

Person-to-person transmission of the gut microbiome

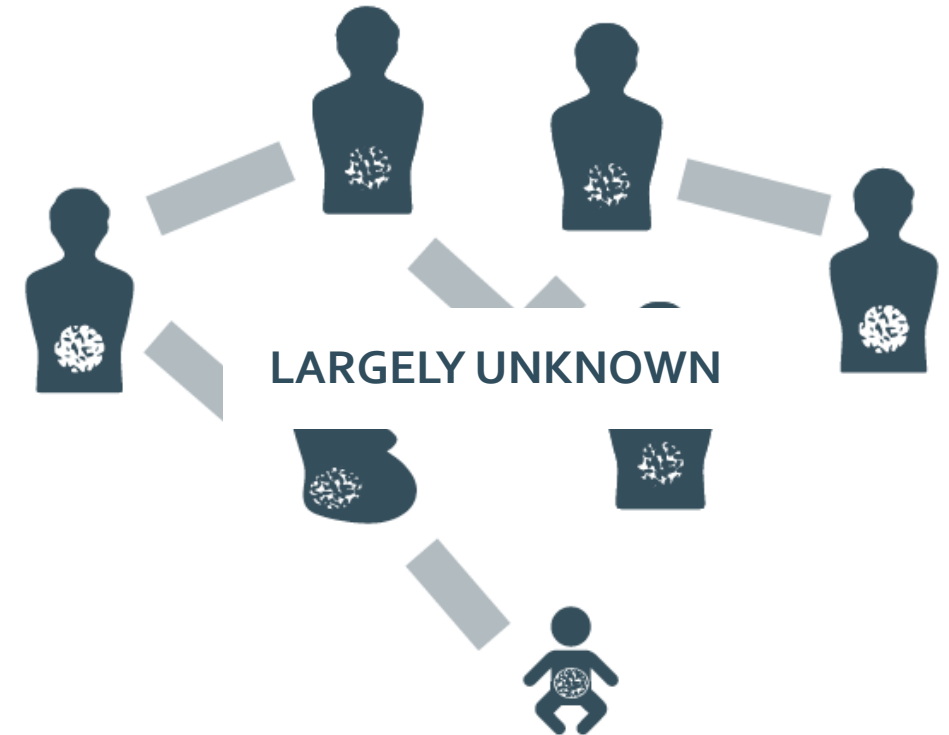
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Transmission of the human microbiome

- Known **role** of the human microbiome in **maintaining host health**
- Some knowledge on **what factors modulate microbiome composition**
- How do we acquire such health- and disease-associated microorganisms?



How are they **transmitted** and **spread** in populations?

Importance of understanding microbiome transmission

- Fundamental question for microbiome research

HYPOTHESIS

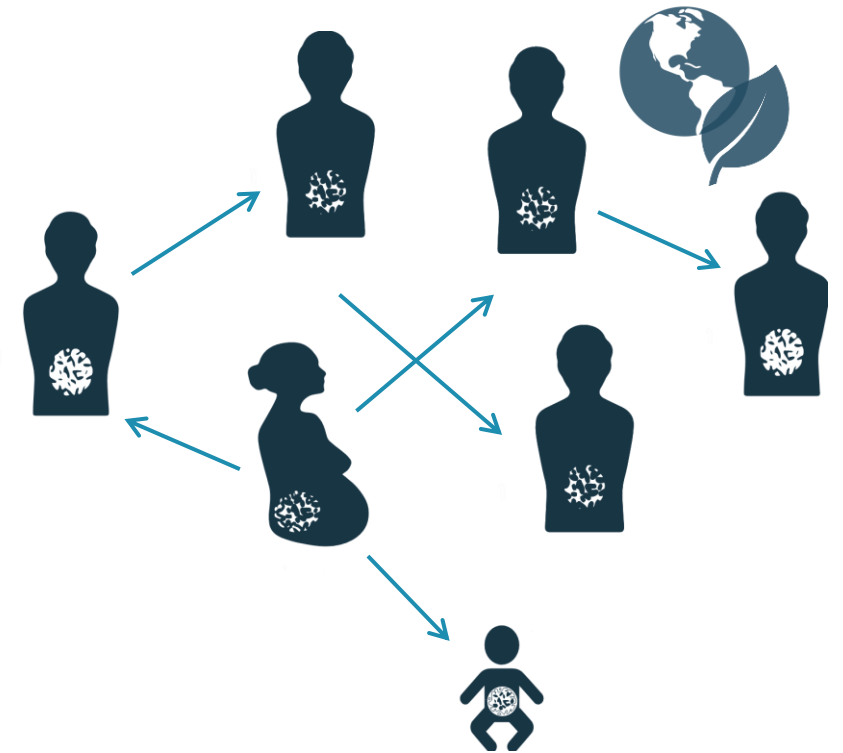
Science

Are noncommunicable diseases communicable?

Numerous noncommunicable diseases could have a transmissible microbial component

By B. B Finlay^{1,2} and CIFAR Humans

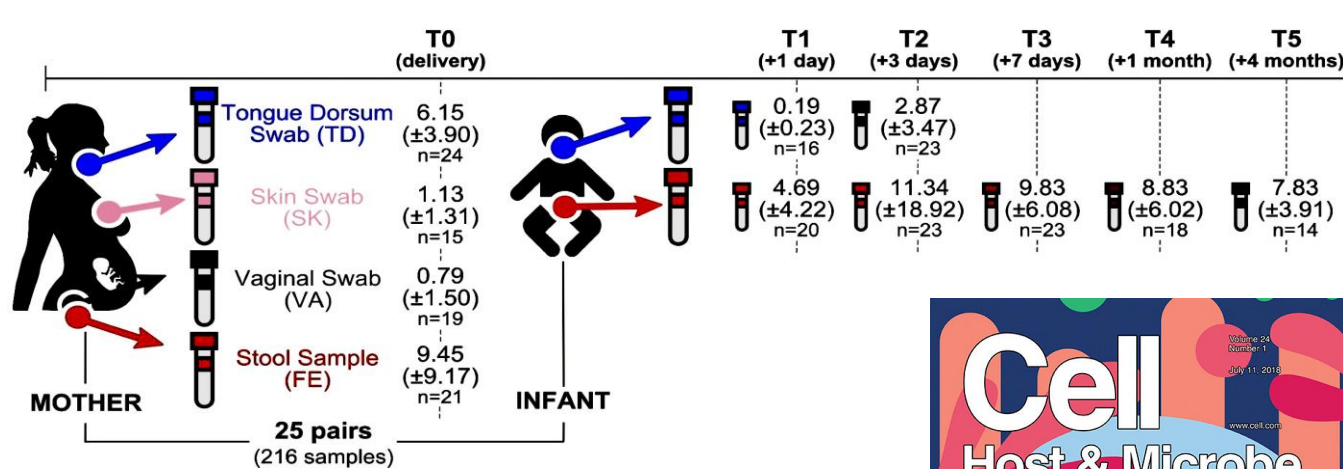
- Potential to alter transmission of health- and disease-associated microorganisms
- Improved microbiota modulations:
 - Timing: early life vs adulthood
 - Composition: specific strains



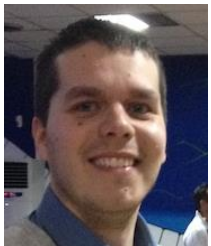
What do we know so far?

Vertical transmission

- First gut colonizers: **maternal microorganisms**, followed by microbial succession



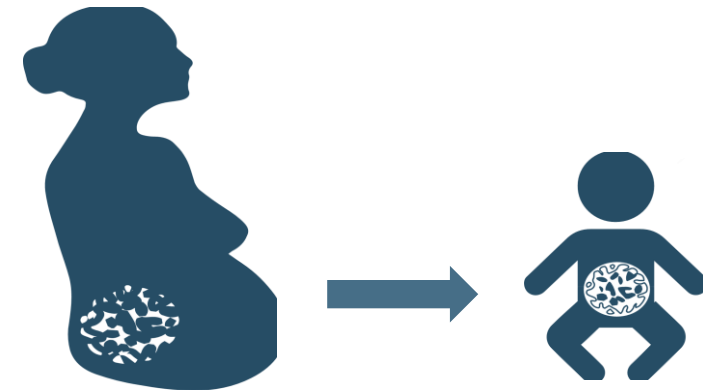
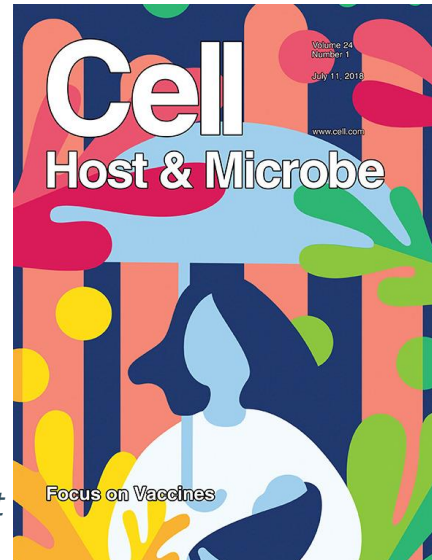
All numbers refer to the avg Gbases after pre-processing (±s.d.)



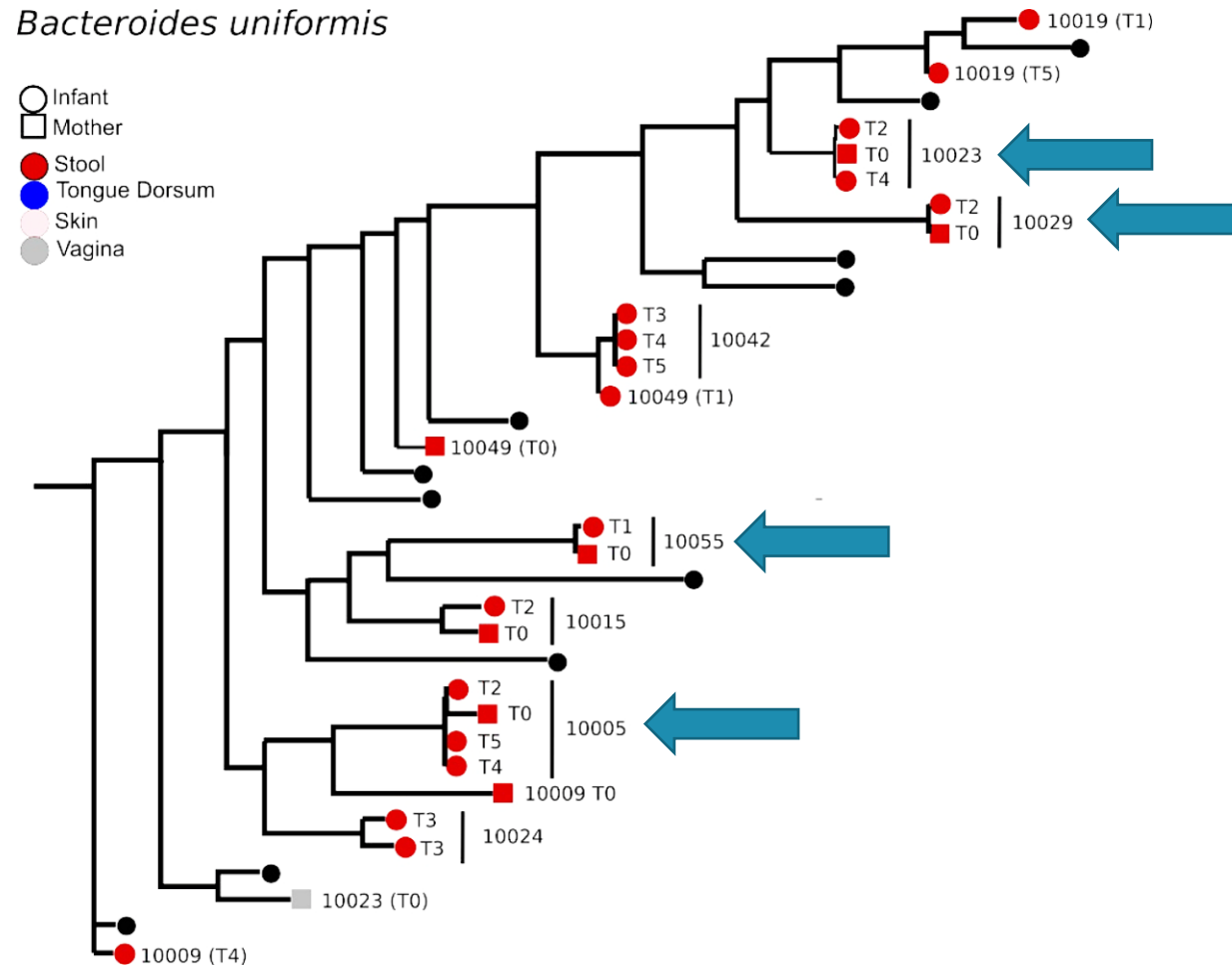
Asnicar, Manara et al, *mSystems* (2017)



Ferretti et al, *Cell Host and Microbe* (2018)



Strain-resolved metagenomics



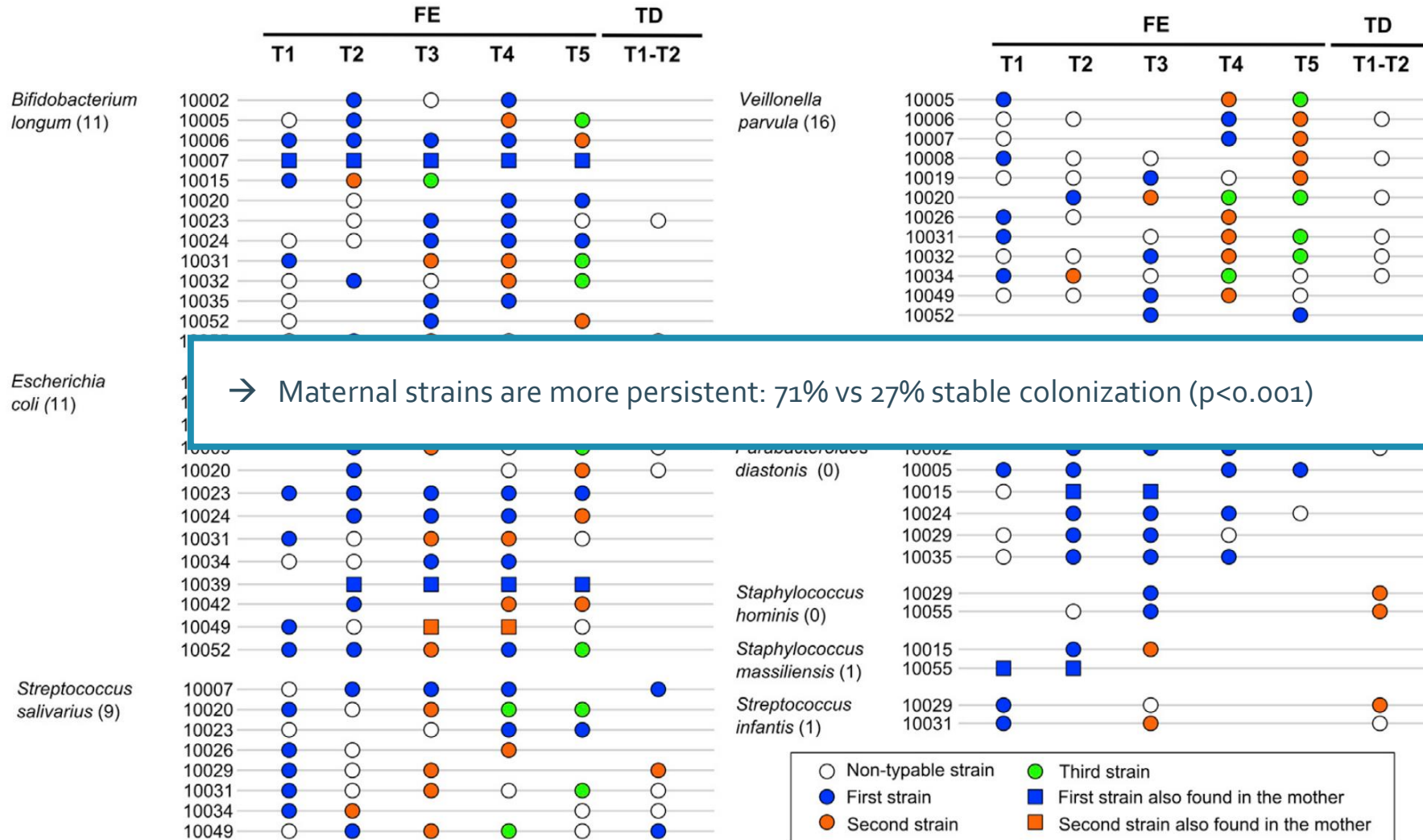
→ Advances in metagenomics:

Strain resolution in

shotgun metagenomic sequencing

to identify potential transmission events

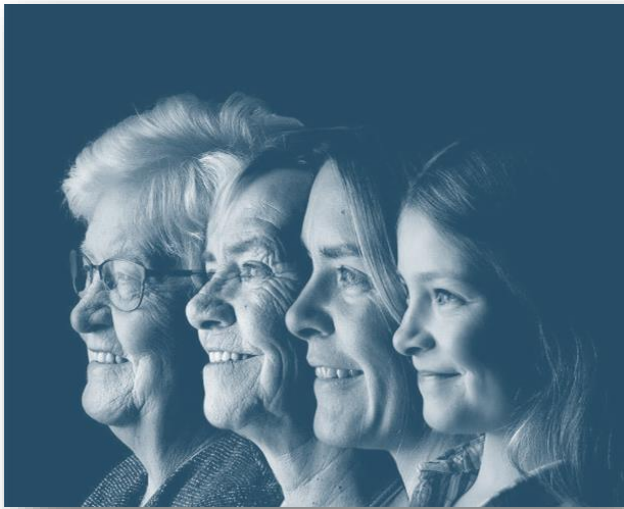
Maternally-transmitted strains are more persistent



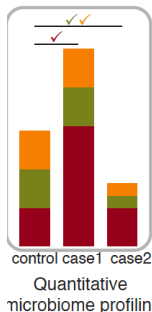
→ But maternal transmission is unlikely to account for all diversity found in adults

Does transmission also occur across multiple familial generations?

A multigenerational family cohort



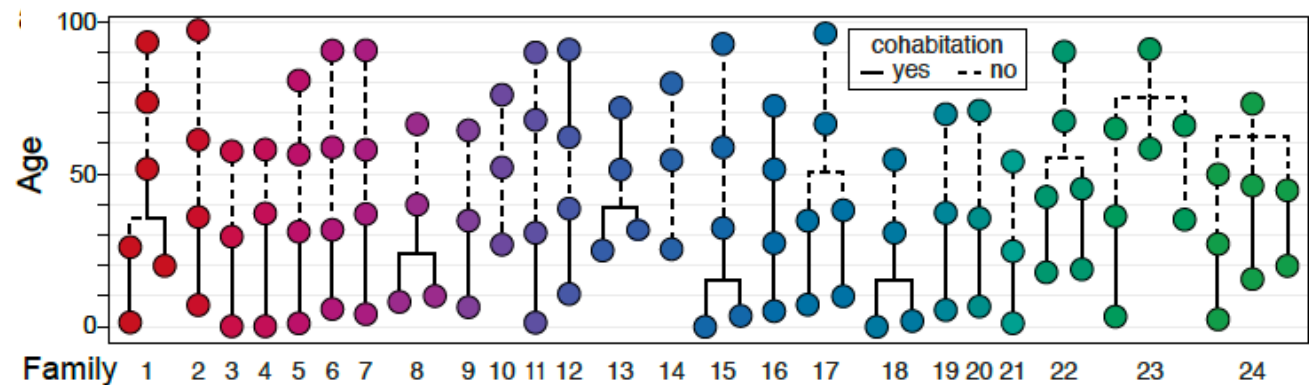
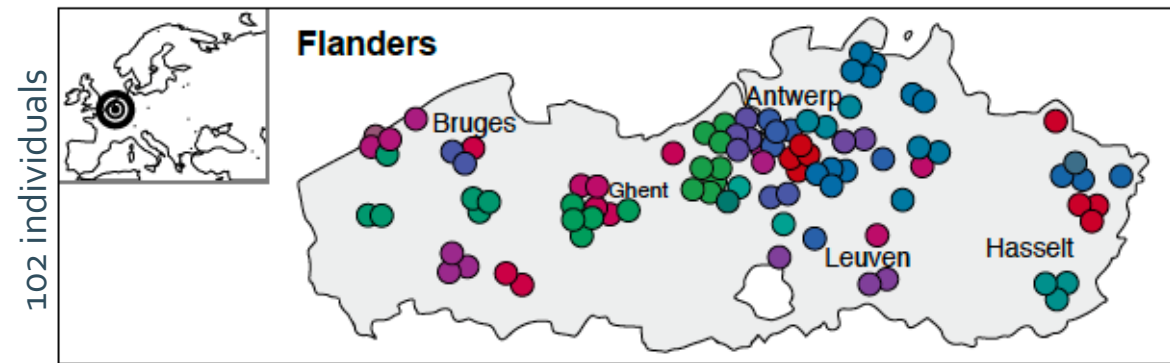
- 24 families
- [3:5] generations of women
- [0:98] years old



Shotgun sequencing + flow cytometry (QMP)

Vandeputte *et al*, *Nature* (2017)

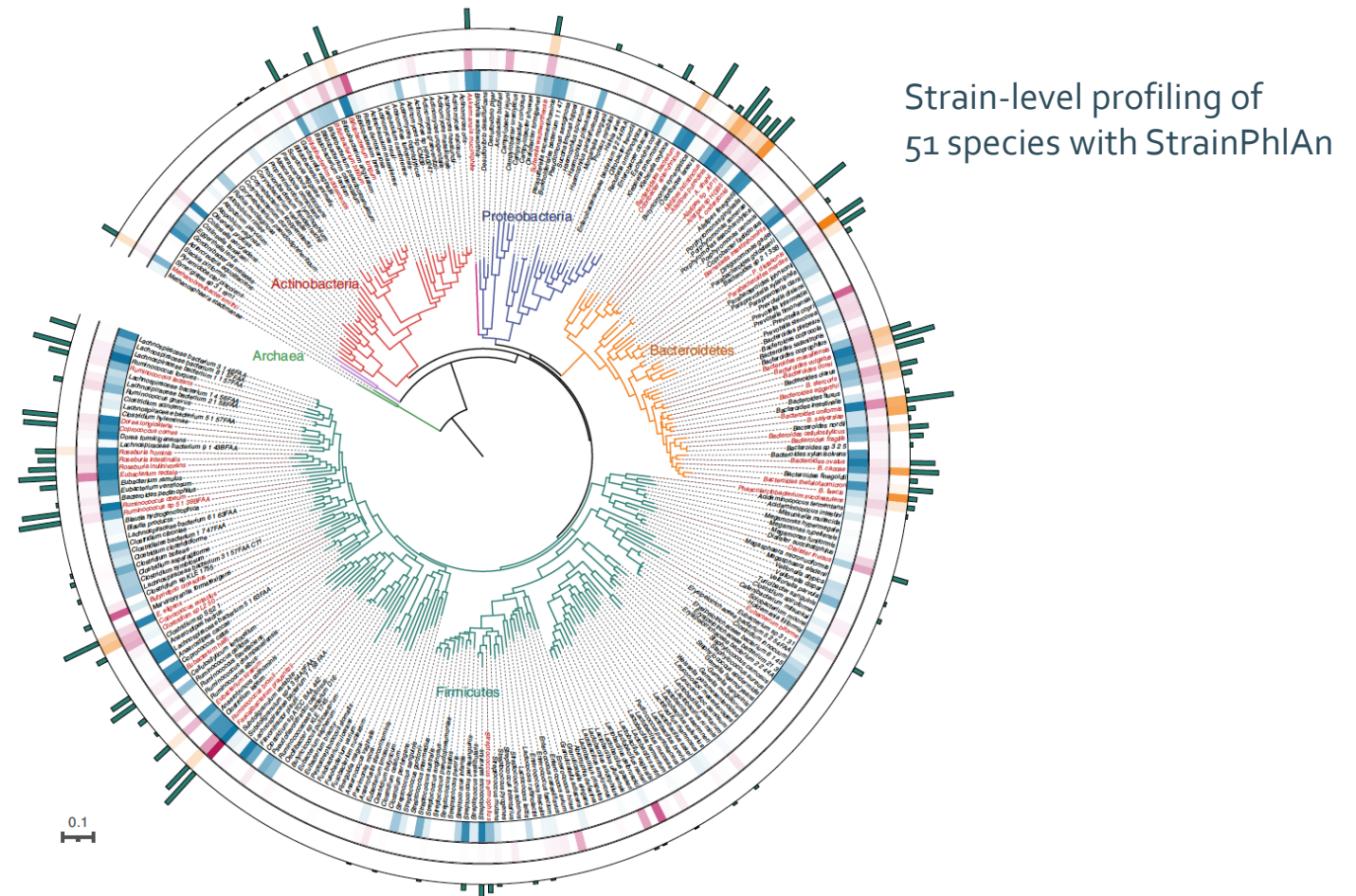
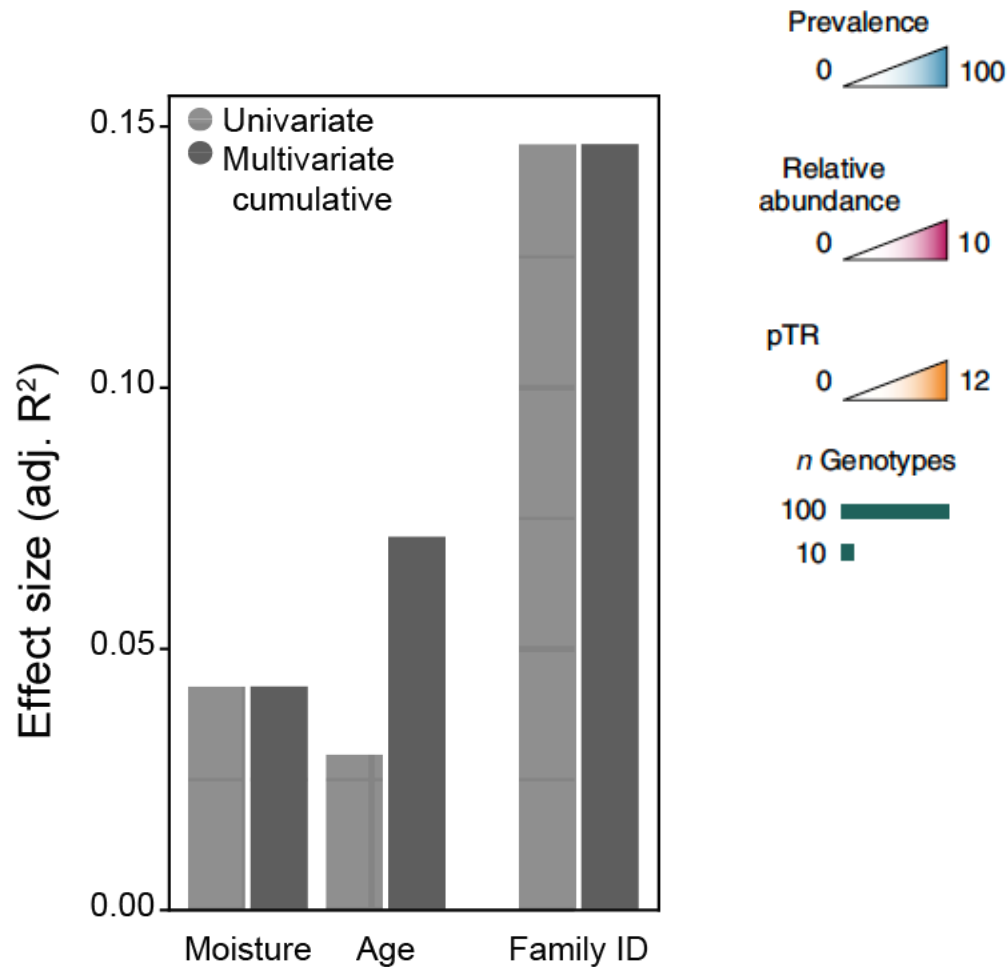
Vieira-Silva *et al*, *Nature Microbiology* (2019)



Valles-Colomer M*, Bacigalupe R* *et al*, *Nature Microbiology* (2022)

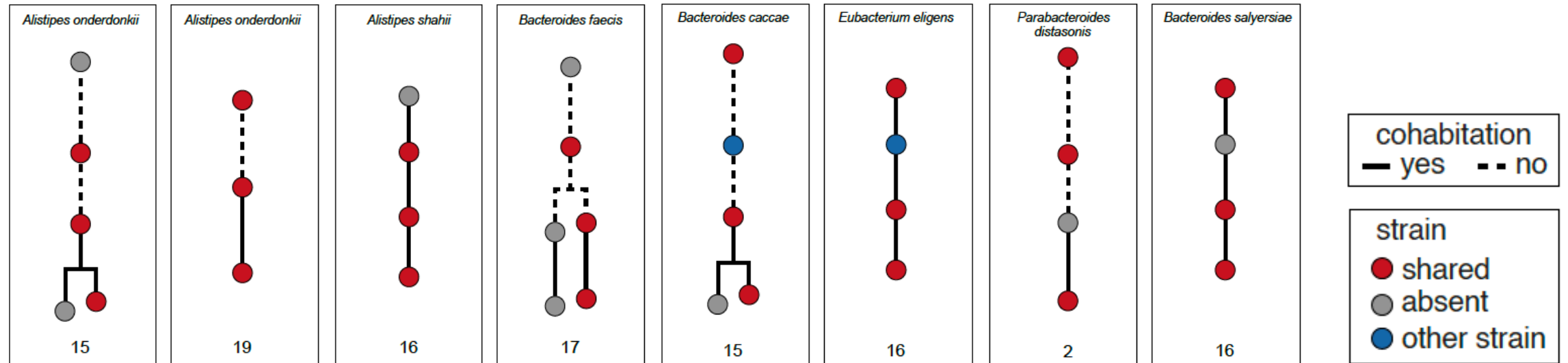
Does transmission also occur across multiple familial generations?

Strain-level profiling



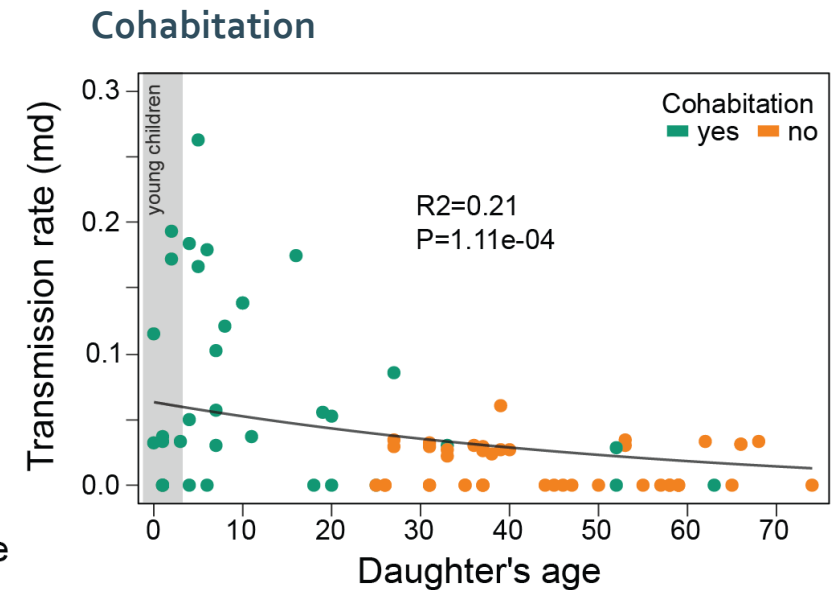
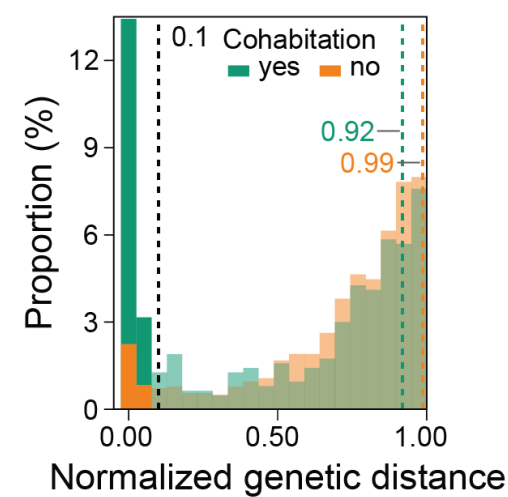
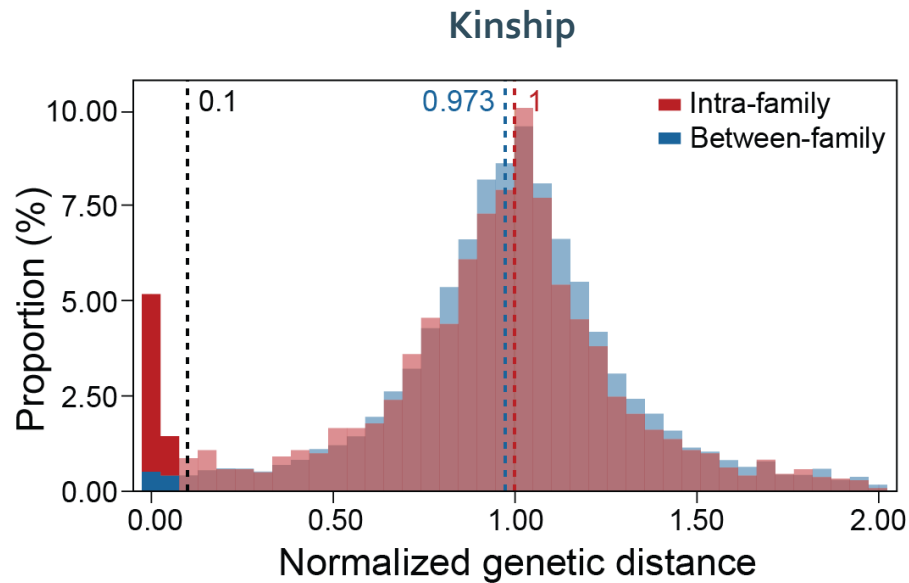
Does transmission also occur across multiple familial generations?

Not frequently, but it does!



Does transmission also occur across multiple familial generations?

But... is that vertical or horizontal transmission?



→ Both?

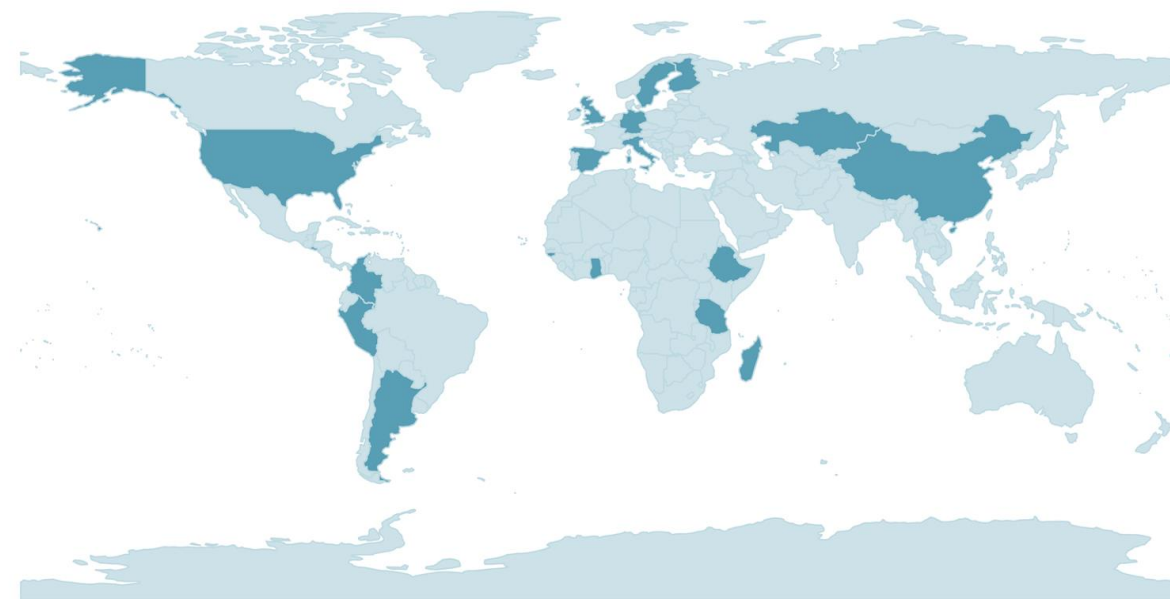
A large-scale study of microbiome transmission

StrainPhlAn 4 (Blanco-Miguez *et al* (2022), *bioRxiv*)

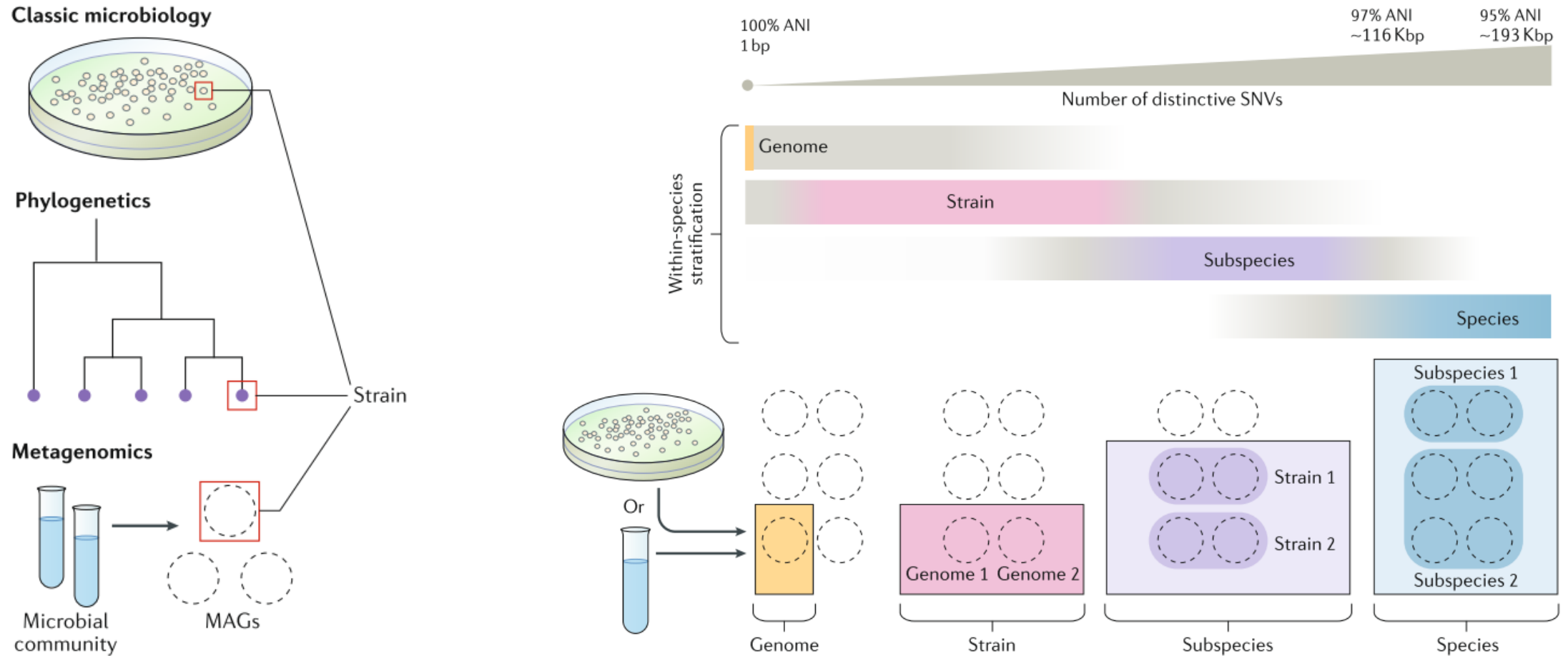
Gut 646 SGBs (365 uSGBs) ➤ 477,141 strains 55% of profiled species are so-far uncultured

9,715 samples [2,880 novel]
31 datasets
20 countries

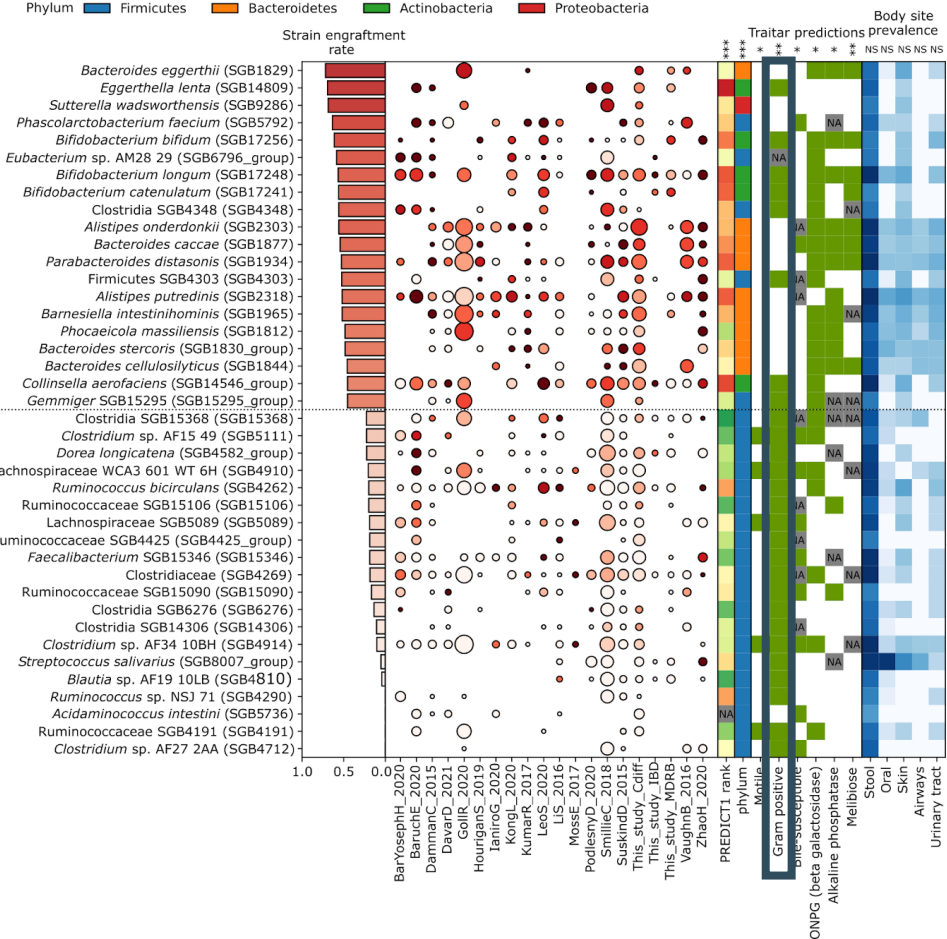
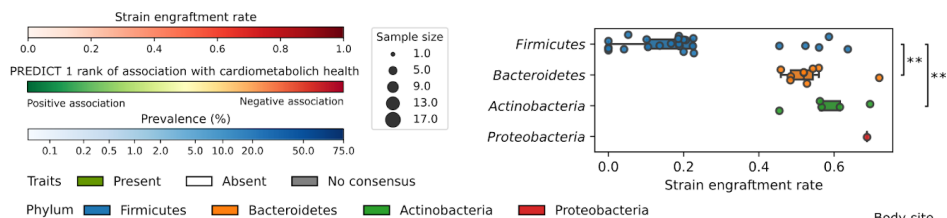
Longitudinal sets	Mother-offspring pairs
1,676 samples [0] 495 individuals [0] 5 datasets [0] 4 countries [0]	3,598 samples [619] 711 pairs [261] 18 datasets [8] 14 countries [3]
Households	Adult twins
1,123 samples [432] 211 households [70] 7 datasets [3] 8 countries [1]	1,734 samples [0] 712 pairs [0] 3 datasets [0] 1 country [0]



Using strains to infer transmission events



... and also strain engraftment upon FMT



- 1,255 metagenomic samples
- 203 FMT procedures (donor, recipient-pre, recipient-post)
- Any disease/condition

- Strain engraftment linked to FMT success
- Combined administration route for best performance
- Antibiotic pre-treatment
- Bacterial phenotypic characteristics
- Predictable (ML)

Take home messages

- Evidence of extensive **vertical** but also **horizontal** transmission of the microbiome
- Sharing an **environment** plays a key role (cohabitation)
- Microbiome transmission is not left to chance:
Dispersal specialists (with certain phenotypical properties) are transmitted more frequently

Thank you!

The Laboratory of Computational Metagenomics



<http://segatalab.cibio.unitn.it>

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