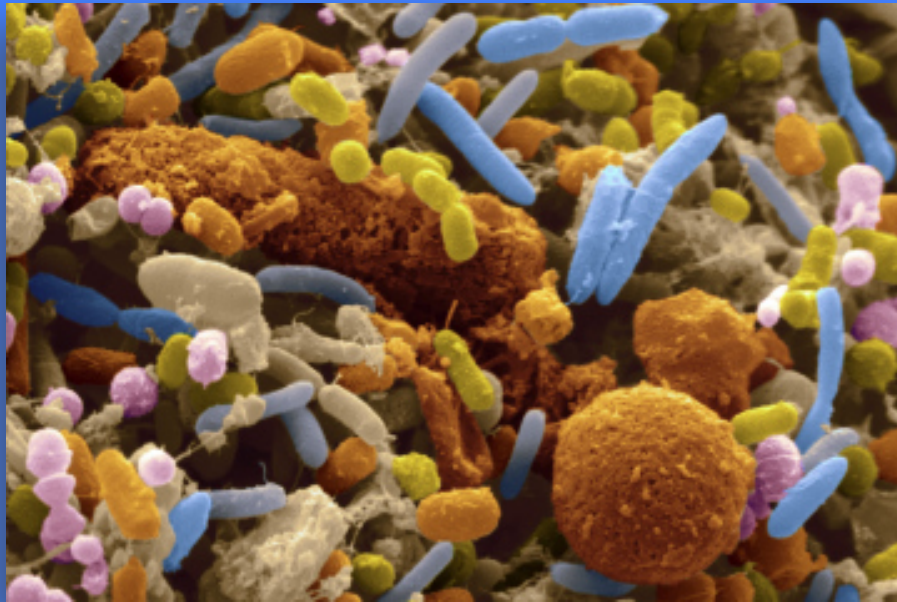


Microbiome Dysbiosis in Health and Disease: Making Predictions



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The University of Michigan

@PatSchloss

http://schlosslab.org/talks/Schloss_NIAID2015.pdf

Call to arms

What are the translatable deliverables that we have to show for all of the recent microbiome work?



James Hadfield
@CIgenomics



 **Follow**

RK: microbiome allows you to predict if someone is obese or not with high accuracy
[#AGBT15](#)

RETWEET

1

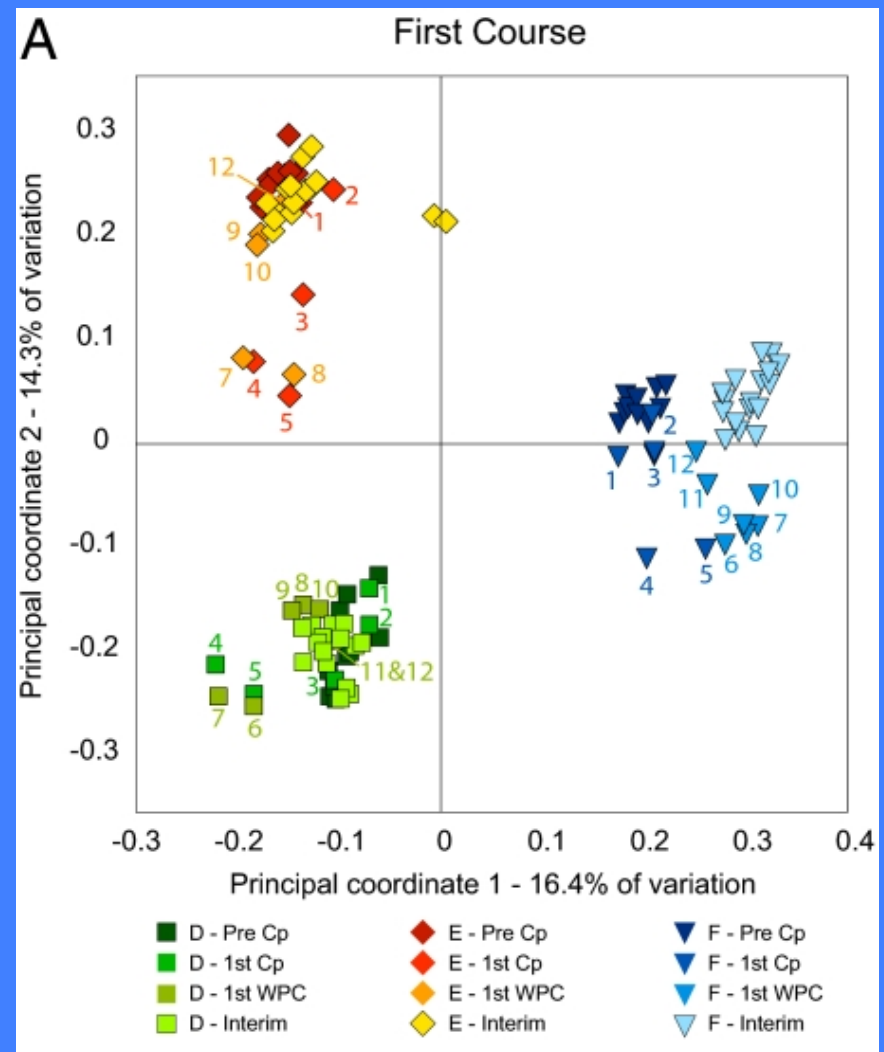


9:52 AM - 28 Feb 2015



Where is there potential?

- Manipulate the microbiome (really hard)
- Diagnostics



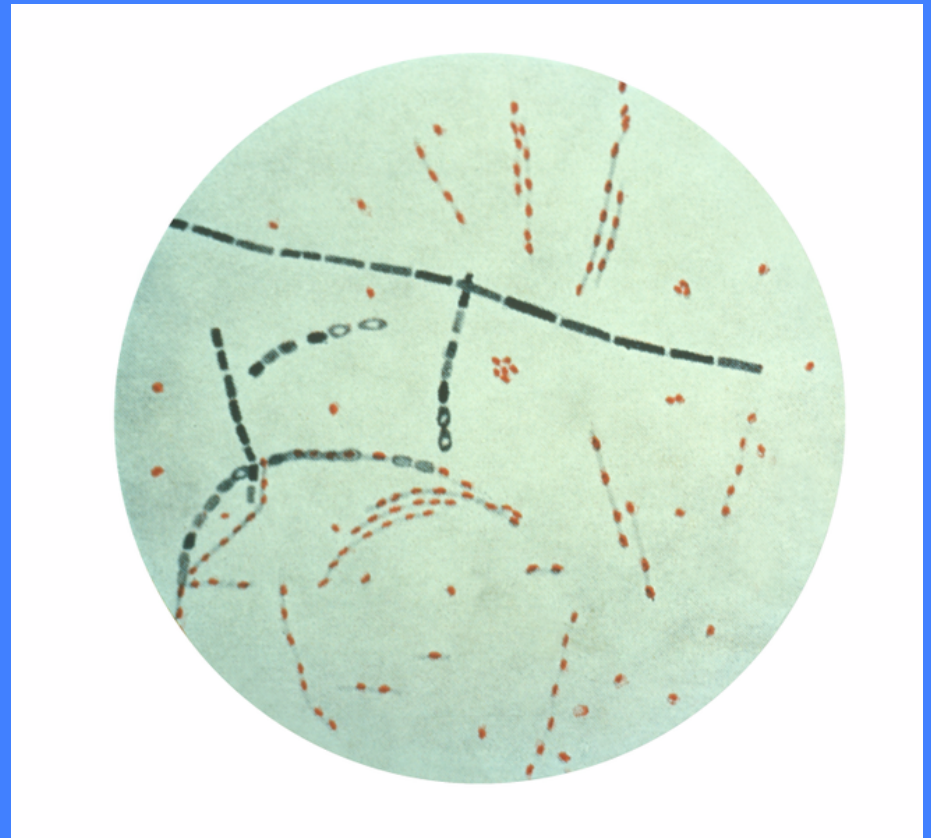
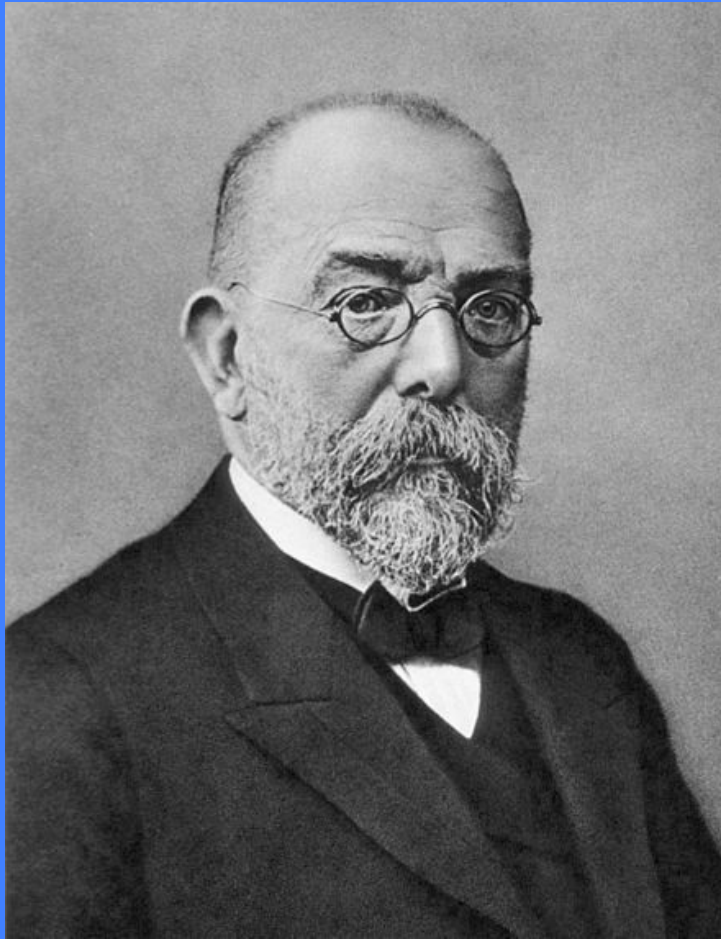
The microbiome is a potential reservoir for biomarkers

- Reservoir
 - $\sim 10^2$ - 10^3 species per subject
 - $\sim 10^2$ - 10^3 bacterial genes per human gene
 - Growing evidence that microbiome is involved in health and disease
- Applications
 - Non-invasive diagnoses
 - Assess risk
 - Predict outcomes

Making predictions using the microbiome

- Experimental predictions
- Whole community analysis
 - Beta diversity
 - Community typing
- Population-level analysis
 - H_1 : Individual populations cause disease
 - H_2 : Mixed and varied populations cause disease

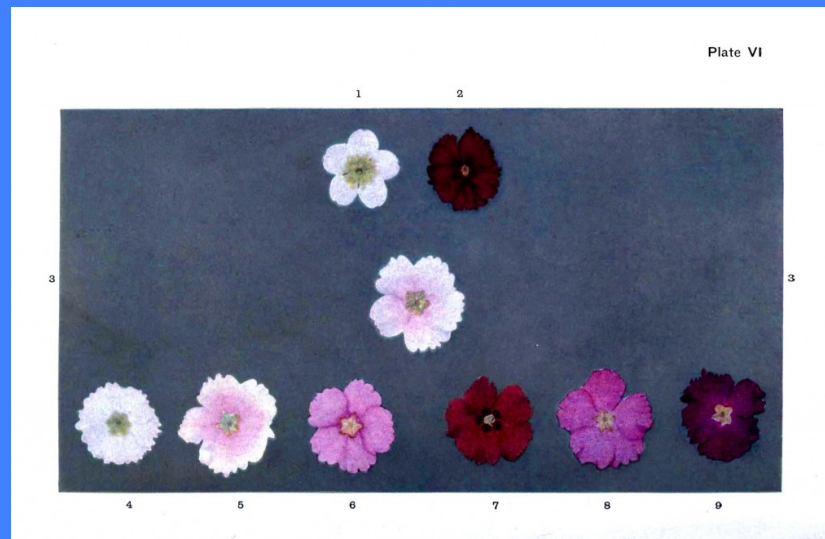
Single bug: The mechanism of disease



Simple model of the genome

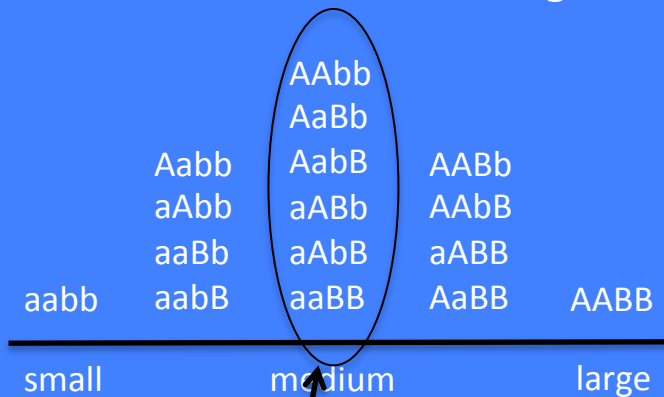
	Aa	
aa	aA	AA
white	pink	red

Huntington's



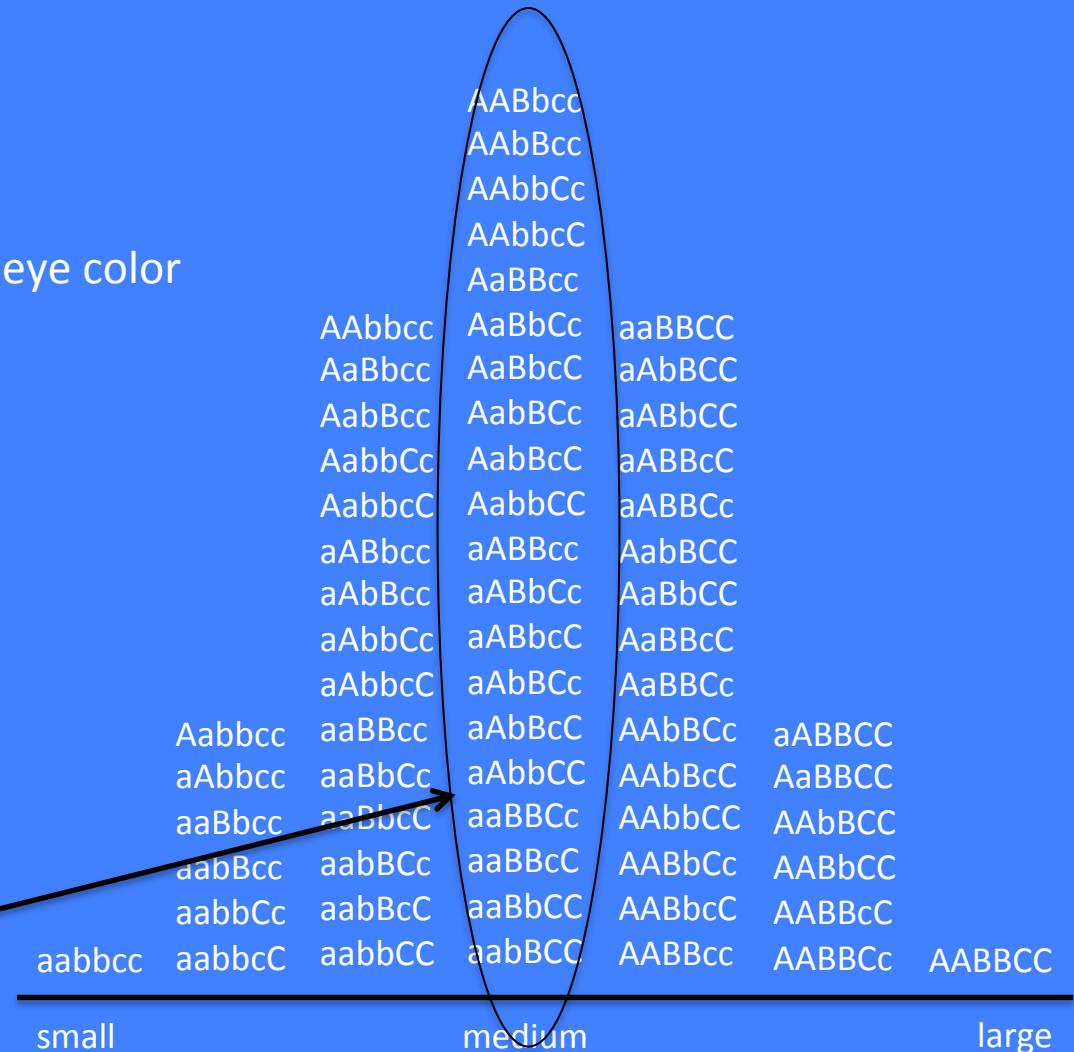
Polygenic trait / polymicrobial infection(?)

e.g. Skin and eye color



Two identical contributing genes

Many different
genotypes can give rise
to the same phenotype



Three identical contributing genes

Complex traits

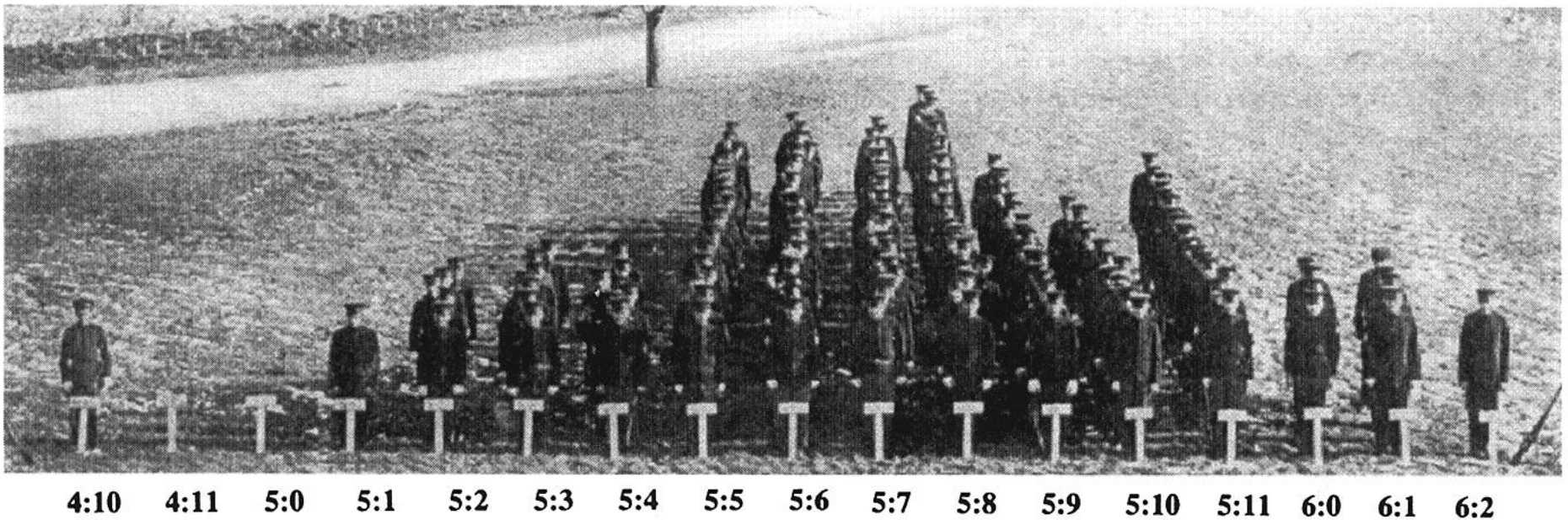
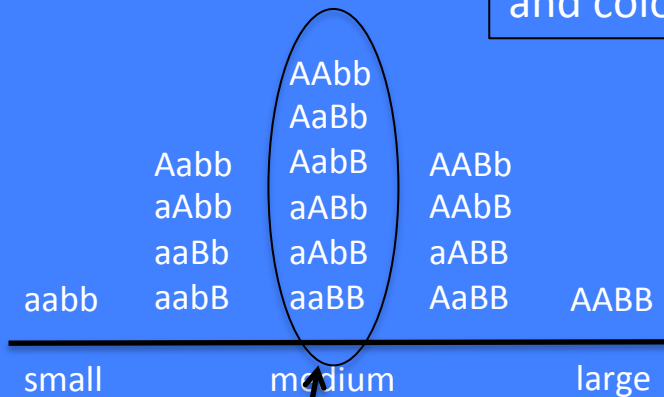


Figure 12. Living histogram of 175 male college students (Blakeslee 1914).

Genetics x Environment (Diet)

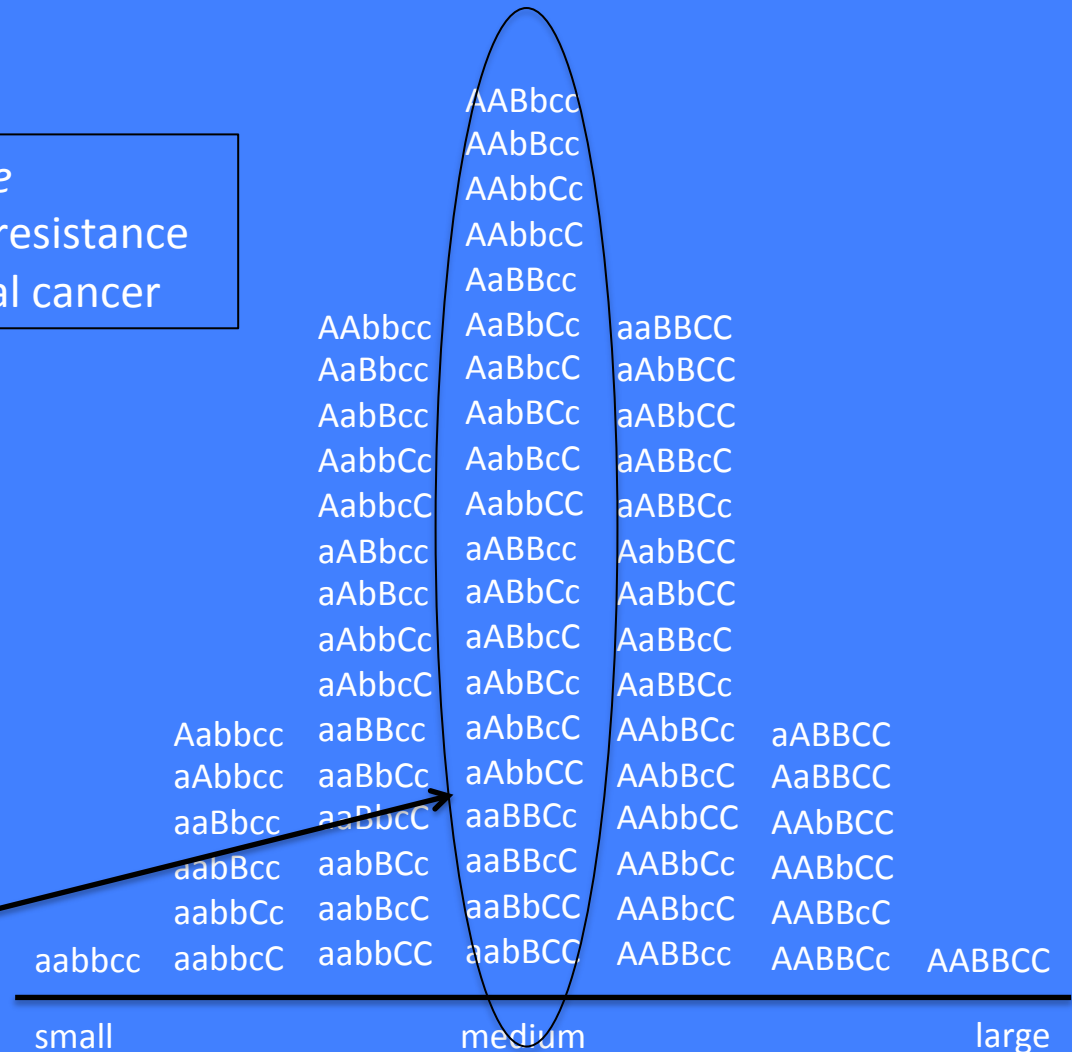
Polygenic trait / polymicrobial infection(?)

e.g. *C. difficile*
colonization resistance
and colorectal cancer



Two identical contributing genes

Many different bacteria
can give rise to the
same phenotype



Three identical contributing genes

Case studies

- **Colorectal cancer**
- *Clostridium difficile* infection

Colorectal cancer

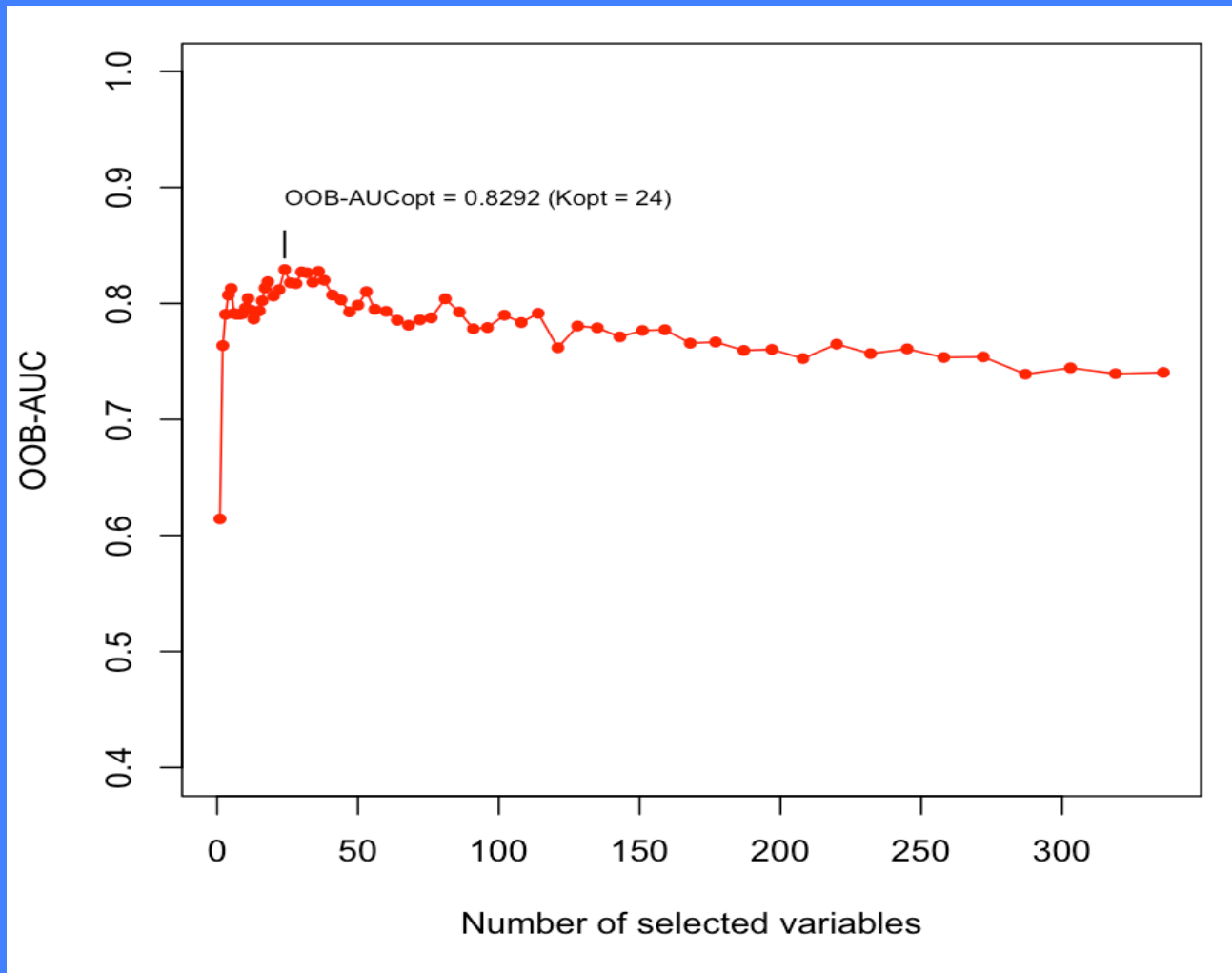
- One-third of individuals do not adhere to screening recommendations partly because they're miserable and expensive
- Growing use of non-invasive diagnostics (FOBT, FIT, ColoGuard); but limited ability to detect adenomas

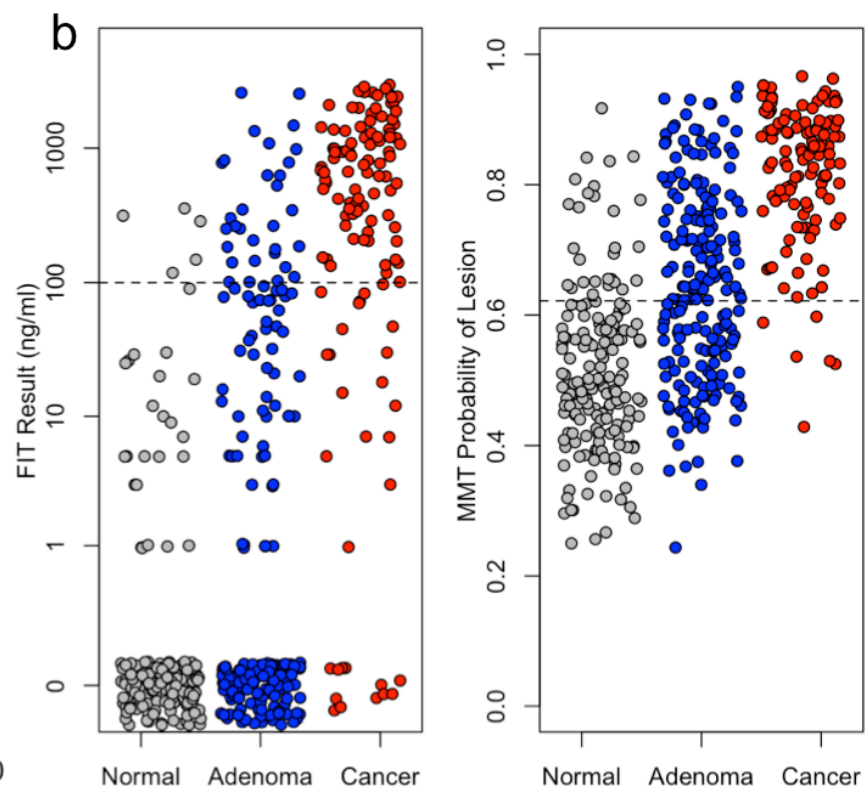
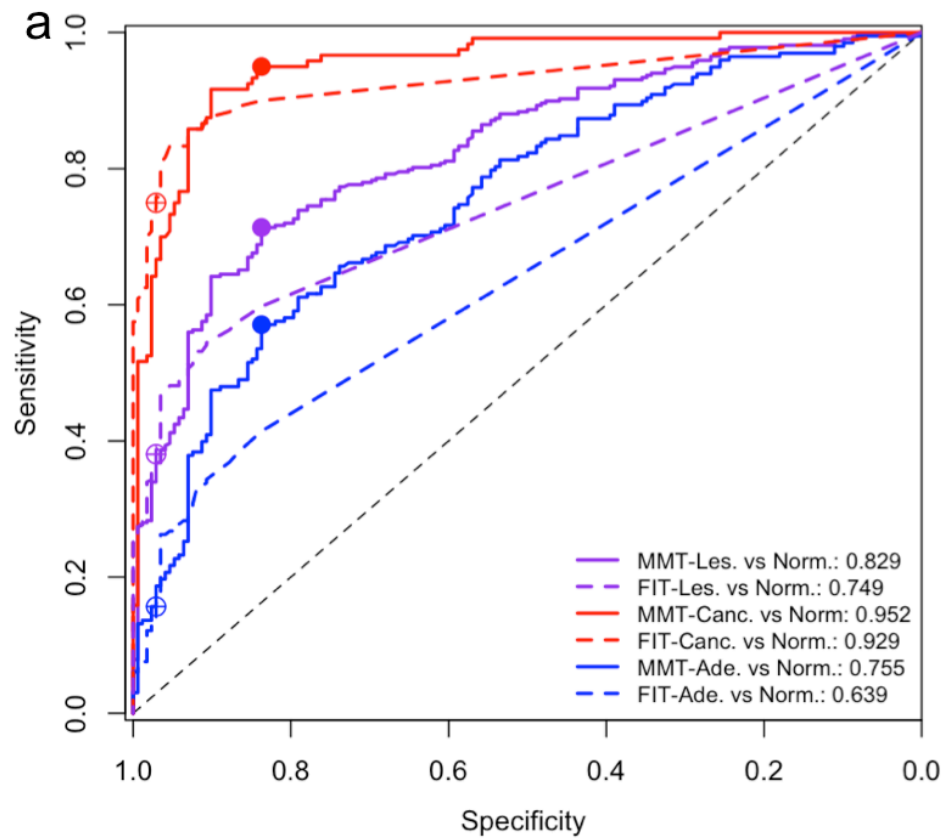
Design

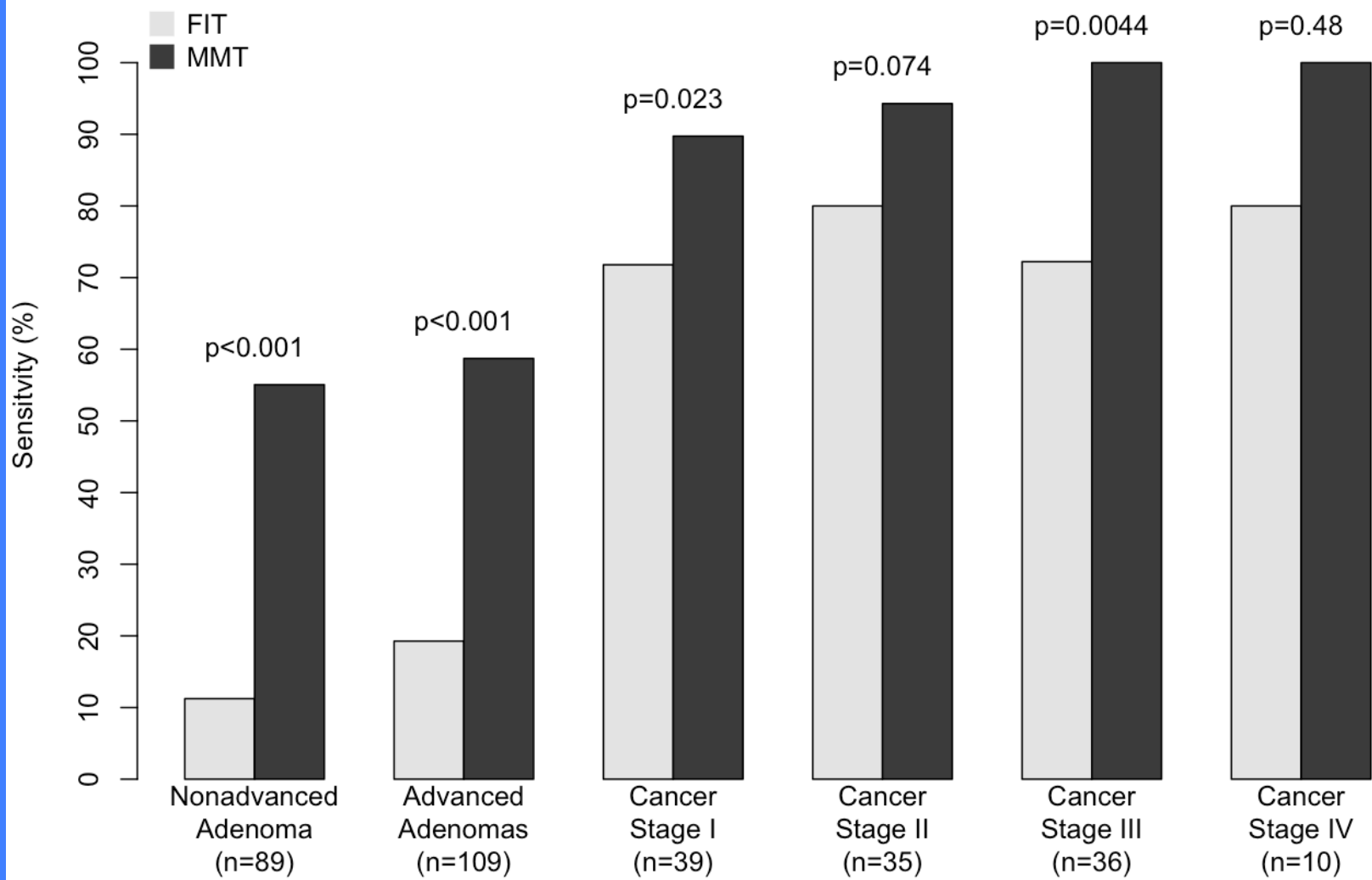
- Cohort of 490 subjects (172 normal, 198 adenoma, 120 carcinoma) with paired colonoscopy
- Generated 16S rRNA gene sequence data from V4 region
- Processed with mothur* to get a sequencing error rate of 0.02%
- Used random forest machine learning algorithm

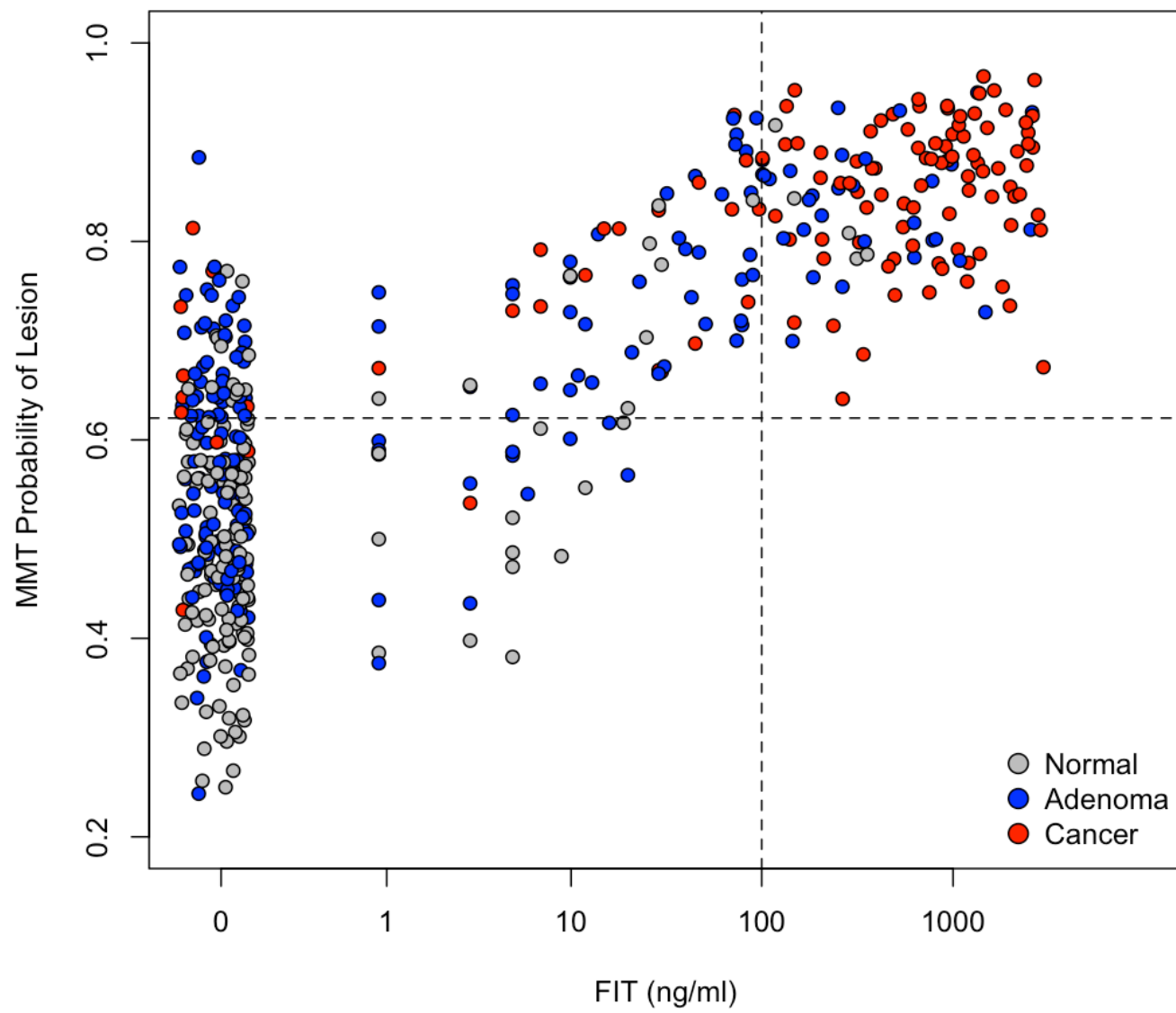
* The best software package for analyzing 16S rRNA gene sequence data (www.mothur.org)

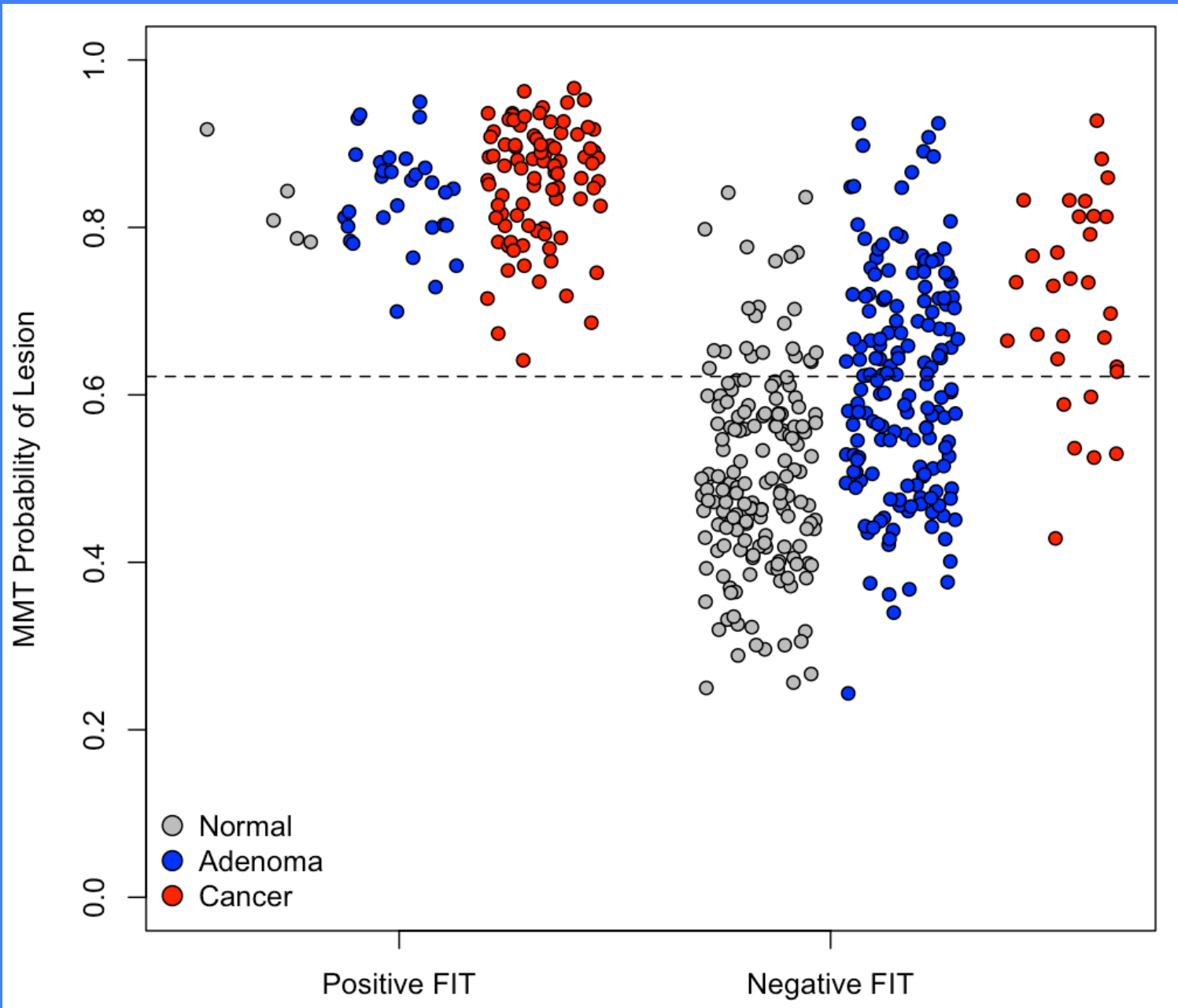
The Multitarget Microbiota Test: Microbiome + FIT

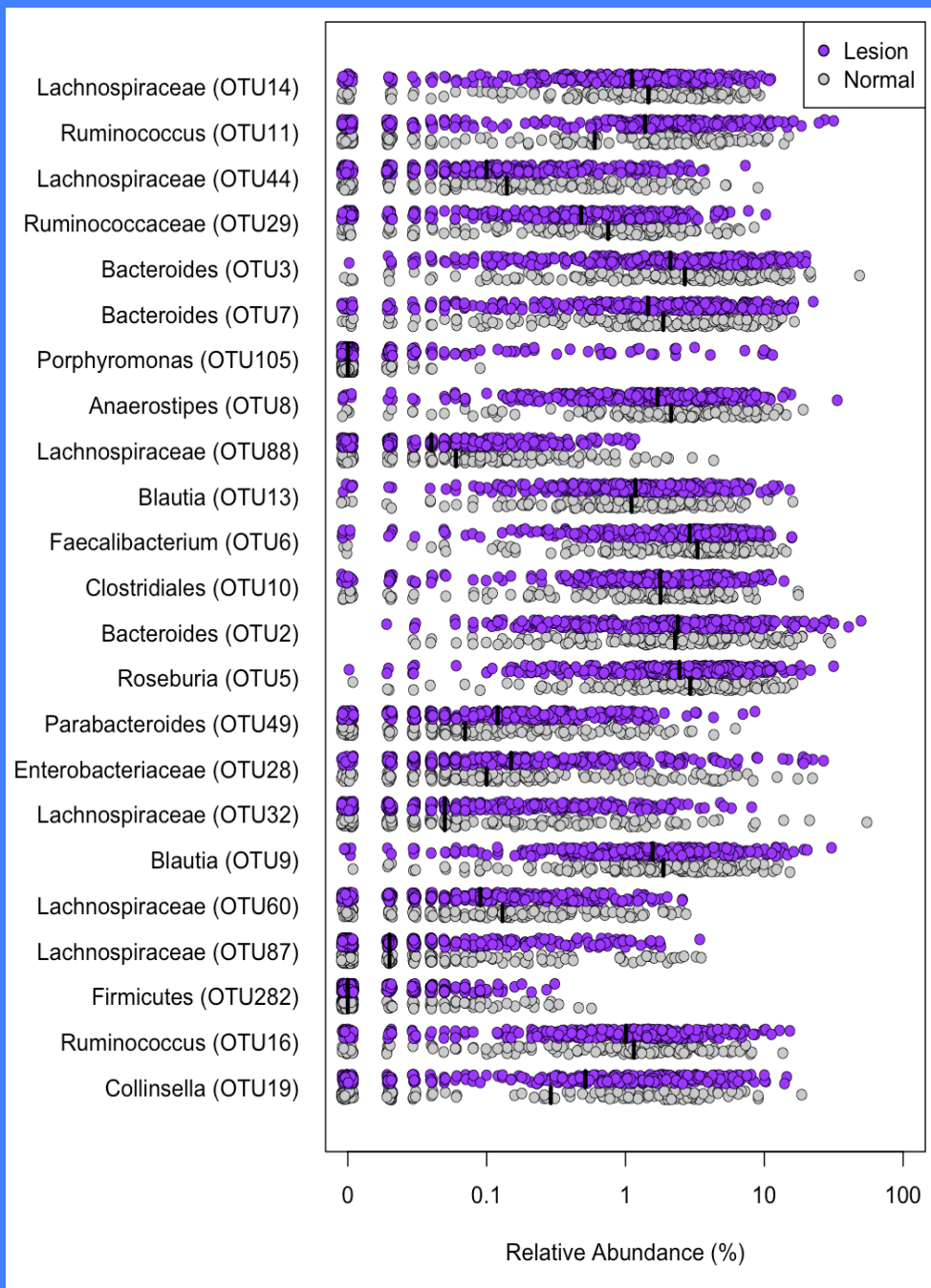










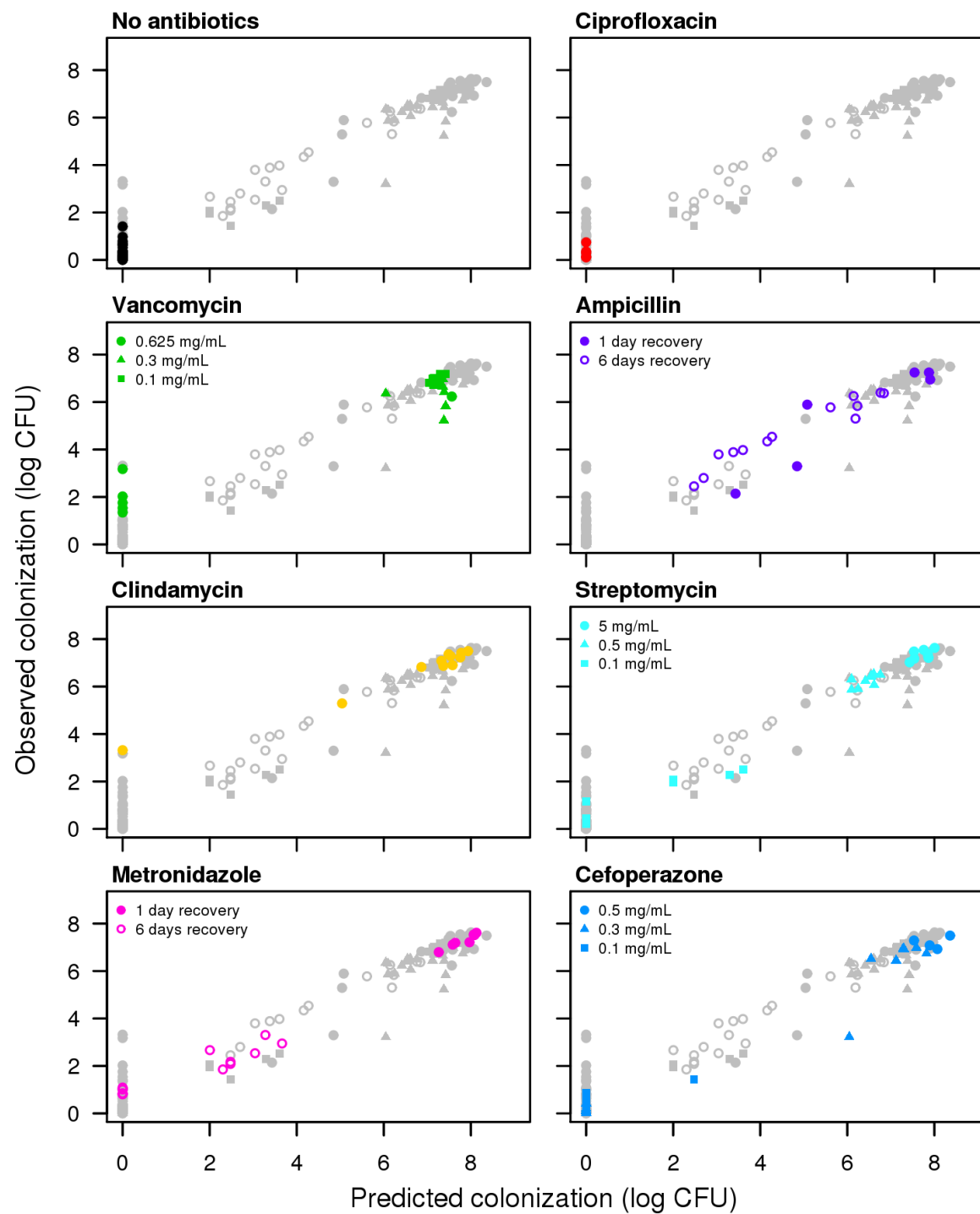


Case studies

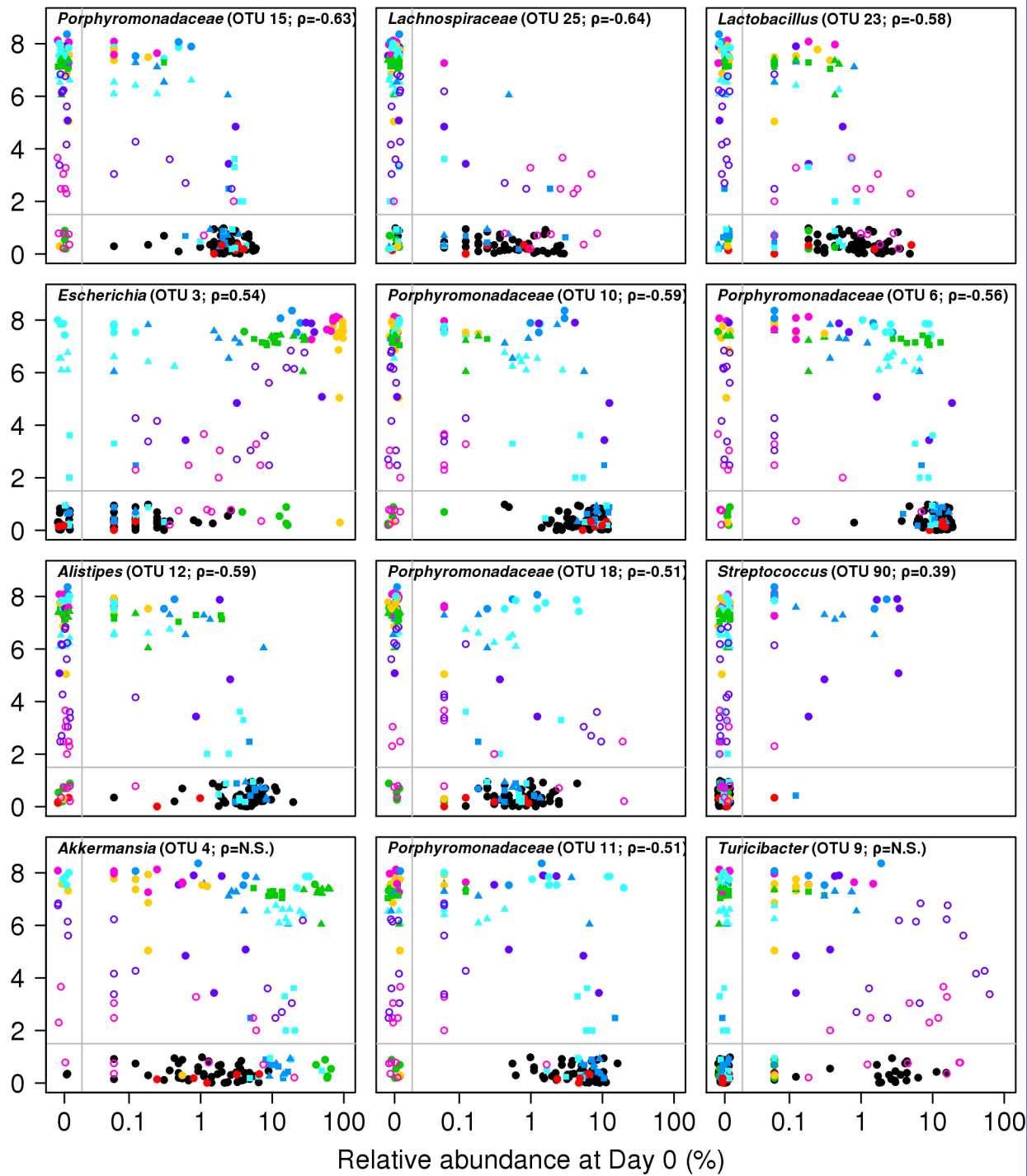
- Colorectal cancer
- *Clostridium difficile* infection

Can we predict who will get *C. difficile*?

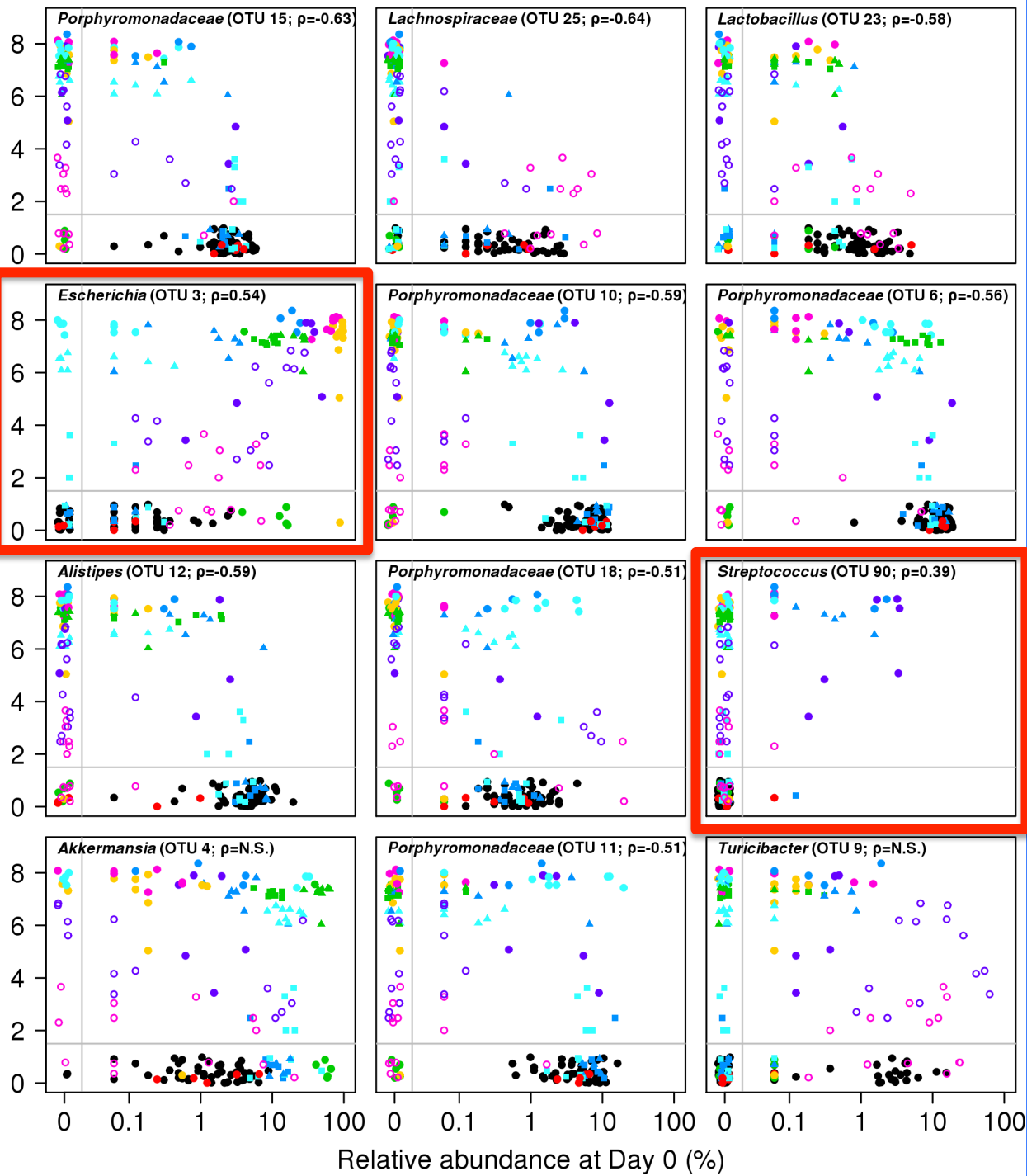
- We can predict who has *C. difficile* based on the other bacteria in their stool (see obesity)
- Imagine getting a rectal swab/stool sample of everyone that comes into the hospital and being able to assess the patient's risk of getting *C. difficile*
- Can do this with mice



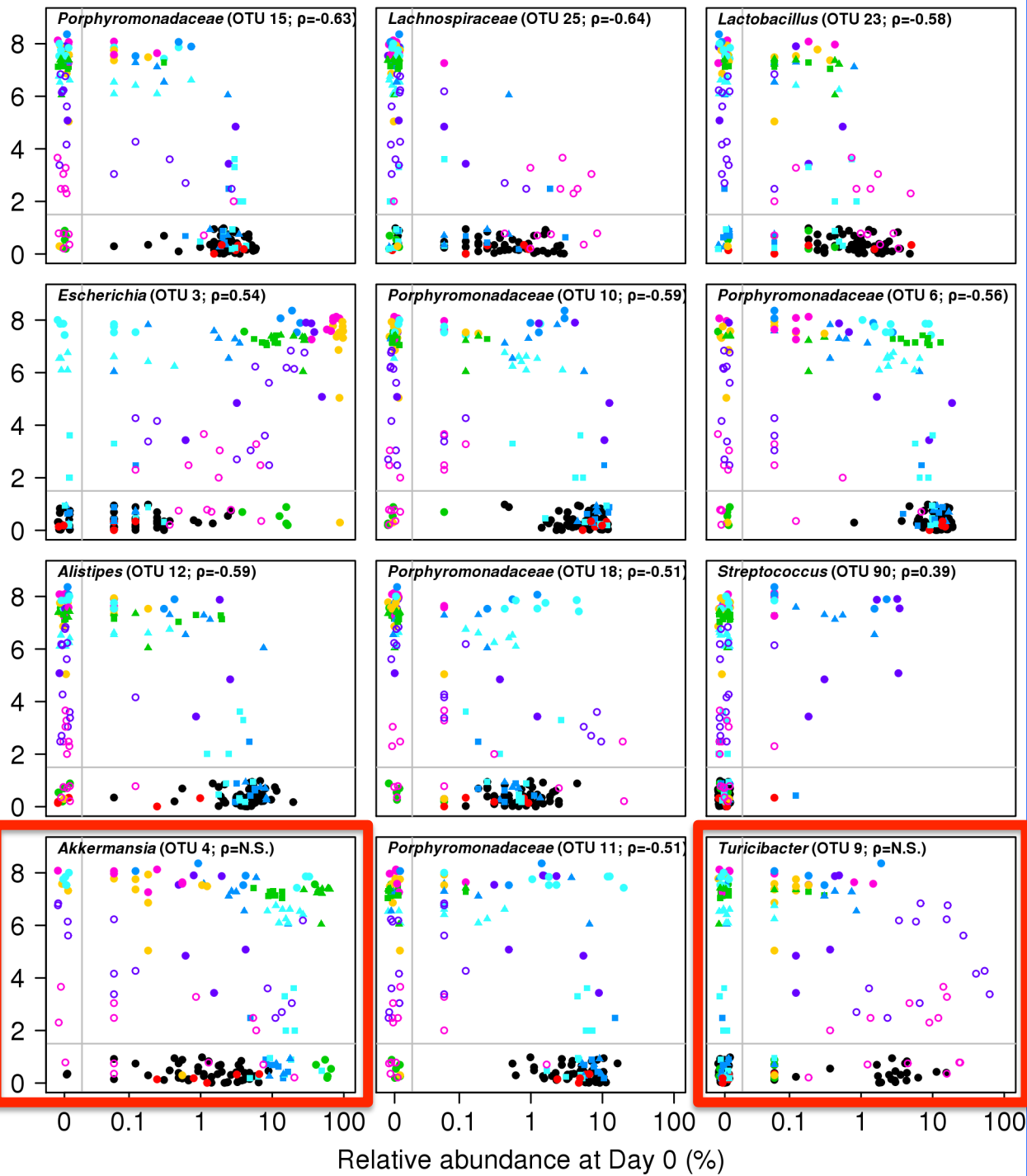
Observed colonization (log CFU)



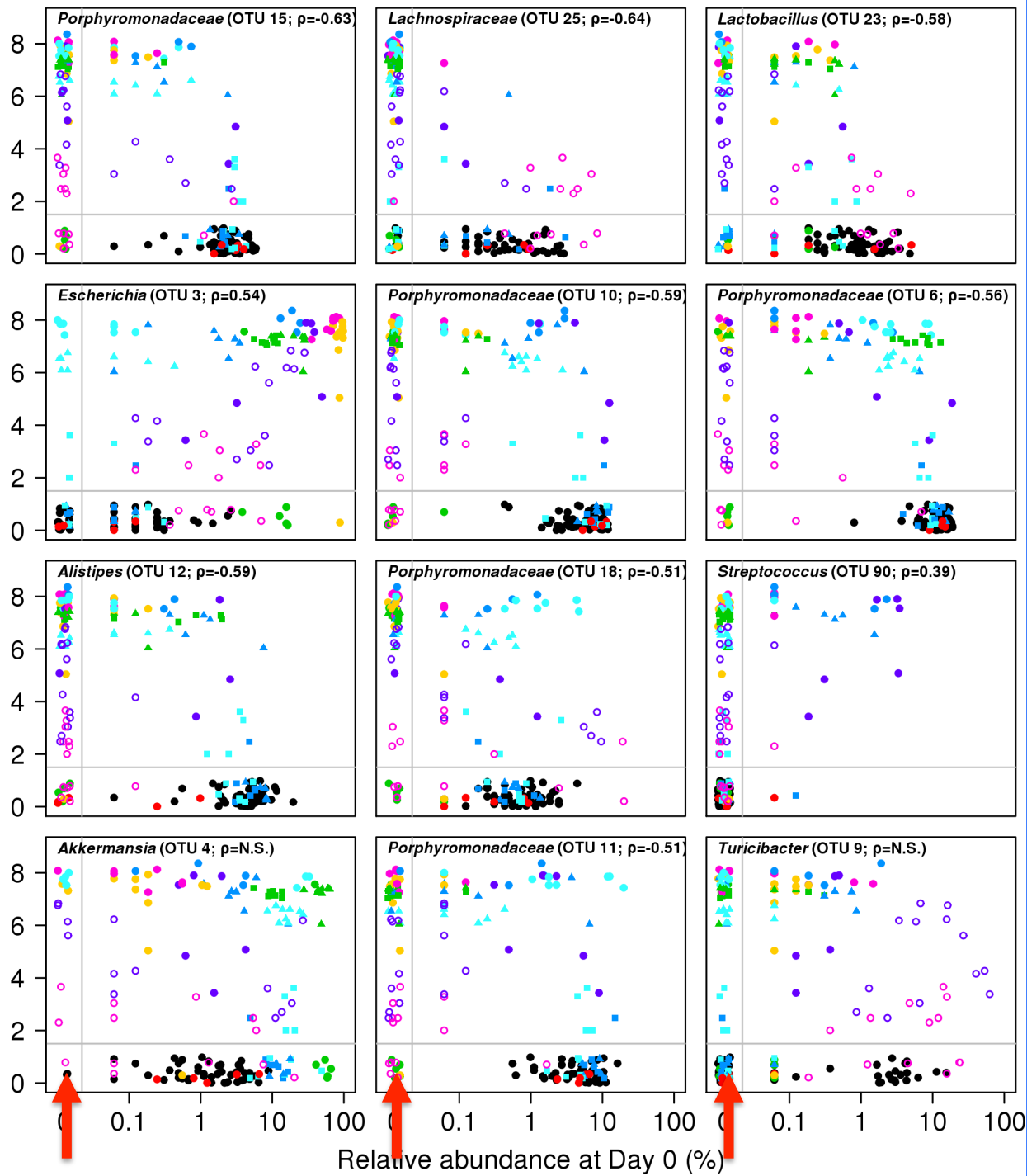
Observed colonization (log CFU)

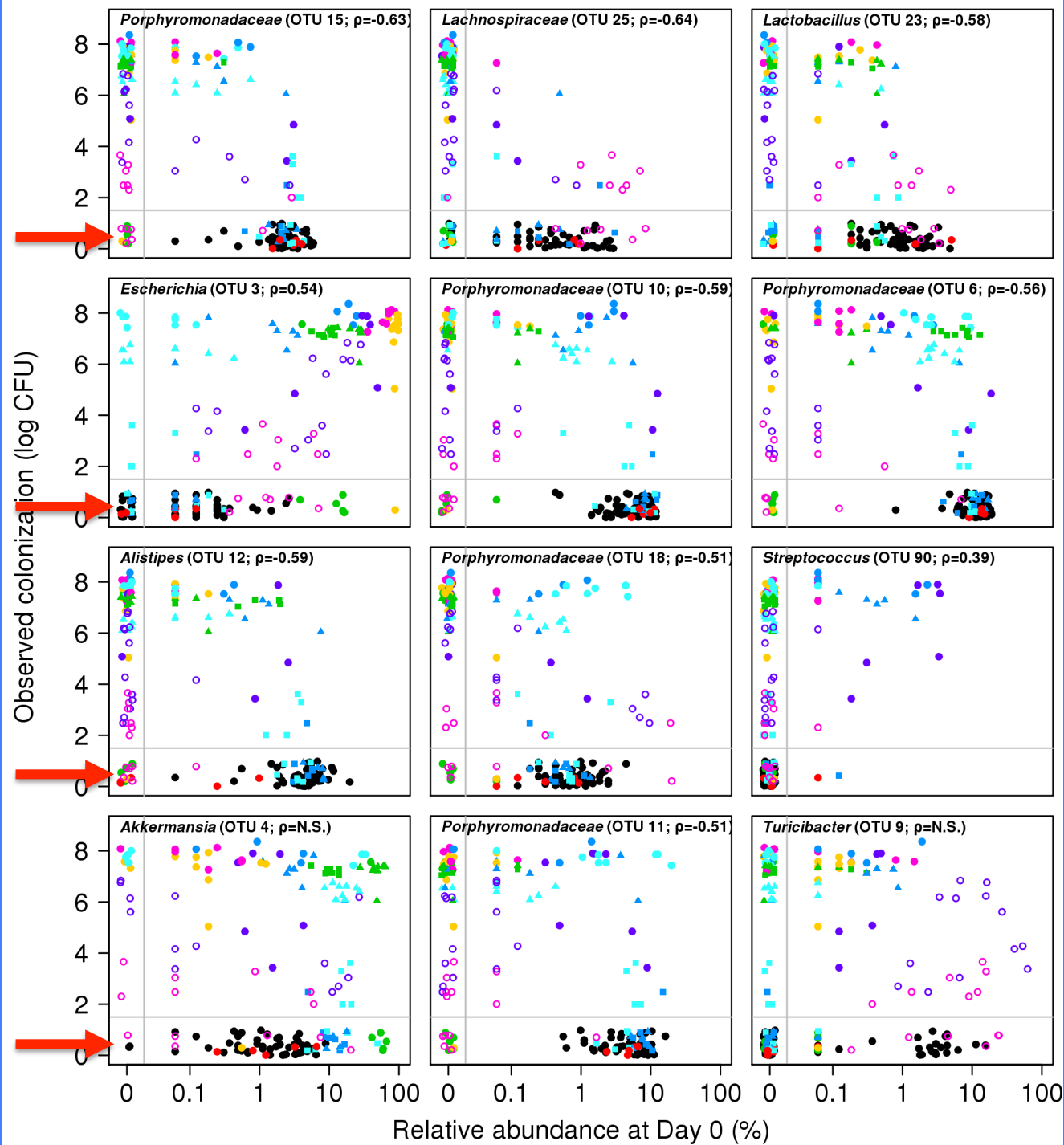


Observed colonization (log CFU)



Observed colonization (log CFU)





Context matters...

- Have shown in the microbial context, but also host context matters
 - Sex, age, co-morbidities
 - Host gene expression
 - Diet, etc.
- Like GWAS, most diseases are not the result of single gene/microbe

You keep using that word

**I do not think it means what you
think it means.**

A photograph of a brown and white dog, possibly a pit bull mix, standing on a grassy area with some dry leaves. The dog is looking down and to the left. The background is a mix of green grass and brown leaves.

**SCOOP
THAT POOP**

**Tips for
Bringing a Fecal
Sample to Your
Veterinarian**

mypawsitivelypets.com

Acknowledgements



Funding

- NIH U19AI090871
- NIH R01HG005975
- NIH R01GM099514
- U of M GI SPORE

<http://github.com/SchlossLab>
<http://www.mothur.org>

CRC

- Niel Baxter
- Joe Zackular, PhD
- Dean Brenner, MD
- Mack Ruffin, MD

C. difficile

- Alyx Schubert, PhD
- Vince Young, MD/PhD
- Mary Rogers, PhD

