

The Family Microbiome and Familial Adenomatous Polyposis

Research Talk

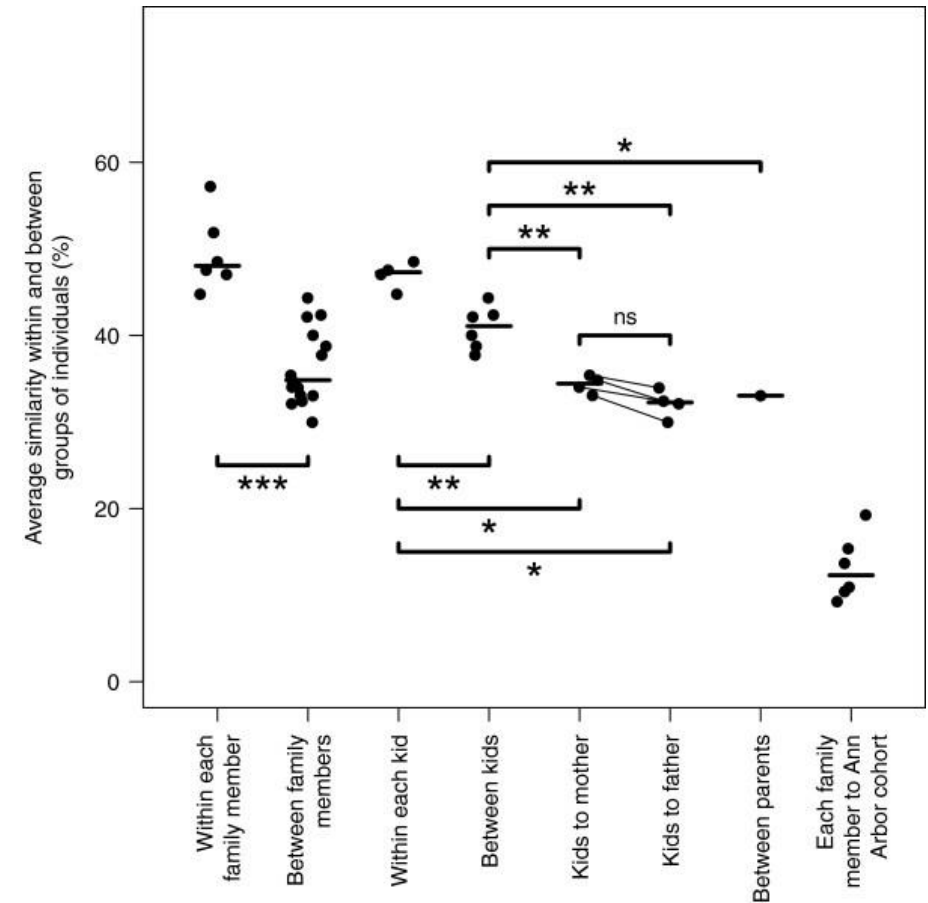
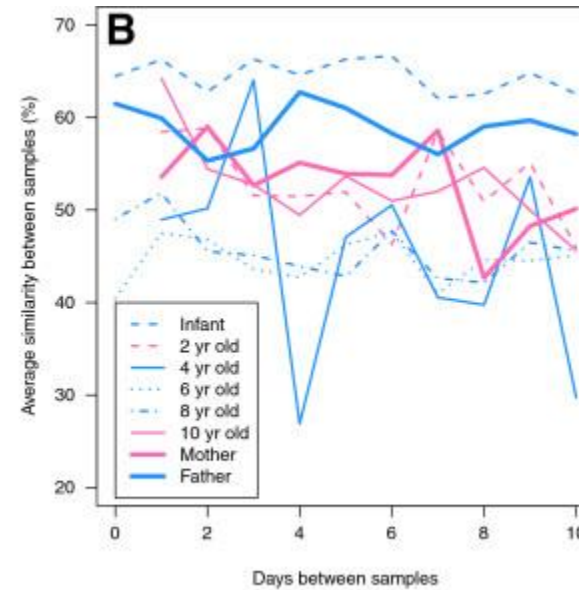
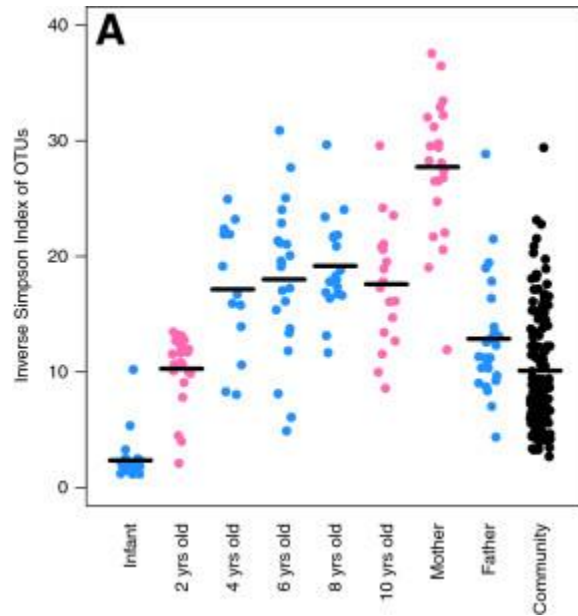
Marc Sze

July 21st, 2016

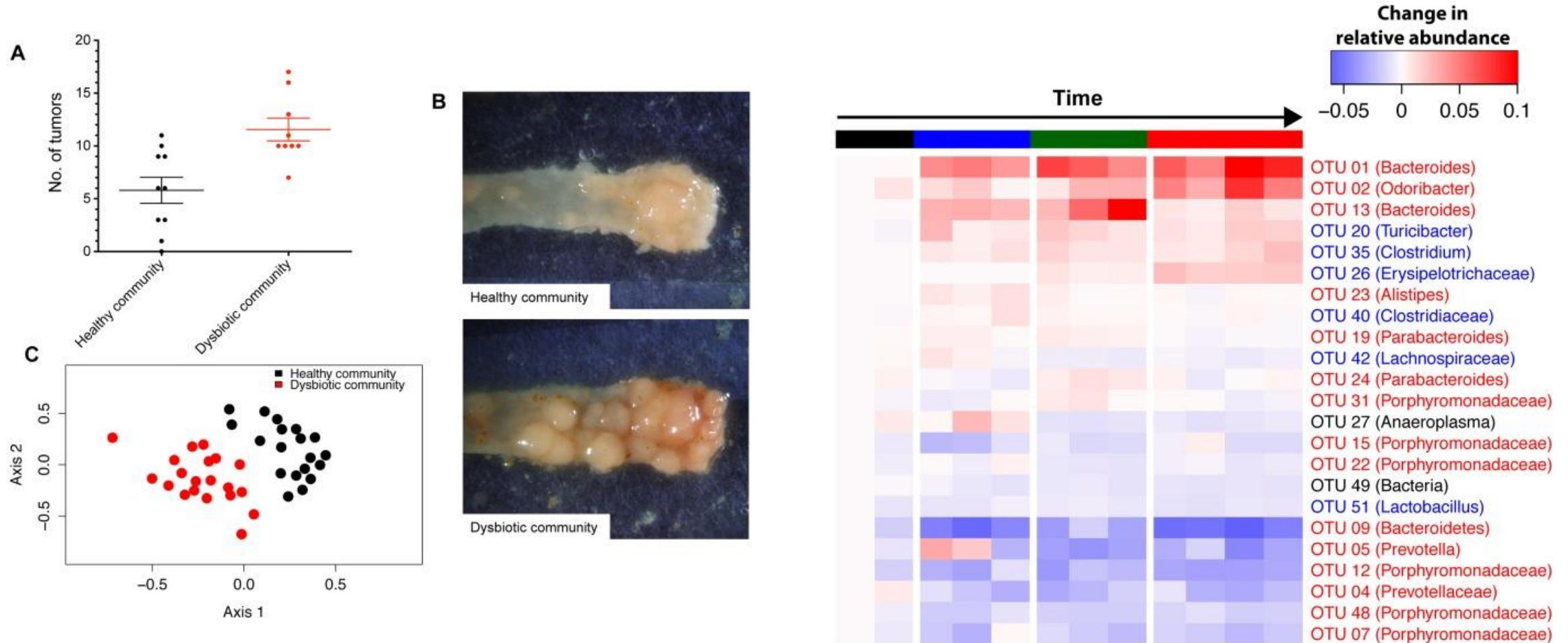
Introduction: Previous Studies

Family Centered Studies	Heritability Centered Studies
Schloss, 2014 (PMID 25061514)	Goodrich, 2014 (PMID 25417156)
Lax, 2014 (PMID 25170151)	Hua, 2015 (bioRxiv)
http://americangut.org/intra-family-microbial-dynamics/ Posted on April 2016	Davenport, 2015 (PMID 26528553)
http://www.ubiomeblog.com/the-microbiome-family/ Posted on July 2016	Lim, 2016 (PMID 27053630)
	Goodrich, 2016 (PMID 27173935)

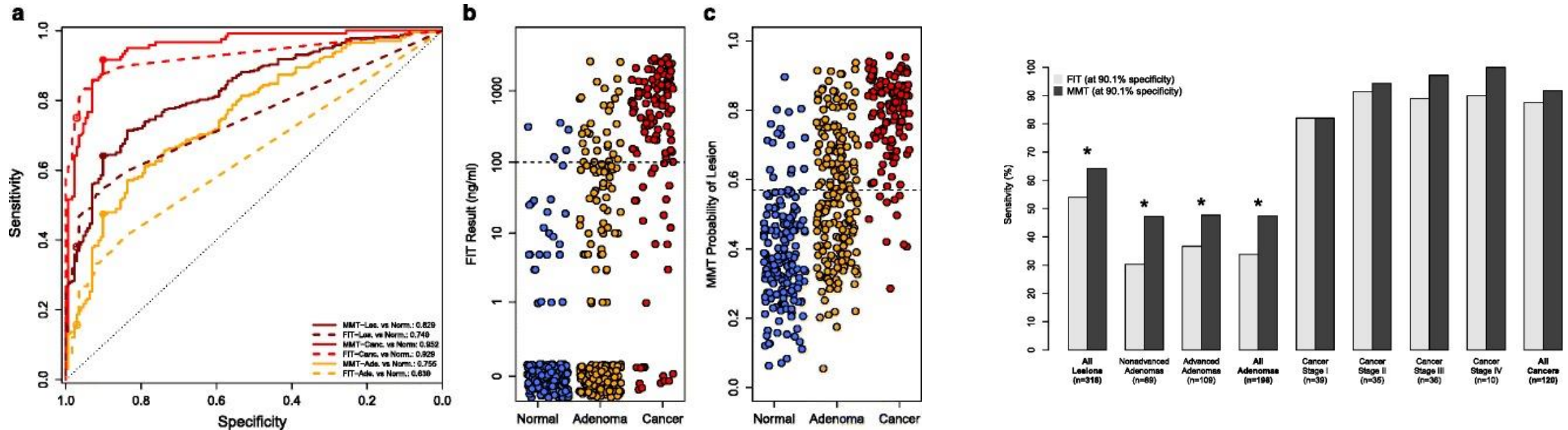
Introduction: Previous Gut Family Study



Introduction: Colorectal Cancer and the Microbiome



Introduction: Colorectal Cancer and the Microbiome



Overarching Hypothesis and Specific Aims

- Whether the bacterial community between normal and FAP families is different and whether specific members' heritability is strongly influenced by the autosomal dominant APC gene defect.
 - Aim 1: Is there a detectable difference in stool in those with and without FAP?
 - Aim2: Within the same family and across families is there a consistent microbiome signature difference between those with FAP and those without disease?
 - Aim3: Is there a detectable difference between the bacterial microbiome of benign and polyp tissue in those with FAP?

Sampling Overview

Repeated every year

Stool

Stool

Stool

1st Sampling

2nd Sampling

3rd Sampling

- Demographics
- Food Frequency Questionnaire
- Medical History

- Whole family sampled
- Assumed average n/family = 4
- Samples kits mailed to families
- Go for 10 years concurrently

Repeated each routine colonoscopy

Stool

5/6 matched polyp and benign
tissue samples

Stool

Before Colonoscopy

Colonoscopy

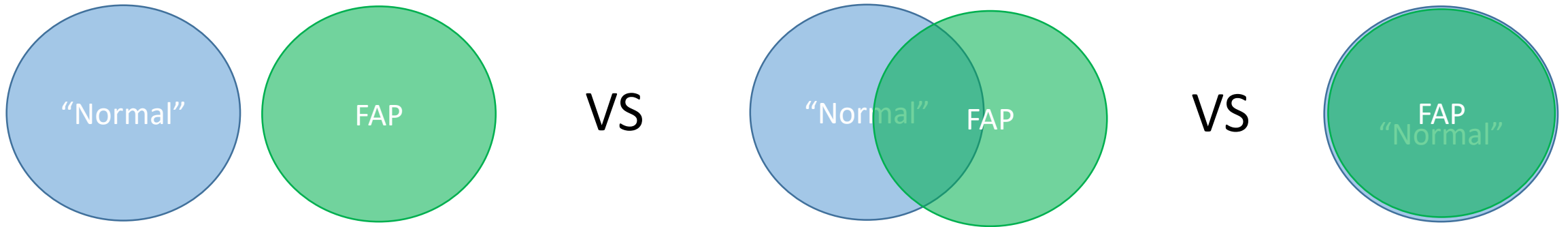
After Colonoscopy

- | | |
|---|---|
| <ul style="list-style-type: none">- Demographics- Food Frequency Questionnaire- Medical History | <ul style="list-style-type: none">- Number of polyps- Size of polyps- Evasiveness of polyps |
|---|---|

- Only those needing endoscopy
- Plan on children being included
- Go for 10 years concurrently

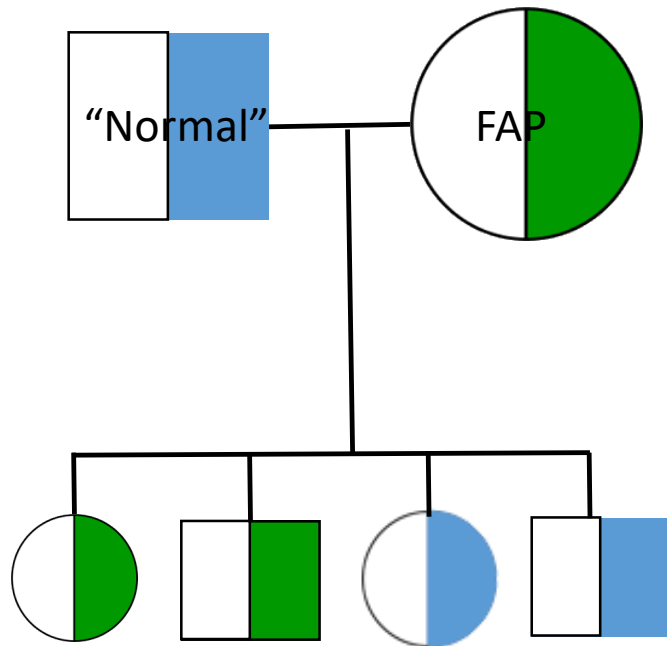
Aim 1

Is there a detectable difference in stool in those with and without FAP?

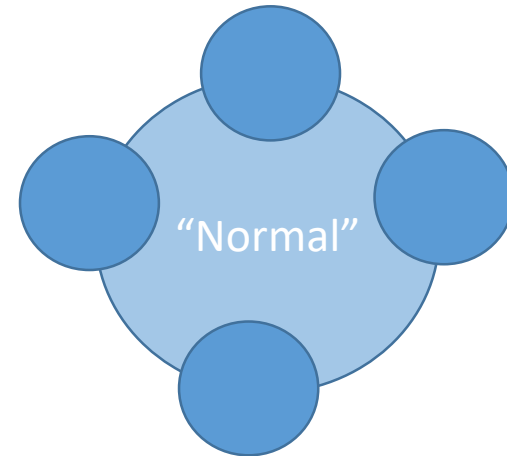


Aim 2

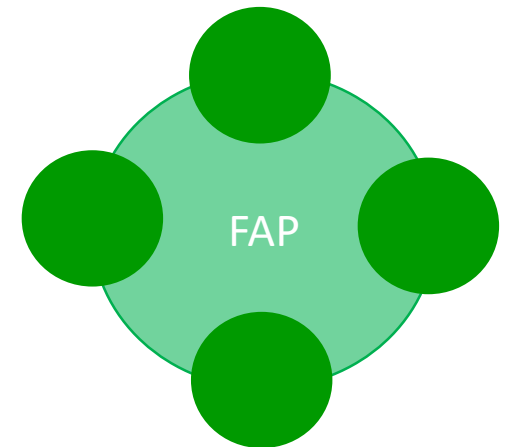
Within the same family and across families is there a consistent microbiome signature difference between those with FAP and those without disease?



AND

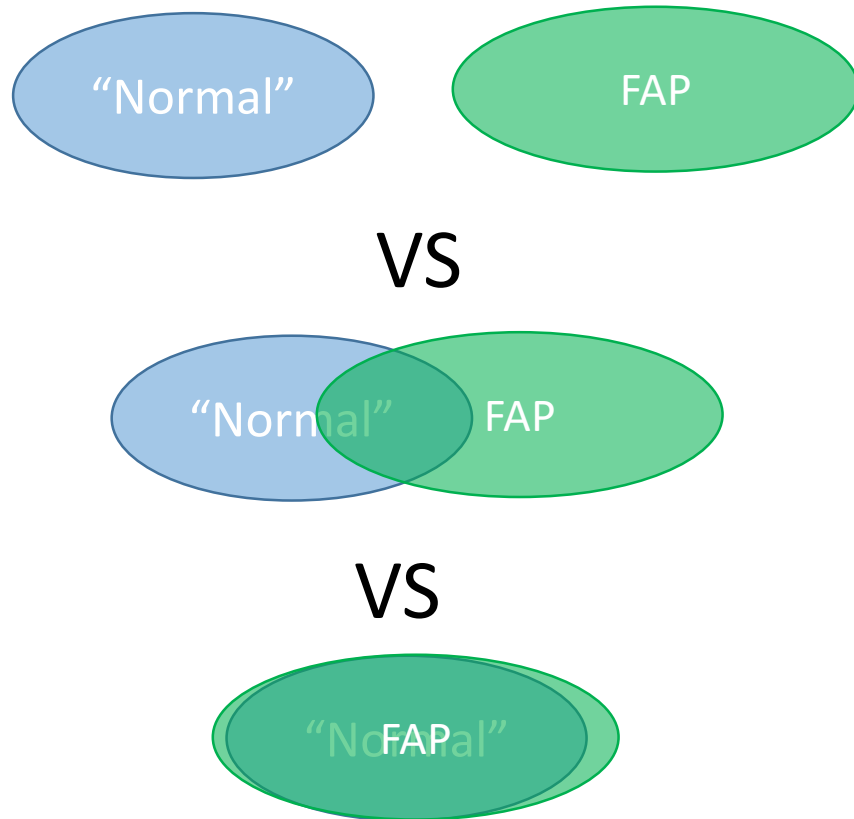


VS



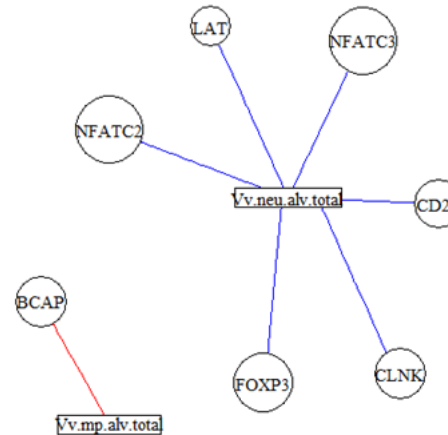
Aim 3

Is there a detectable difference between the bacterial microbiome of benign and polyp tissue in those with FAP?

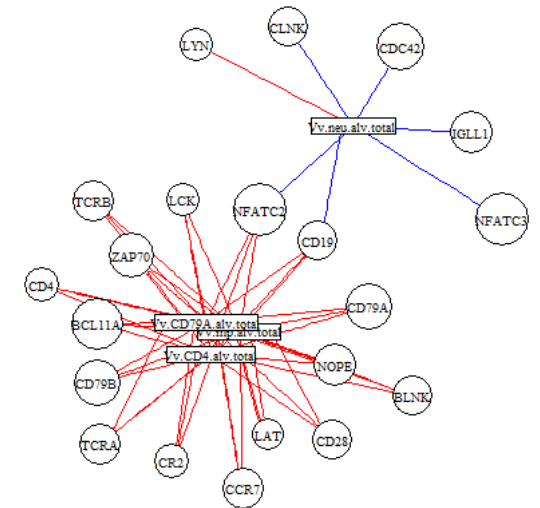


AND

Taxa 1 on normal tissue



Taxa 1 on polyp tissue



Study Progress

Overall Study Milestones

IRB - *Submitted*

Clinical Section Milestones

Procedures and cohort identified – *Completed*

Find half time study coordinator – *Underway*

REDCap Registry Launch – *Final Approvals and User testing*

Wet Lab Section Milestones

Fecal Collection Tubes – *Currently testing Zymo versus OmniGeneGut* 

DNA/RNA joint extraction (Tissue) – *Identified a working method, need to confirm and try with electronic pipette*

- <https://github.com/marcsze/WetLabStuff/tree/master/LabReports>

Dry Lab Section Milestones

None currently underway

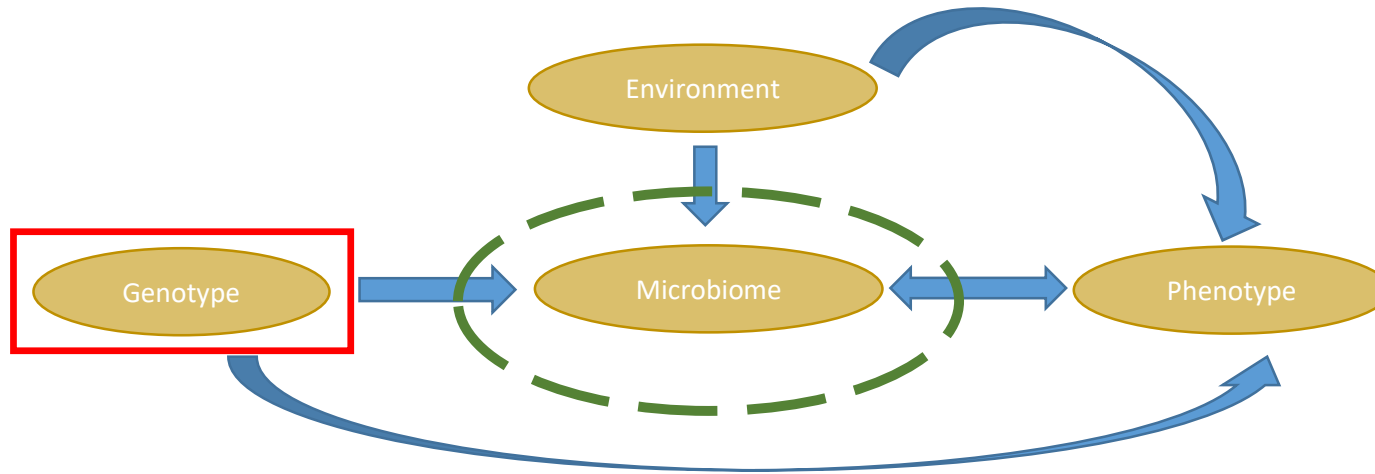
One Final Thought on Analysis

- Used ACE model
 - A (additive genetics)
 - $A = 2 * (r_{mz} - r_{dz})$
 - r_{mz} = correlation of trait in identical twins
 - r_{dz} = correlation of trait in fraternal twins
 - C (common environment)
 - $C = r_{mz} - A$
 - E (unique environment)
 - $E = 1 - r_{mz}$
- Falconer's formula to calculate Heritability
 - $H^2 = A = 2 * (r_{mz} - r_{dz})$

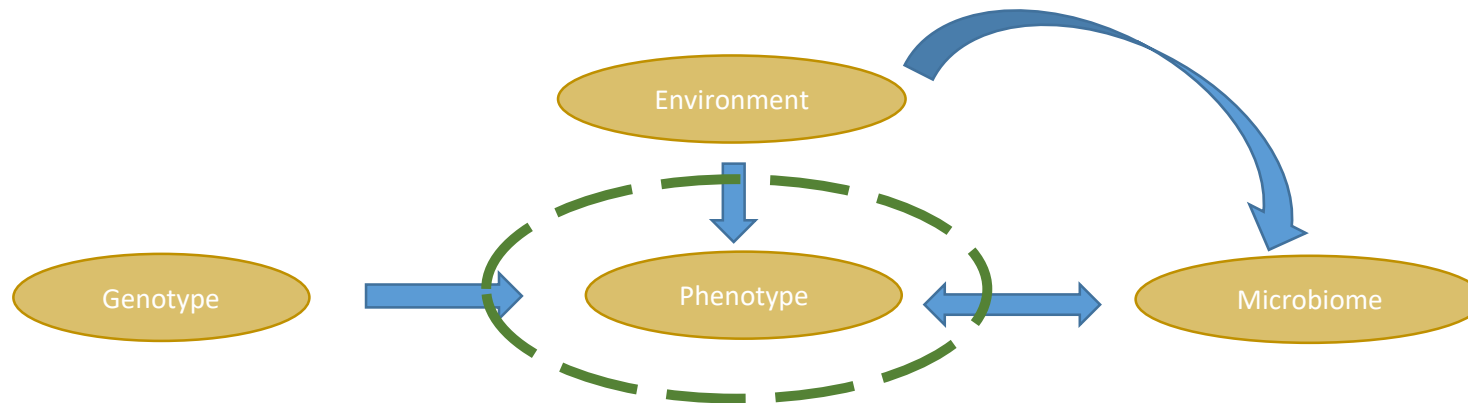


One Final Thought on Analysis

All previous Genotype microbiome studies (e.g. Goodrich, et al. 2016):



An alternative hypothesis



Thanks for your time and attention.

One Final Thought on Analysis

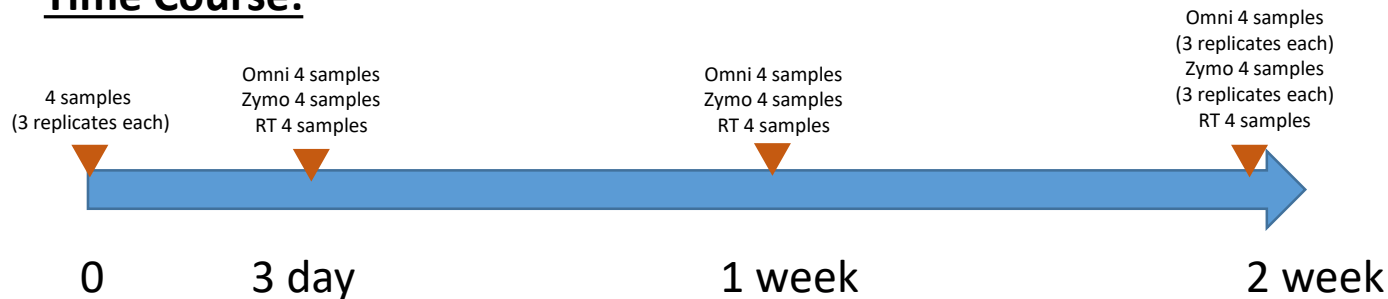
Goals:

- 1) Test which collection kit is better at preventing growth

Needed Disposables:

16 Zymo Fecal Collection Kits
16 OmniGene Gut Collection Kits
1 MO BIO Powersoil DNA extraction Kit
BR DNA Qubit
70 rxns 16S V4 PCR
1 MiSeq Run (or part of one)

Time Course:



Number of Samples Needed:

- *Need 4 control stool samples (20 samplings for each)
 - Added 2 extra (1 Omni and 1 Zymo)
 - Test DNA extraction with collection kit ahead of time
 - Take an aliquot, solid chunks, etc.

Wet Lab Overview:

