Metagenome-assembled genomes from a population-based cohort uncover novel gut species and strain diversity, revealing prevalent disease associations

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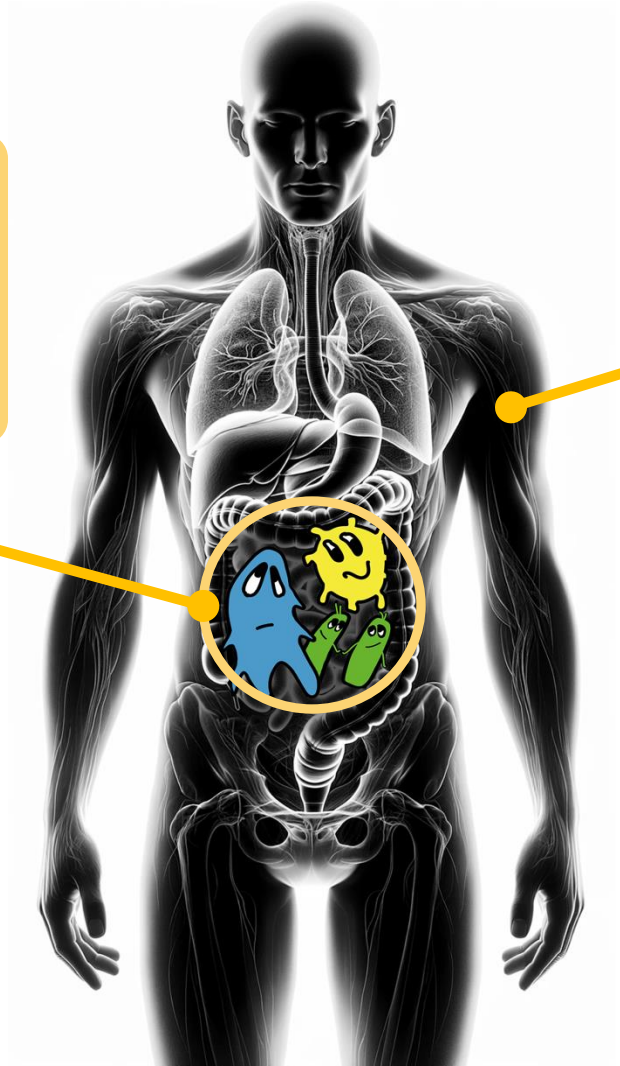
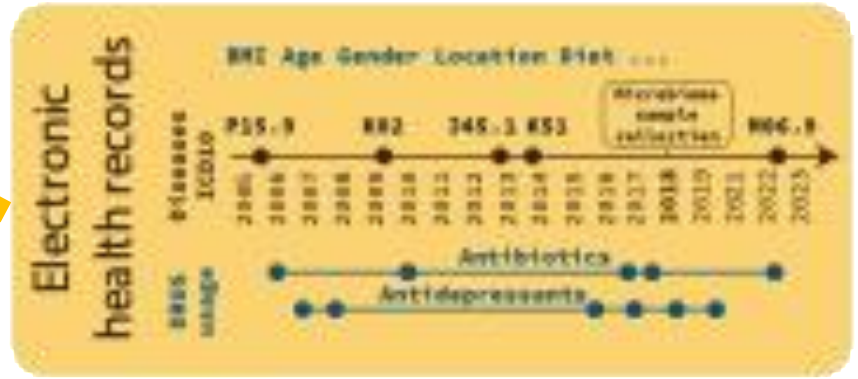
Estonian Microbiome Cohort

- 2,500 human gut microbiome samples
- 2nd TP for 332 samples





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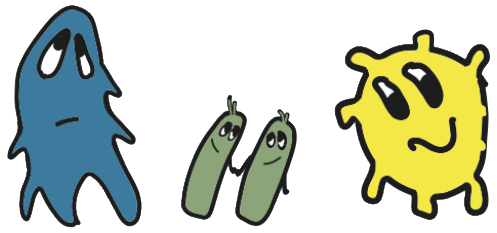

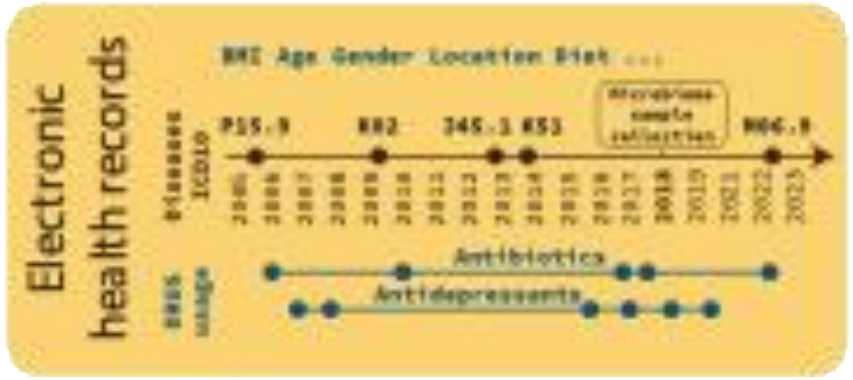

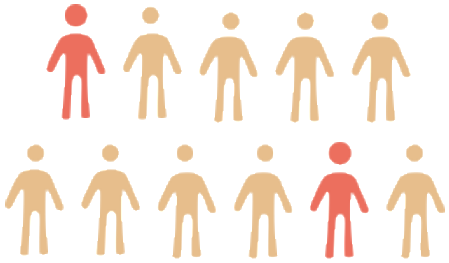

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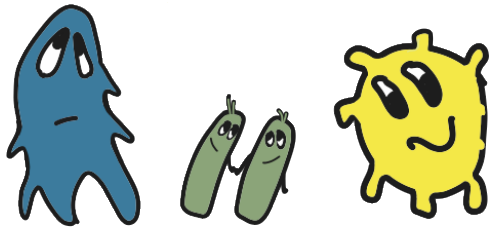
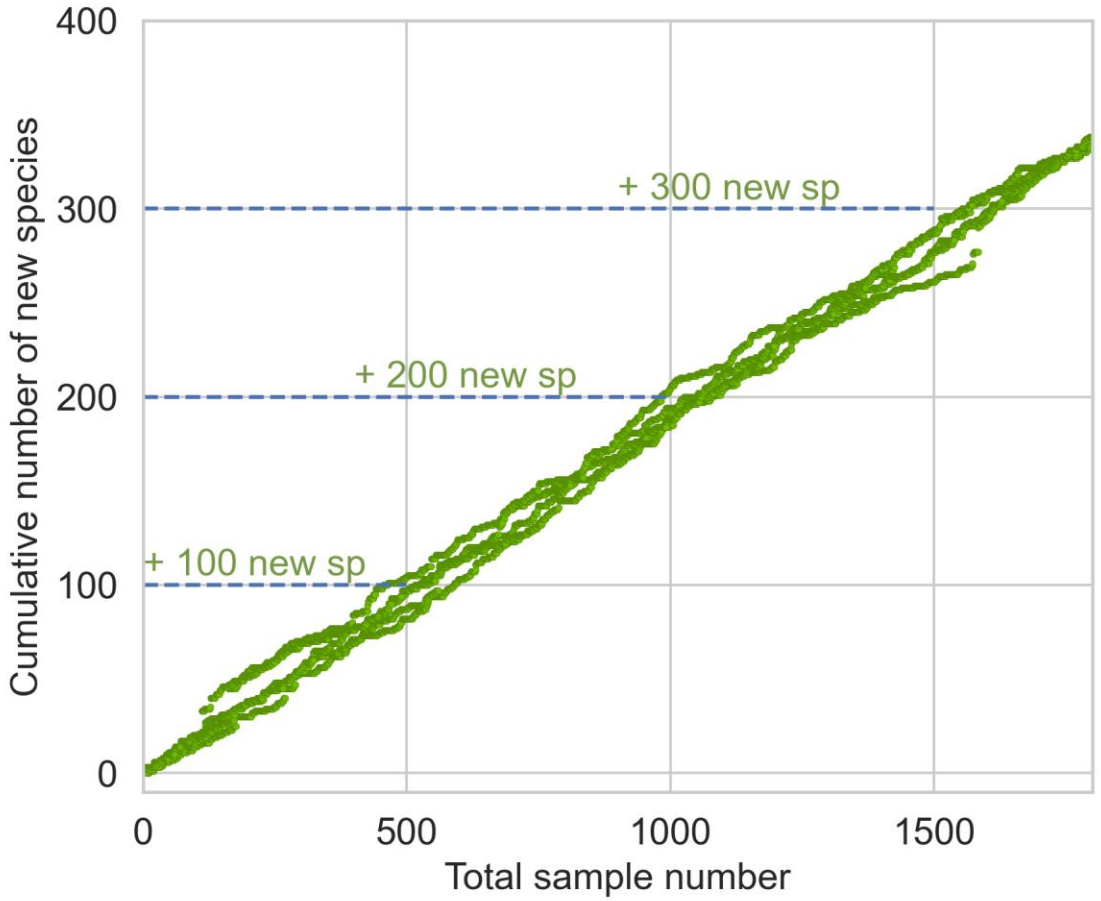


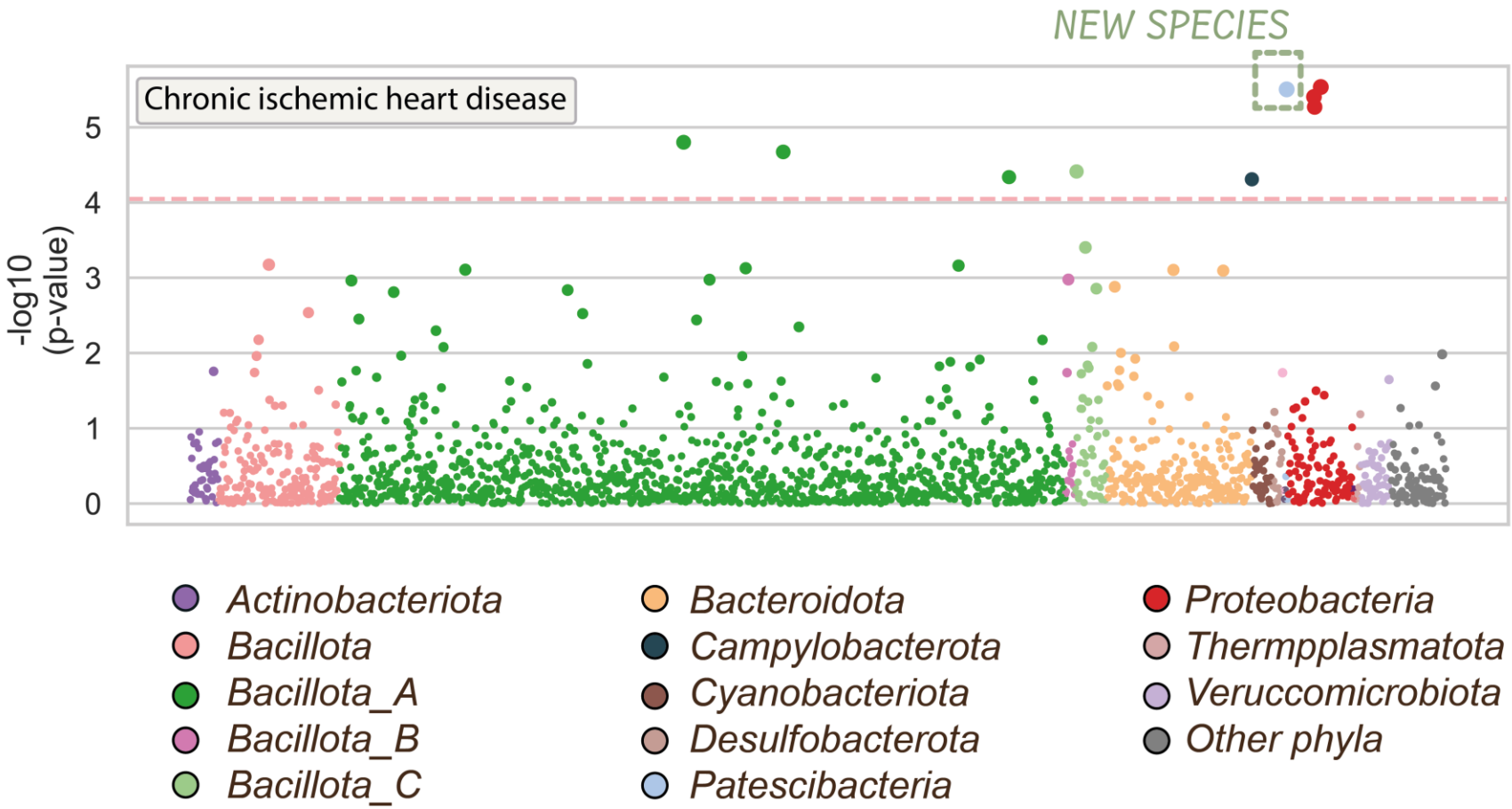
- Many gut bacteria are missing from databases
- Bacterial species form a continuum, not strict groups



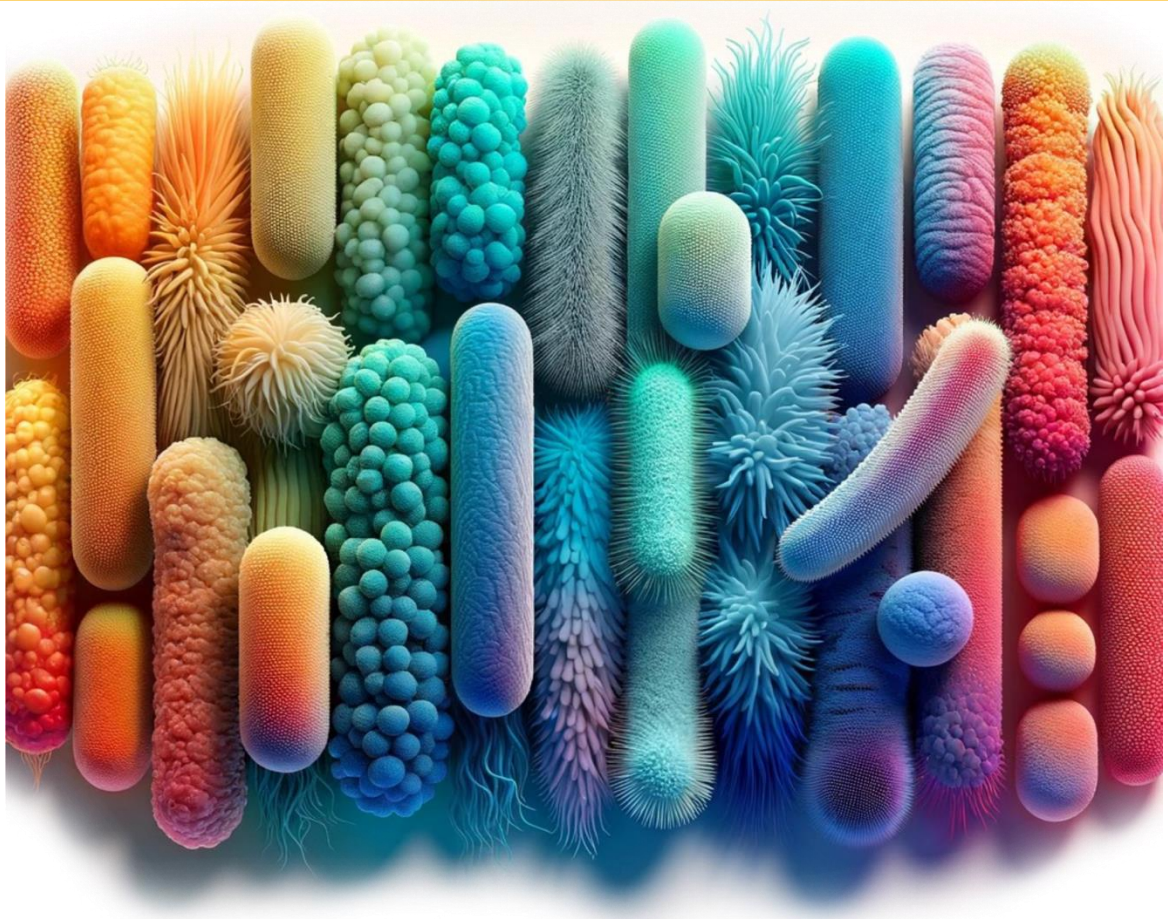
Association study on species level

- 84,254 MAGs
- 2,257 species
- 353 new species

- **33** diseases analysed
- Species-level associations identified in **25** diseases
- **9** diseases showed links to **newly** discovered species



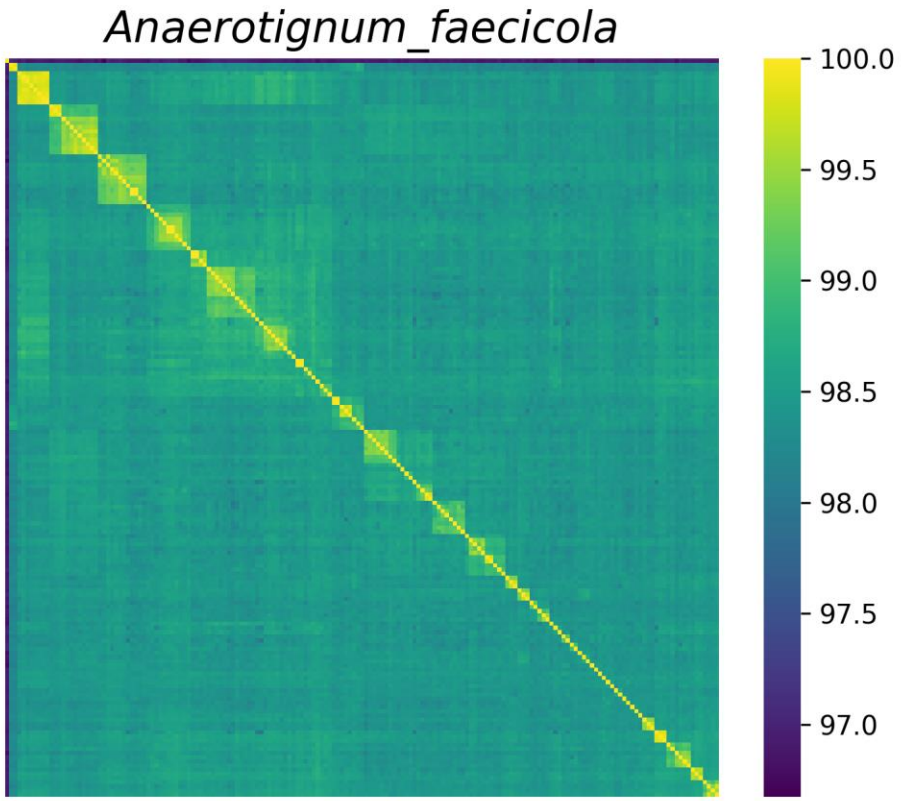
When species is just not enough

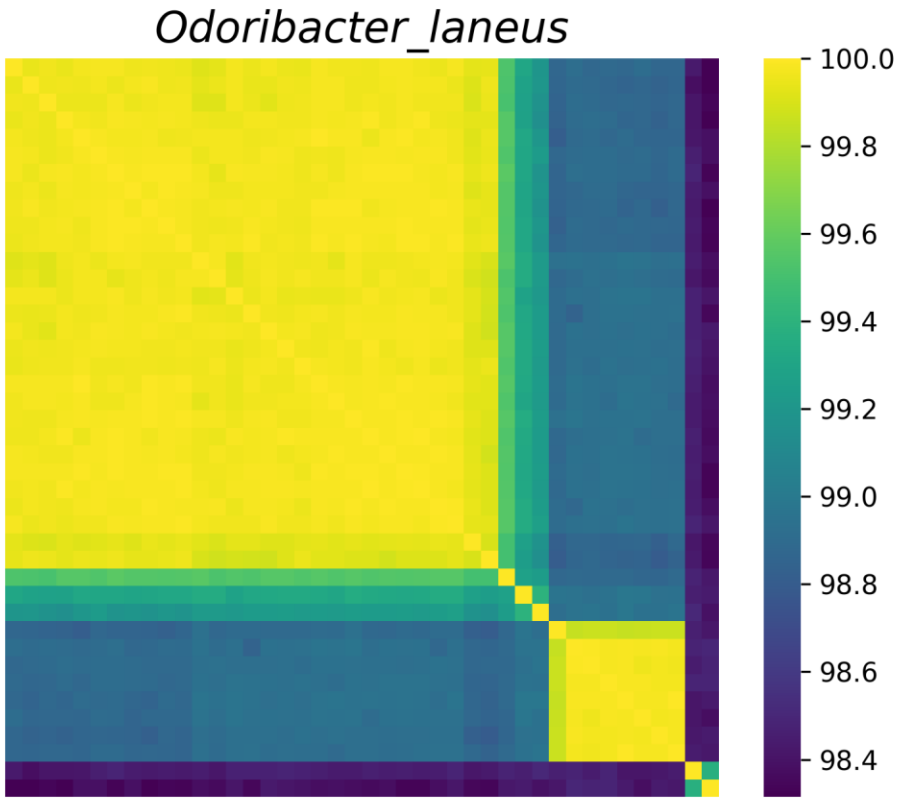


Species 1 *Species 2* *Species 3*

Bacteria with
genome similarity > 95%
are different species

When species is just not enough





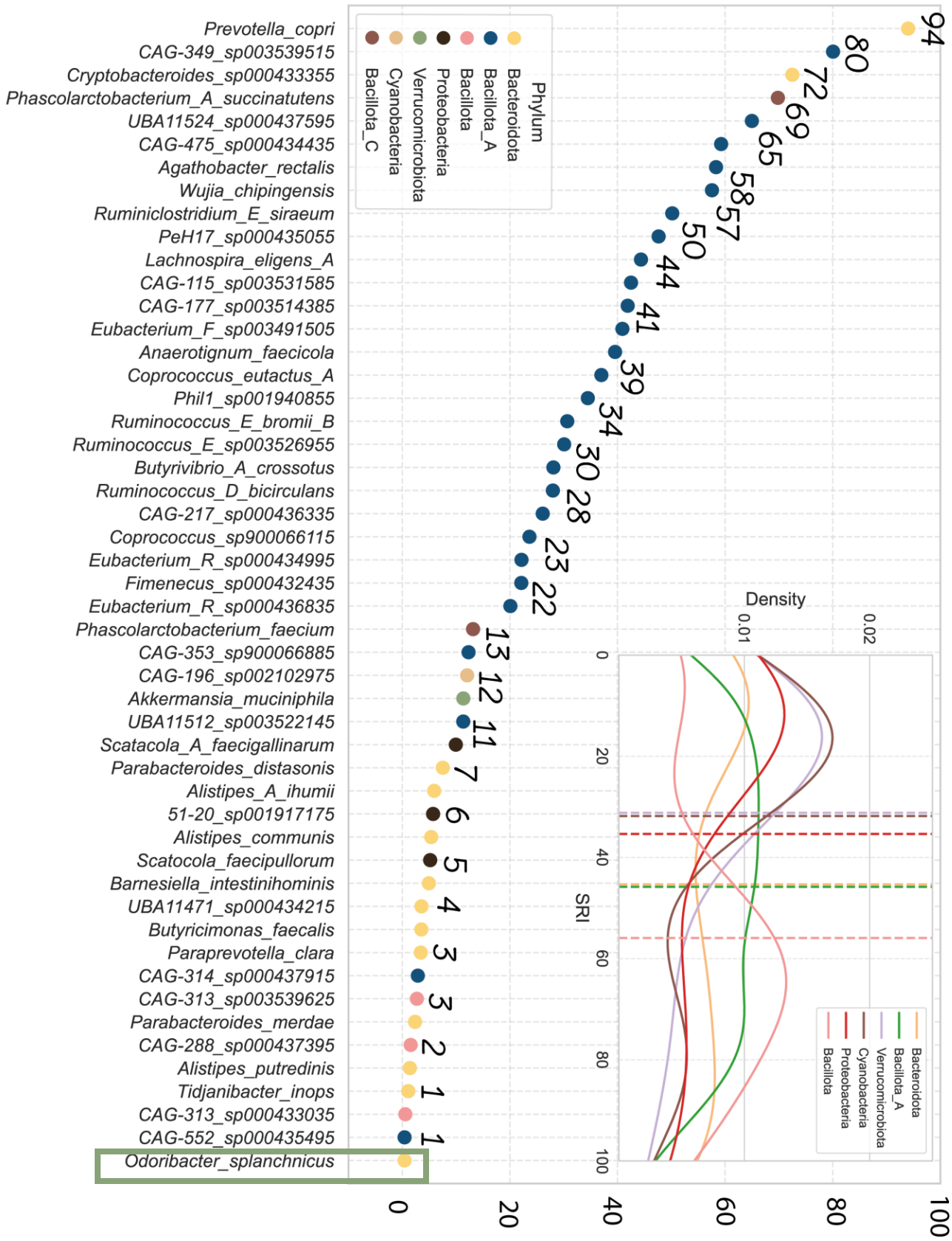
The Strain Richness Index - SRI

$$SRI = \frac{Number\ of\ strain\ cluster}{Total\ number\ of\ MAGs} * 100\%$$

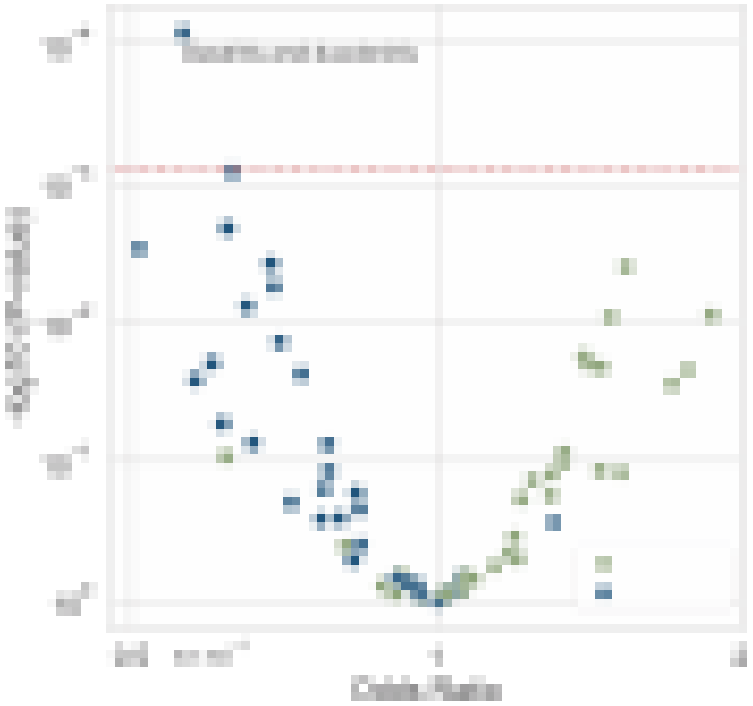
The Strain Richness Index (SRI) expresses the level of genetic diversity within a species by quantifying the number of distinct strains present in a given population or sample set.

SRI=94 means that per each 100 genomes of particular species we expected 94 different strains
-> Each strain cluster has 1-2 participant

Strain richness index (SRI)

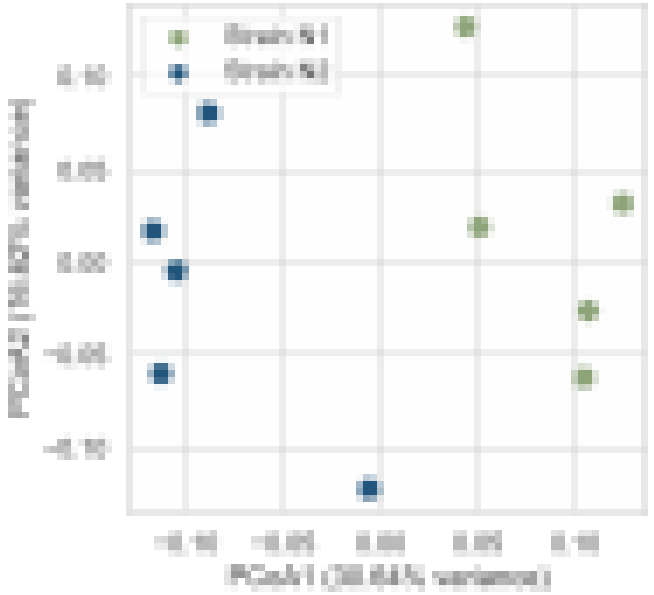


Strain level association study



Volcano plot showing the associations between the two major *O. splanchnicus* strains and 33 disease phenotypes. The red line indicates the Bonferroni-corrected significance threshold.

Pan-genome analysis of five representative MAGs from each *O. splanchnicus* strain (N1 and N2).



Principal coordinates analysis (PCoA) of *O. splanchnicus* representative MAGs based on predicted gene cluster presence/absence profiles.

Thoughts

- Not all species may be suitable for strain-level analysis
- Differences in strain richness need to be further explored using broader global microbiome data
- Why are some gut species highly diverse while others are not?

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