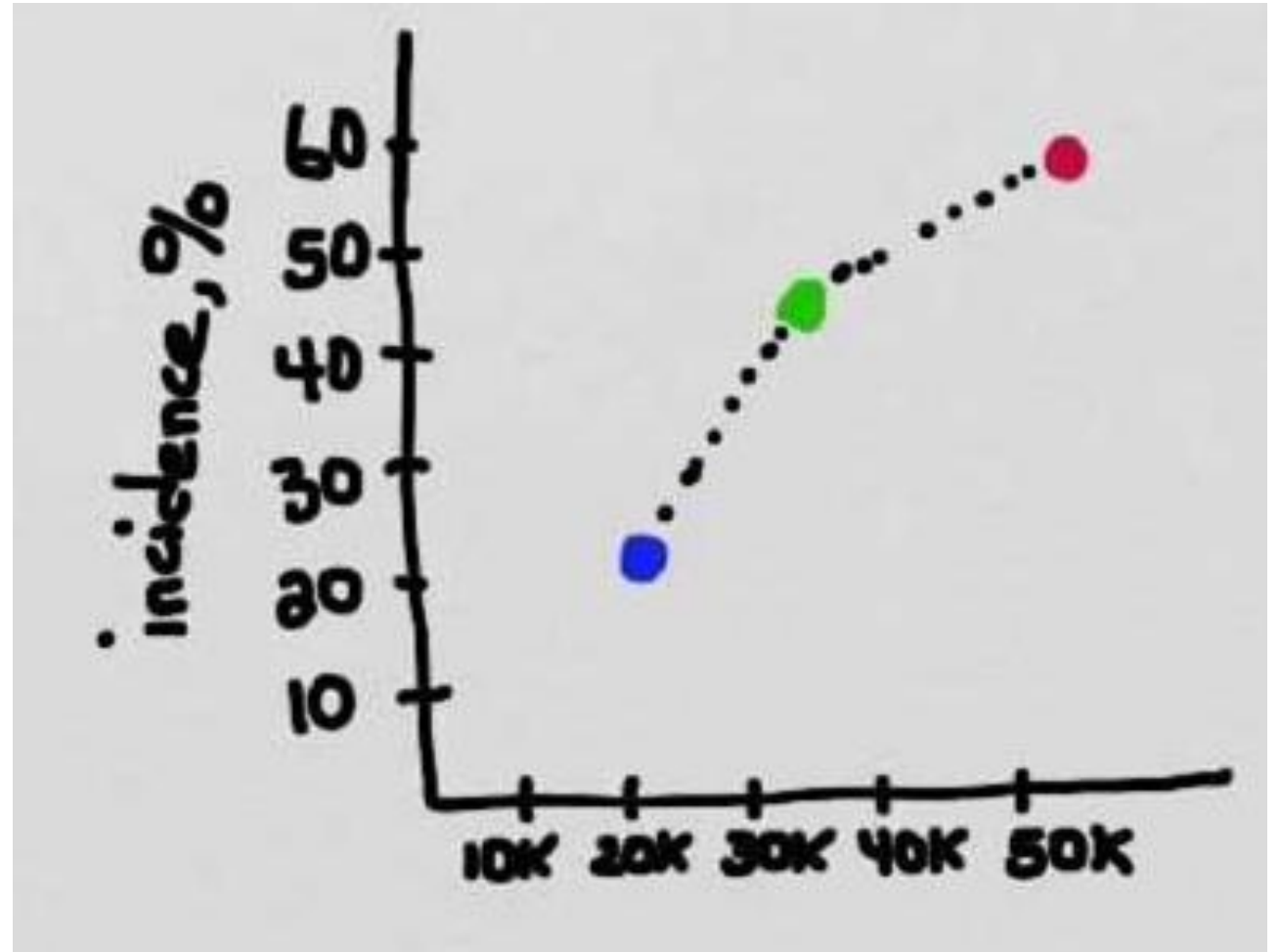


Taxonomical analysis: Group based analyses

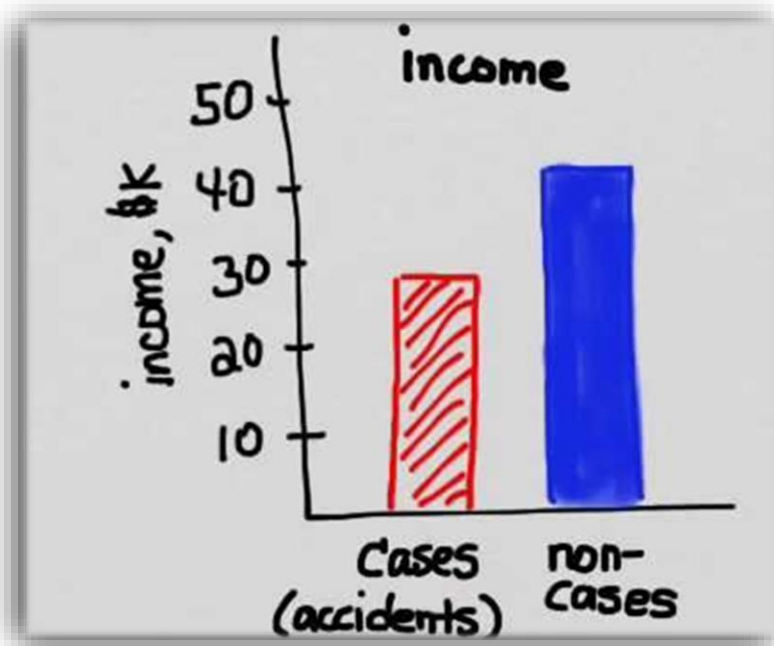
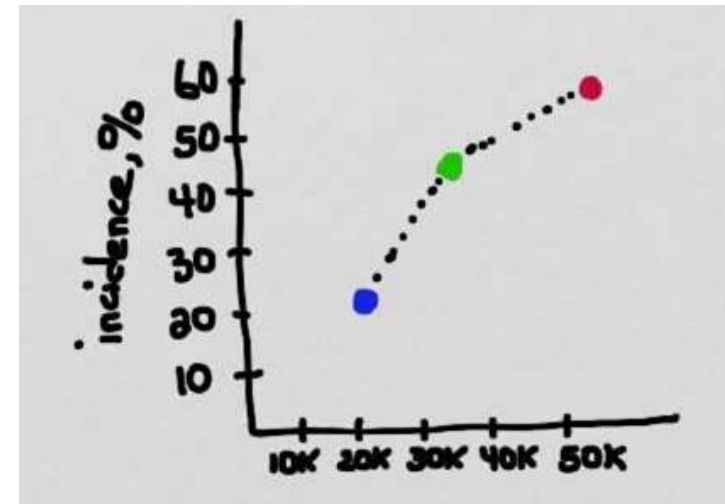
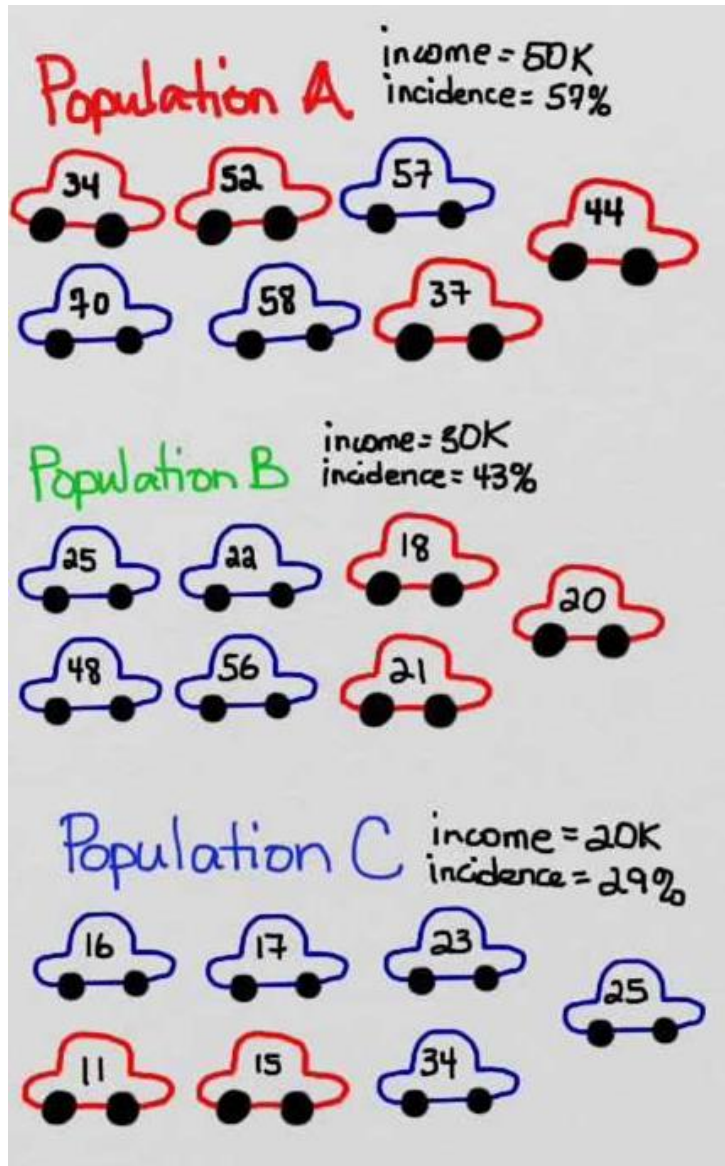
Population A income = 50K
incidence = 57%

Population B income = 30K
incidence = 43%

Population C income = 20K
incidence = 29%



Ecological fallacy: Group based analyses



Reverse causal reasoning

SOMEDAY, I WANT TO
GET MARRIED BECAUSE
STUDIES SHOW THAT
MARRIED PEOPLE ARE
HAPPIER.



Dilbert.com DilbertCartoonist@gmail.com

A SMARTER
INTERPRETATION IS
THAT NO ONE WANTS
TO MARRY AN
UNHAPPY PERSON.



2-10-12 © 2012 Scott Adams, Inc. /Dist. by Universal Uclick

YOU'RE
ANNOY-
ING.



WITH ANY
LUCK, YOUR
SOUL MATE
WON'T BE
PERCEPTIVE.



Choosing the correct transformation

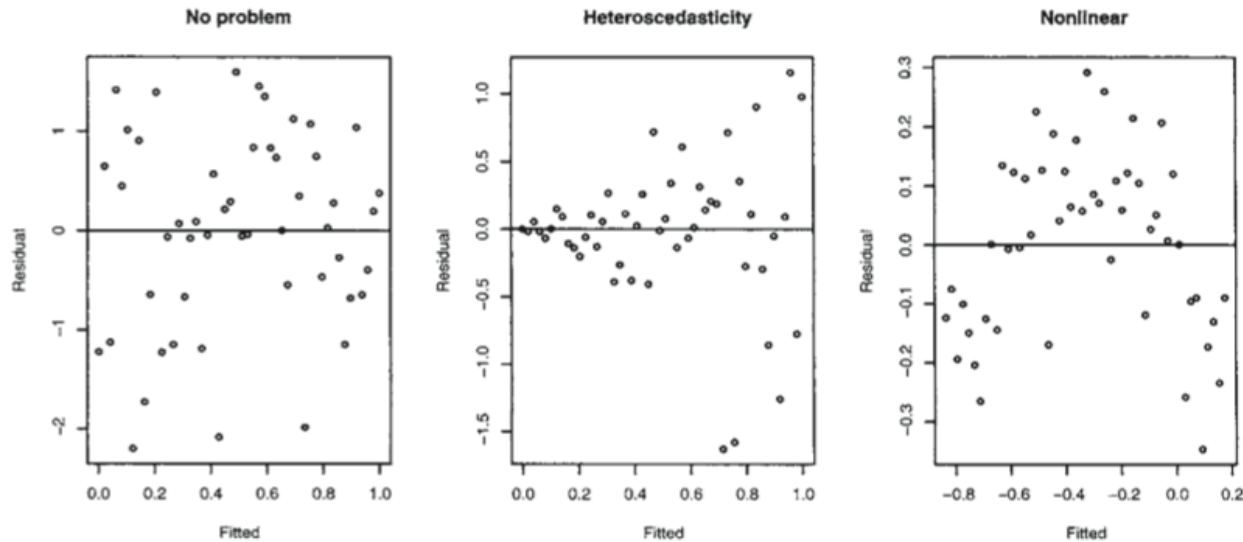
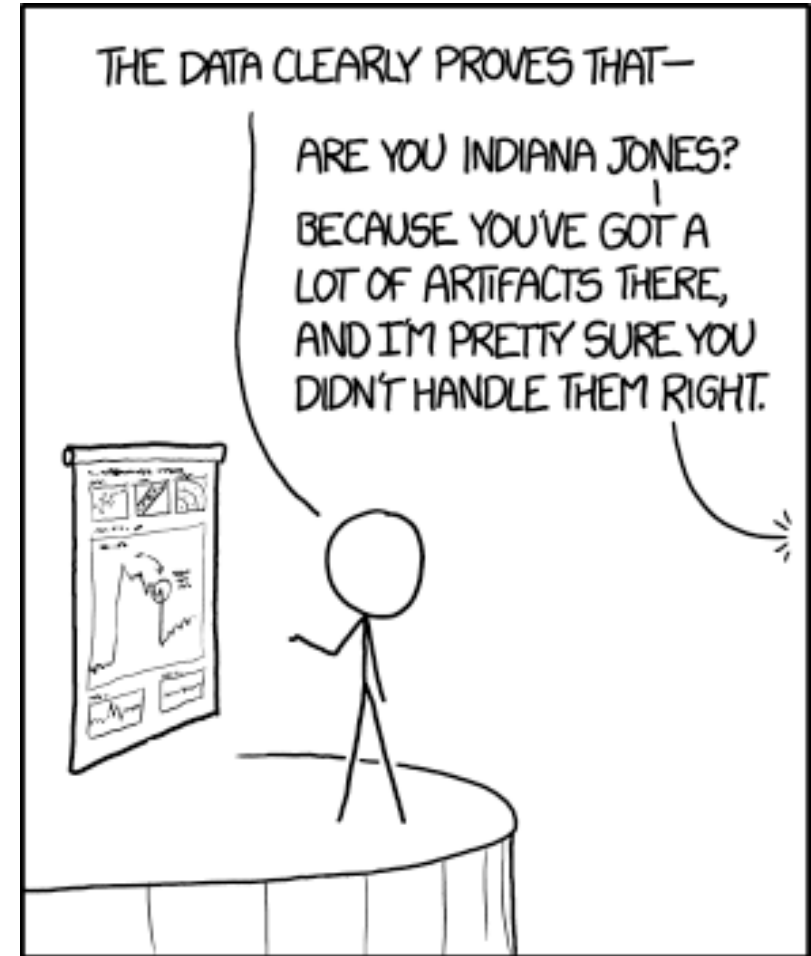


Figure 4.1 *Residuals vs. fitted plots—the first suggests no change to the current model while the second shows nonconstant variance and the third indicates some nonlinearity, which should prompt some change in the structural form of the model.*



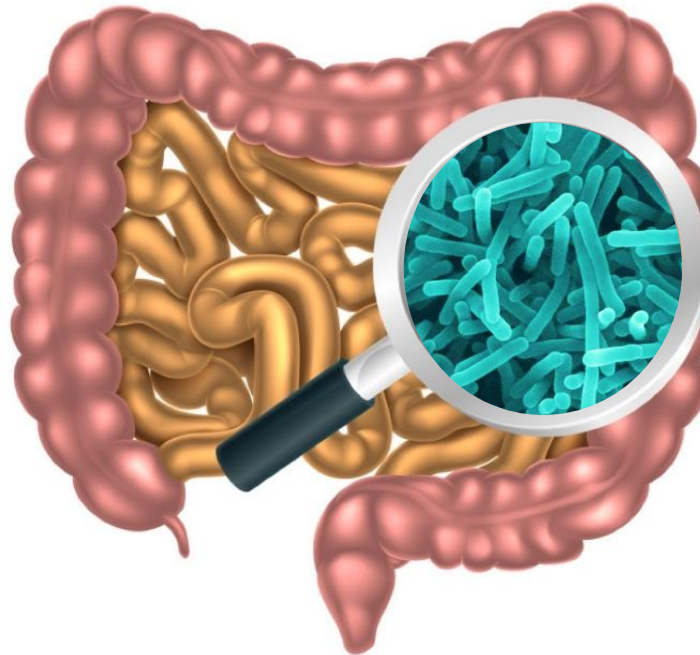
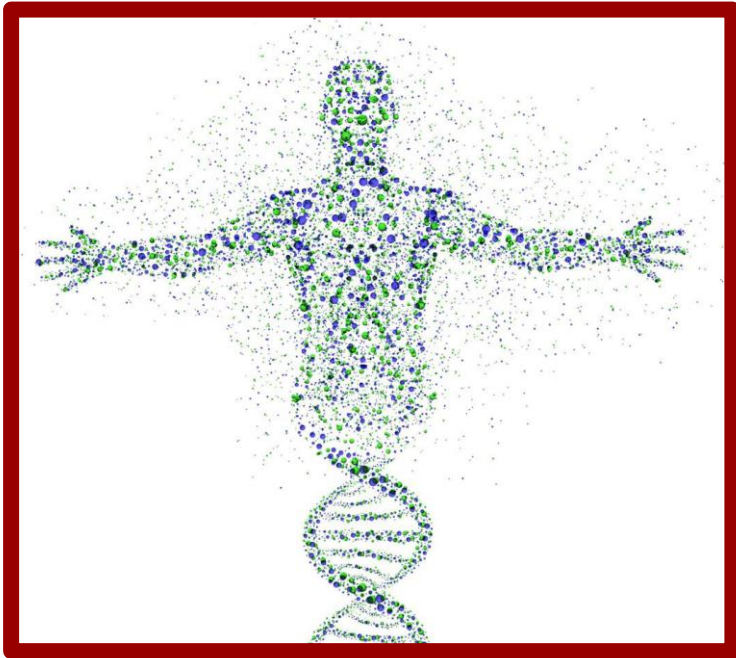
How can we measure and interpret GM?

- As no “gold standard” methods are still available yet for the analysis of microbiome, there is a lot of flexibility in the methods to be used. However, you need to be conscious of the pros/contras of this decision.
- New methodologies will surely emerge as, in other fields, the advances to acquire more and better data are going faster than the development of analysis algorithms. Therefore, in such an emergent field you need to update yourself constantly to keep in the cutting-edge loop

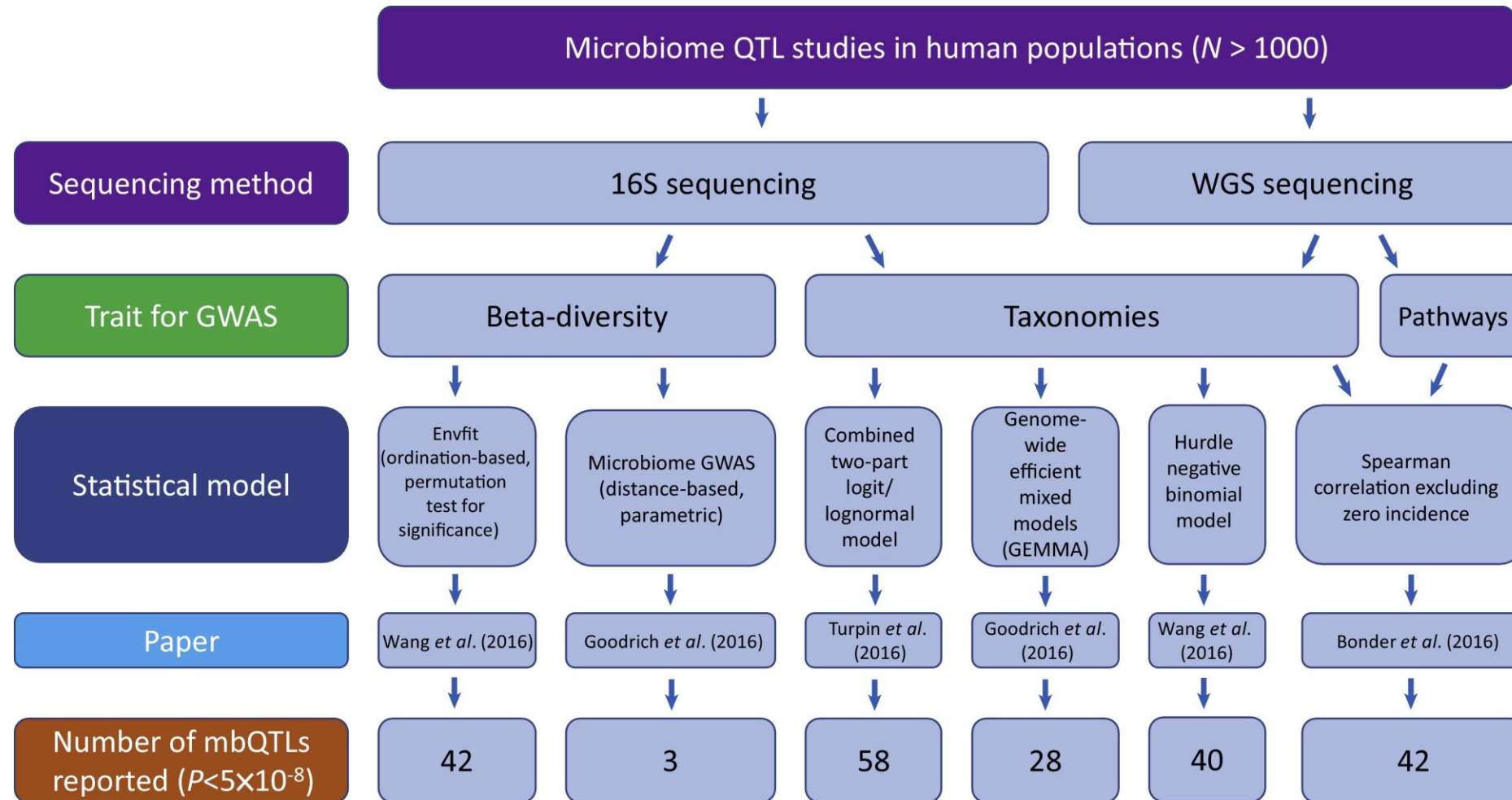
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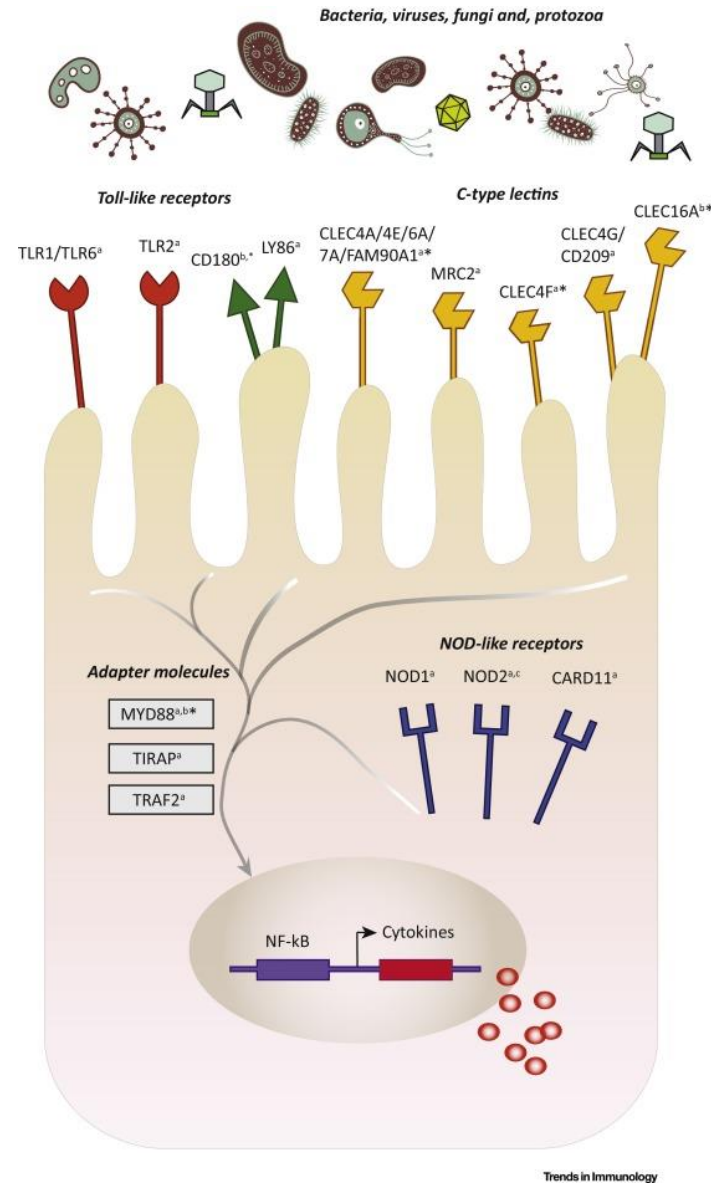
Influences on Gut Microbial Composition



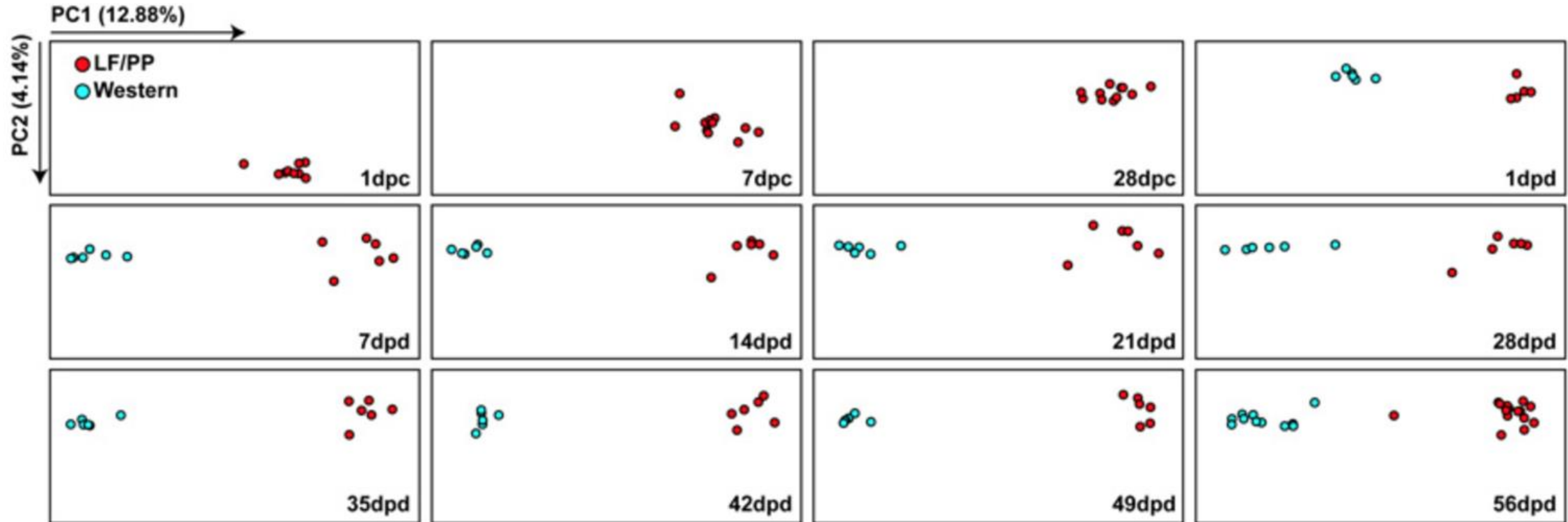
Main Driver: Diet or Genetics?



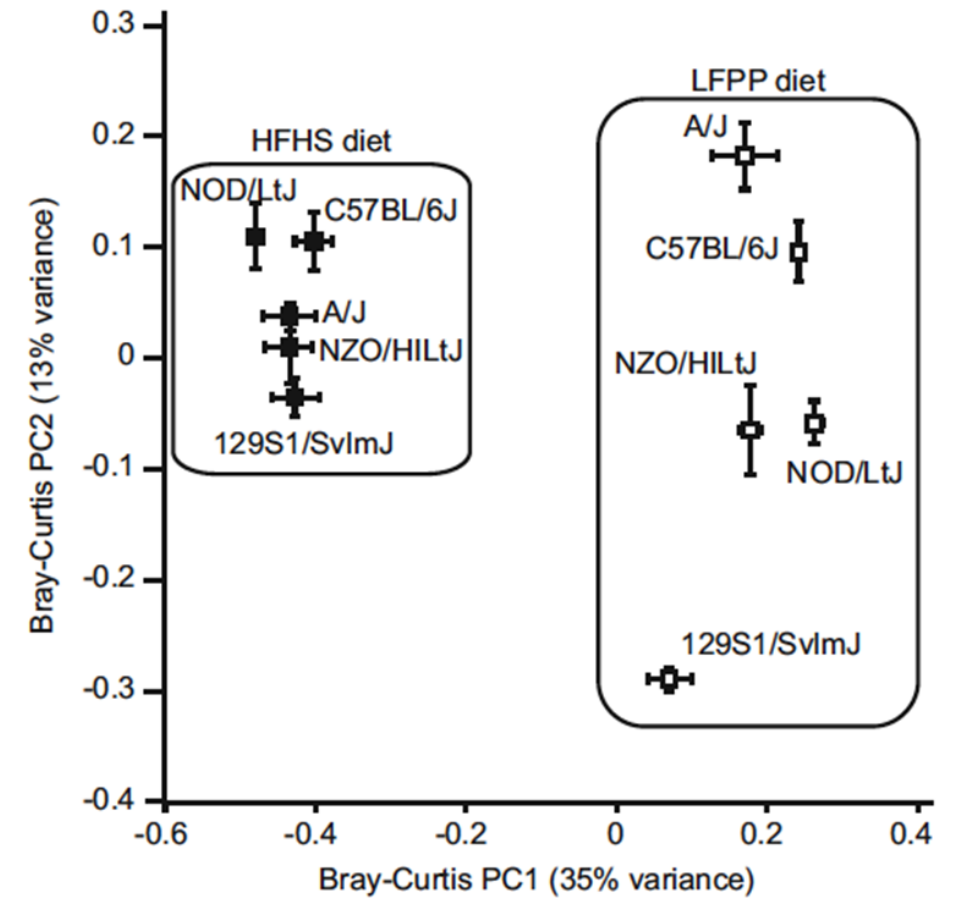
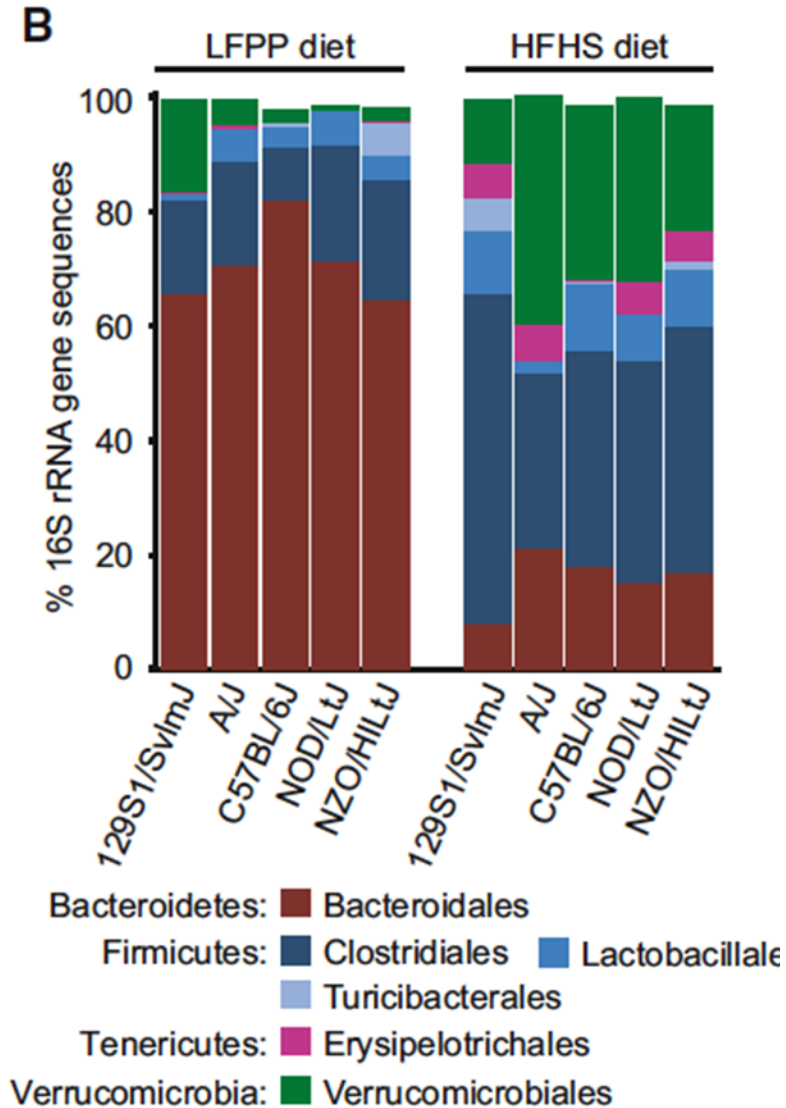
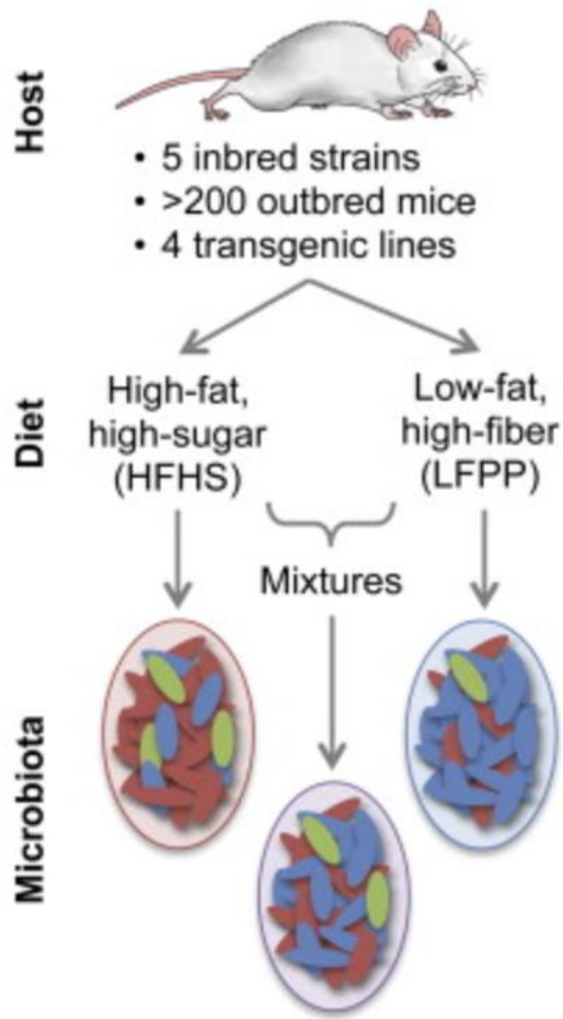
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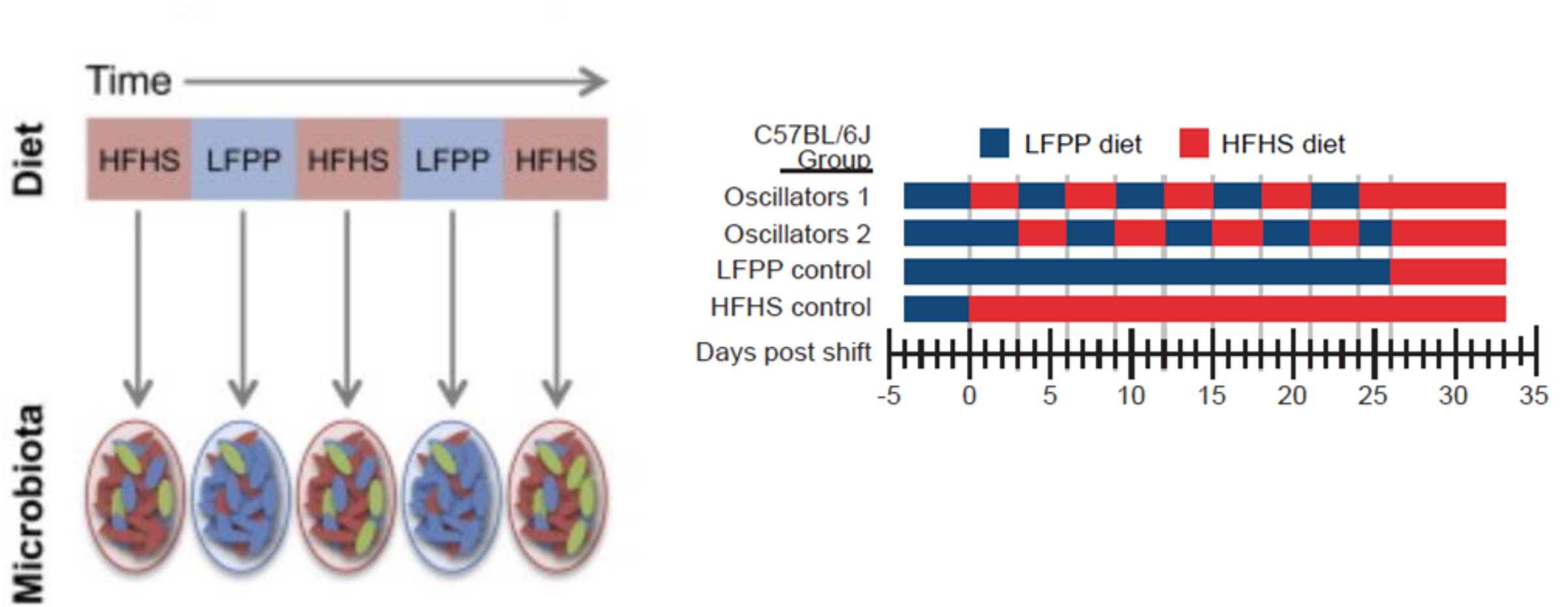
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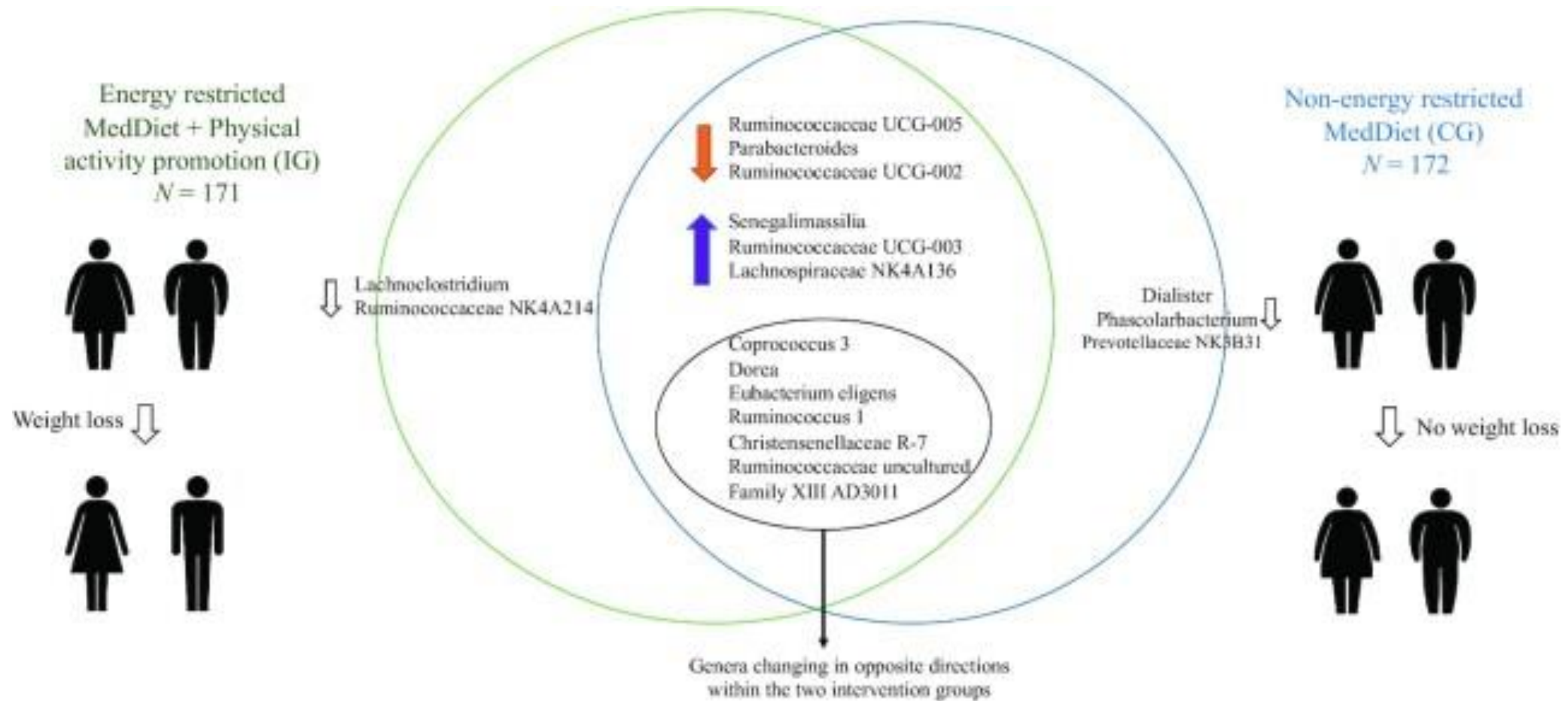
Diet vs Host Genotype



Responsiveness to Shifts in Diet

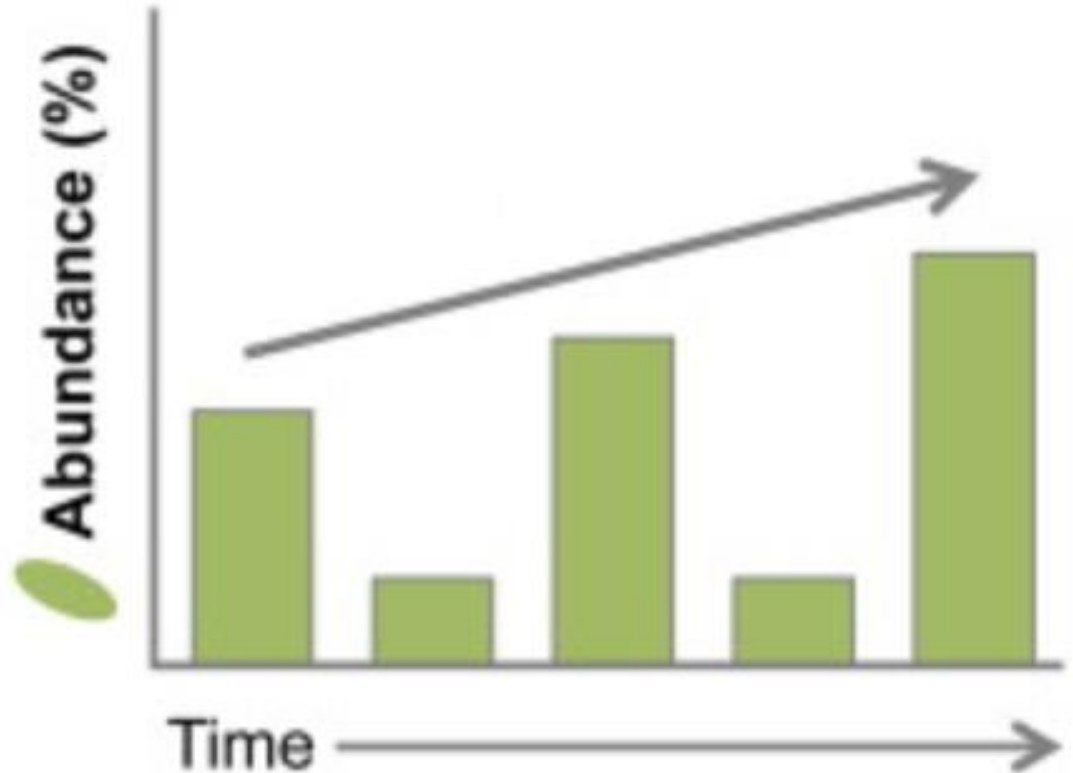


Responsiveness to Shifts in Diet



Memory Associated with Past Diets

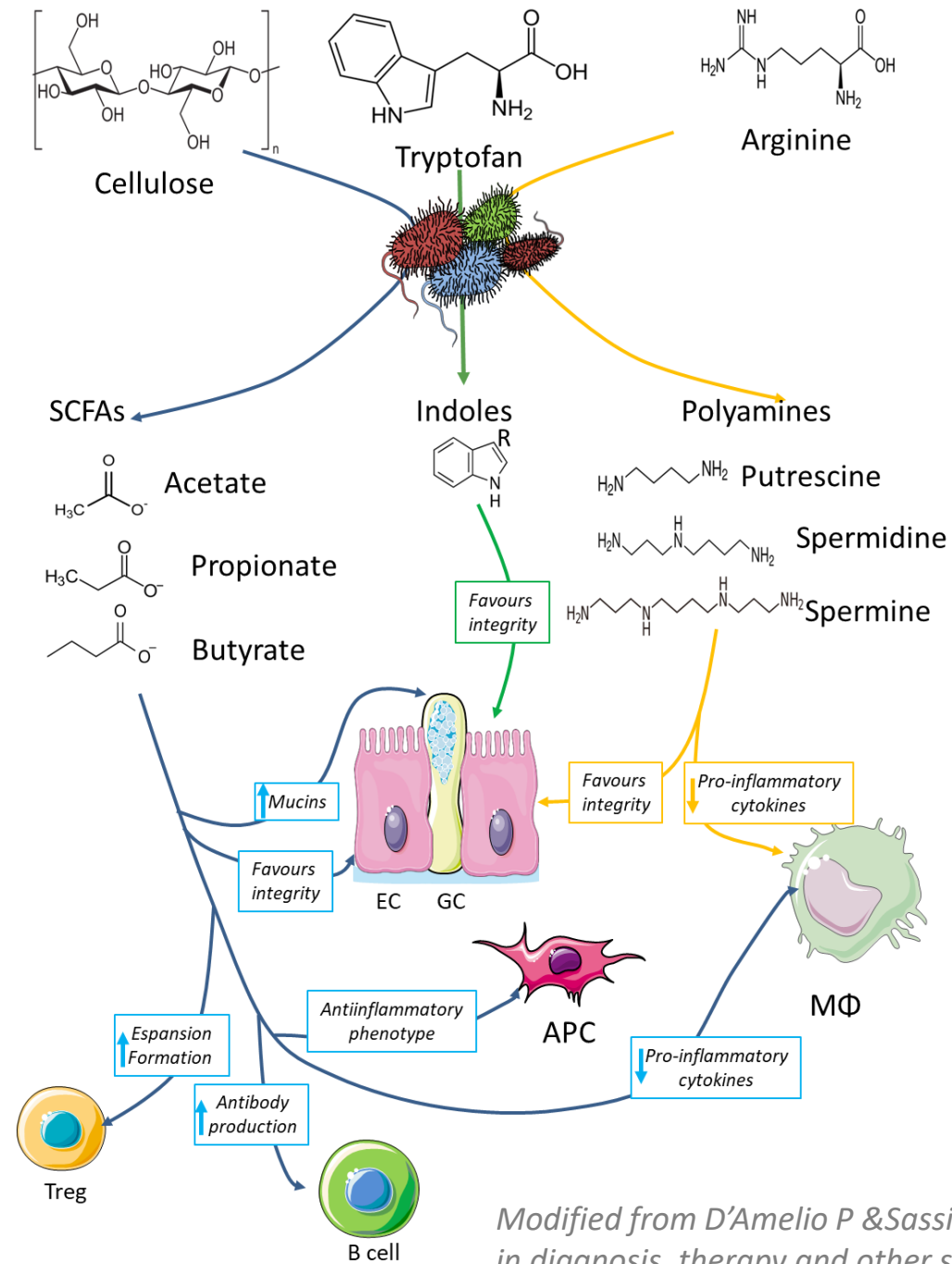
- Oscillation of number dependent or stable abundances for OTUs
- Determination of “microbial memory”



Agenda

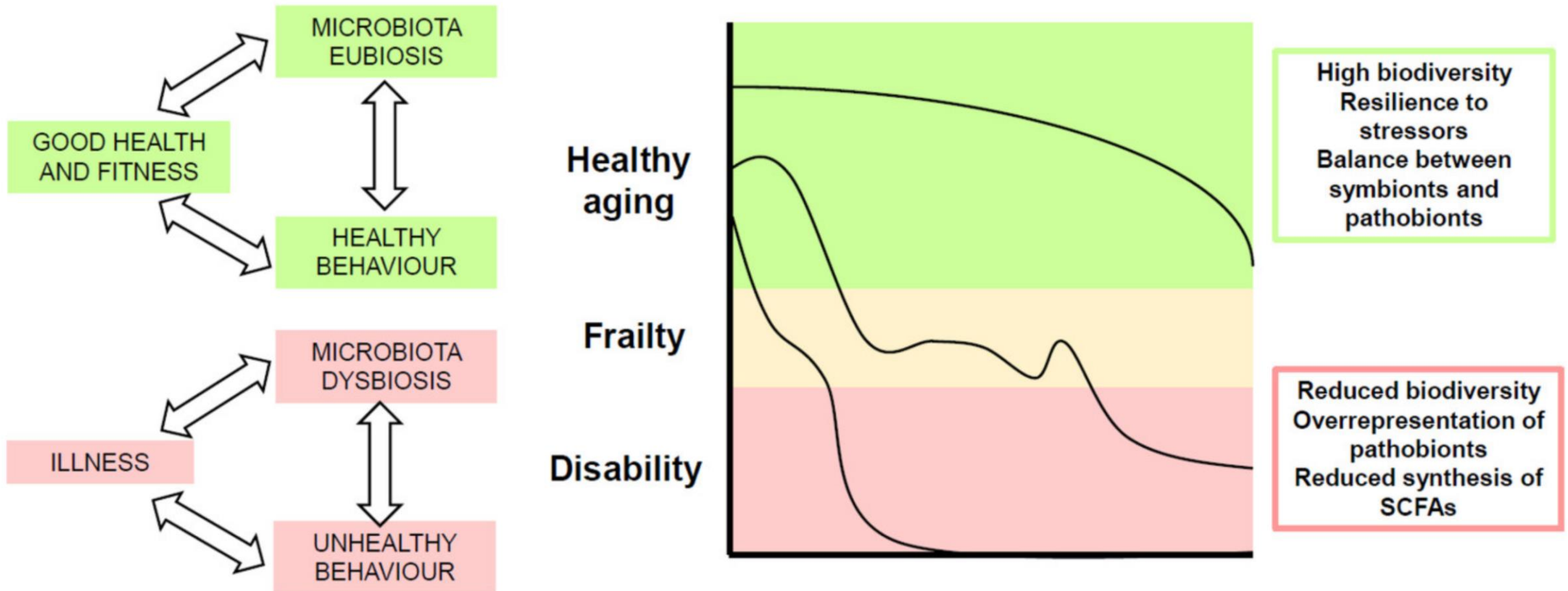
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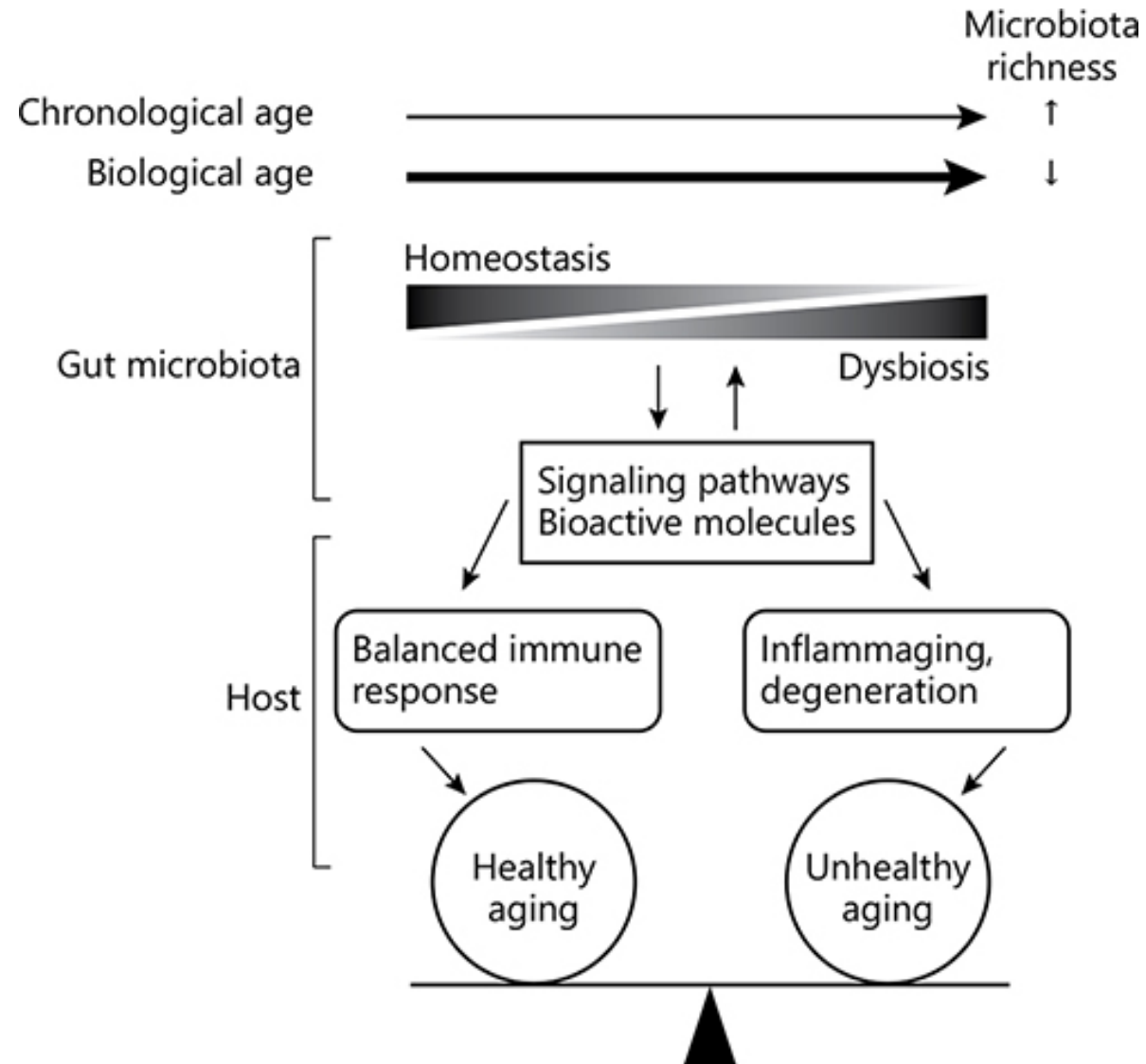


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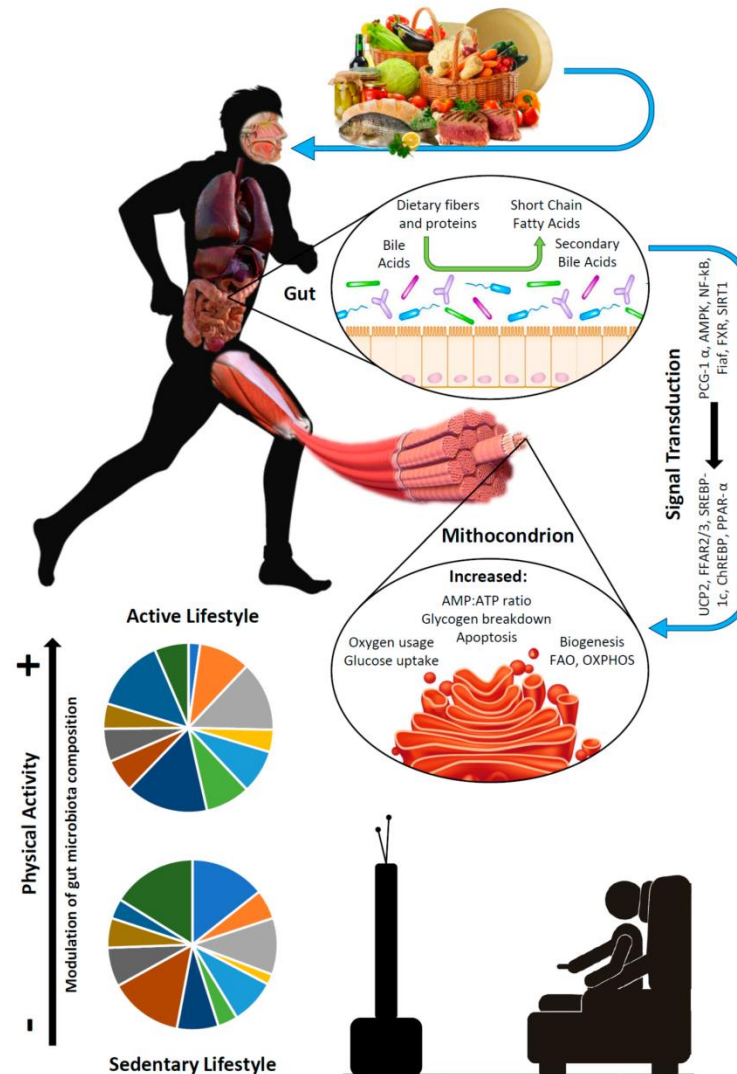
GM in aging: is there a role in frailty?



GM in aging: is there a role in frailty?



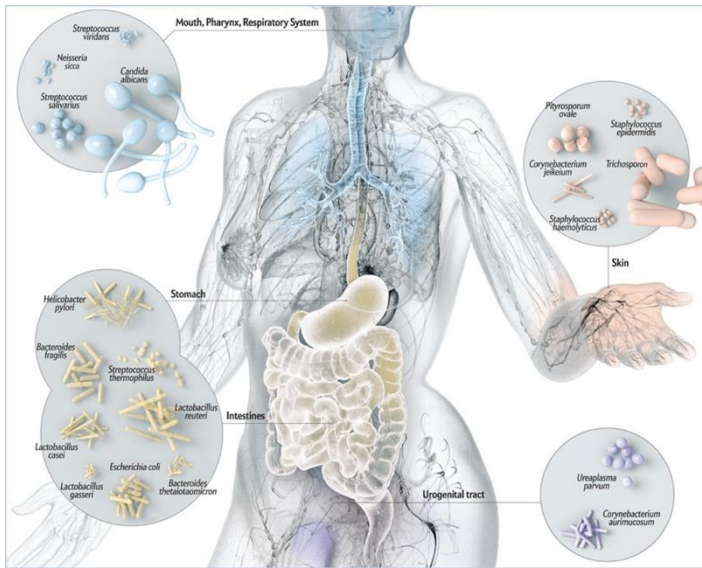
Aging Gut Microbiota at the Cross-Road between Nutrition, Physical Frailty, and inflammation



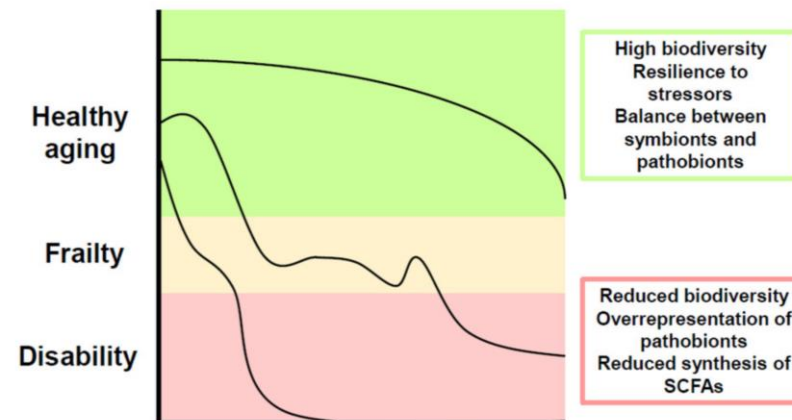
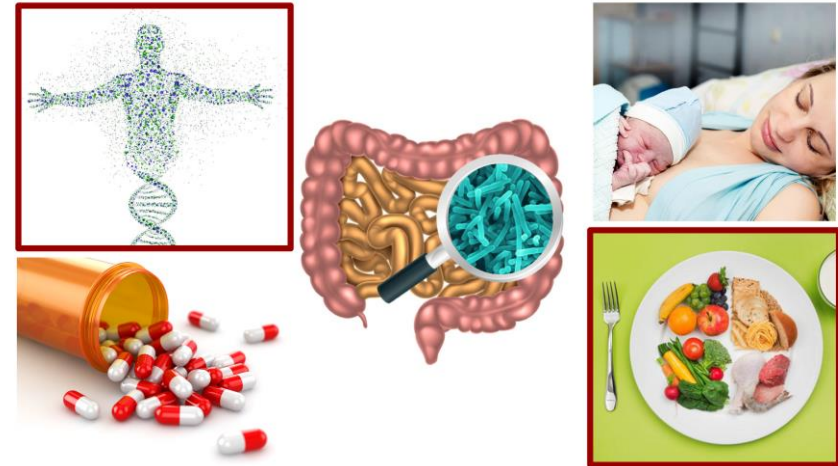
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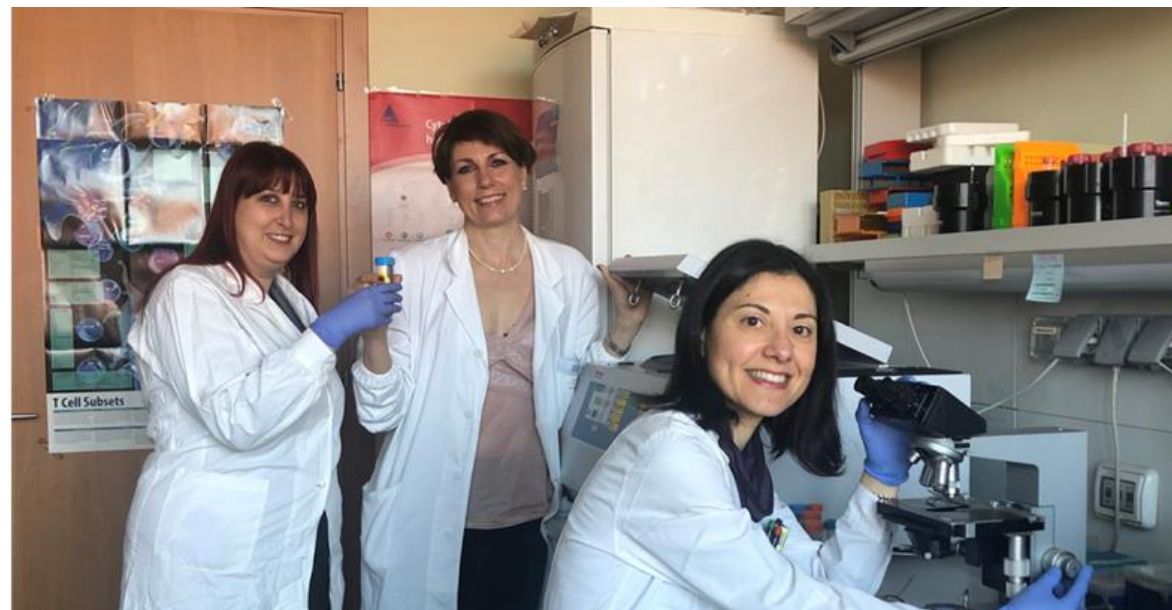
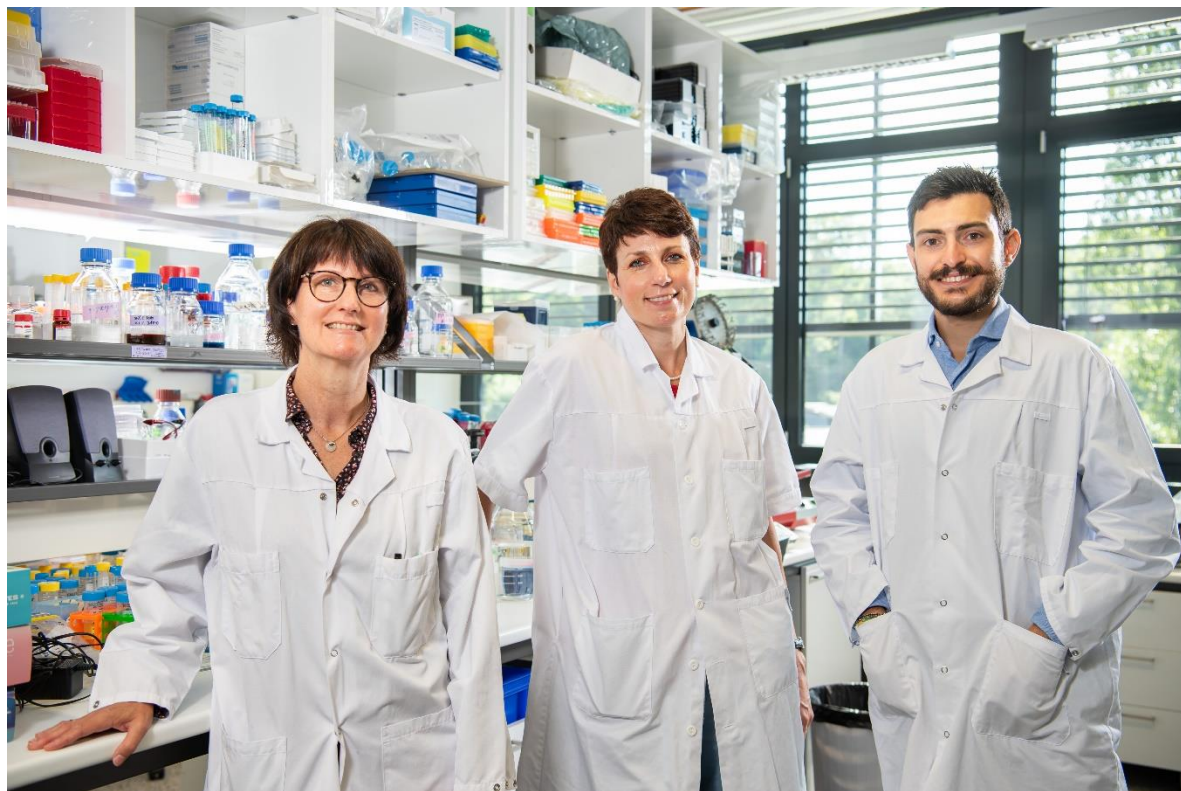




Thank you!



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