

# The Family Microbiome and Familial Adenomatous Polyposis

Research Talk

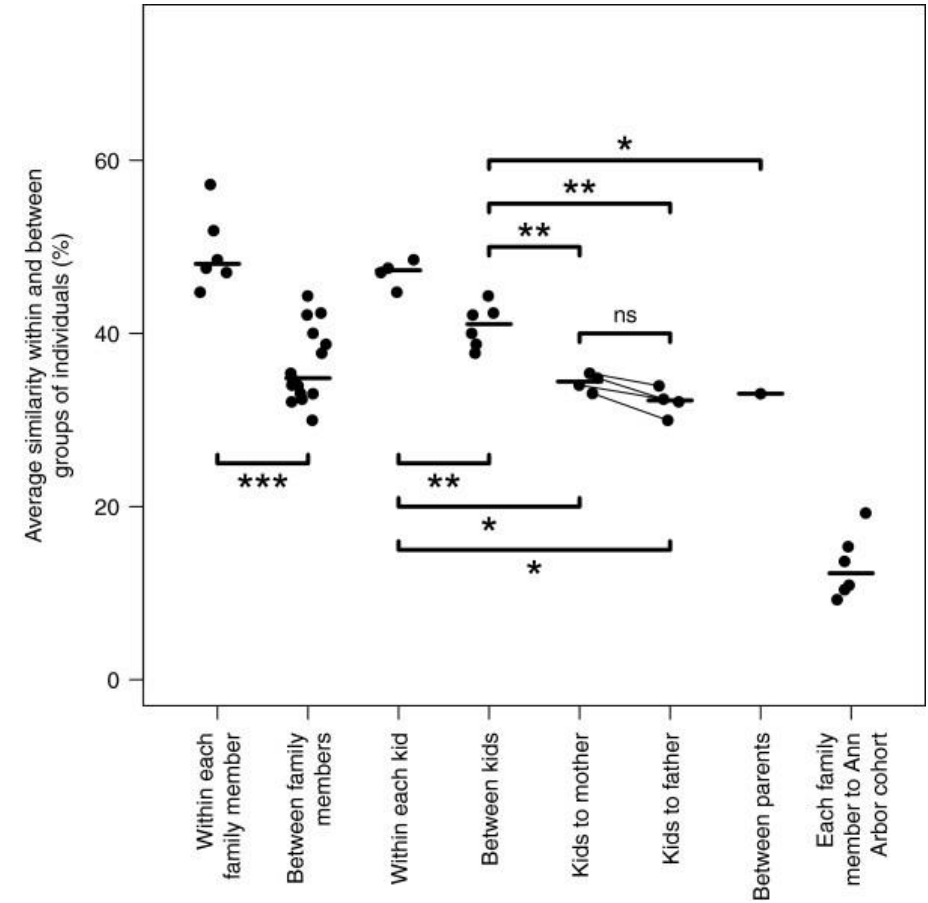
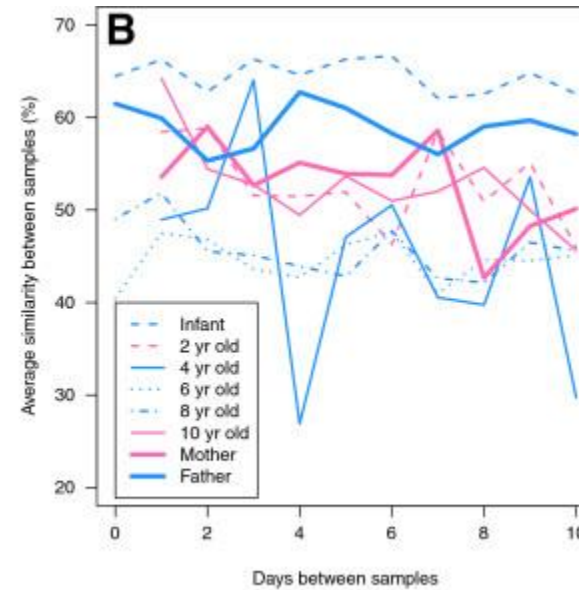
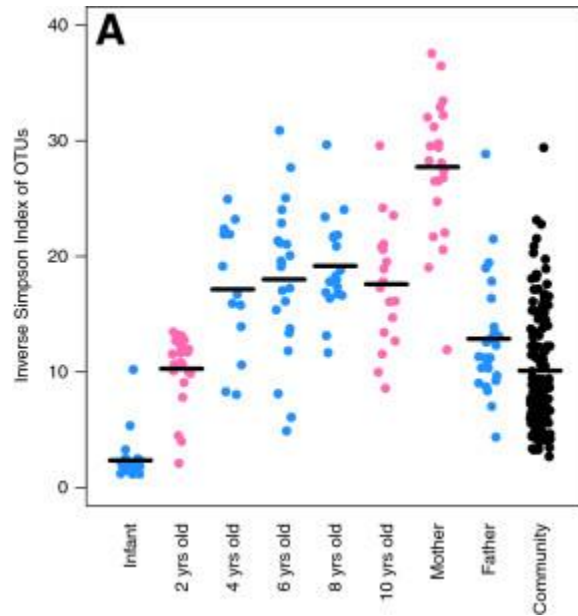
Marc Sze

July 21<sup>st</sup>, 2016

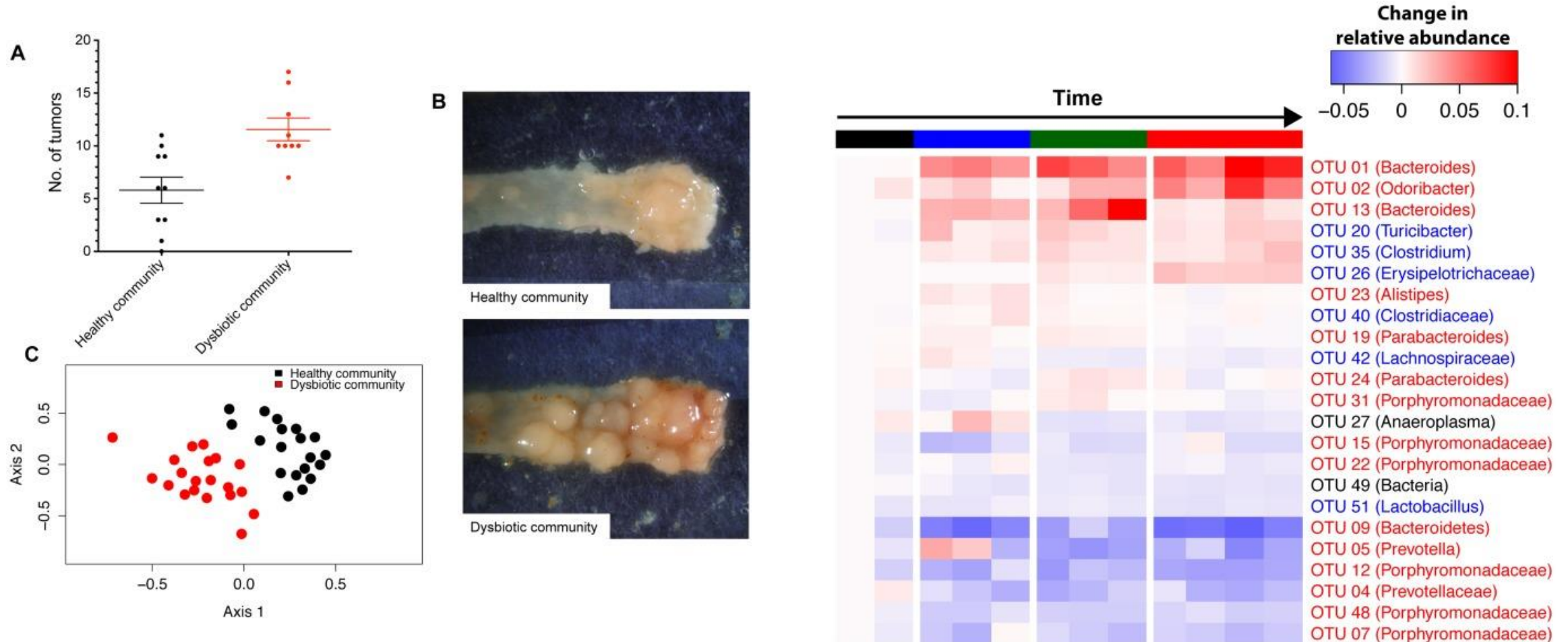
# Introduction: Previous Studies

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

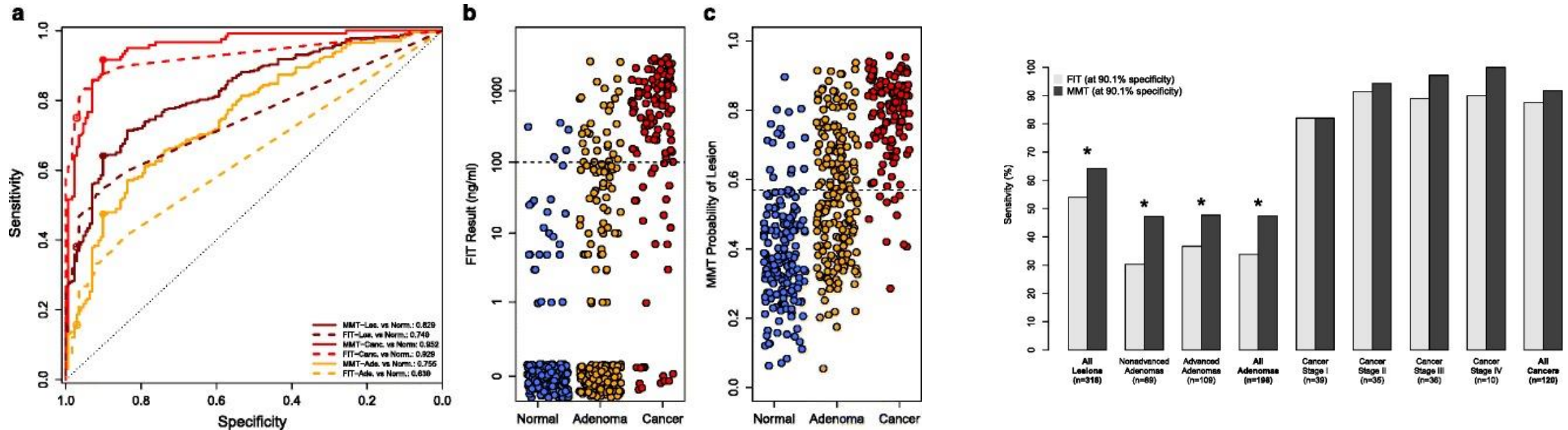
# Introduction: Previous Gut Family Study



# 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

1<sup>st</sup> Sampling

2<sup>nd</sup> Sampling

3<sup>rd</sup> 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

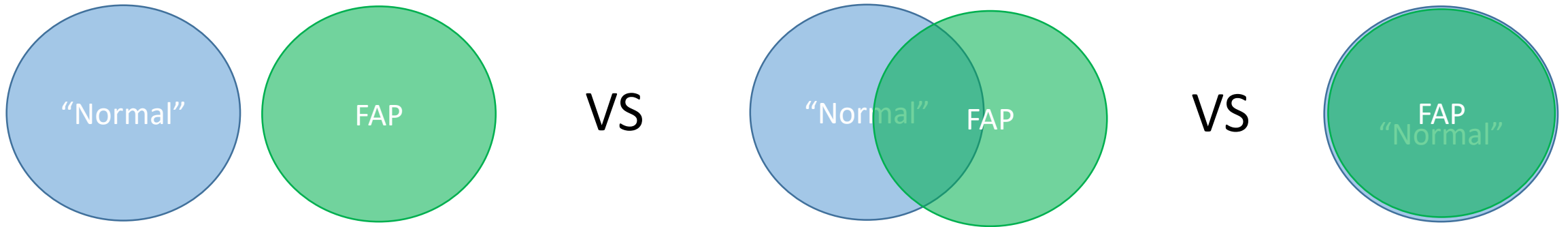
After Colonoscopy

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

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

# Aim 1

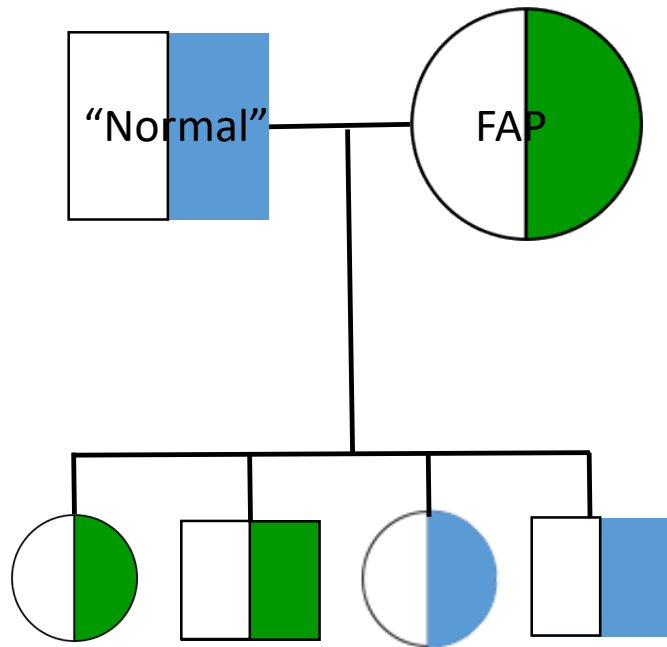
Is there a detectable difference in stool in those with and without FAP?



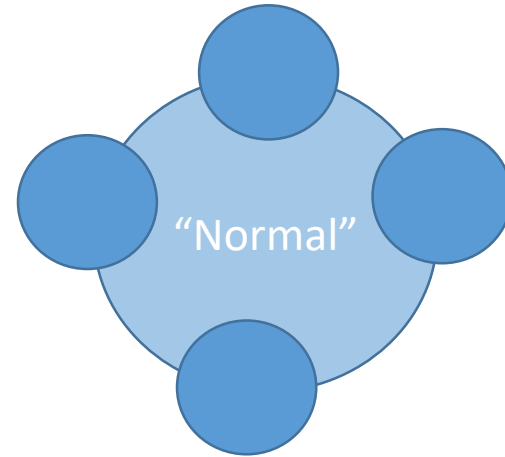


# Aim 2

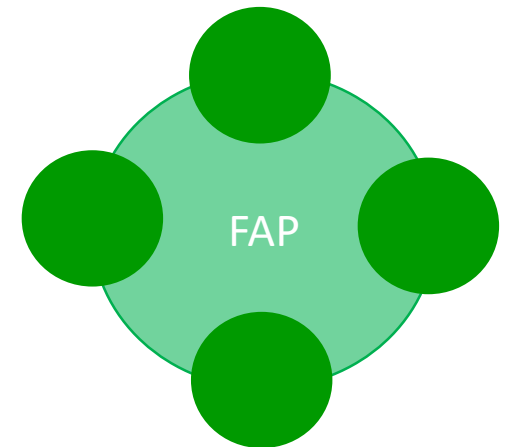
Within the same family and across families is there a consistent microbiome signature difference between those with FAP and those without disease?



AND

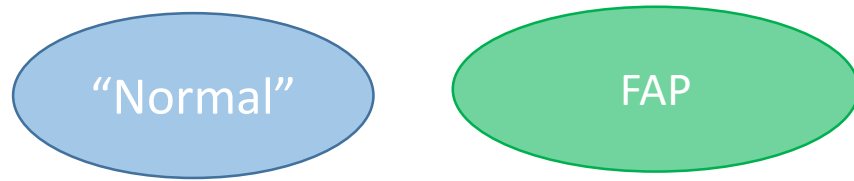


VS

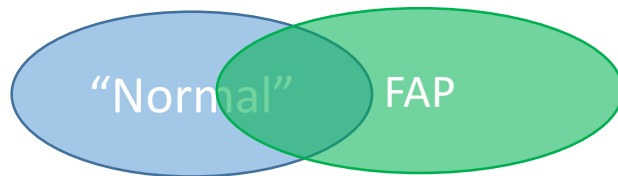


# Aim 3

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



VS

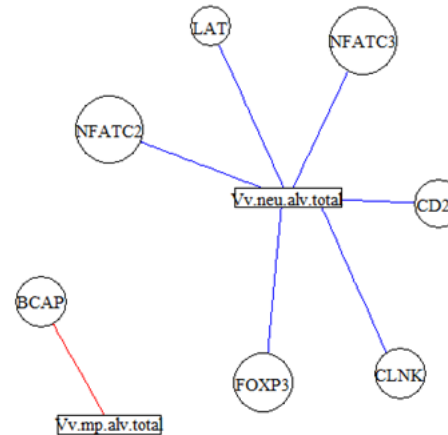


VS

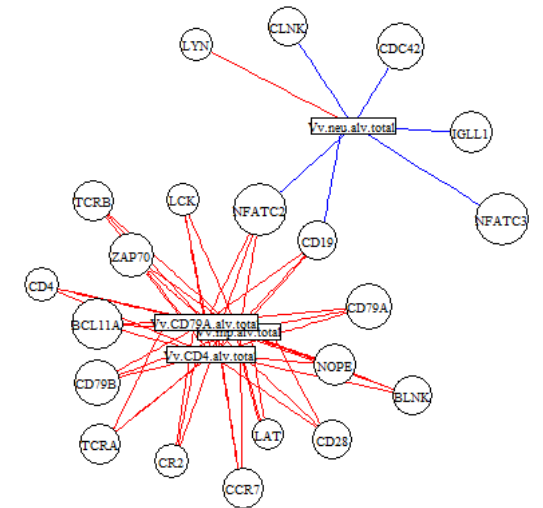


AND

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

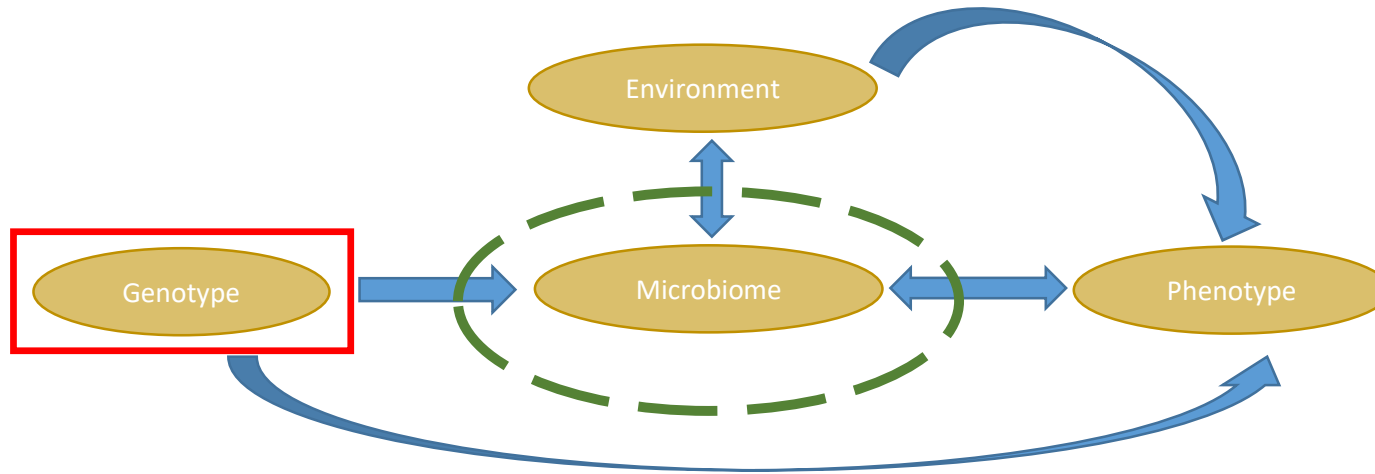
# One Final Thought on Analysis

- 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
  - $H^2 = A = 2 * (r_{mz} - r_{dz})$

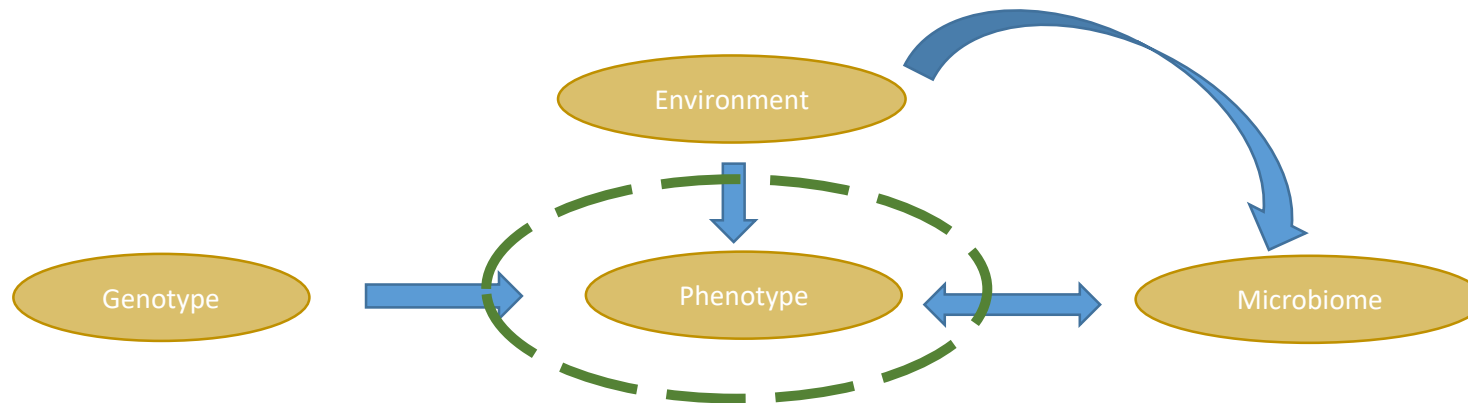


# One Final Thought on Analysis

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

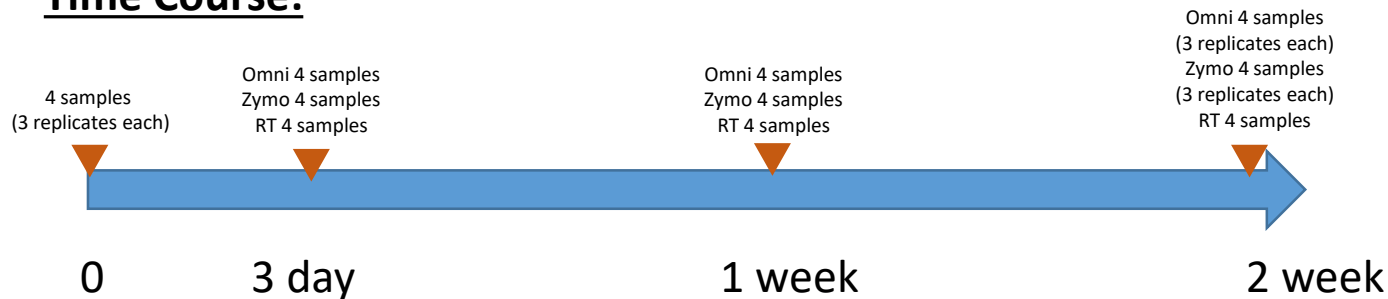
## Goals:

- 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:

