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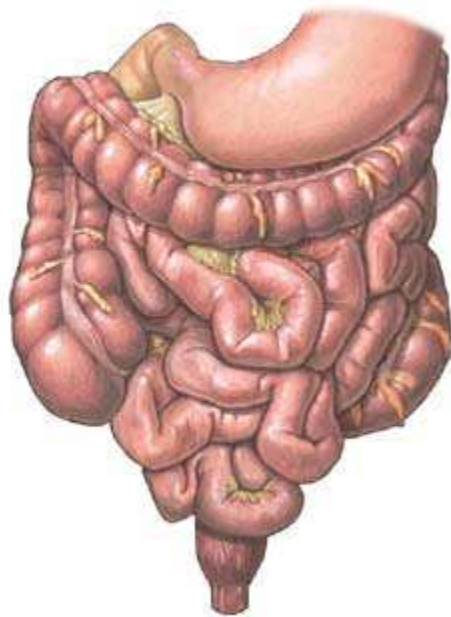
HITChip

Human Intestinal Tract Chip

In Health and Disease

Mirjana Rajilić-Stojanović

- Diversity of the microbiota
- Microbiota of healthy adults
 - Dynamics of the microbiota
- Microbiota in disease
 - Specific composition of the microbiota of UC and IBS patients
- Conclusions

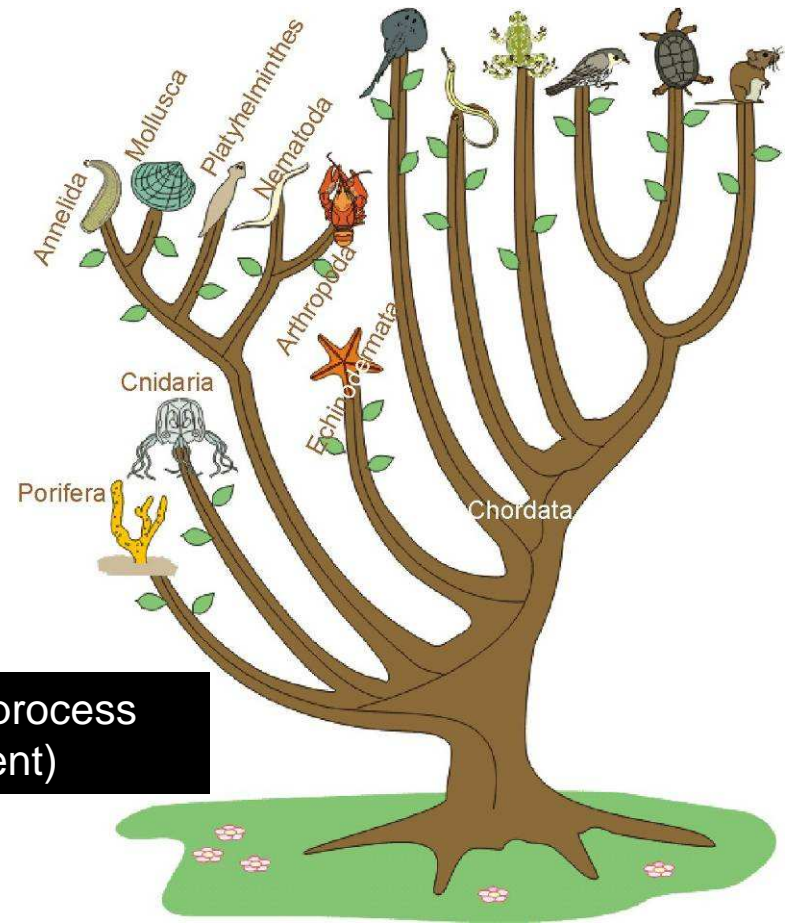
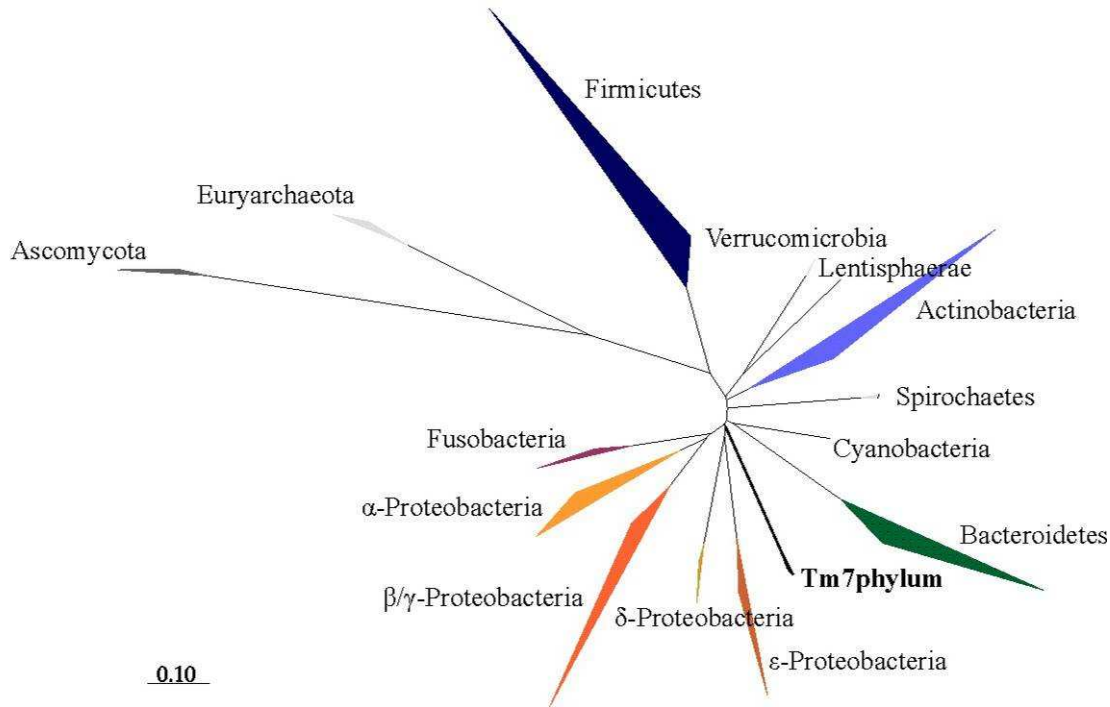


Dimensions of the gastrointestinal microbiota

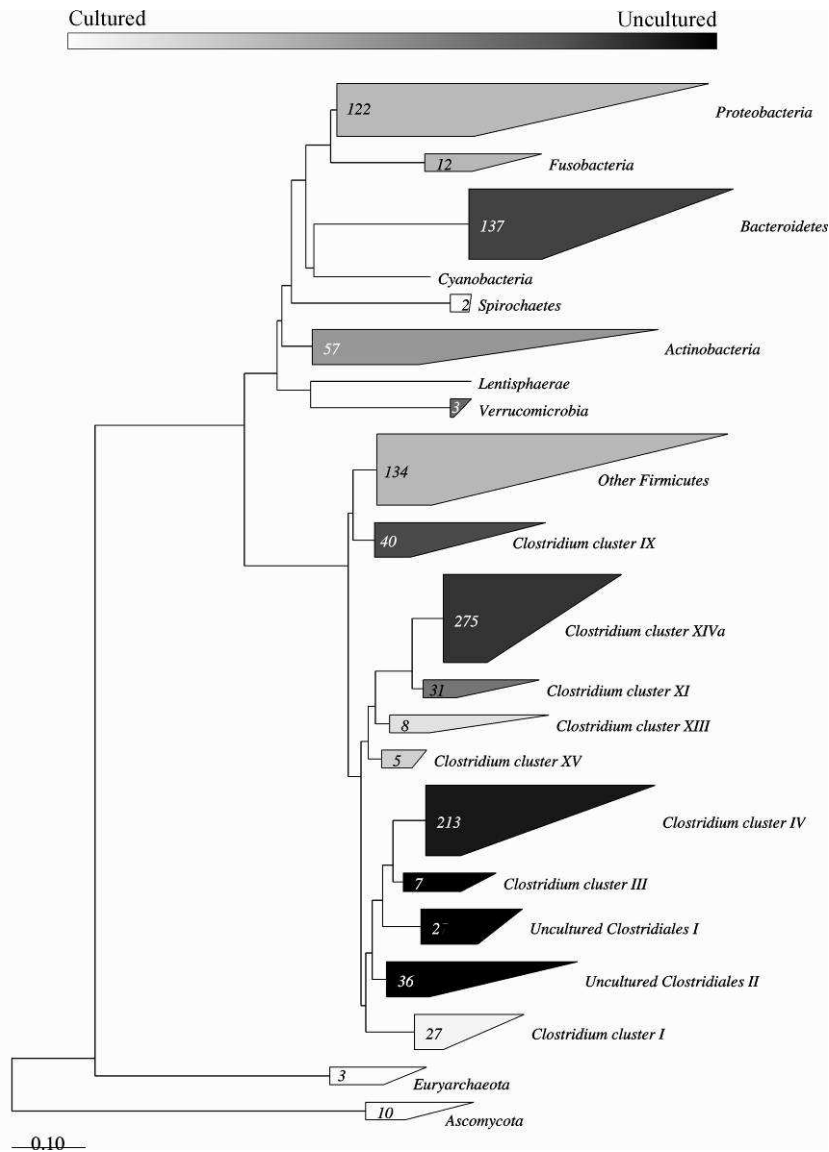
- 10^{12} cells per gram of intestinal content
- Microbes in gut = 1,000 x humans on Earth
- 95% of cells in our body are microbial
- Total mass ~1.5 kg
- Microbes comprise 30% of faecal volume

Functions of the gastrointestinal microbiota

- Digests ~100g of food per day
- Digests ~1,000 kg of host secreted substances
- Provides SCFA (food) to the gut epithelial cells
- Synthesises essential amino acids
- Synthesises vitamins K and B12
- Metabolises sex hormones
- Makes first line of protection against pathogens
- Modulates our immunity



- Description of the diversity of HIT microbiot is ongoing process
- Higher diversity than initially anticipated (13 phyla present)



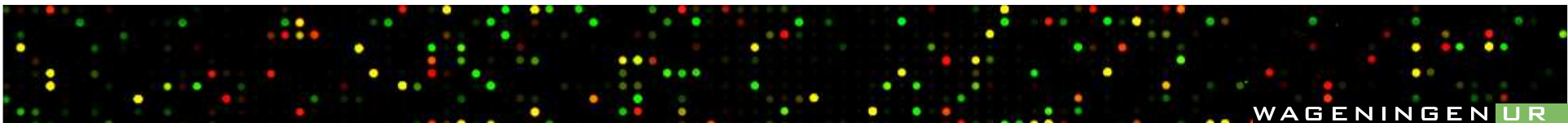
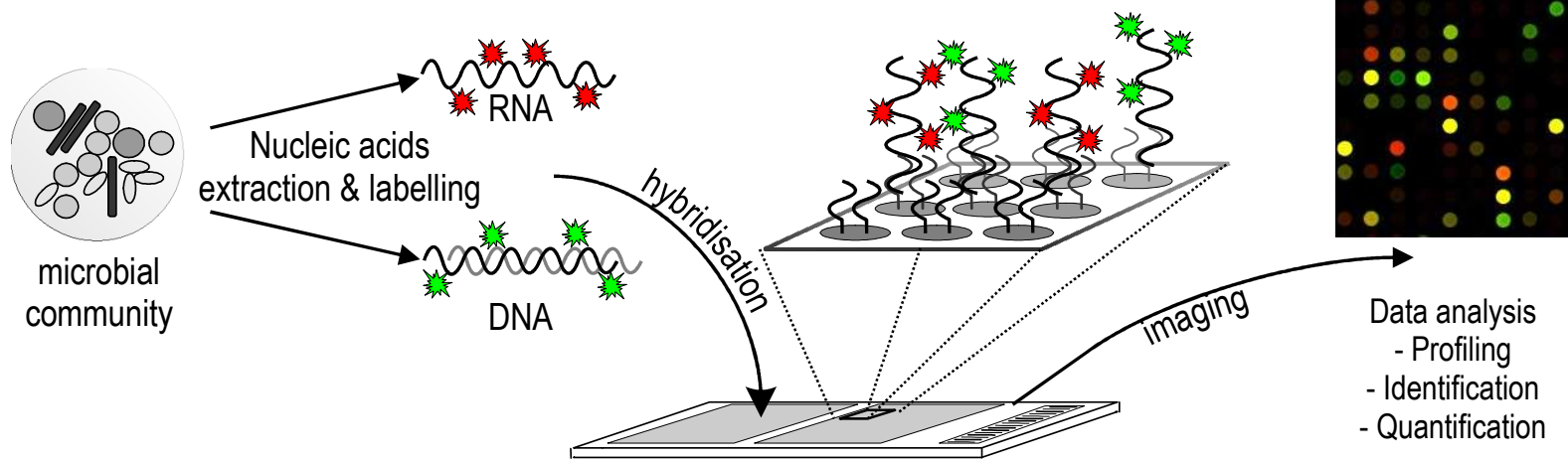
- Phylotypes recovered in cultivation-dependent studies
- ▨ Phylotypes recovered in both cultivation-dependent and -independent studies
- Phylotypes recovered in cultivation-independent studies

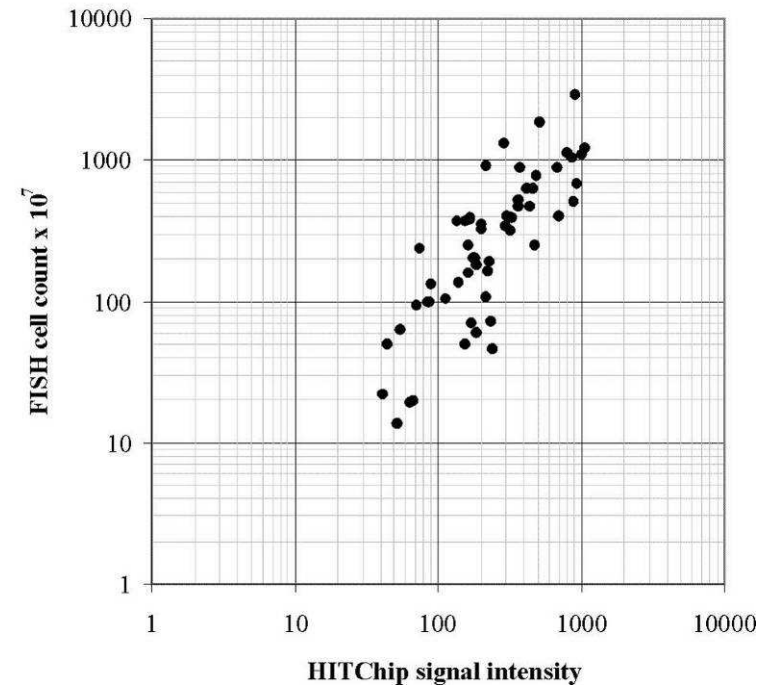
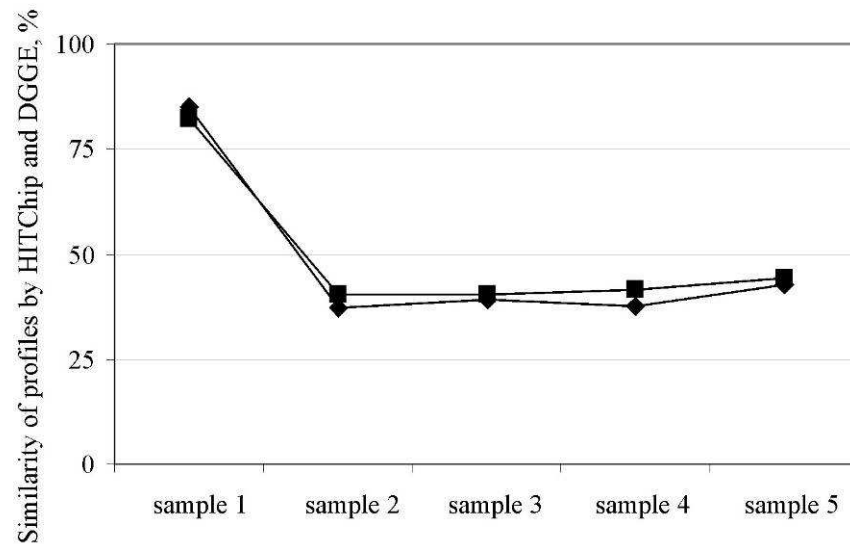
~ 65% of 1,200 organisms has not yet been cultured
 Diversity can be analysed only on the bases of the 16S rRNA gene

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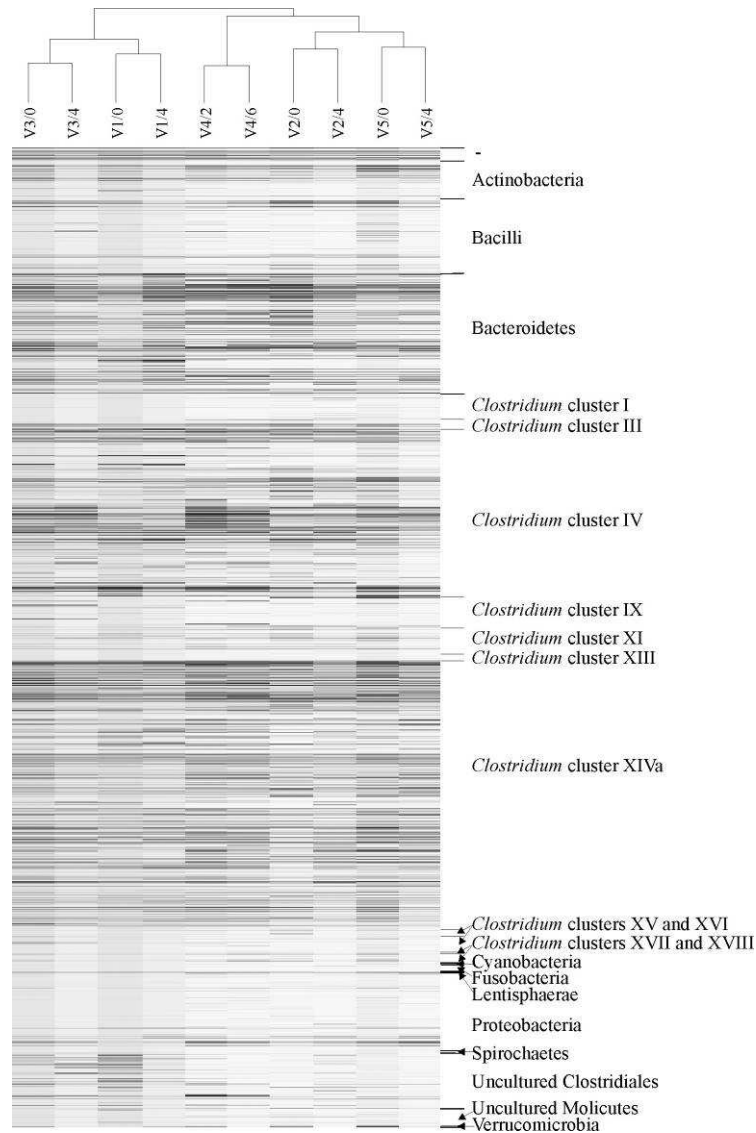
Human Intestinal Tract Chip

~ 5,500 probes printed in duplo
~ 1,000 organisms targeted



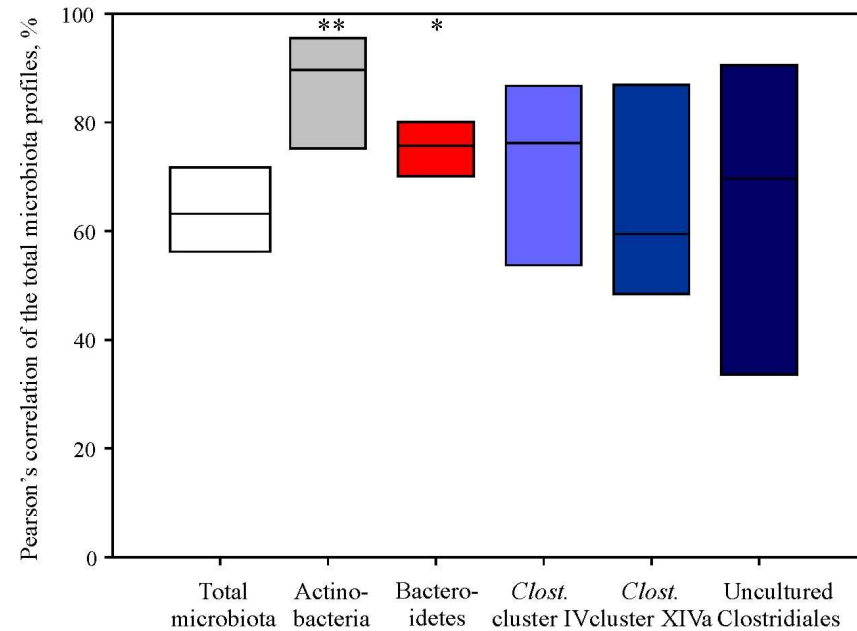
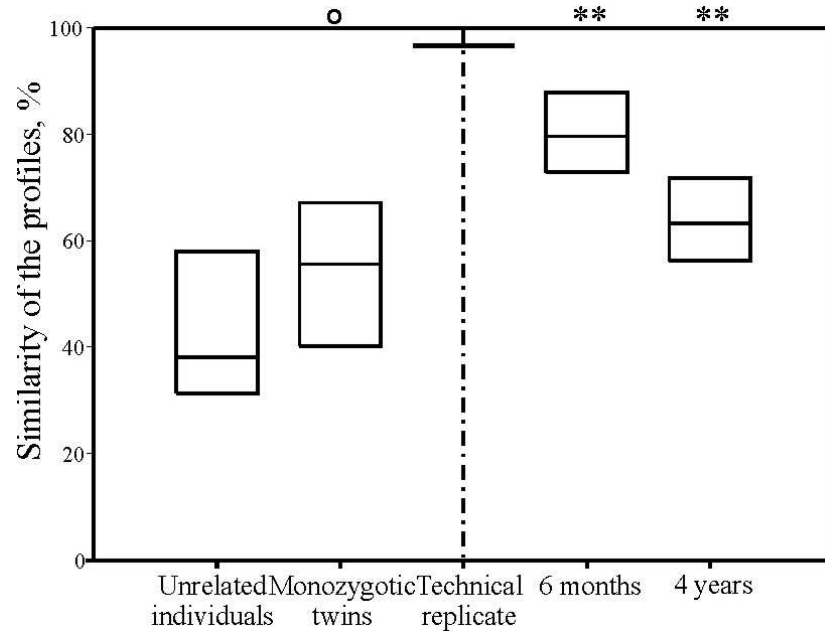


- Good agreement with another profiling technique
 - Improved resolution
 - Additional information (phylogeny)
- Good agreement with another quantifying technique
 - Targeting 130 phylogenetic groups simultaneously



Previous short term analysis (up to 1 year) →
Microbiota is stable and individual-specific

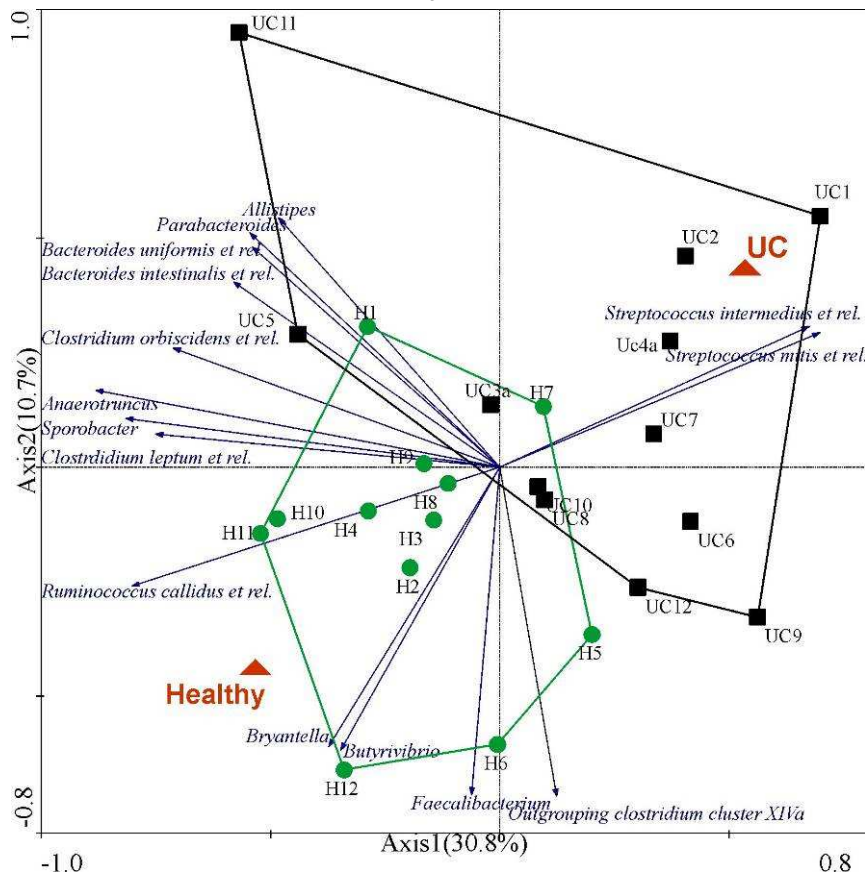
- After 4 year period microbiota of an individual is individual-specific
- The microbiota profile is a unique fingerprint



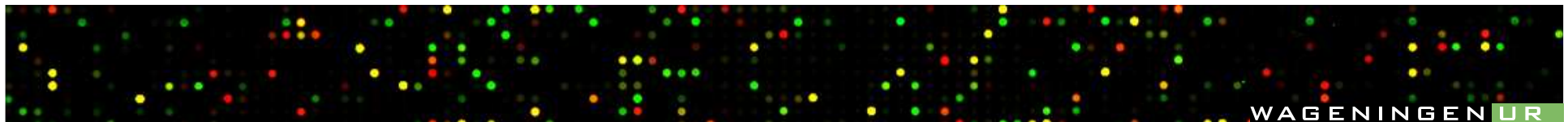
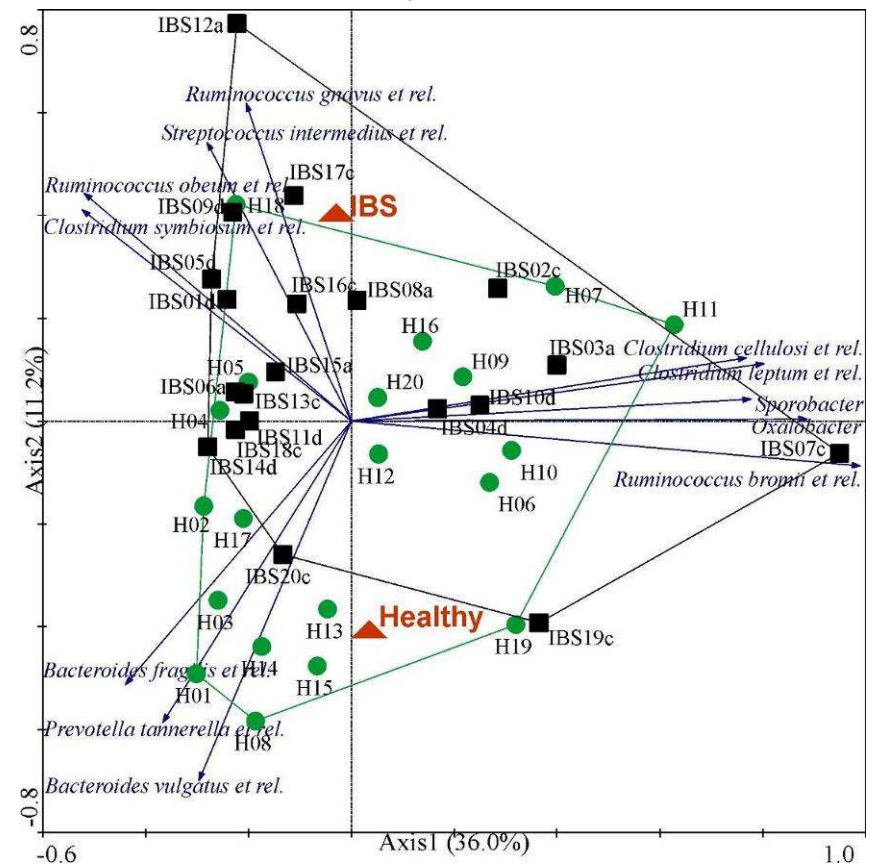
- The similarity of the microbiota of an individual decreases with the time
- Microbiota of monozygotic twins notably more similar ($p=0.06$)
- *Bifidobacterium* spp. and some Bacteroidetes have significantly increased stability

Microbiota is shaped by genetic and environmental factors

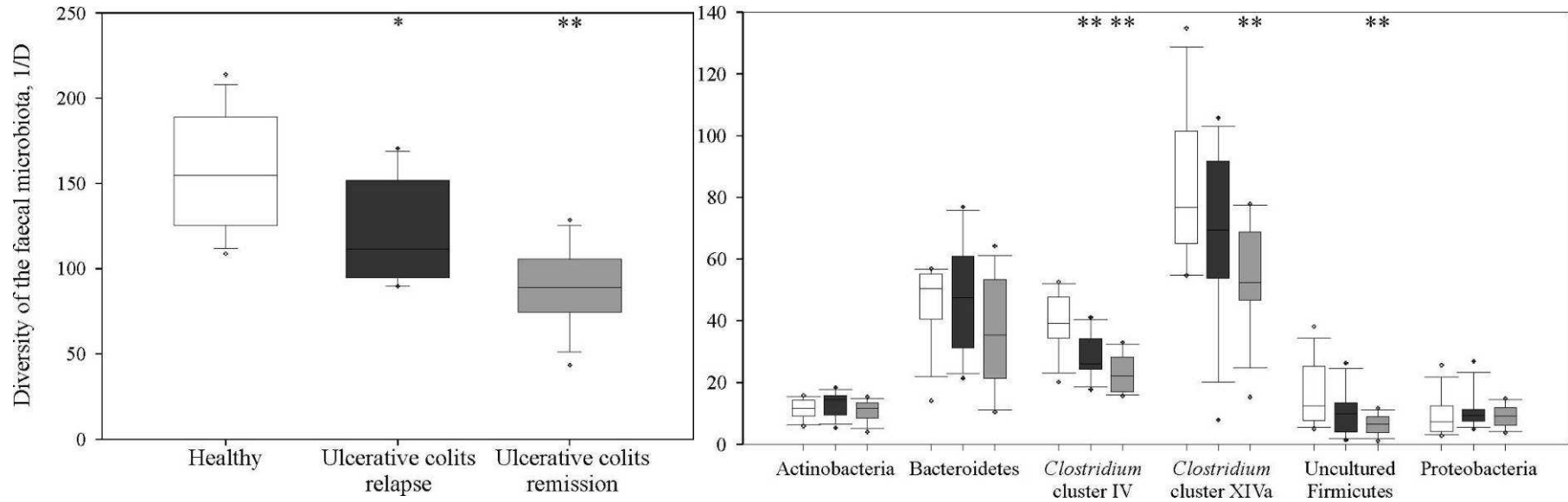
Healthy vs. UC - P=0.002



Healthy vs. IBS - P=0.152

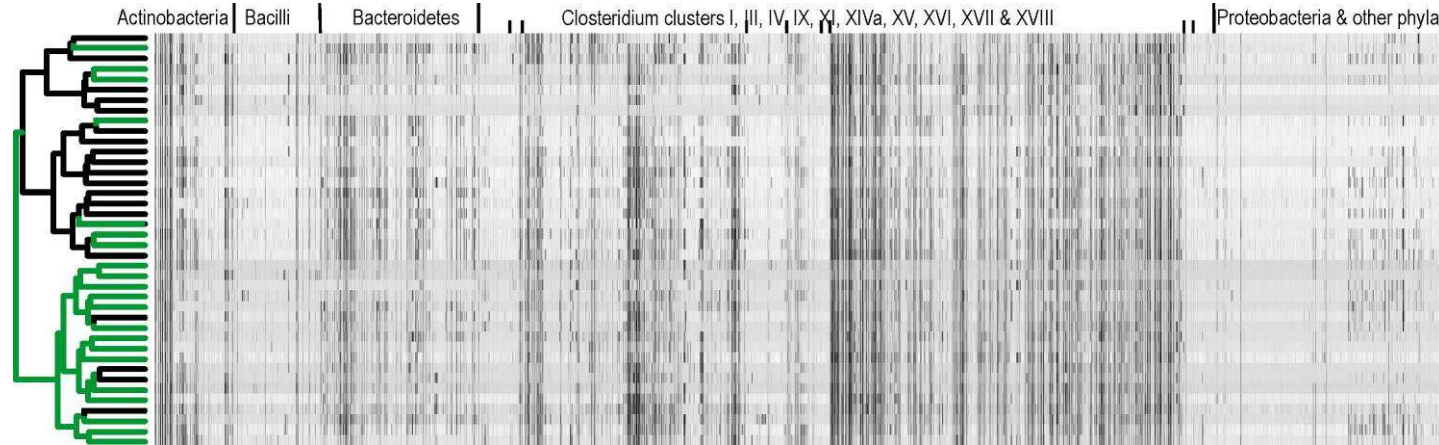


Reduced diversity in UC patients

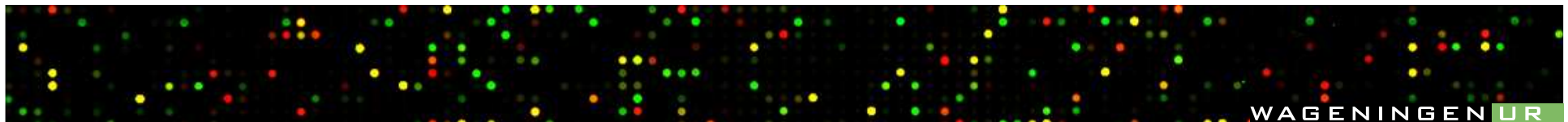
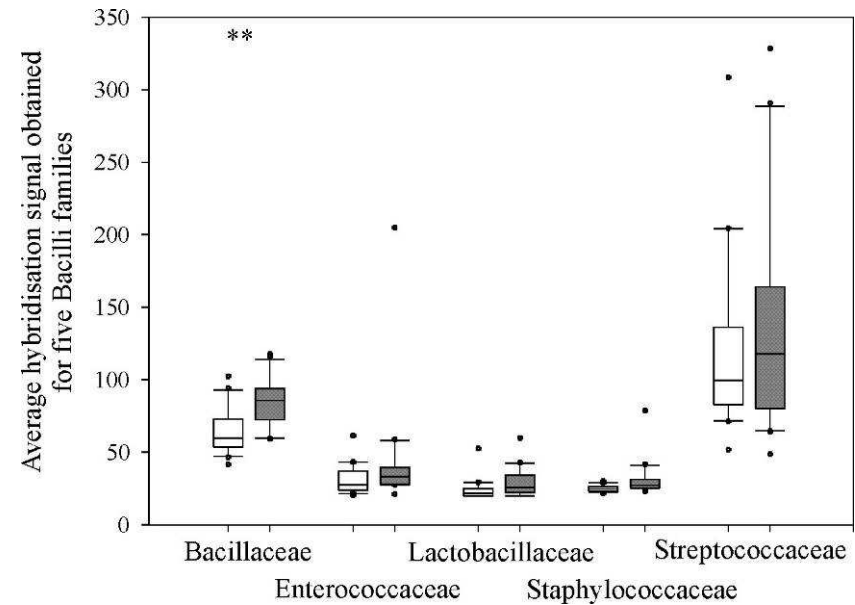
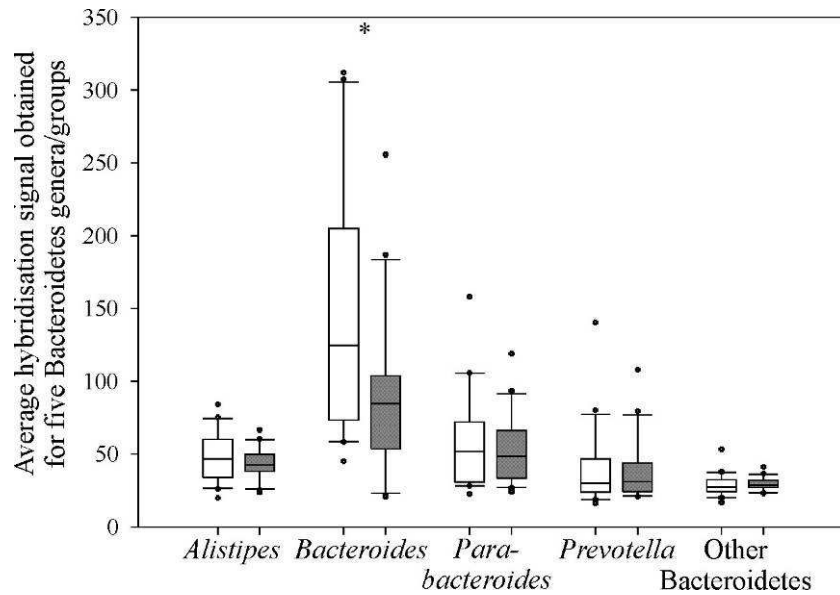


Presence of specific microbes – *Peptostreptococcus* spp. and *Clostridium difficile*

	<i>Clostridium difficile</i>	<i>Peptostreptococcus</i> spp.
UC1	Present	Absent
UC2	Present	Absent
UC3	Present	Absent
UC4	Absent	Present
UC5	Present	Absent
UC6	Present	Absent
UC7	Absent	Present
UC8	Present	Absent
UC9	Absent	Present
UC10	Absent	Present
UC11	Absent	Present
UC12	Absent	Present



Different microbiota composition in IBS patients (symptome specific)



- HITChip is comprehensive tool for high throughput studies of the HIT microbiota
- The HIT microbiota of healthy adults is a dynamic ecosystem influenced by genetic and environmental factors with a core of permanent colonisers (bifidobacteria and some Bacteroidetes)
- The HIT microbiota of UC, in both relapse and remission, is significantly reduced, and different from the microbiota of healthy subjects
- The HIT microbiota of IBS patients differs in composition from the microbiota of healthy subjects. Increased abundance of *Bacteroides* spp. and bacilli are typical for all subtypes of IBS



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Acknowledgements

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**Thank you
for your attention!**