Identification of a Gut Microbial Signature Linked to Severity of Irritable Bowel Syndrome

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Identification of a Gut Microbial Signature Linked to Severity of Irritable Bowel Syndrome

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#DDW15
@julientap

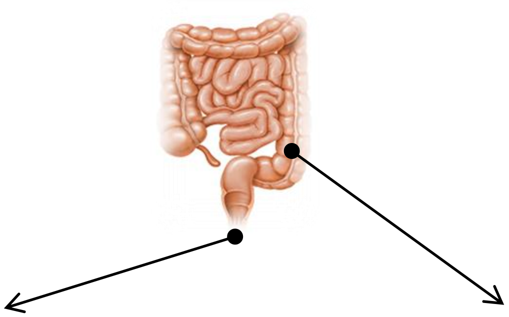
IBS and Gut Microbiota hypothesis

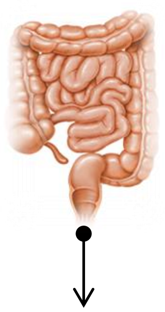
- Irritable Bowel Syndrome (IBS) : most common GI disorder (10-15% western pop.)
- Symptom severity and pattern are used to stratify IBS patients (IBS-SSS, ROME III)

- Gut microbiota might play a role in IBS pathophysiology
- Gut microbiota studies on IBS vs healthy showed differences but **low sample size (n < 50)** may explain heterogeneity of outcomes

Aim: to explore gut microbiota in a larger IBS cohort and to establish a potential link with symptom severity.

Large dataset





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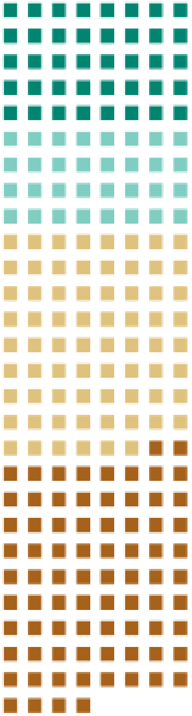
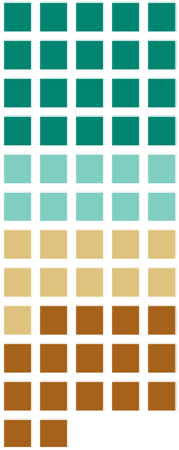
Stool samples
(exploratory set)



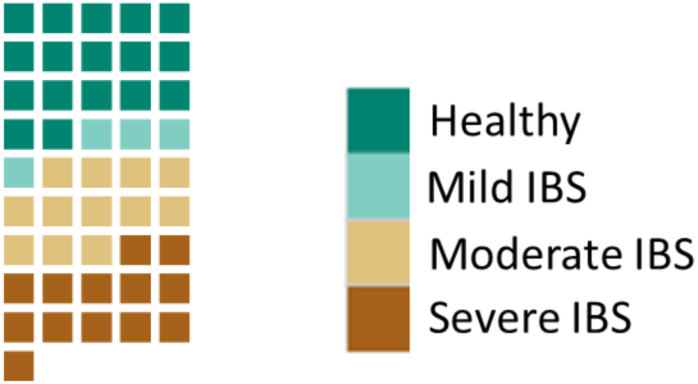
(n= 220)

Unprepared
sigmoid biopsies



(n= 57)

Stool samples
(validation set)



(n= 46)

Clinical data

- Age, BMI, gender
- Symptom severity and pattern :
  - IBS-SSS,
  - ROME III subtypes
- Psychological symptoms
- Quality of Life
- Exhaled gas : CH_4, H_2

Gut microbiota analysis

16S rRNA gene targeted metagenomics
Quantitative PCR targeted on Archaea

Sample (stool, biopsy)

↓ *Extract*

DNA

↓ *Sequence*

Reads

↓ *Denoising & clustering*

Numerical Data

Ecological and statistical data analysis

Numerical Data

Richness and beta-diversity assessment

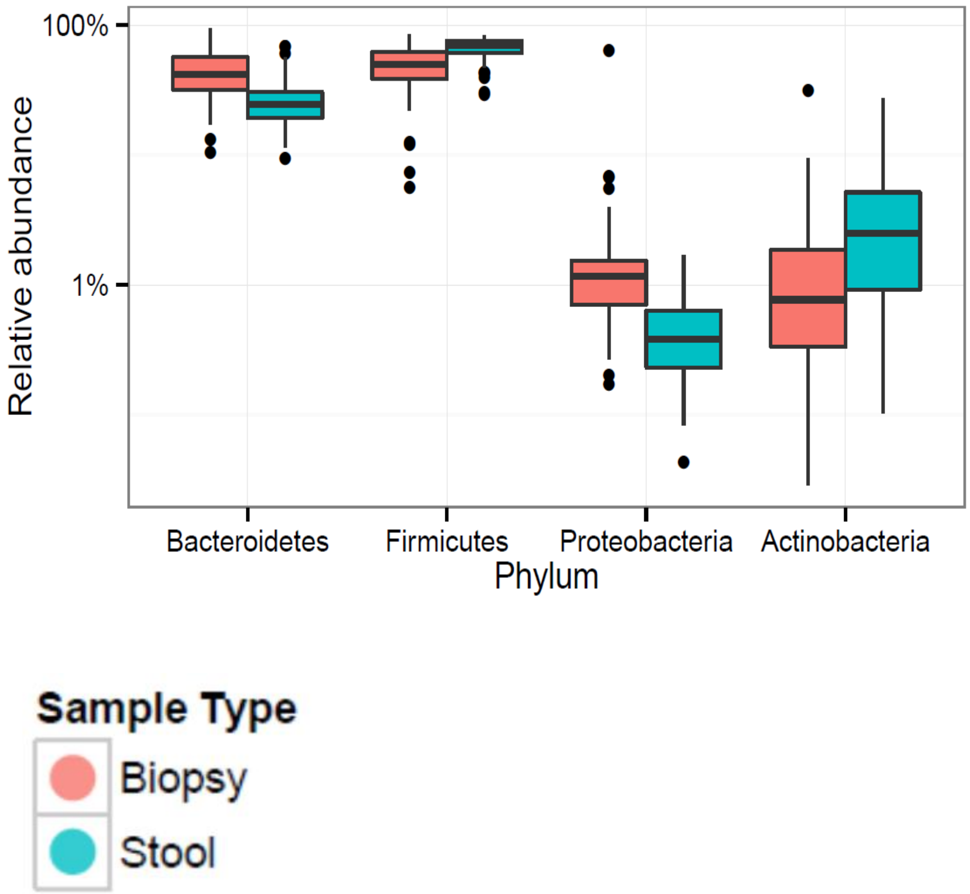
Unsupervised enterotyping

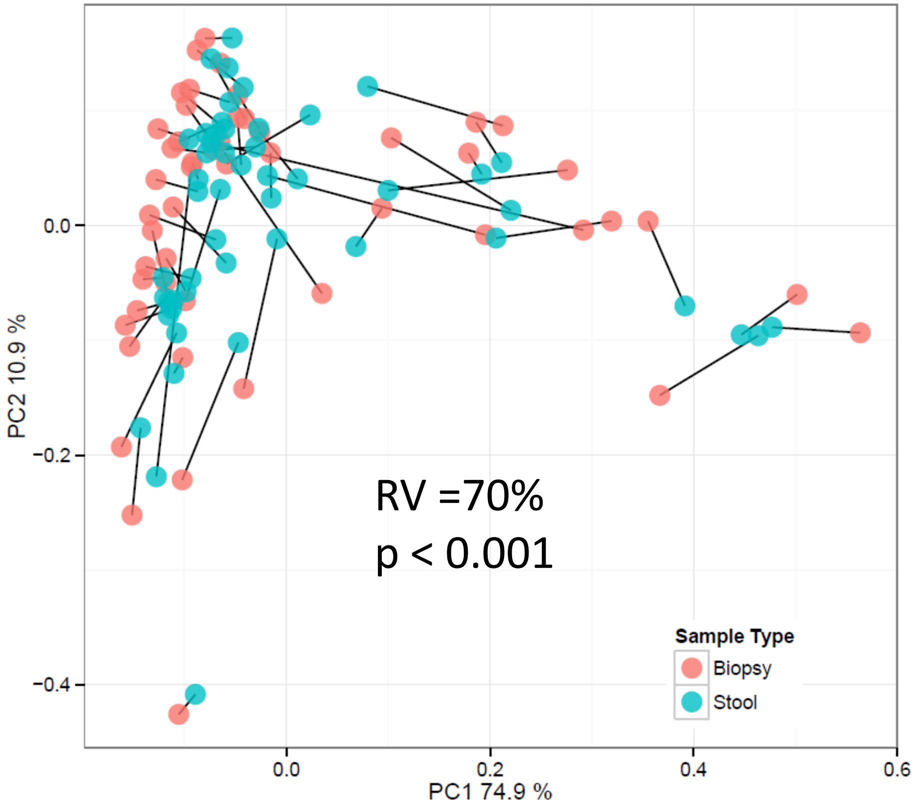
Univariate and multivariate analysis

Machine learning procedure

Gut Microbial Signature for IBS Severity

Fecal microbiota is a good proxy for mucosal microbiota



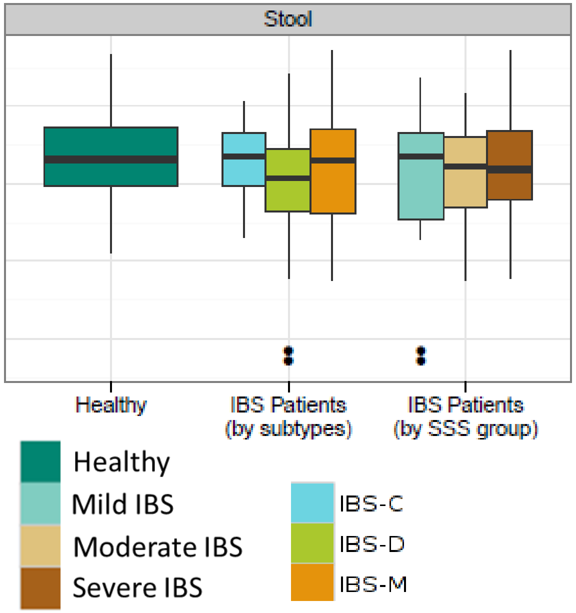


RV =70%

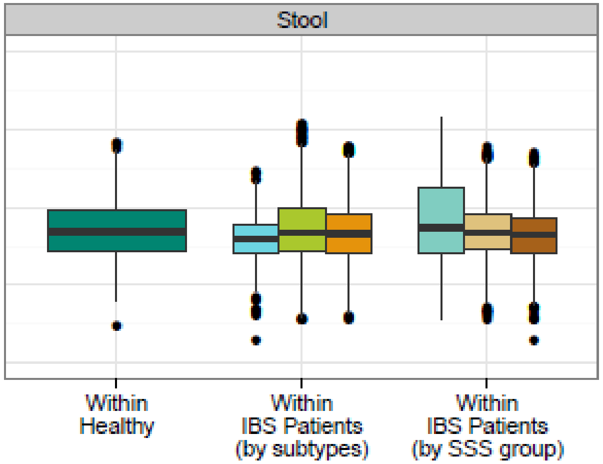
$p < 0.001$

No major global microbial ecological difference between IBS and healthy

Microbiota richness among groups



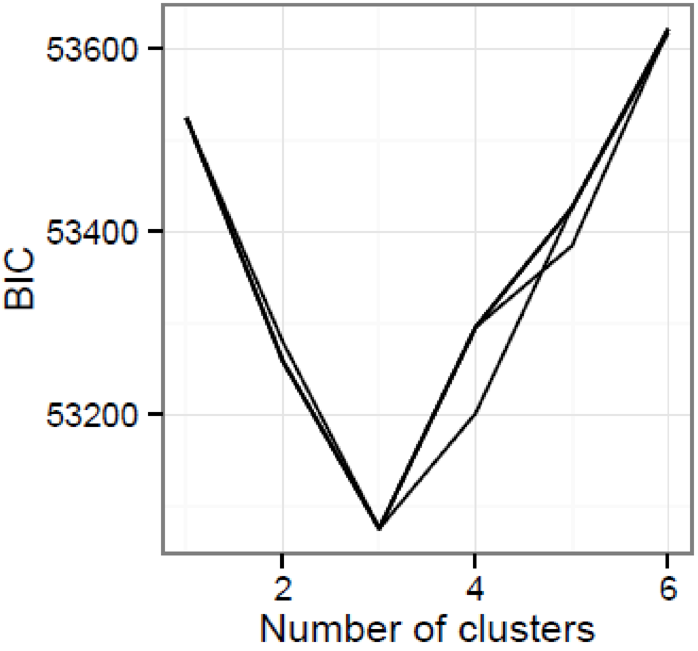
Microbiota variation within groups

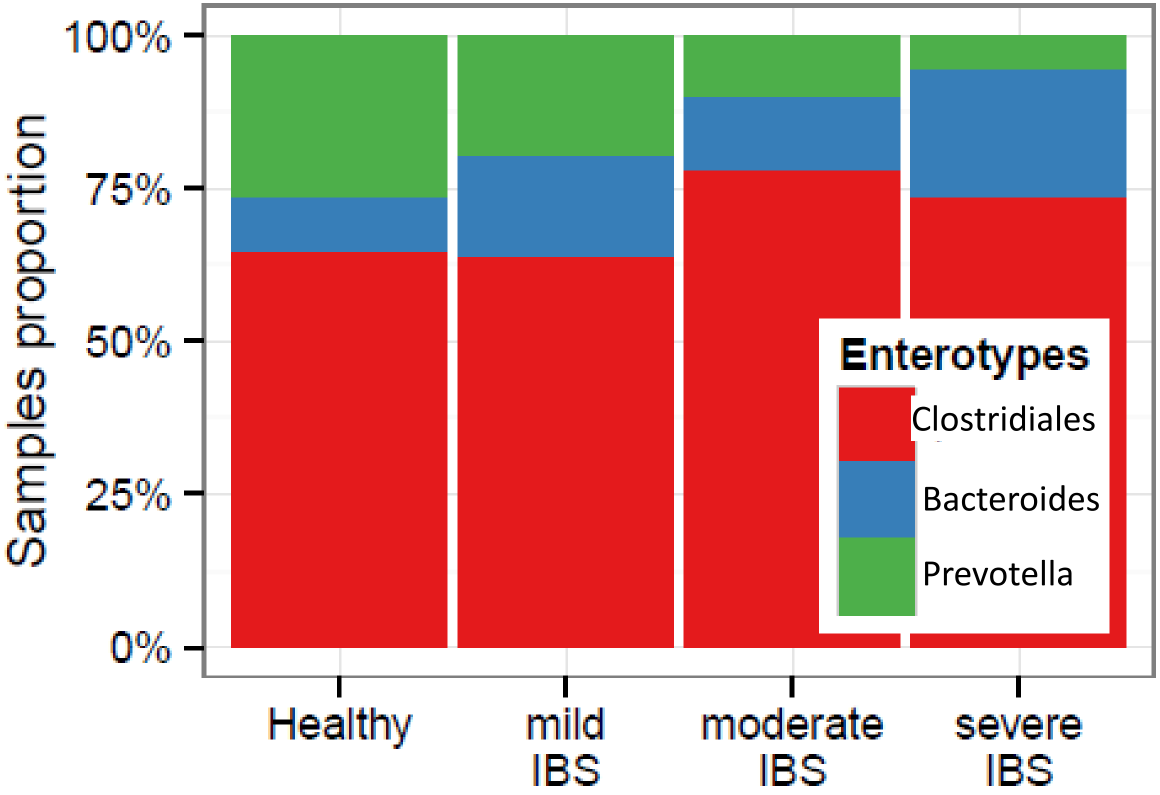


Microbiota distance between IBS and Healthy

- Microbiota richness did not differ between IBS and healthy
- Gut microbiota variation was homogenous across groups
- No difference with global microbial distance between Healthy and IBS

Gut microbiota enterotypes in IBS

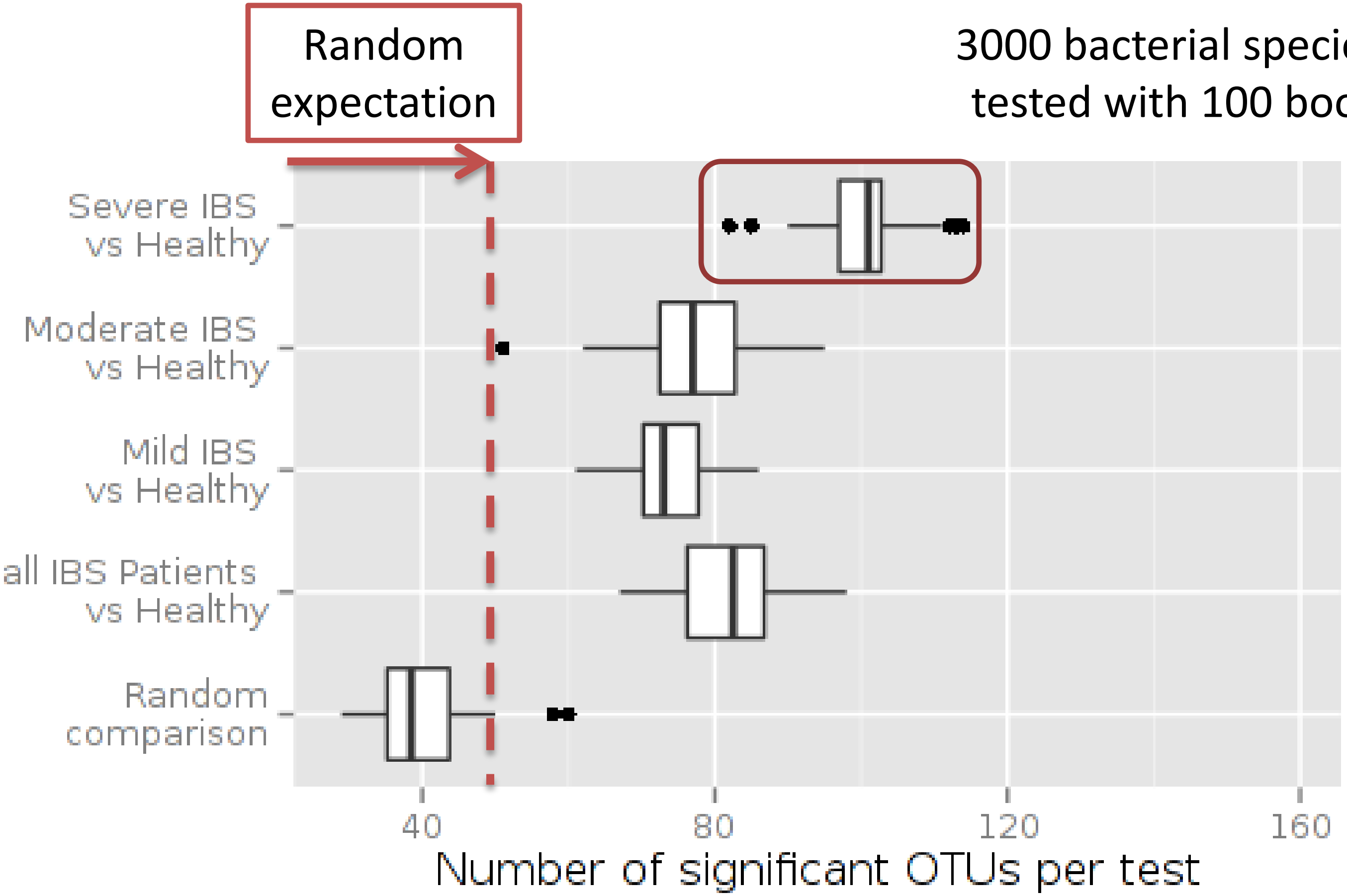




3 enterotypes found in the stool dataset equivalent to those published elsewhere

Link between IBS severity score and enterotypes distribution

Towards a gut microbial signature for IBS severity



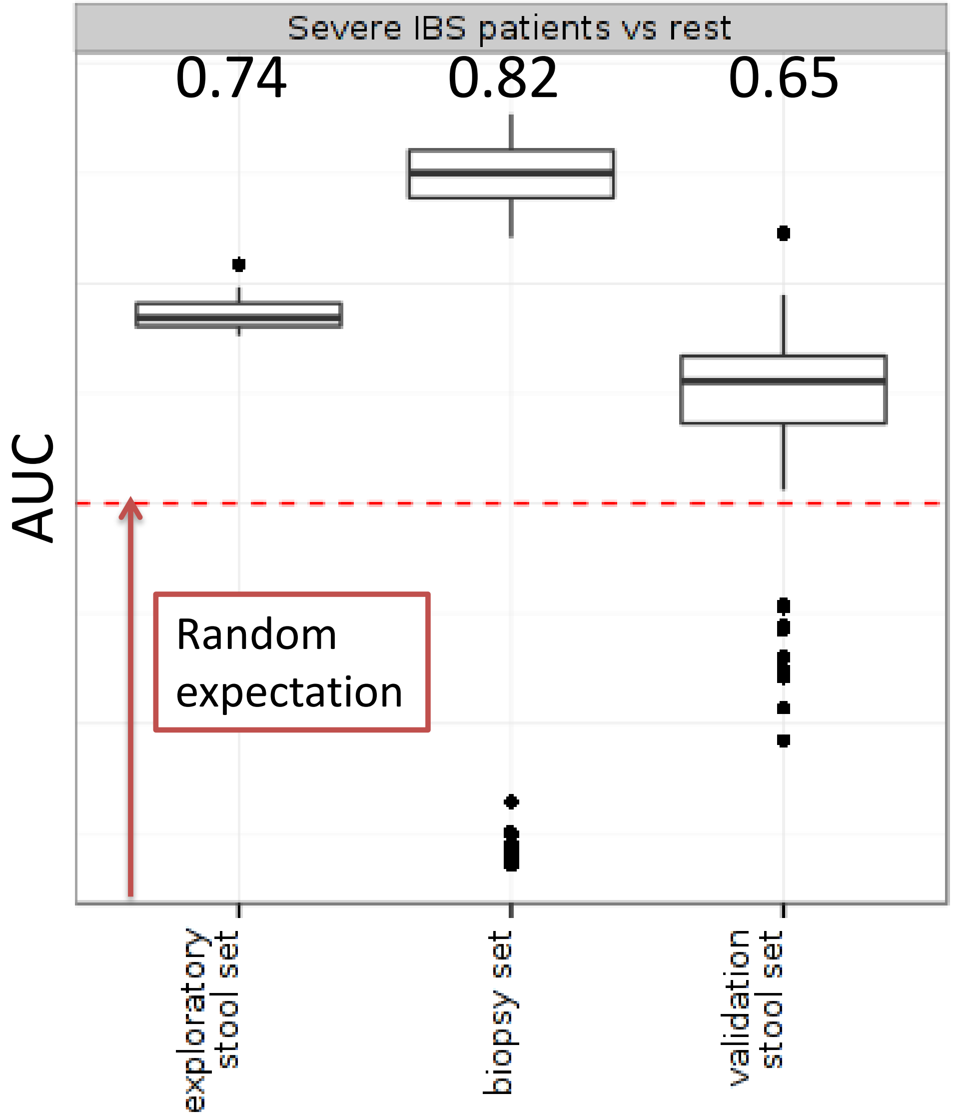
3000 bacterial species (OTU) tested with 100 bootstraps

100 bacterial species might be significant for severe IBS but 50 might be just random!

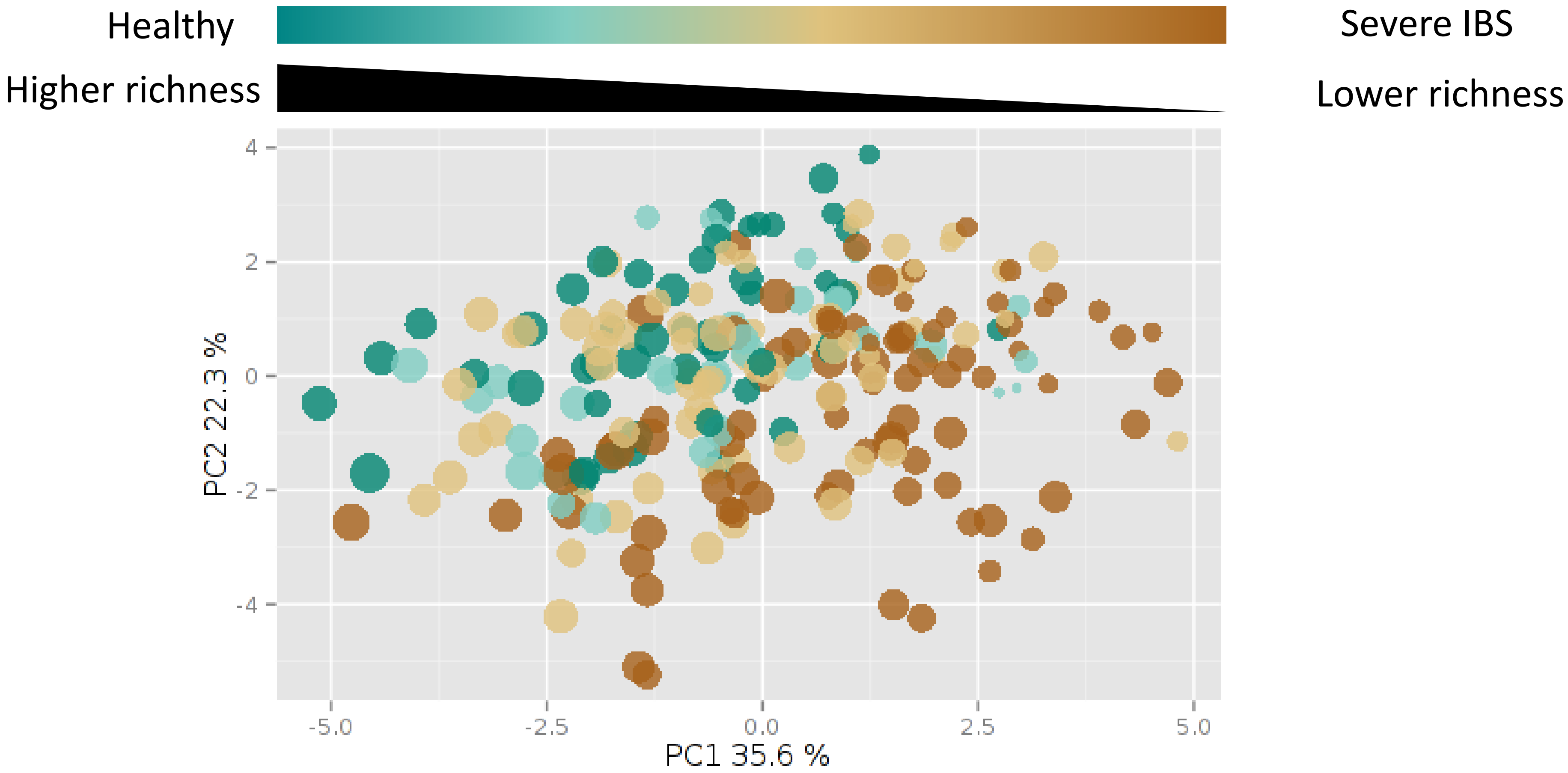
Towards a gut microbial signature for IBS severity

-Machine learning procedure allows finding a microbial signature for IBS severity

-This signature is validated in biopsies and an independent stool samples set

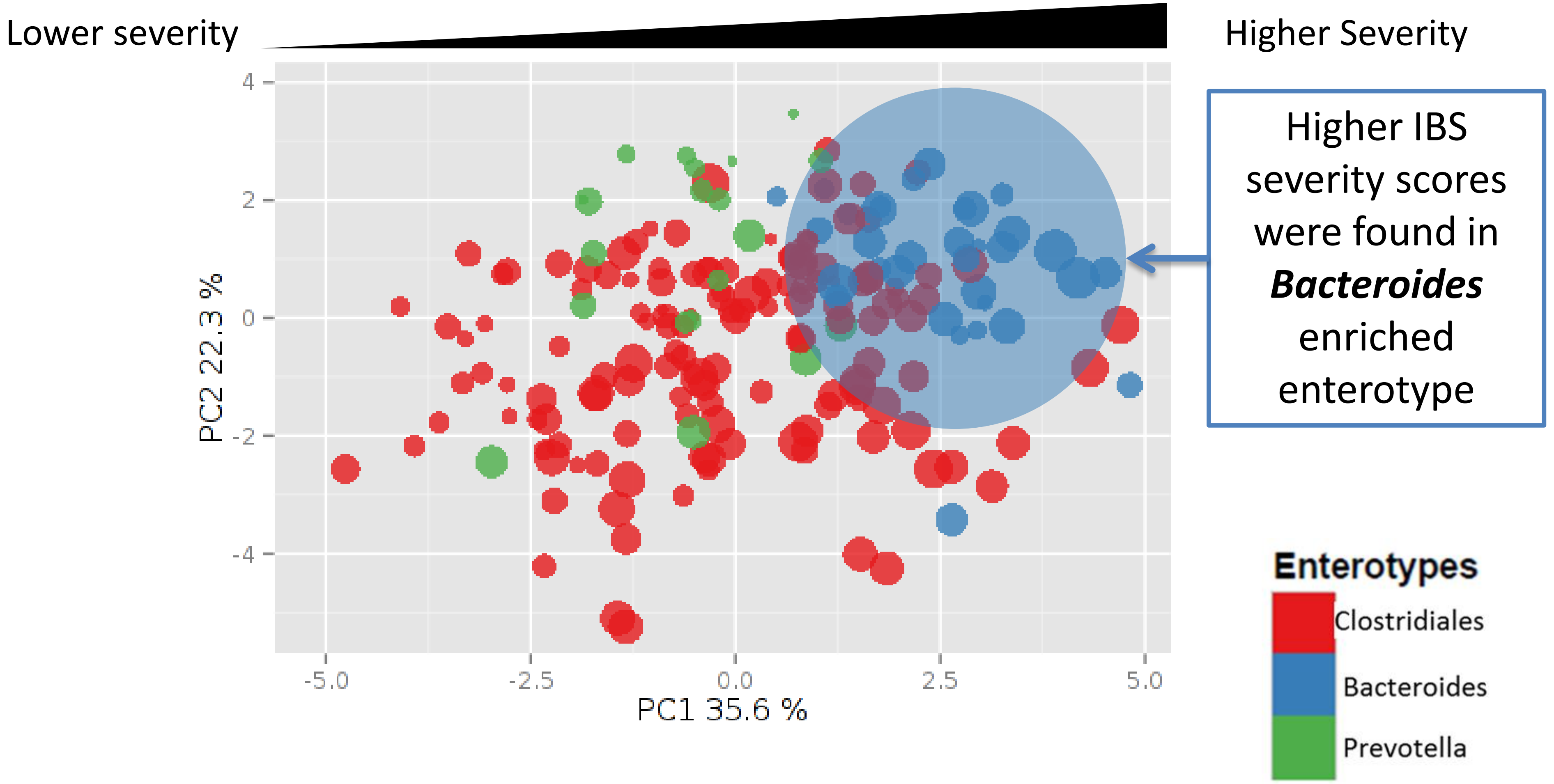


Gut microbial signature for IBS severity is linked with lower microbial richness



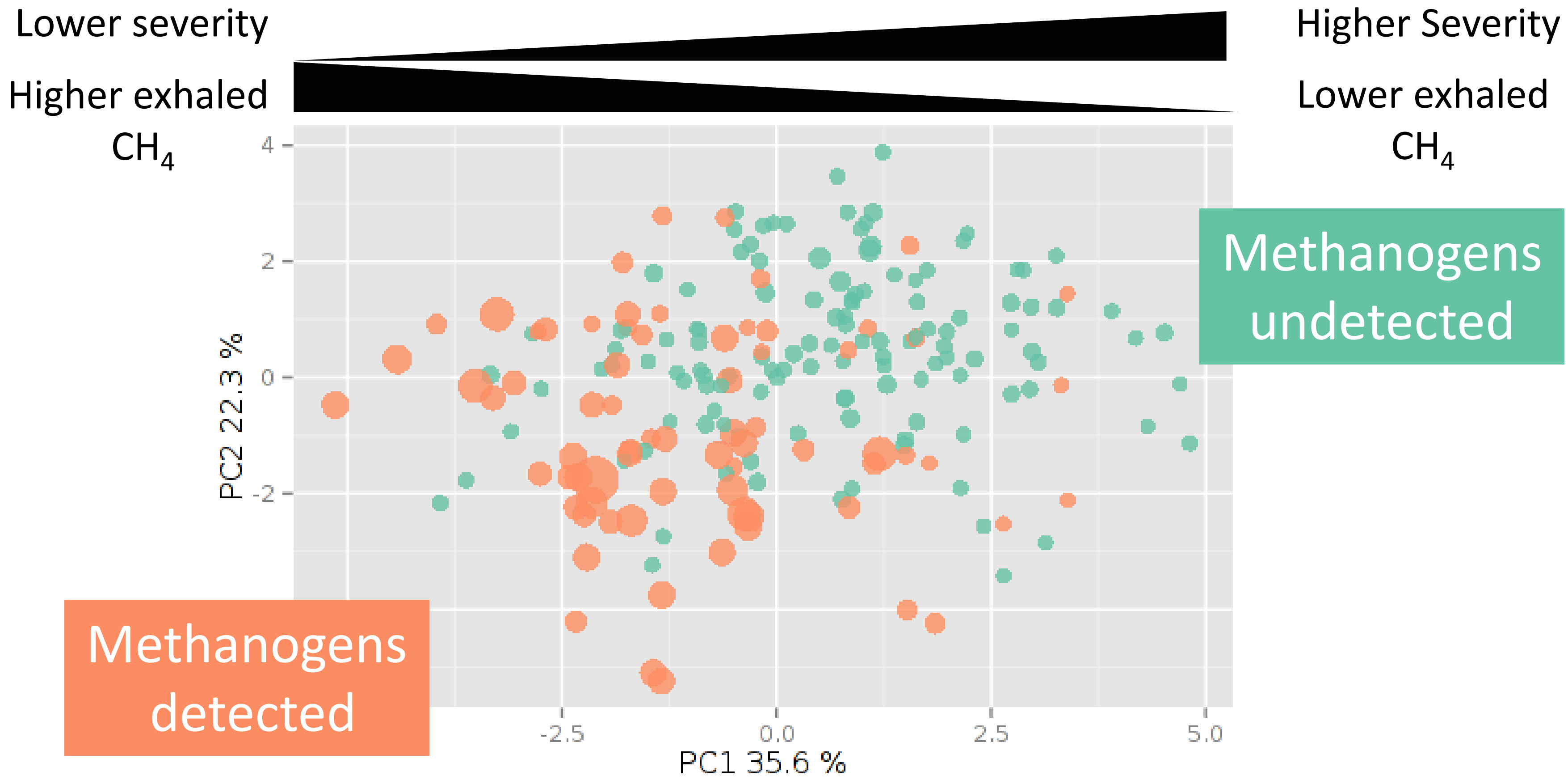
Bacterial species extracted from IBS severity signature
allowed to order samples in association with clinical metadata

Gut microbial signature for IBS severity is linked with *Bacteroides*-enriched enterotype



Higher IBS severity scores were found in ***Bacteroides*** enriched enterotype

Gut microbial signature for IBS severity is linked with lower exhaled CH_4



Lower severity

Higher exhaled CH_4

Higher Severity

Lower exhaled CH_4

Methanogens undetected

Methanogens detected

Take home messages

- A larger cohort of IBS patients (n>200) allows finding gut microbiota alteration **over random expectation**

- IBS symptom severity is associated with a distinct signature at fecal microbiota level

- Gut microbial signature for IBS severity is linked with
  - low microbial richness
  - *Bacteroides* enriched enterotype
  - low Archea methanogens and exhaled CH_4

The role of gut microbiota alterations
in the genesis of IBS remains to be investigated

Acknowledgments

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