

Microbiome Dysbiosis in Health and Disease: Making Predictions



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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?

The image shows a tweet from James Hadfield (@Clgenomics) on February 28, 2015, at 9:52 AM. The tweet content is: "RK: microbiome allows you to predict if someone is obese or not with high accuracy #AGBT15". The tweet has 1 retweet. The interface includes standard Twitter interaction icons like reply, retweet, favorite, and more.

James Hadfield
@Clgenomics

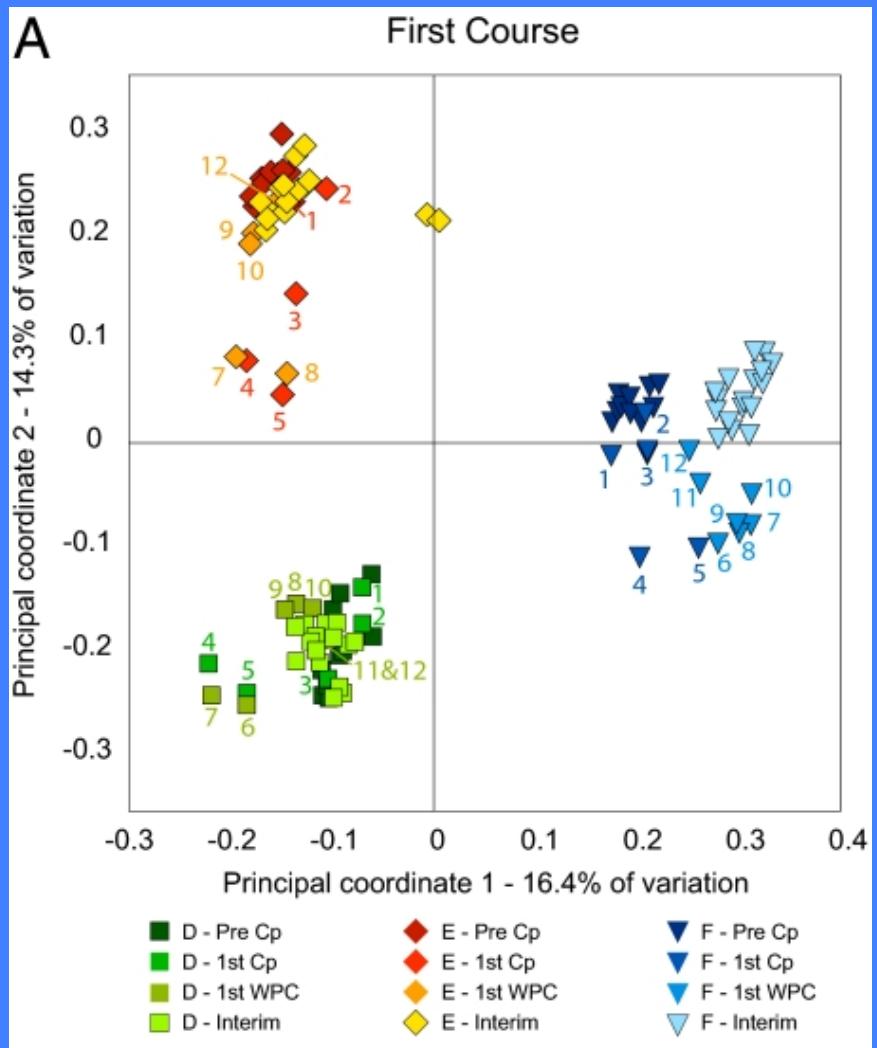
RK: microbiome allows you to predict if someone is obese or not with high accuracy
#AGBT15

RETWEET 1

9:52 AM - 28 Feb 2015

Where is there potential?

- Manipulate the microbiome (really hard)
- Diagnostics



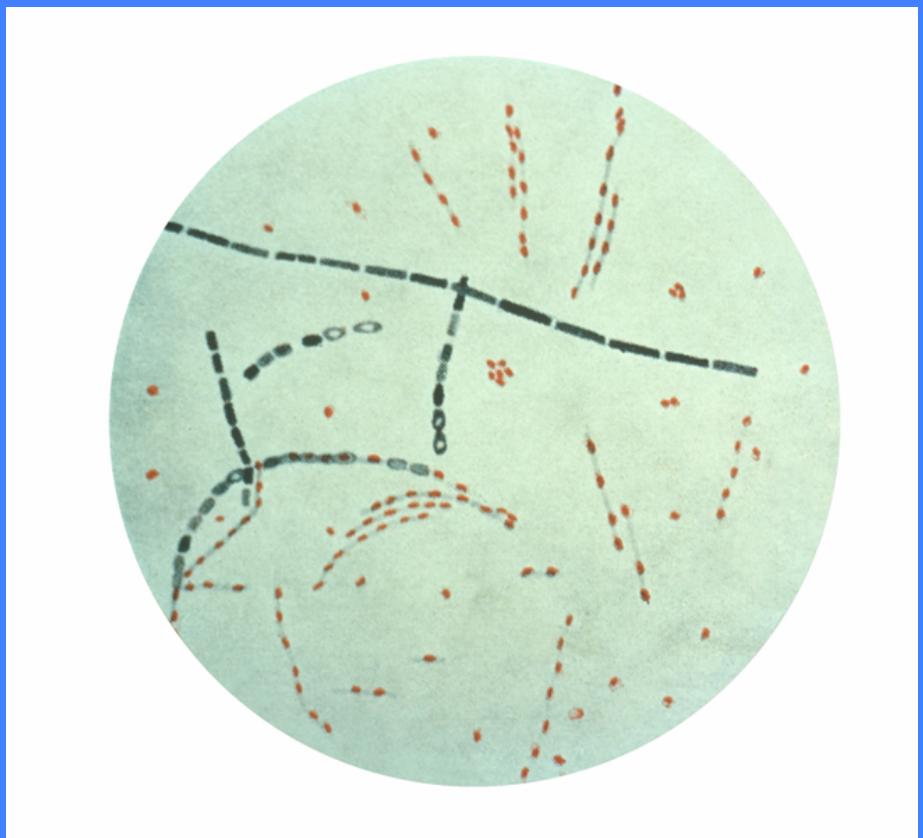
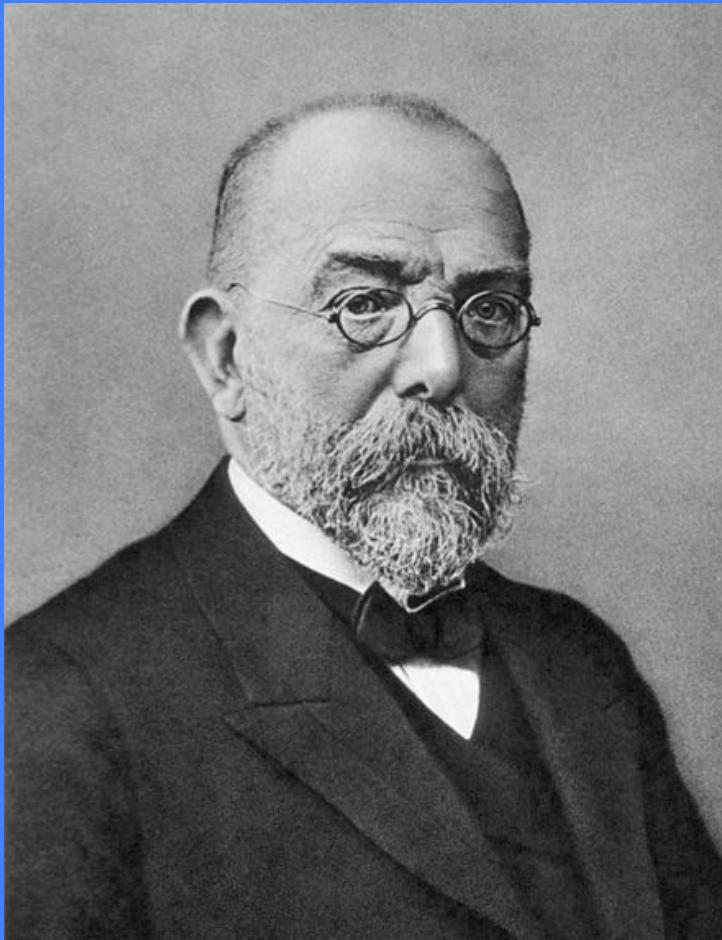
The microbiome is a potential reservoir for biomarkers

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

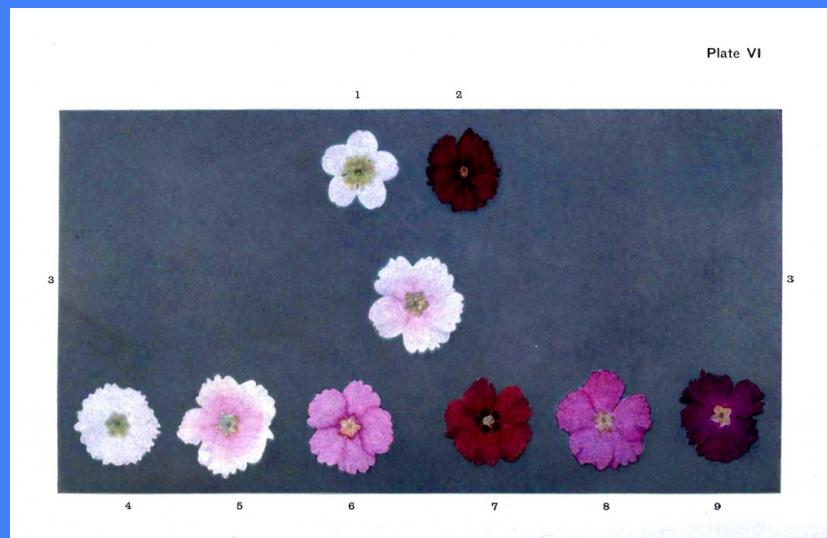
Making predictions using the microbiome

- 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

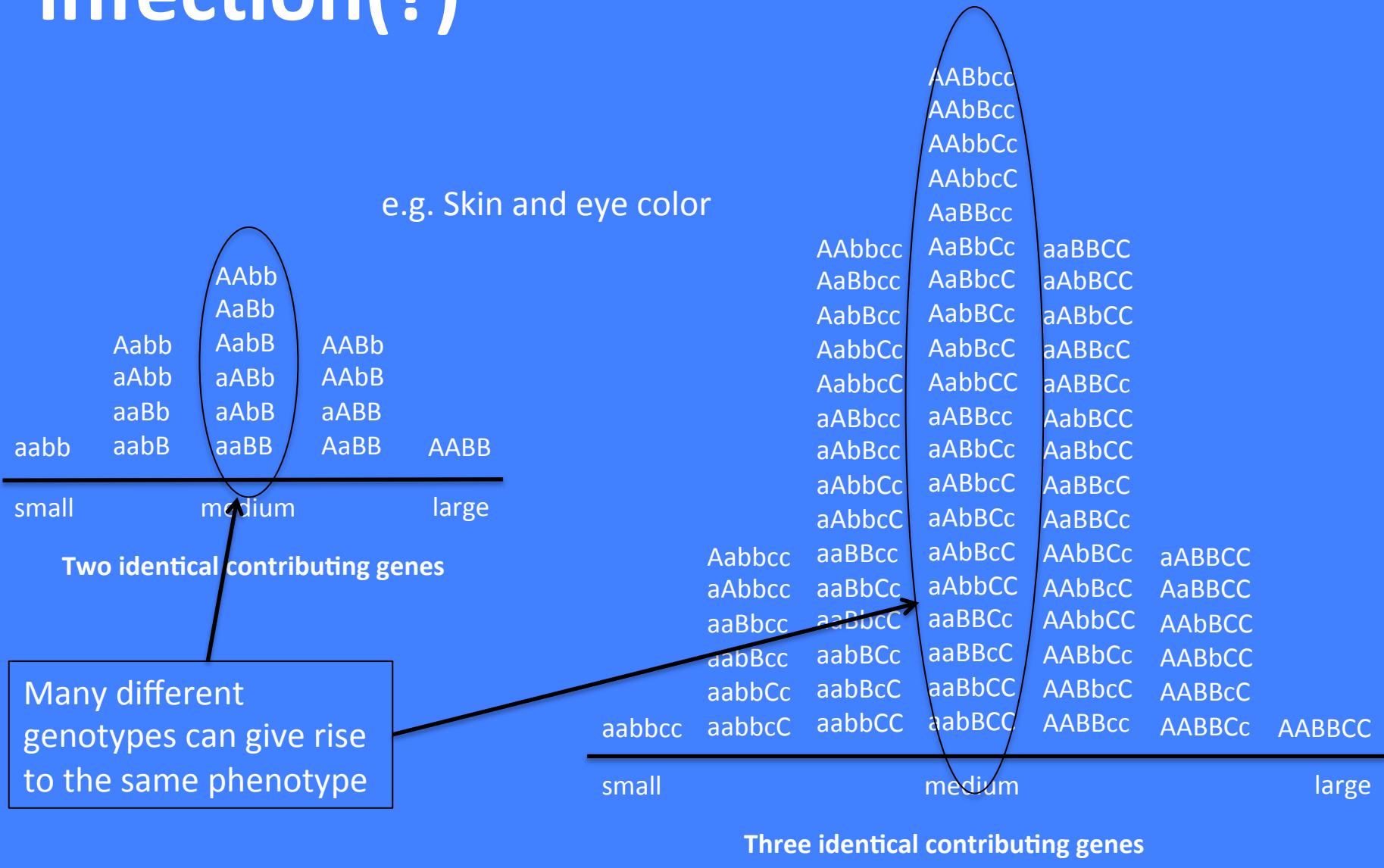


Simple model of the genome



Polygenic trait / polymicrobial infection(?)

e.g. Skin and eye color



Complex traits

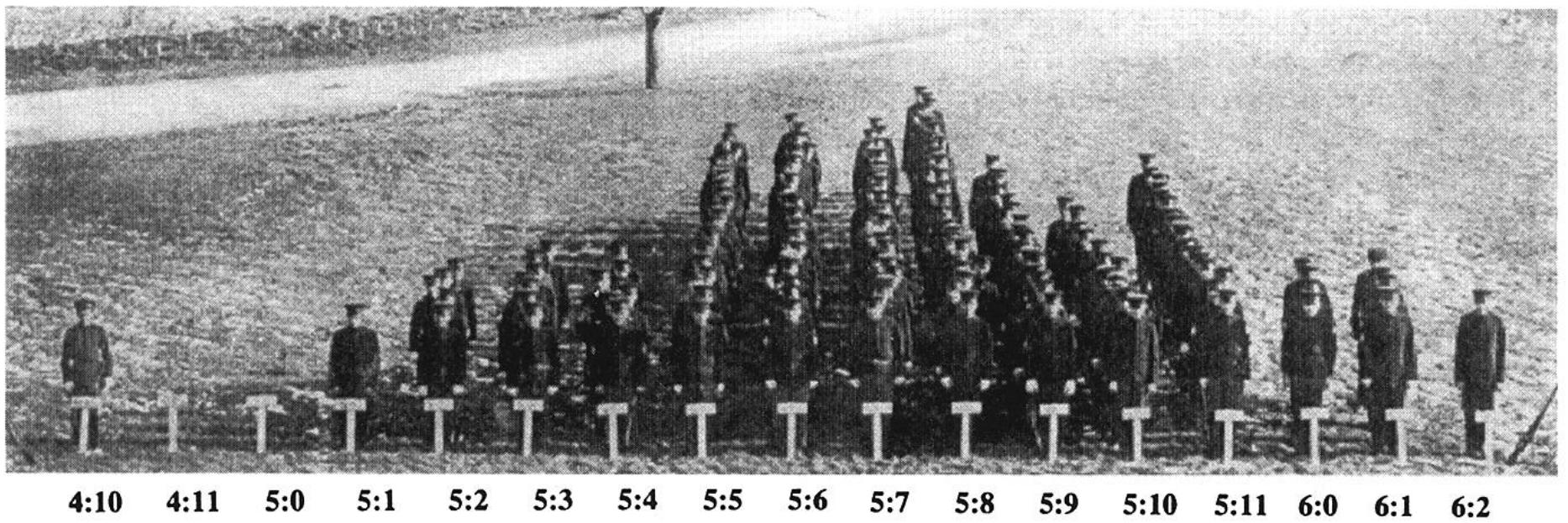
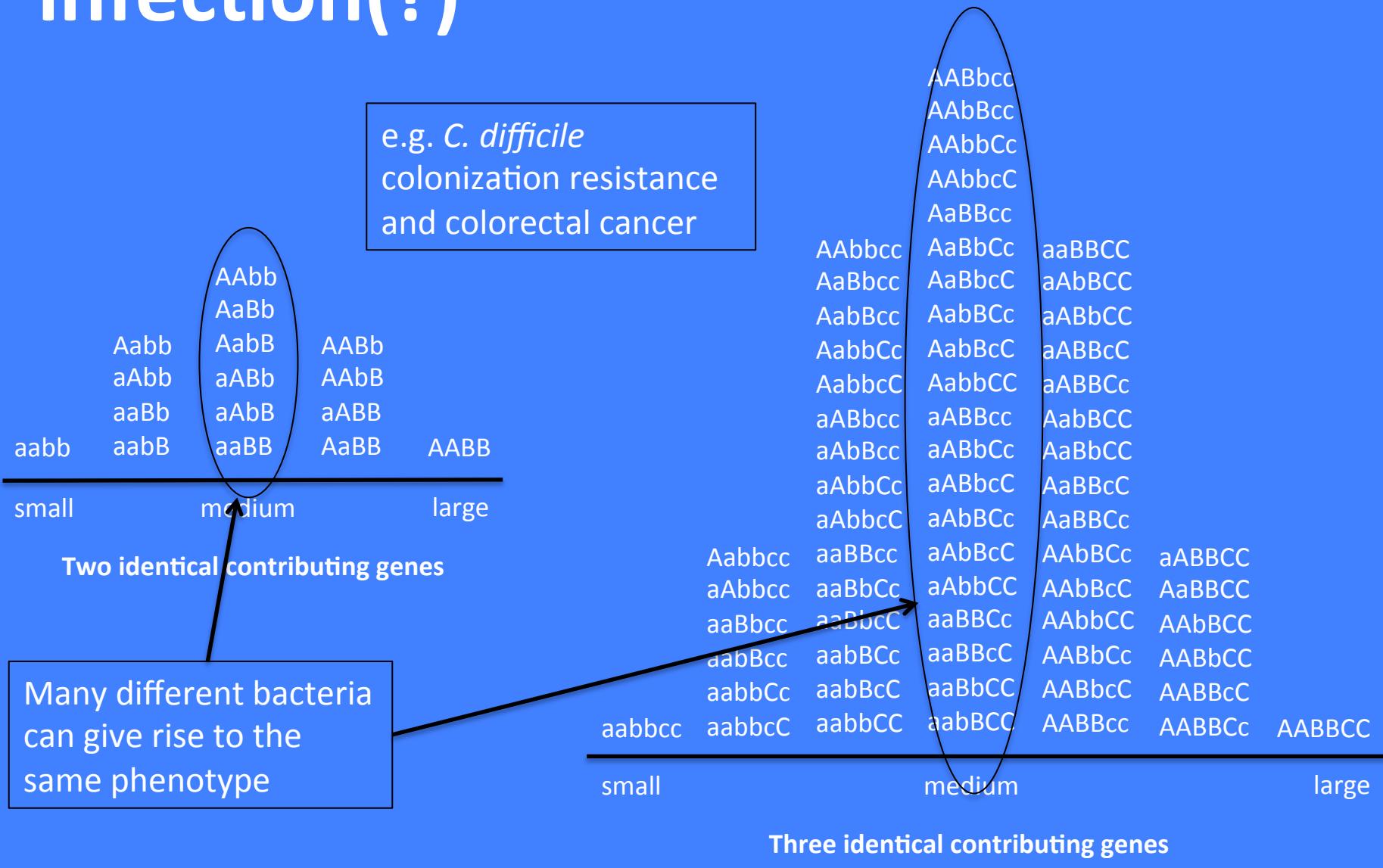


Figure 12. Living histogram of 175 male college students (Blakeslee 1914).

Genetics x Environment (Diet)

Polygenic trait / polymicrobial infection(?)

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



Case studies

- Colorectal cancer
- *Clostridium difficile* infection

Colorectal cancer

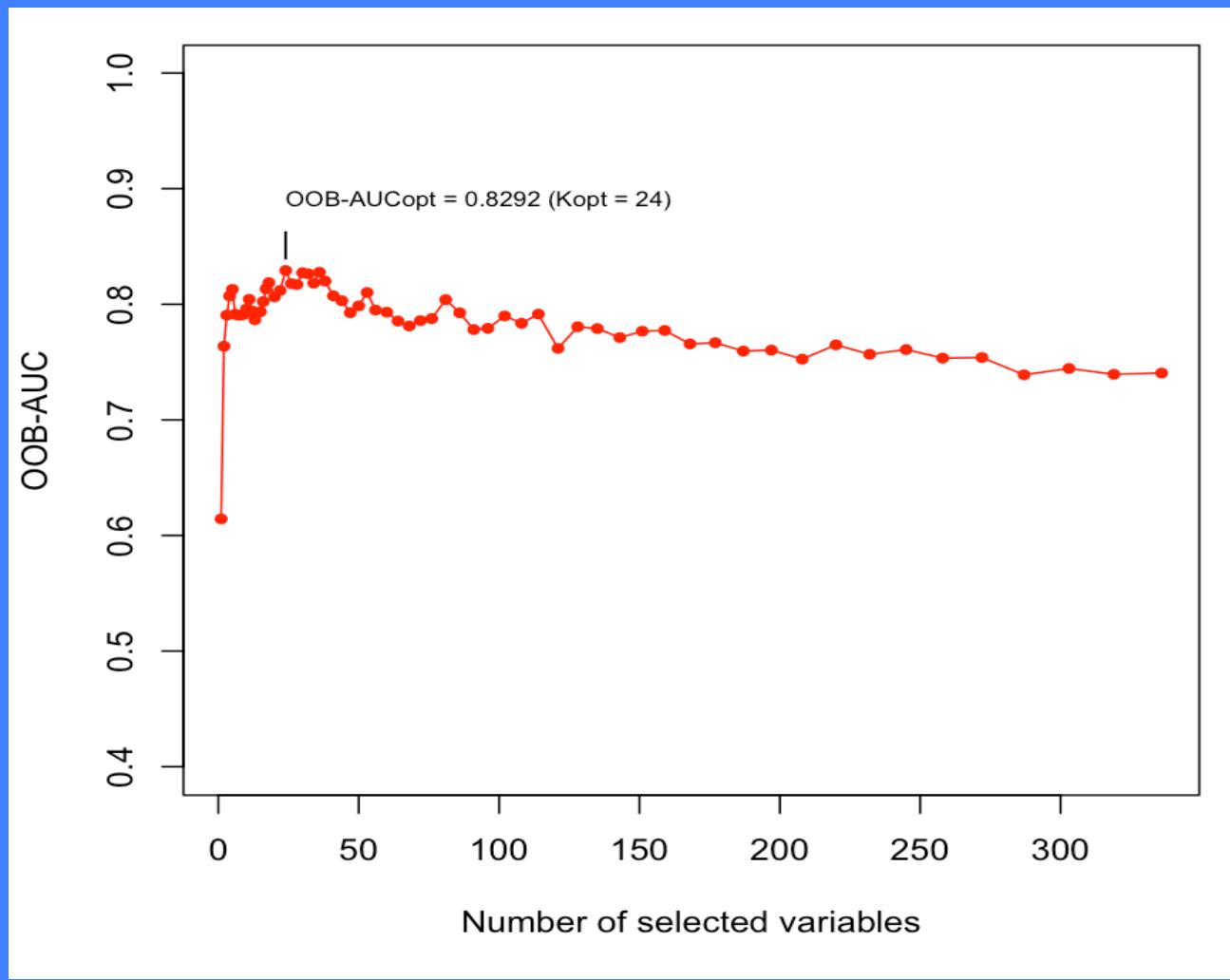
- One-third of individuals do not adhere to screening recommendations partly because they're miserable and expensive
- Growing use of non-invasive diagnostics (FOBT, FIT, ColoGuard); but limited ability to detect adenomas

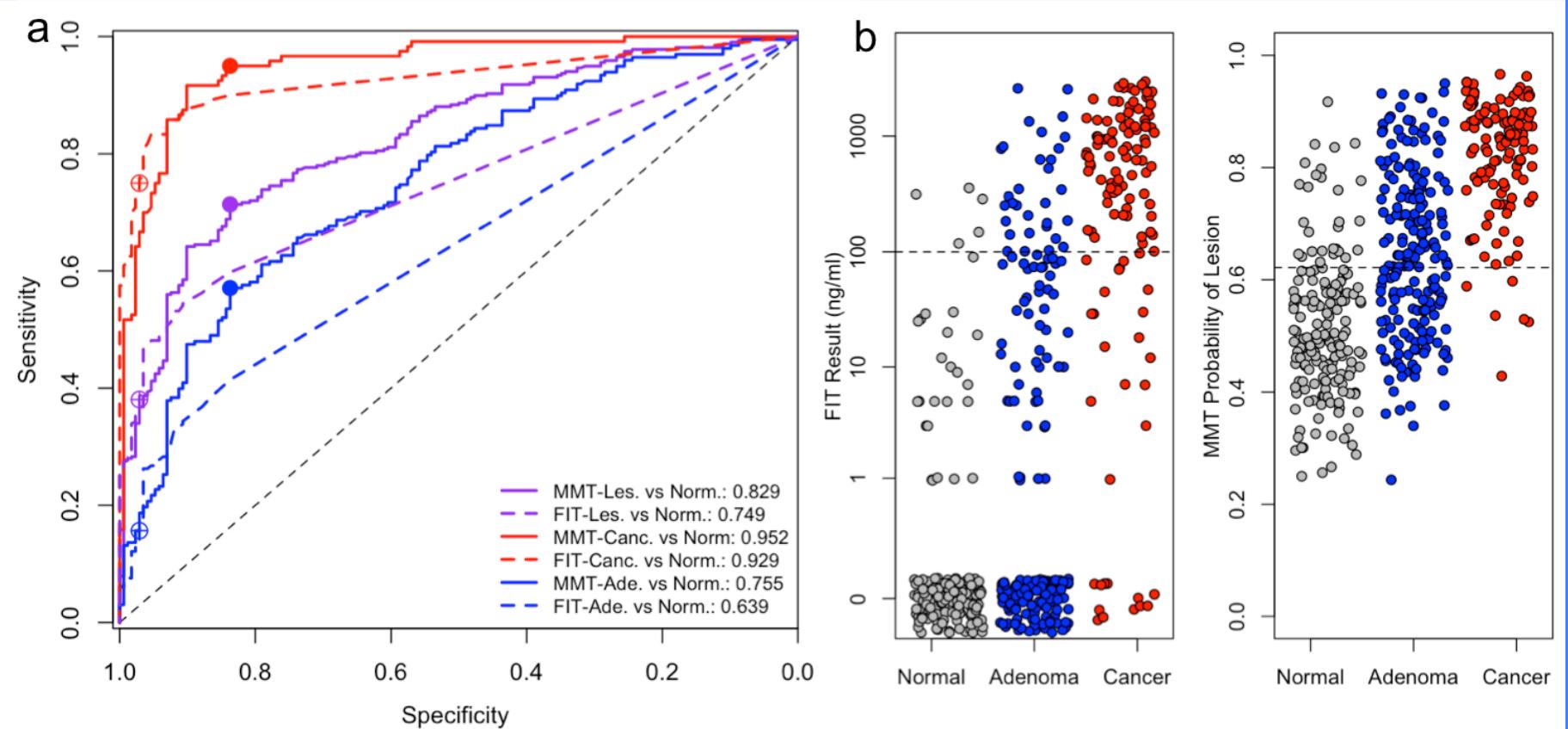
Design

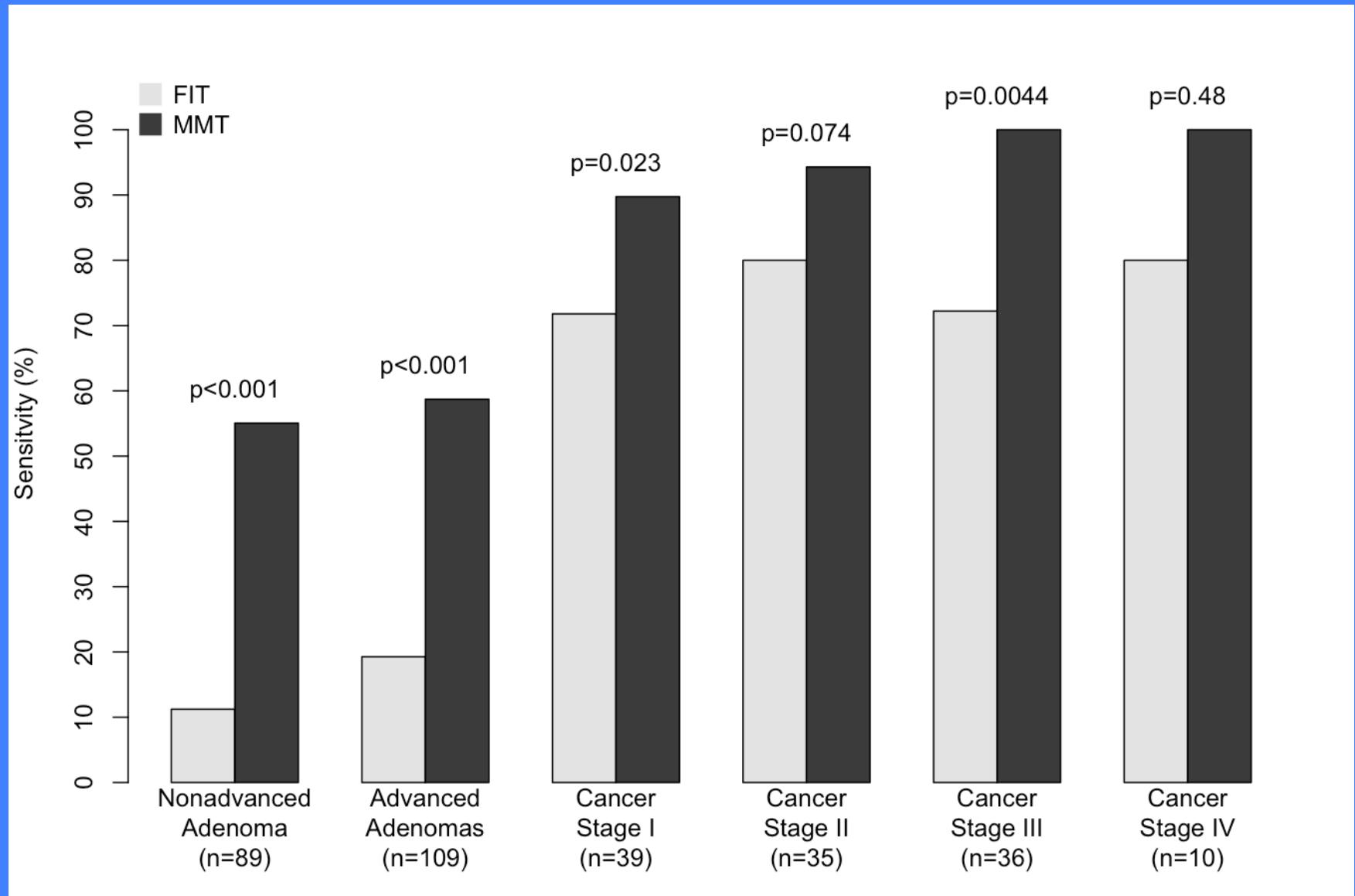
- Cohort of 490 subjects (172 normal, 198 adenoma, 120 carcinoma) with paired colonoscopy
- Generated 16S rRNA gene sequence data from V4 region
- Processed with mothur* to get a sequencing error rate of 0.02%
- Used random forest machine learning algorithm

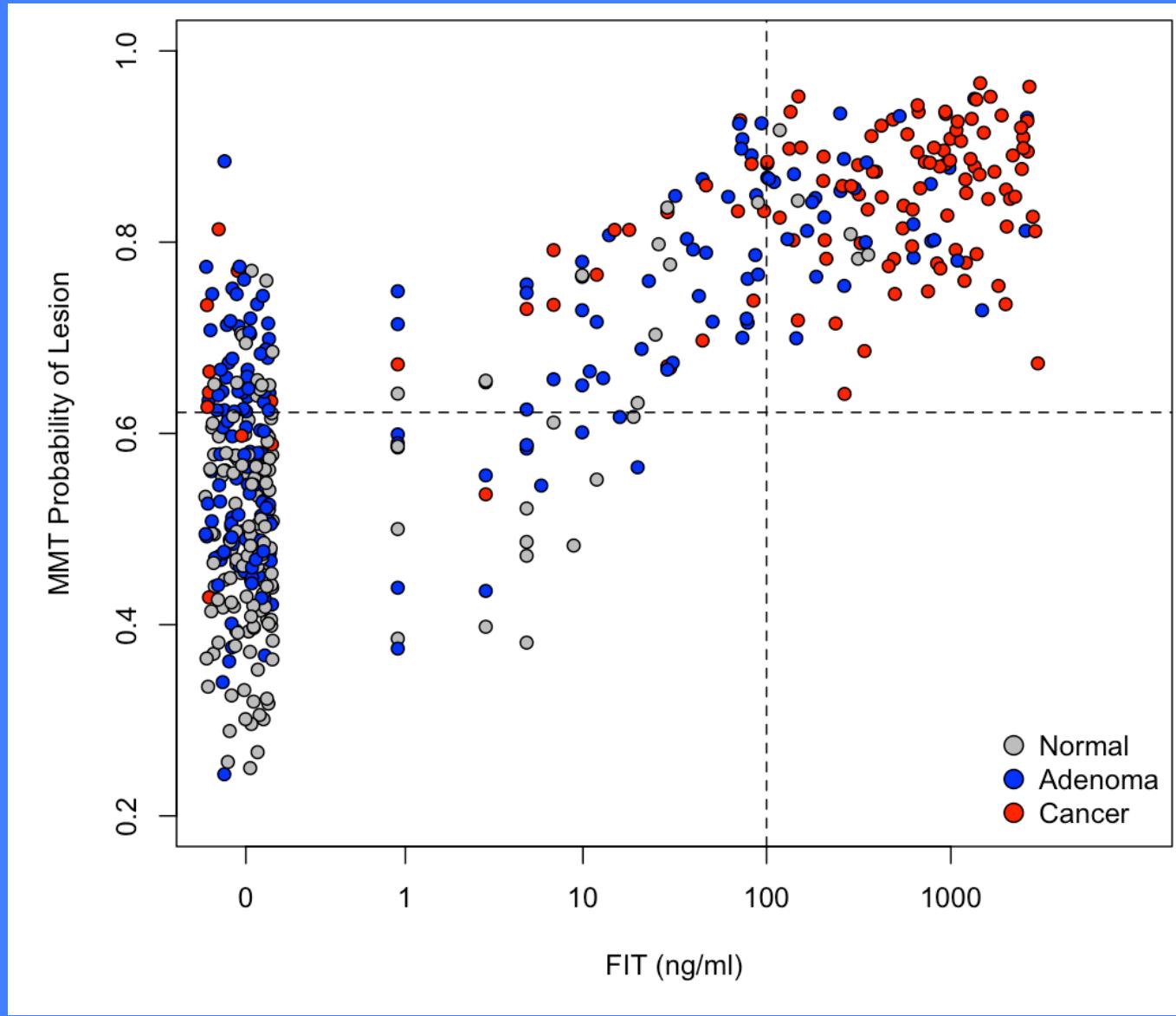
* The best software package for analyzing 16S rRNA gene sequence data (www.mothur.org)

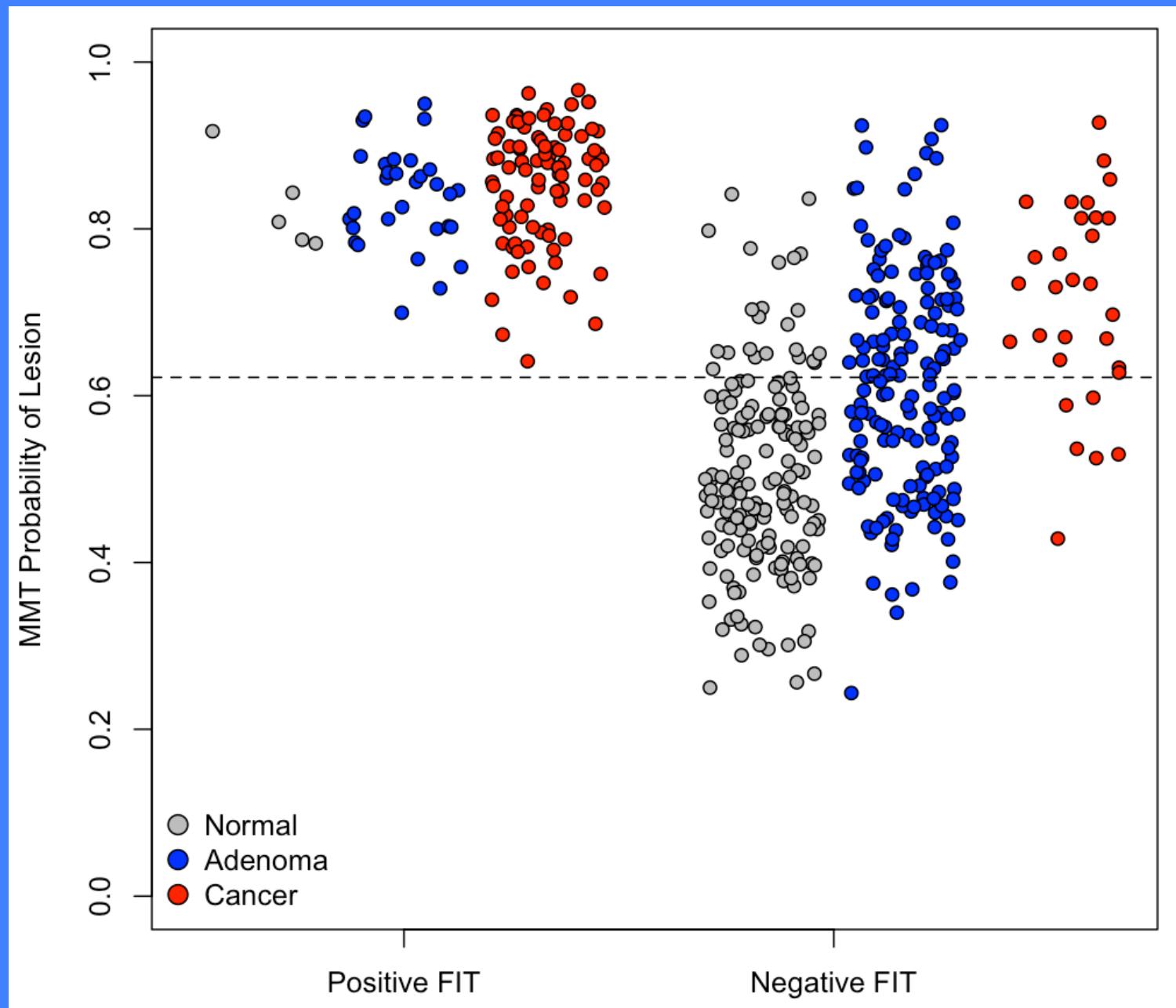
The Multitarget Microbiota Test: Microbiome + FIT

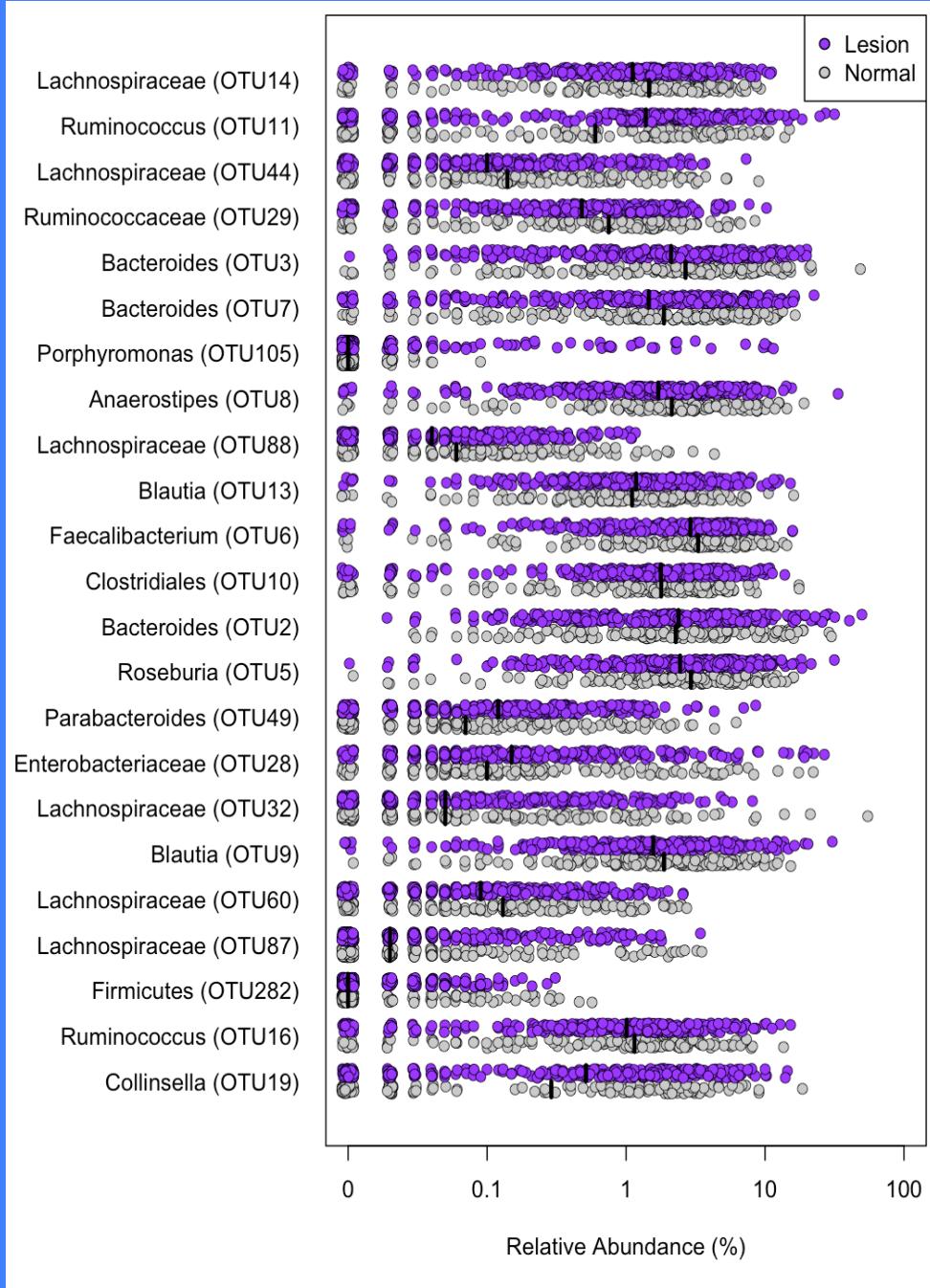










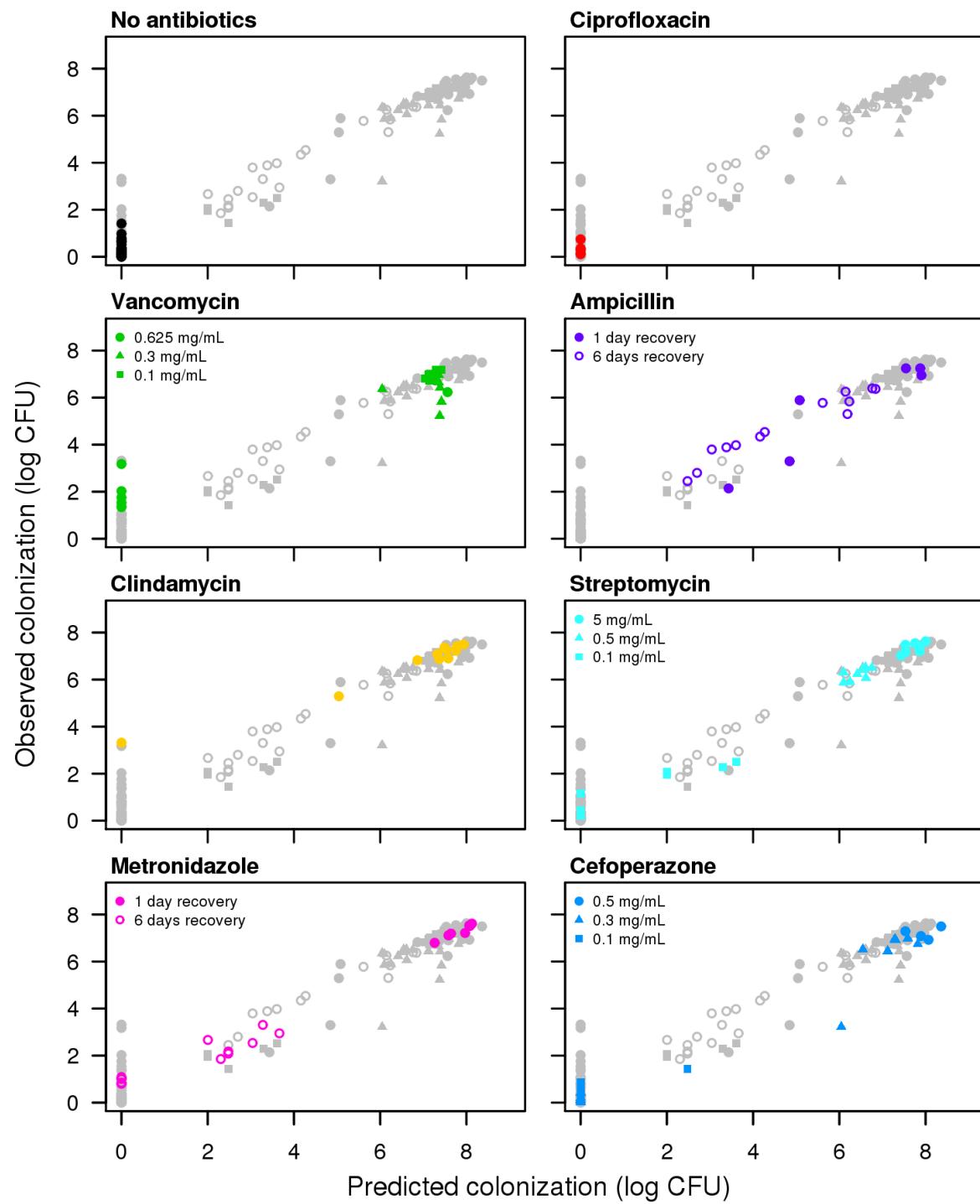


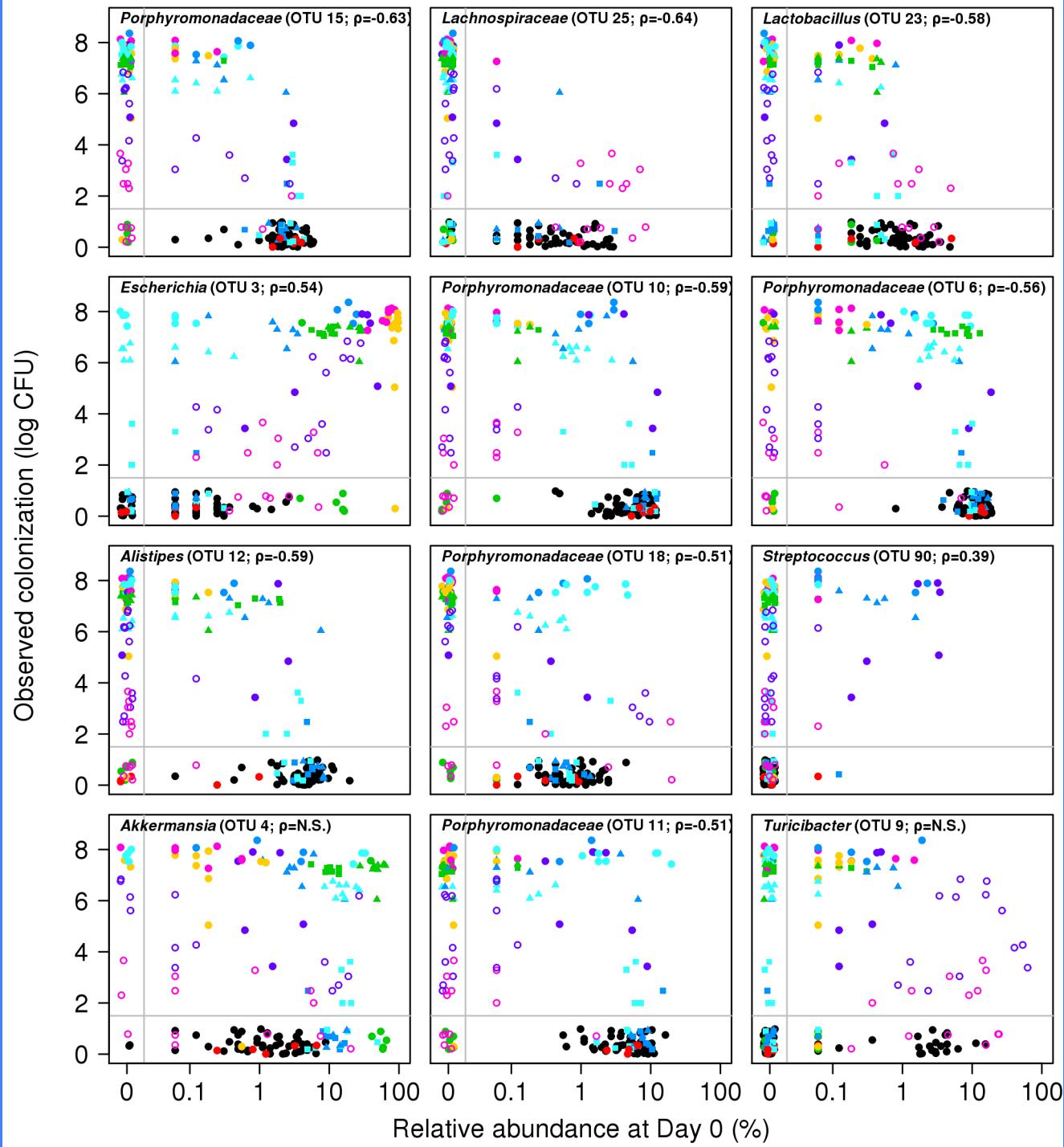
Case studies

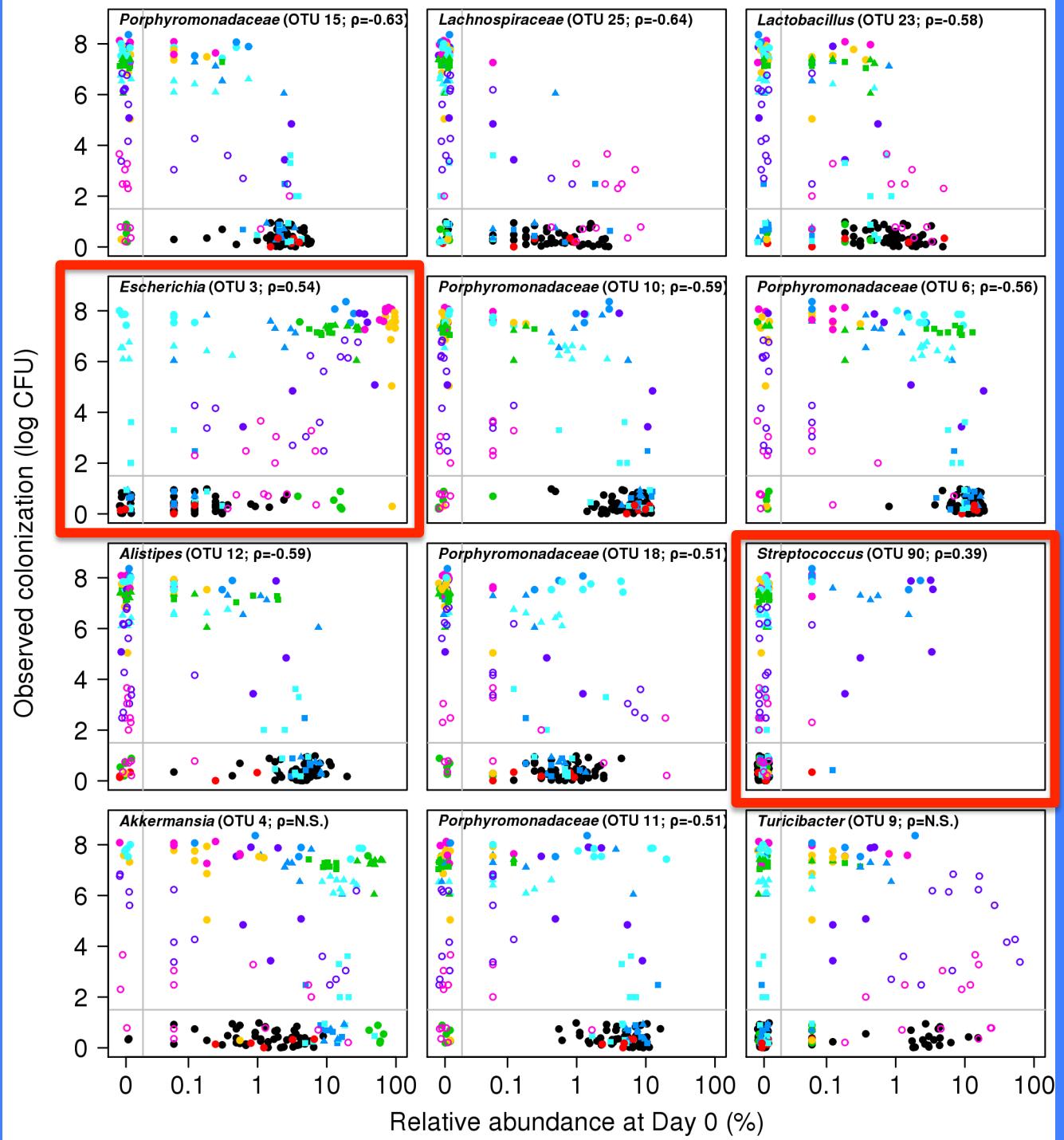
- Colorectal cancer
- *Clostridium difficile* infection

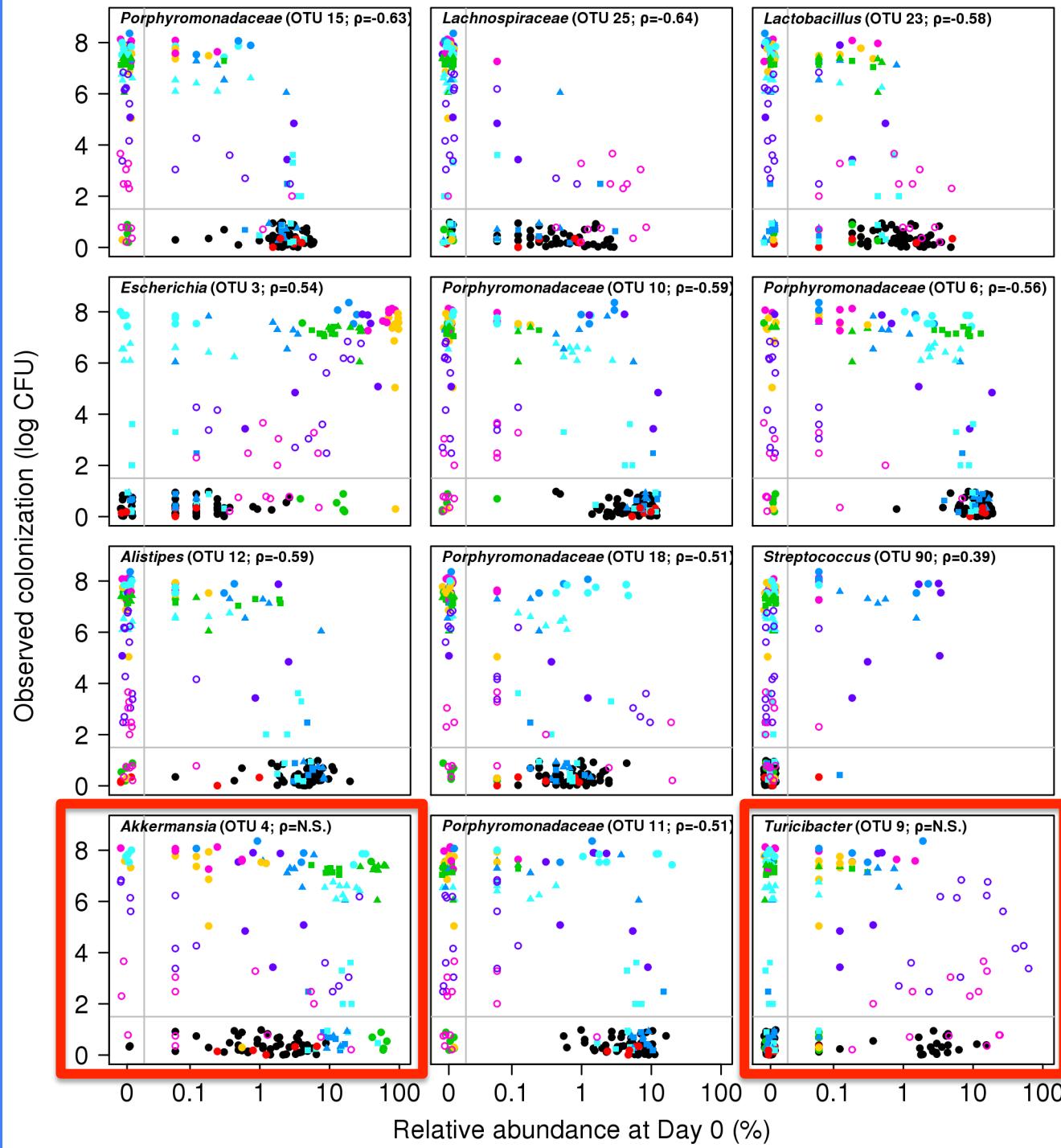
Can we predict who will get *C. difficile*?

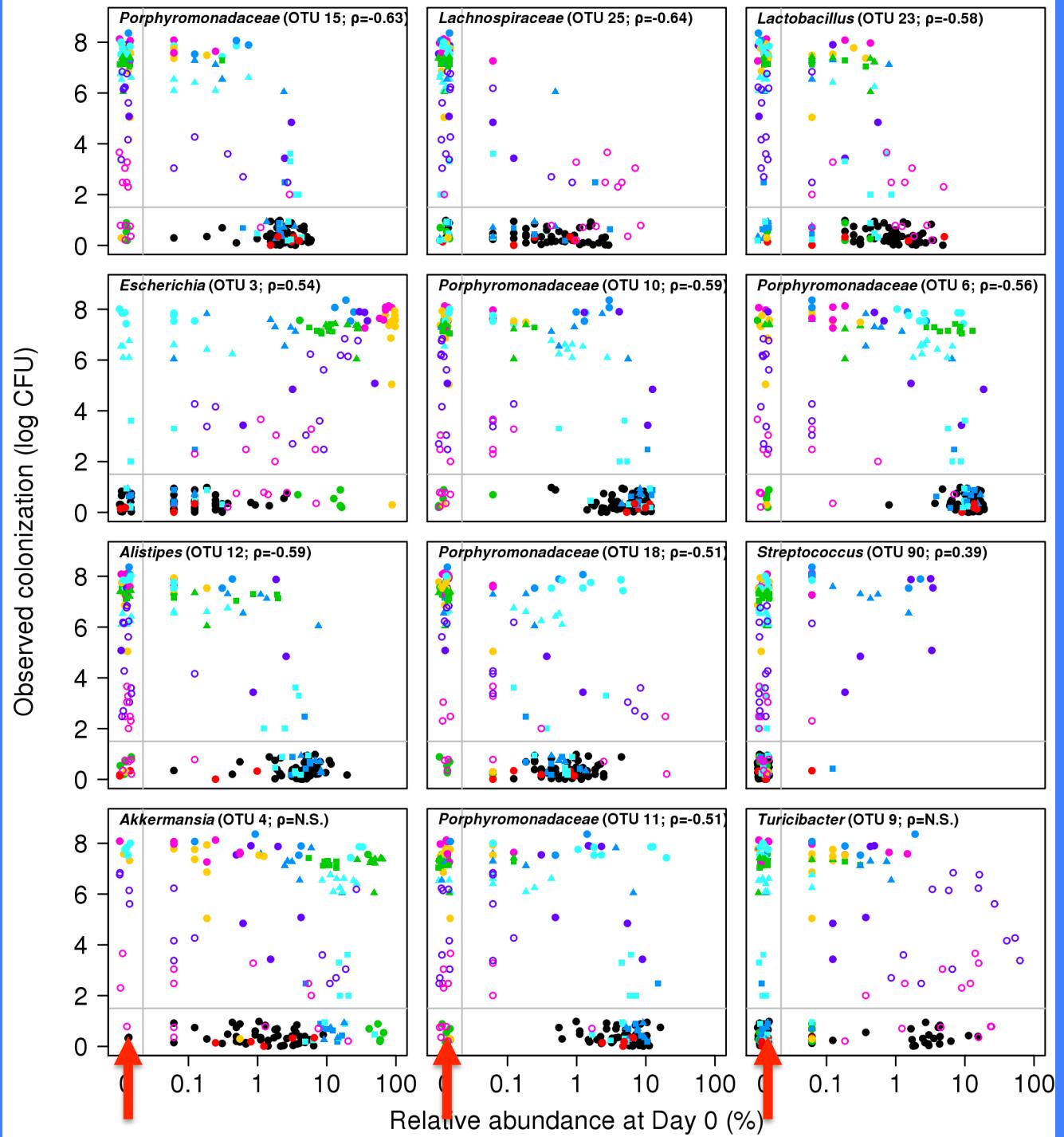
- We can predict who has *C. difficile* based on the other bacteria in their stool (see obesity)
- Imagine getting a rectal swab/stool sample of everyone that comes into the hospital and being able to assess the patient's risk of getting *C. difficile*
- Can do this with mice

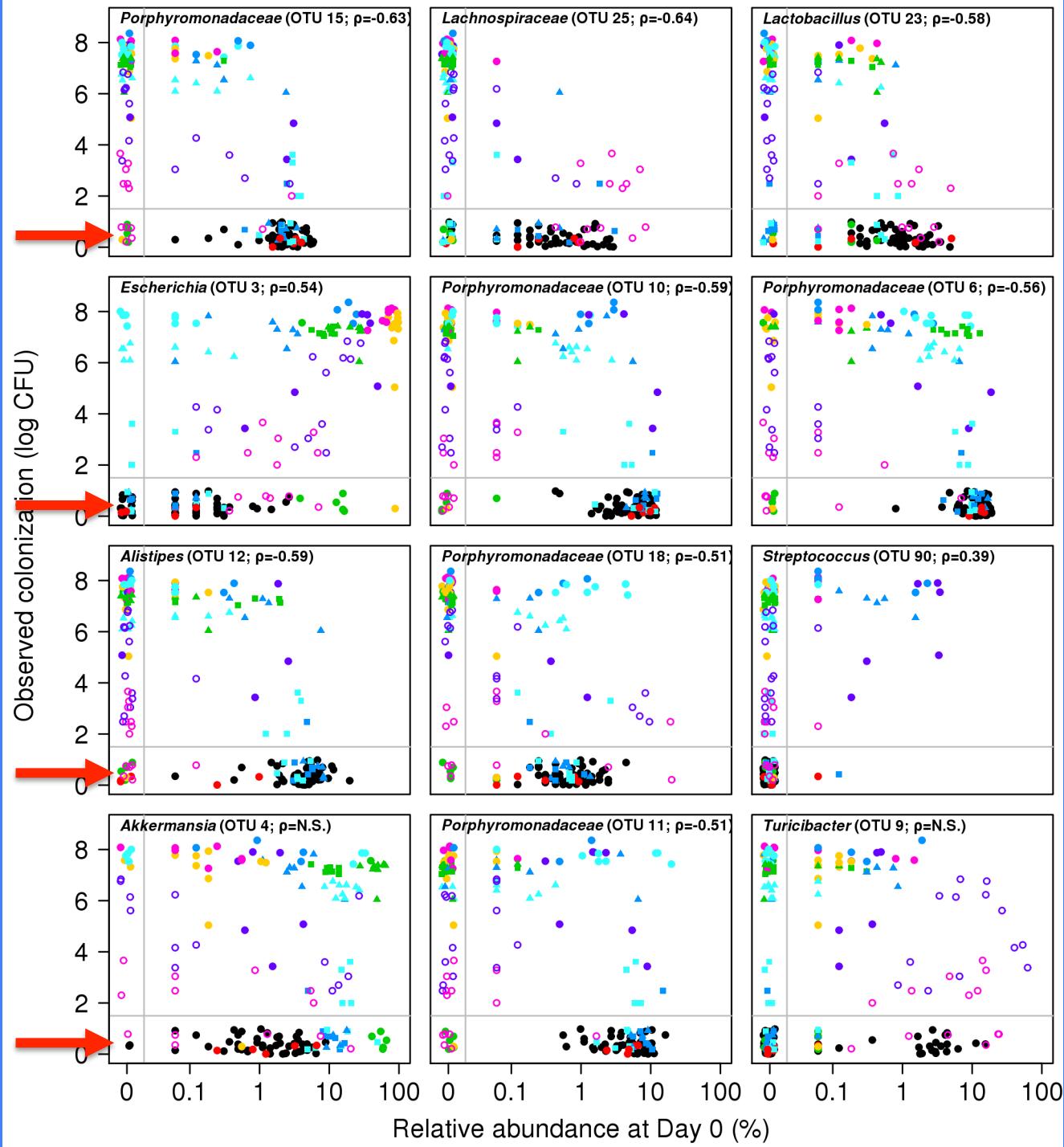






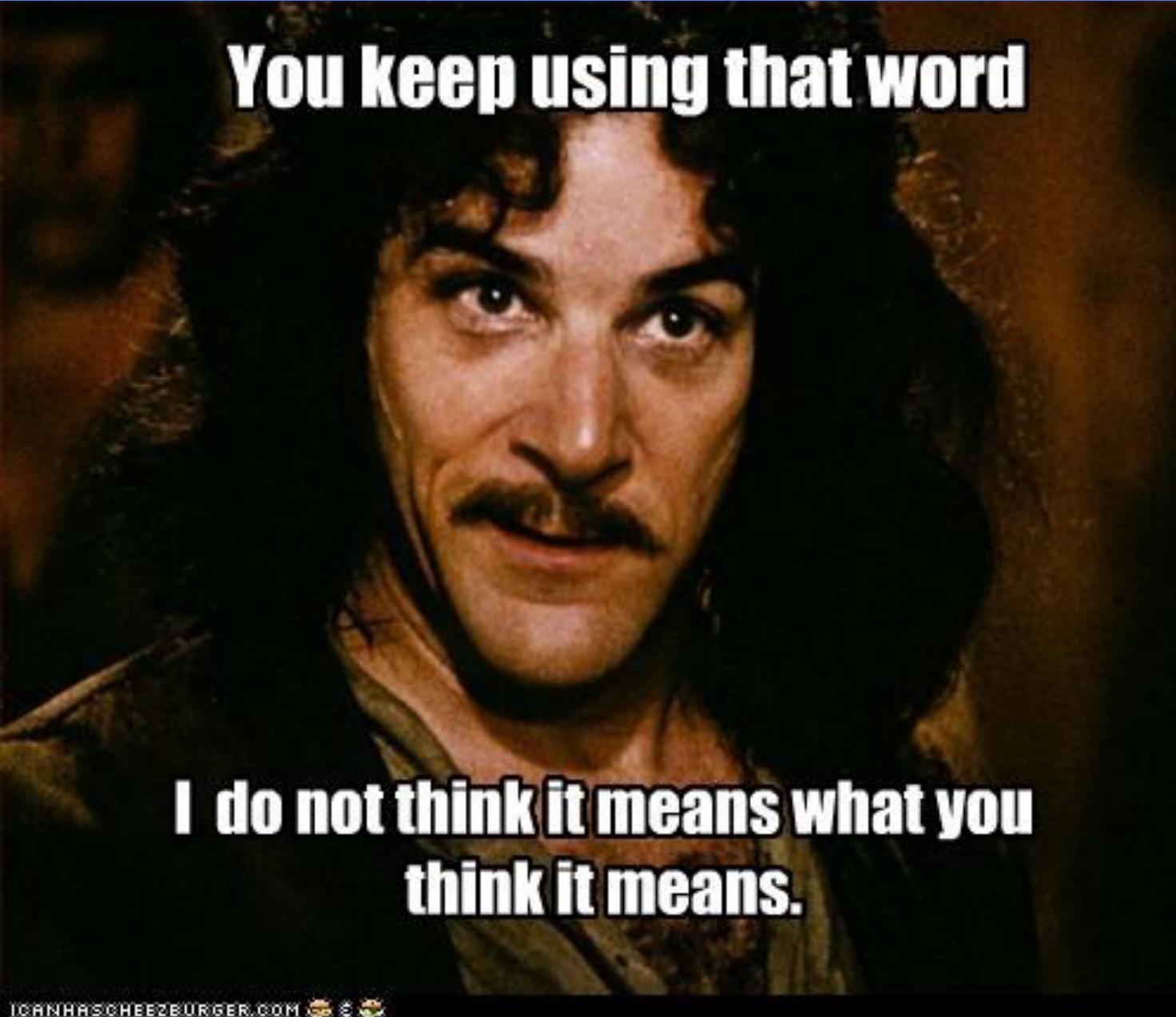






Context matters...

- 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.**



**SCOOP
THAT POOP**

Tips for Bringing a Fecal Sample to Your Veterinarian

mypawsitivelypets.com

Acknowledgements



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

CRC

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- Mack Ruffin, MD

C. difficile

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

