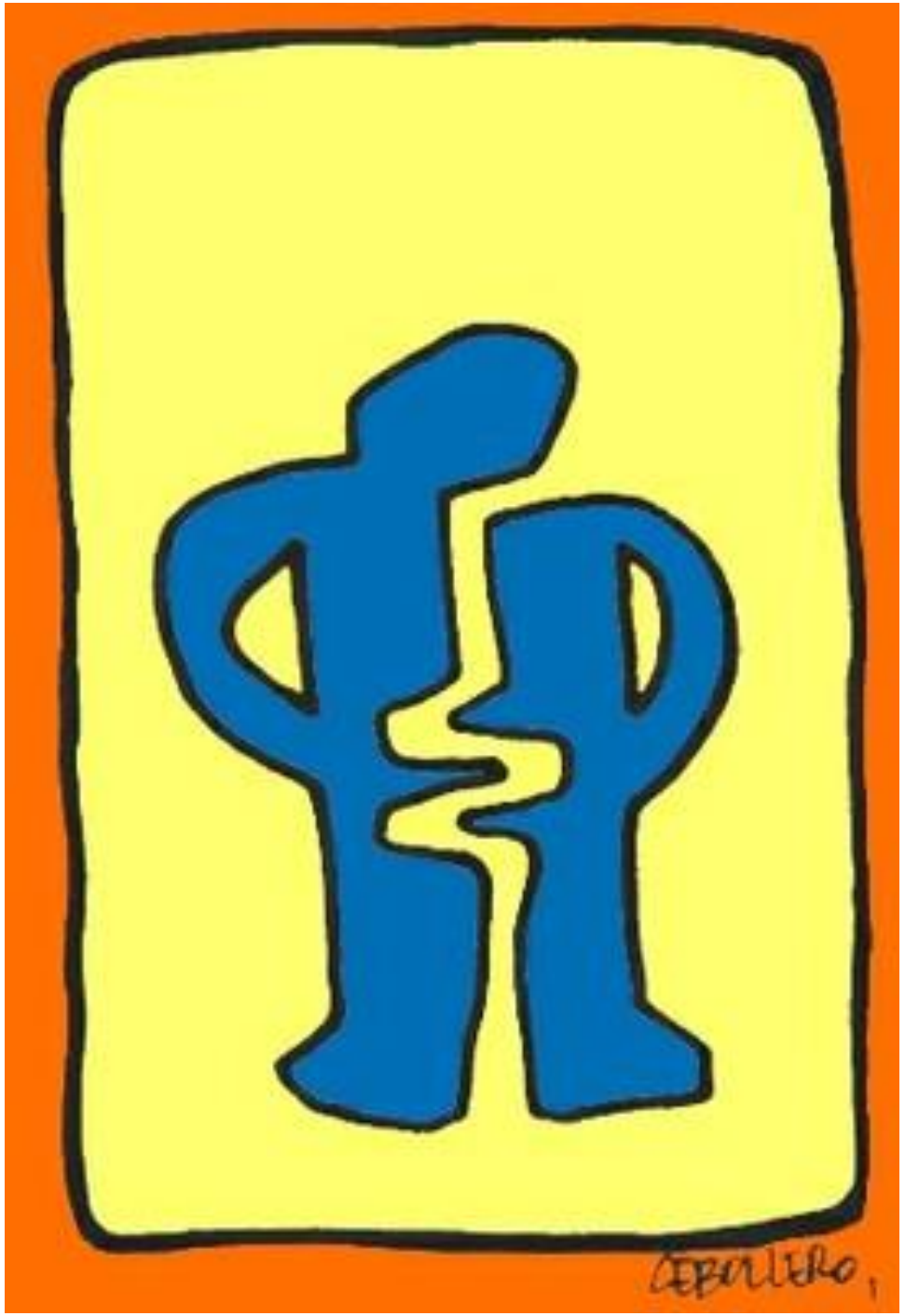
Microbiomes of Pregnancy and Infancy: Implications for Child Health Outcomes

Sarah S. Comstock

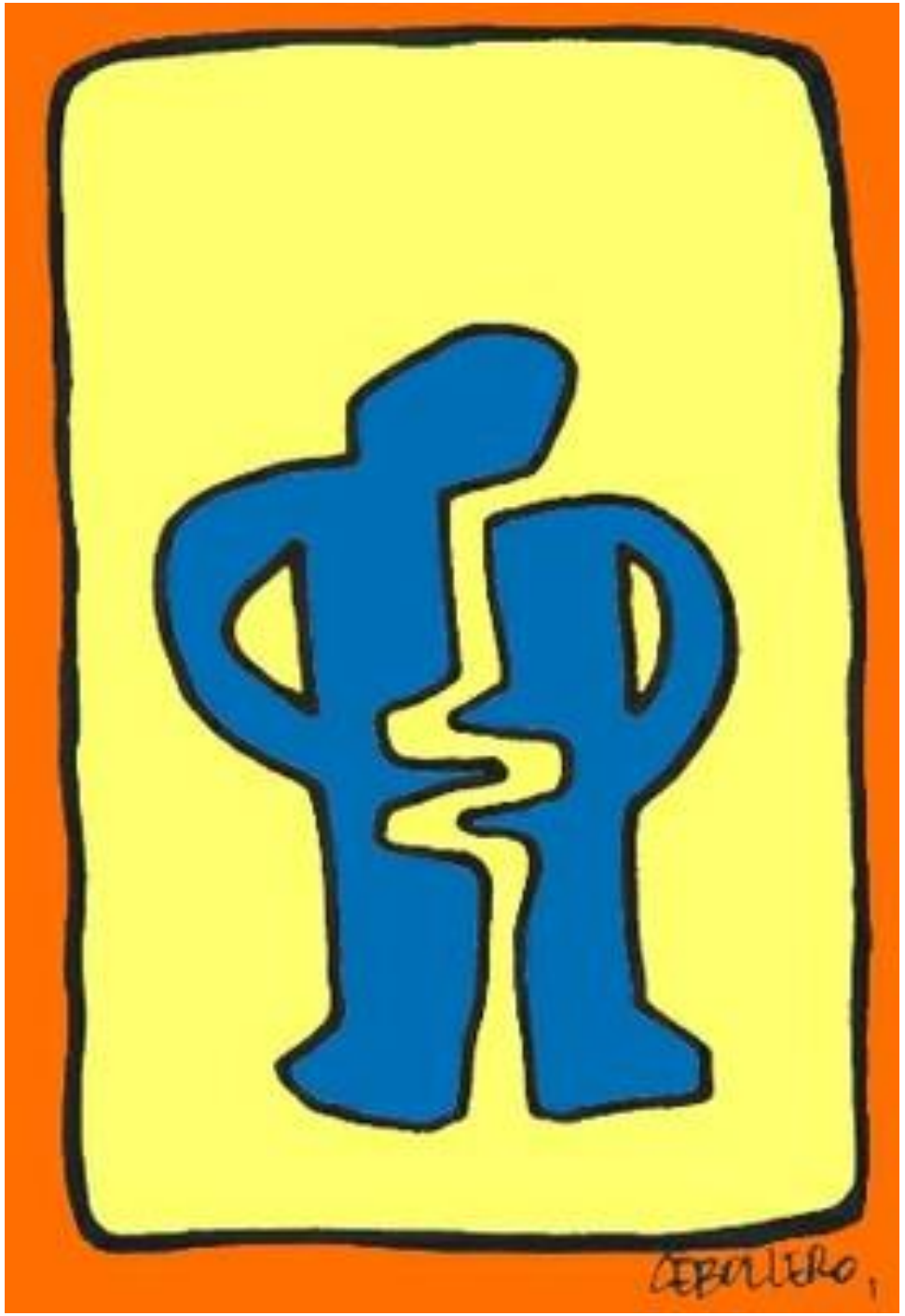
Michigan State University

Overview

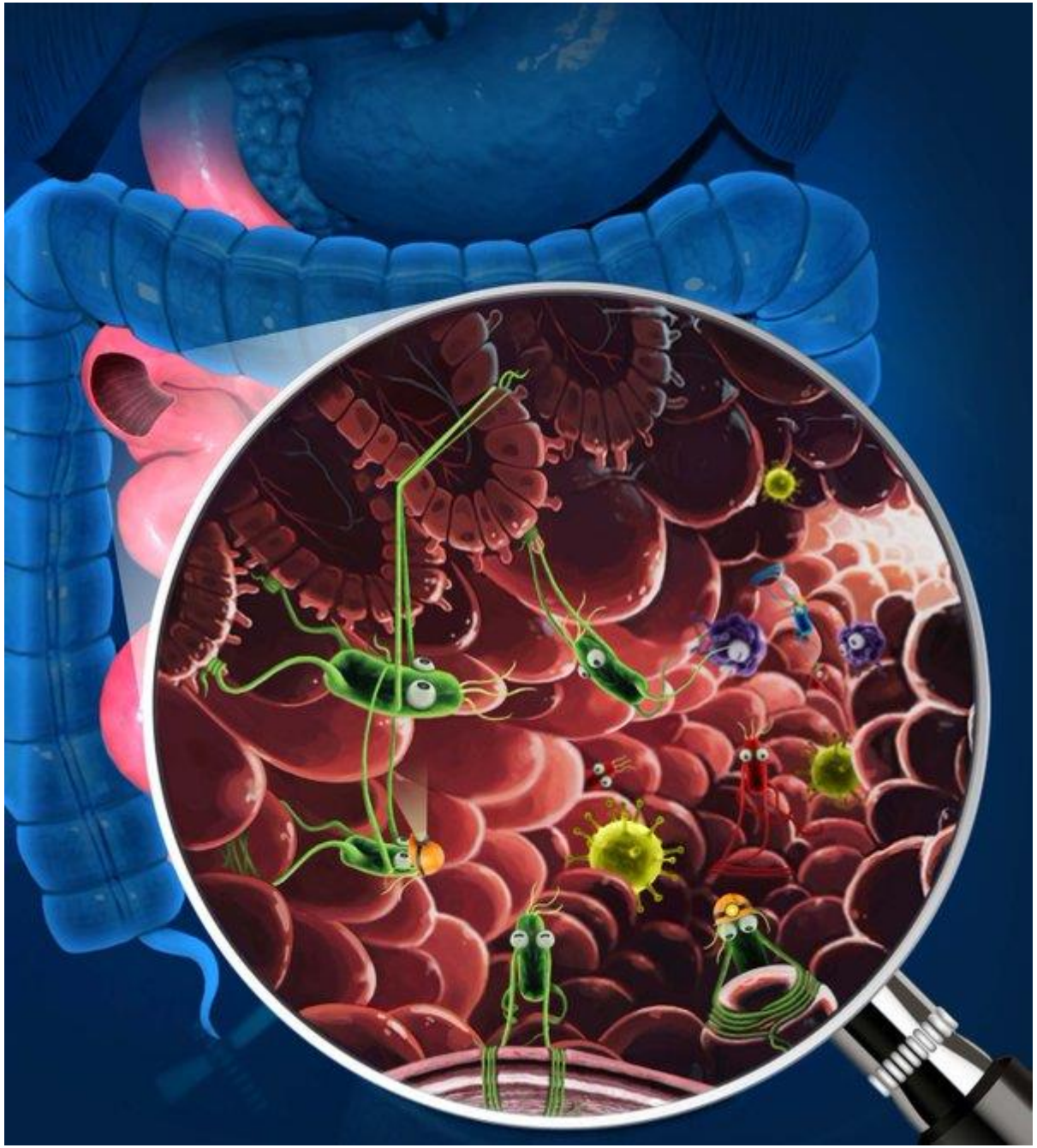
- The microbiome
- Microbiome collection efforts in ECHO
- ECHO-wide microbiome results
- Cohort-specific microbiome results
- Summary & Outlook



The Intestinal Tract

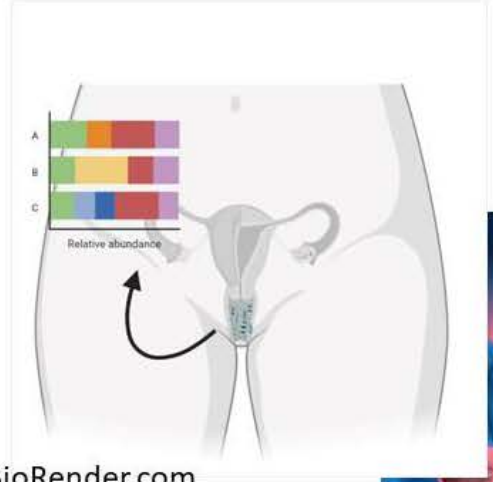


The Microbiome

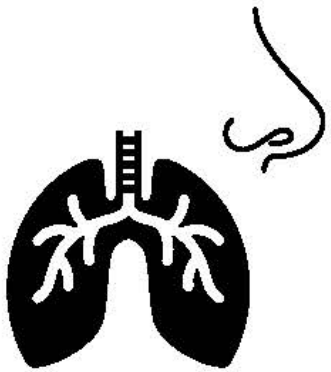


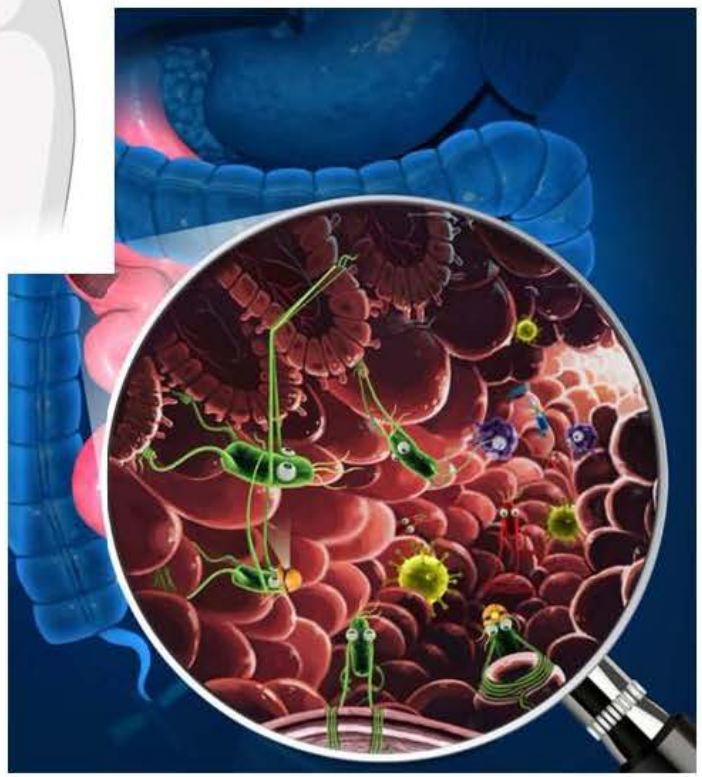
Cell Press

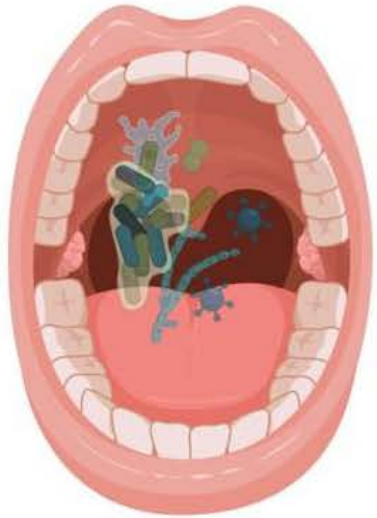
Microbiomes



BioRender.com







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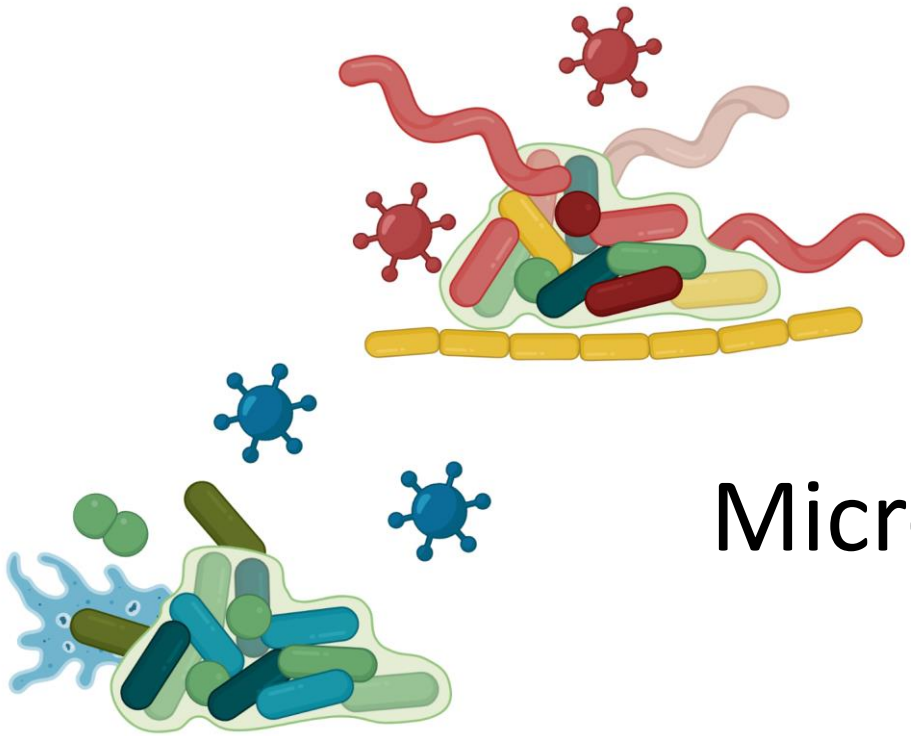
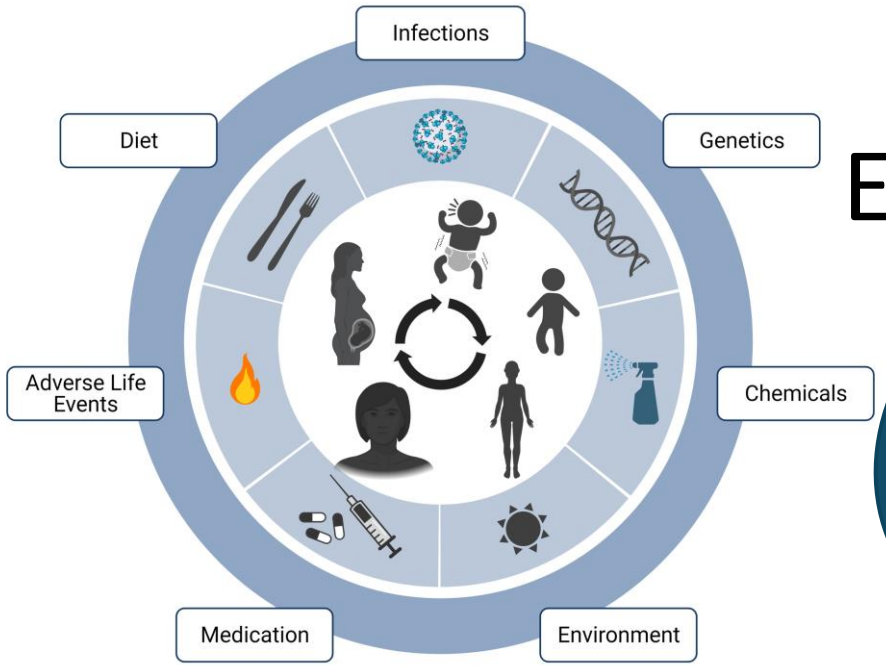
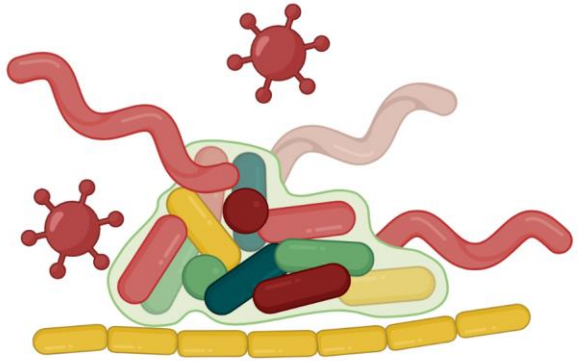
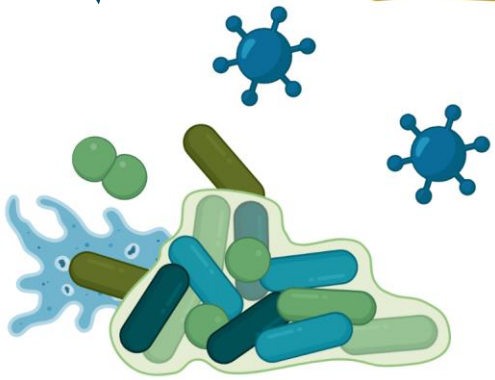


Microbiomes



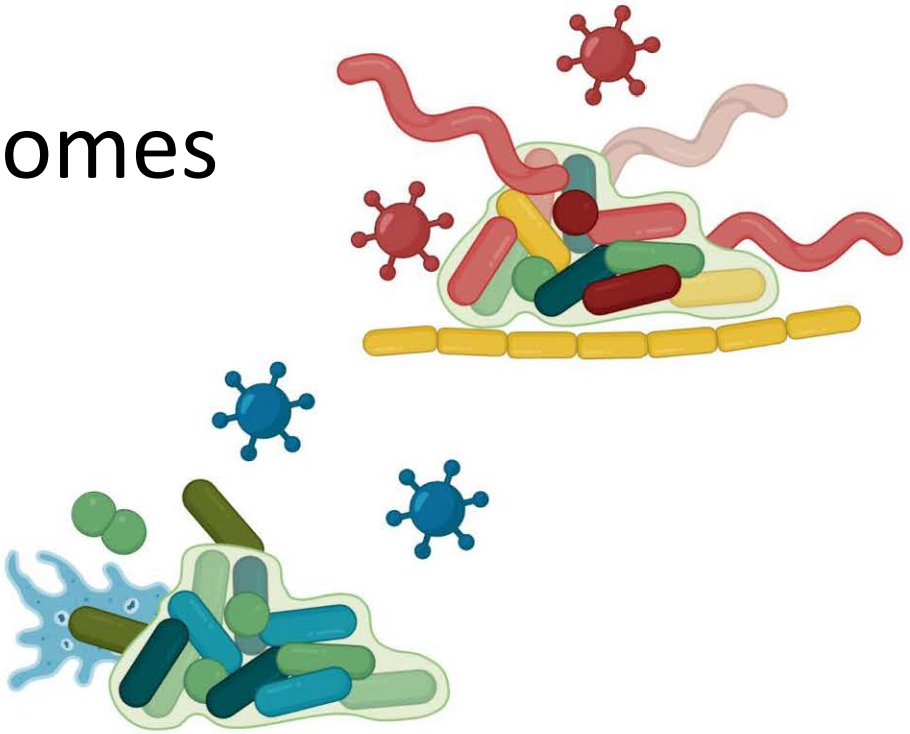
Exposures



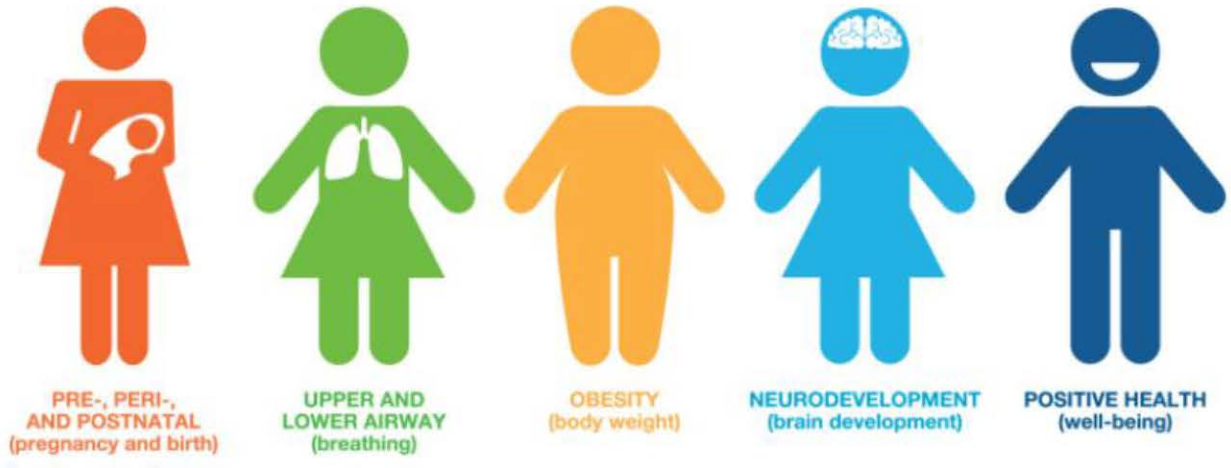


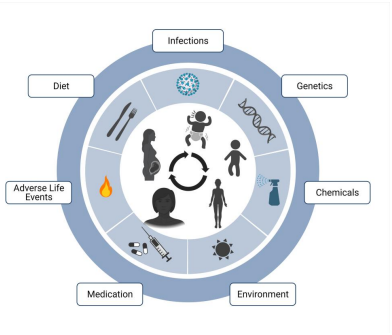
Microbiomes

Microbiomes



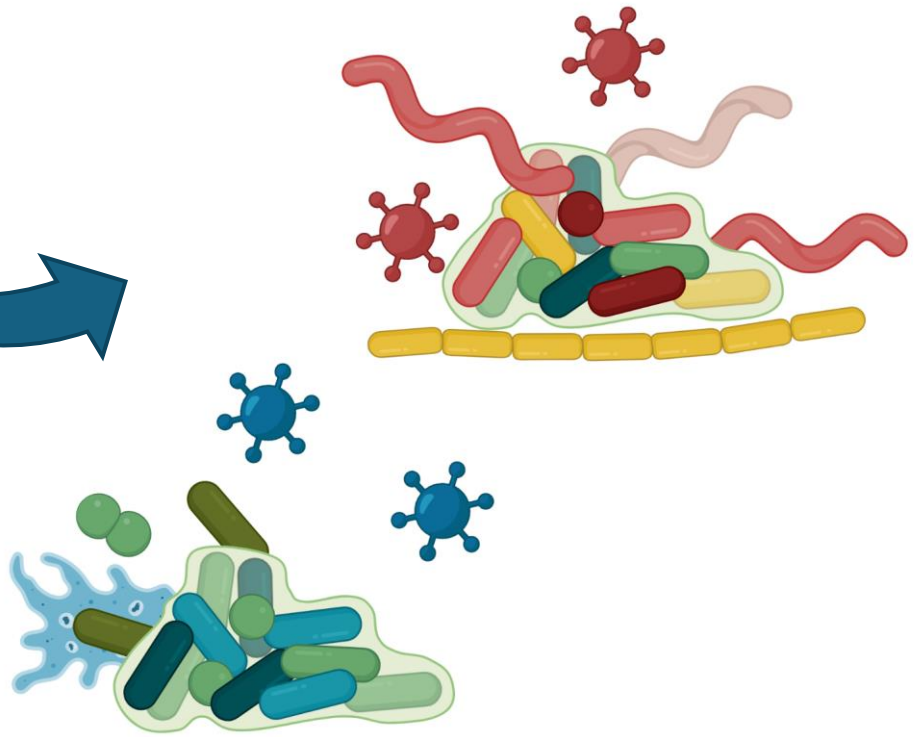
Outcomes



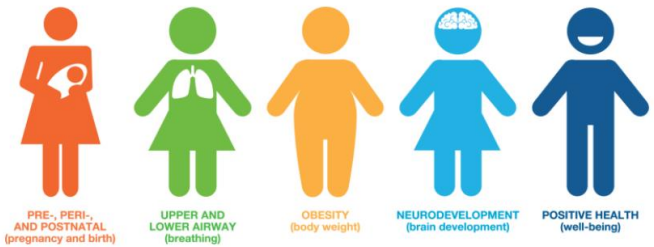


Exposures

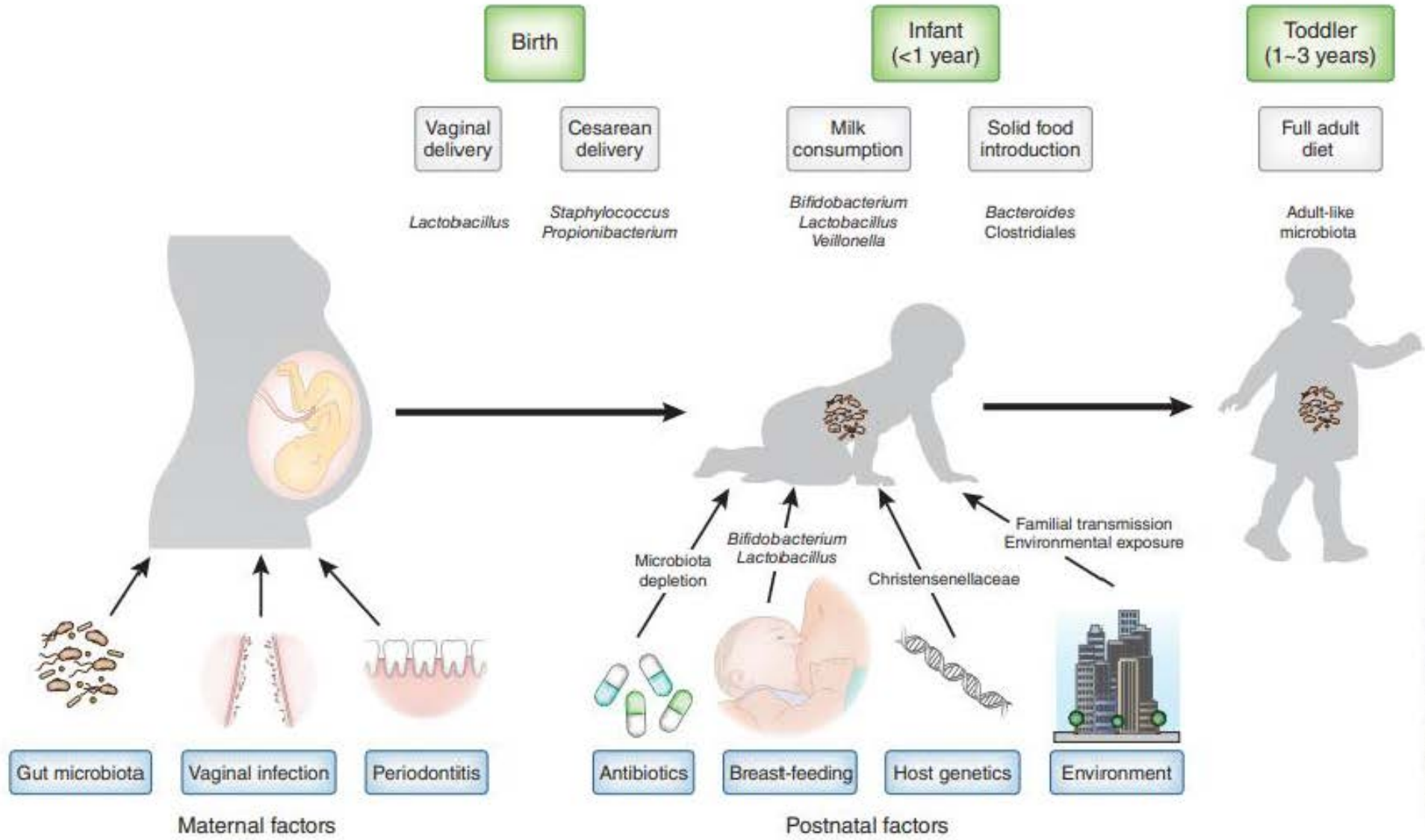
Microbiomes



Outcomes



Exposures which Influence the Gut Microbiome



Marina Corral Spence/Nature Publishing Group

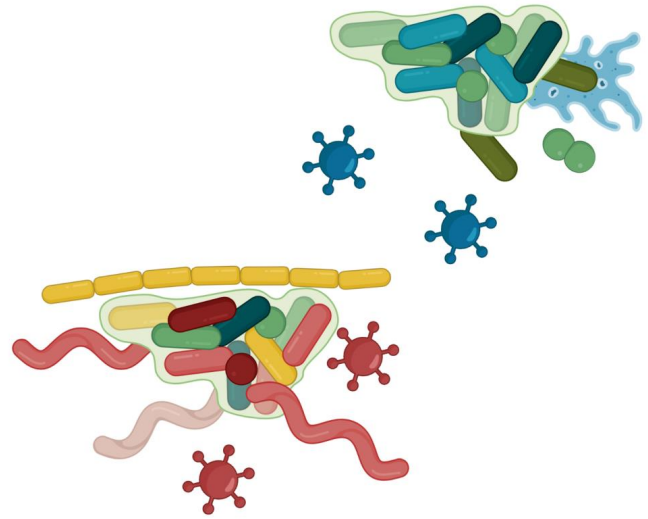
What We Can Do in ECHO

Determine which exposures build host-associated microbiomes that ensure appropriate child development.

The Power of a Longitudinal Pregnancy, Birth, and Pediatric Cohort

- Unique study design that collects information on exposures before outcomes are known

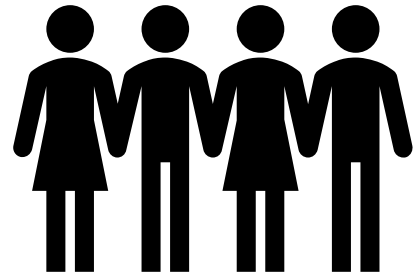
ECHO Microbiome



- Extant data
  - Prenatal vaginal, prenatal fecal, child fecal, child airways
- Existing biospecimens
  - human milk, stool, saliva, nasal mucus
- New biospecimen collections ECHO-wide
- New biospecimen collections through specialized protocols

ECHO Extant Data – Microbiota (16S)

- 16 cohort sites
- ~7,000 participants
  - Pregnant people
  - Children
- Over 16,000 samples

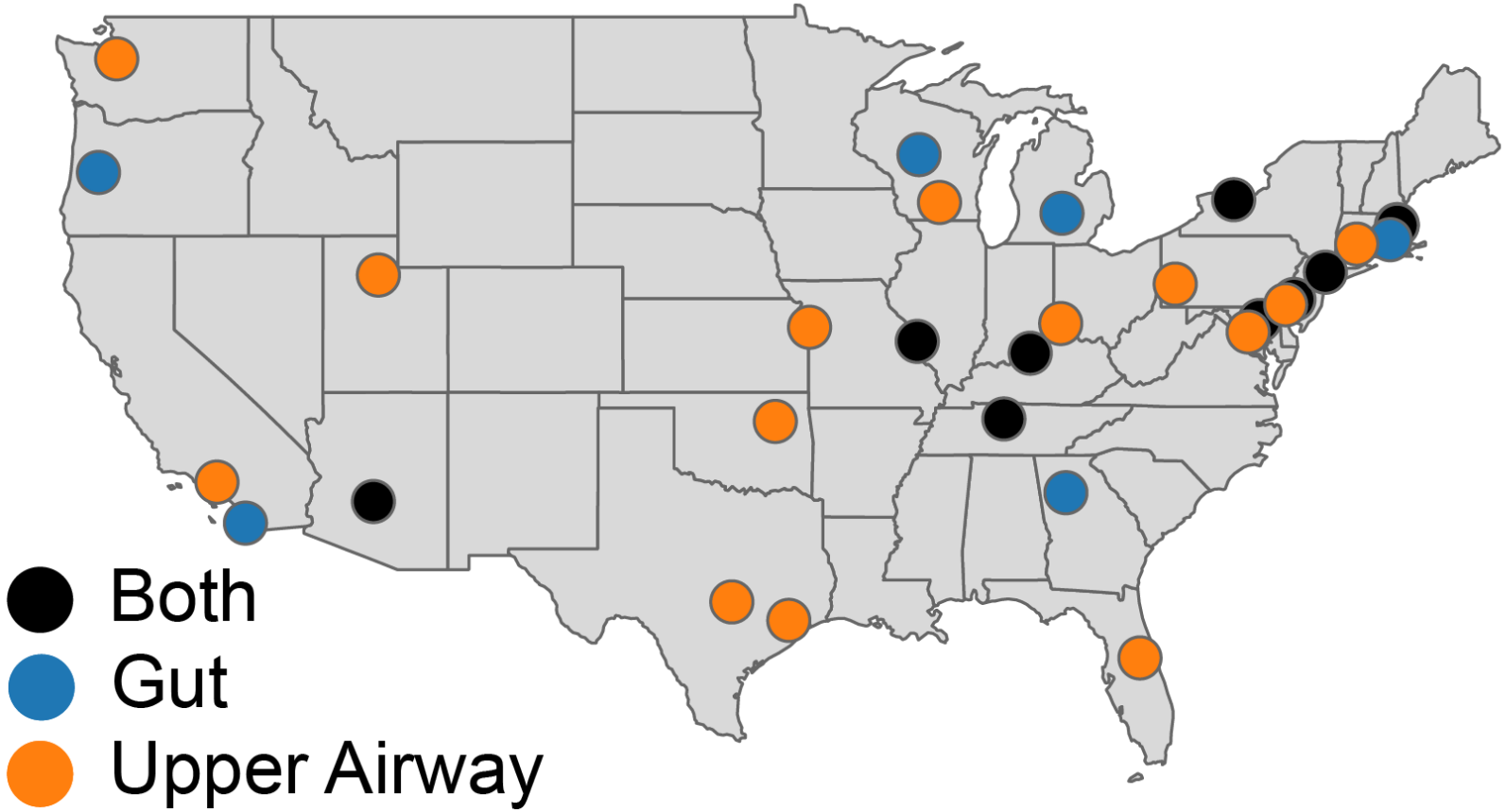


ECHO Extant Data – Microbiota (16S)

- 16 cohort sites
- ~7,000 participants
  - Pregnant people
  - Children
- Over 16,000 samples

	People	Samples
Vaginal – Prenatal	770	780
Fecal - Prenatal	700	770
Fecal – Child	3300	7000
Airways - Child	2900	6900

ECHO Recruitment Sites with Extant Microbiota (16S) Data



Justine Debelius
DAC

ECHO Extant Biospecimens

	Prenatal	Infant: Perinatal	Infancy	Early Childhood	Middle Child-hood	Adolescence
Meconium/Stool	560	350	690	1000	400	500
Human Milk		500				
Nasal Mucus			100	500		
Saliva	13,400		1,600	5,000	4,500	2,300

ECHO Collections in Cycle 2

- ECHO wide
  - Child stool 0-5mos

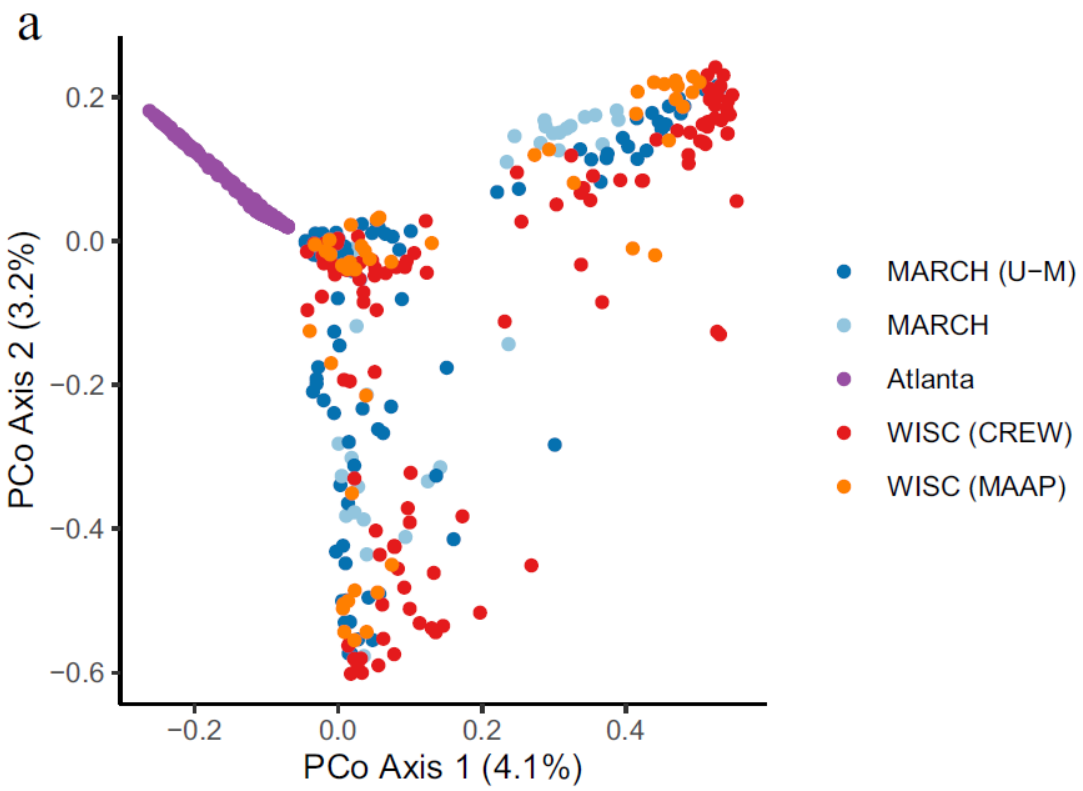
- Obesity Specialized Protocol
  - Prenatal 3rd trimester stool
  - Child stool at: 6-11mos, 12-23mos, 24-35mos, 3-5yr, 6-10yr, 11-17yr, 18-20yr

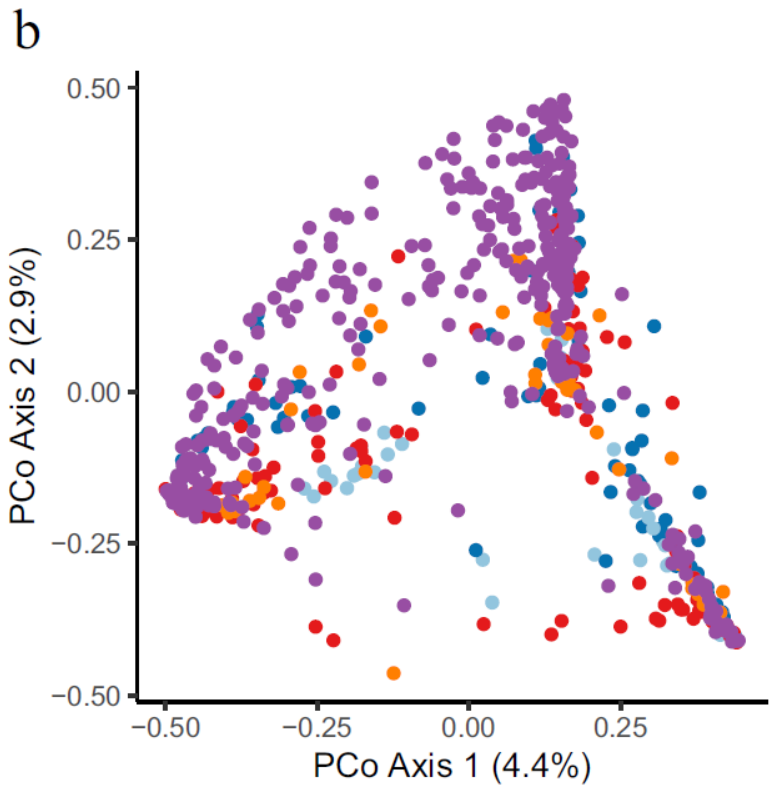
- Airways Specialized Protocol
  - Nasal airway mucosal sample (brush &/or filter) 0-11 mos (preferably 0-5mos) and 6 years

- Lifestyle Specialized Protocol
  - Human milk

ECHO-Wide Analyses with Extant Data

Phylogenetic Placement of ASVs on a Reference Tree Removed a Large Degree of Variation by Site



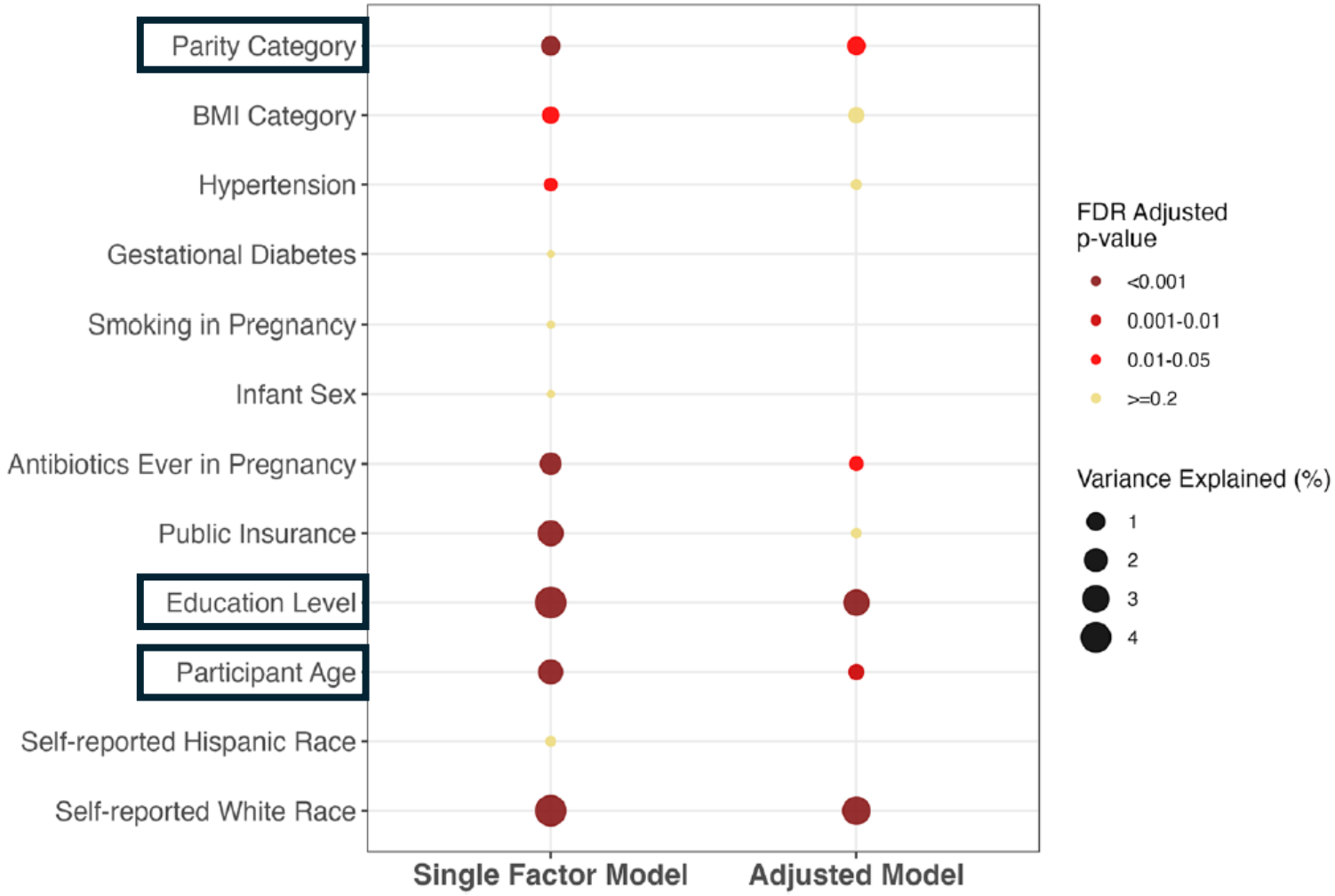


Jonathan Golob

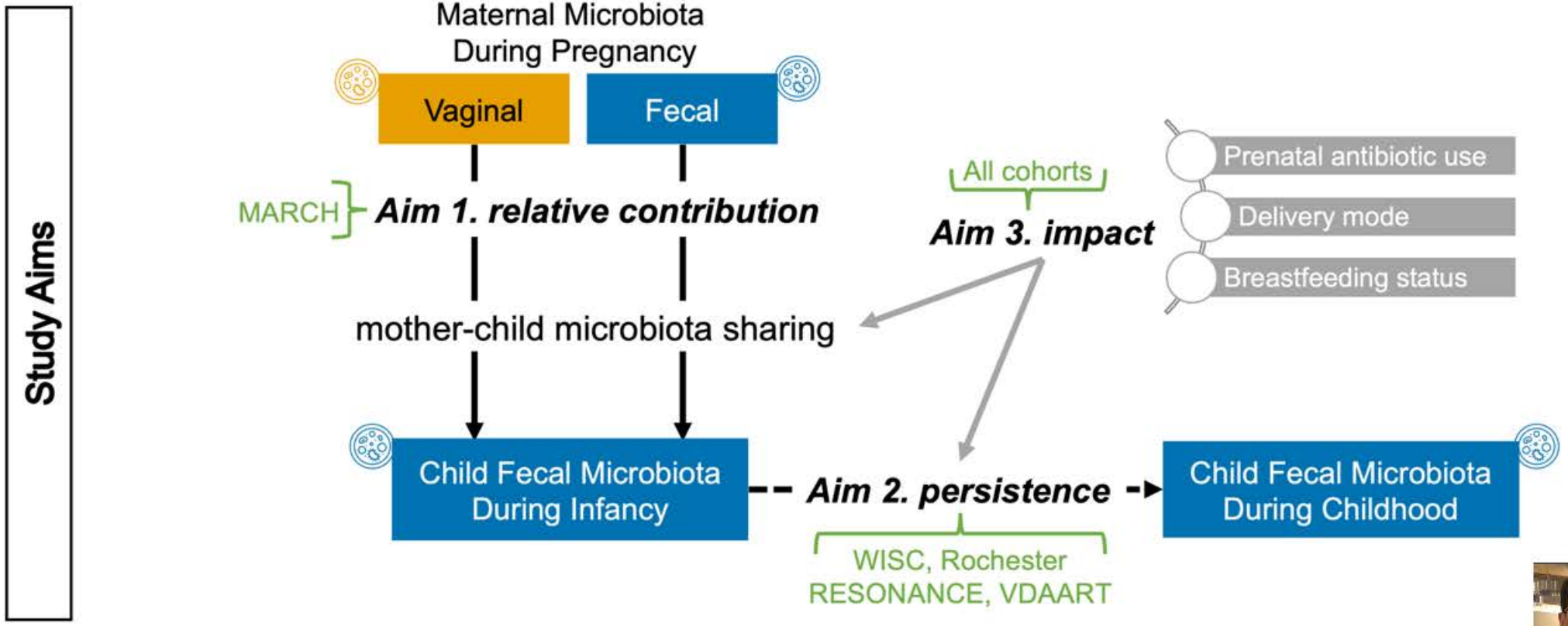
Kimberly McKee

Bray-Curtis, Vaginal Microbiota

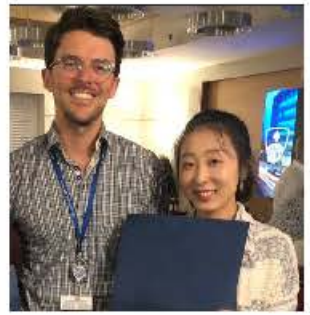
Factors Associated with Vaginal Community Structure in Pregnancy



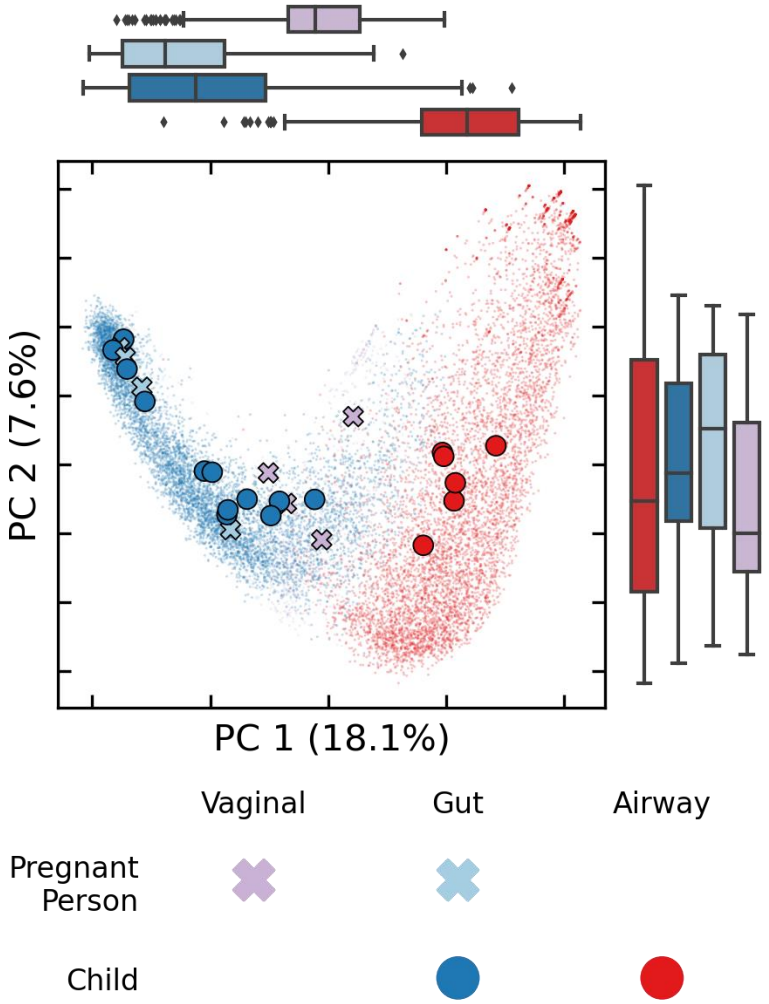
Contributions of the Pregnancy Vaginal & Fecal Microbiota to Offspring Fecal Microbiota Development

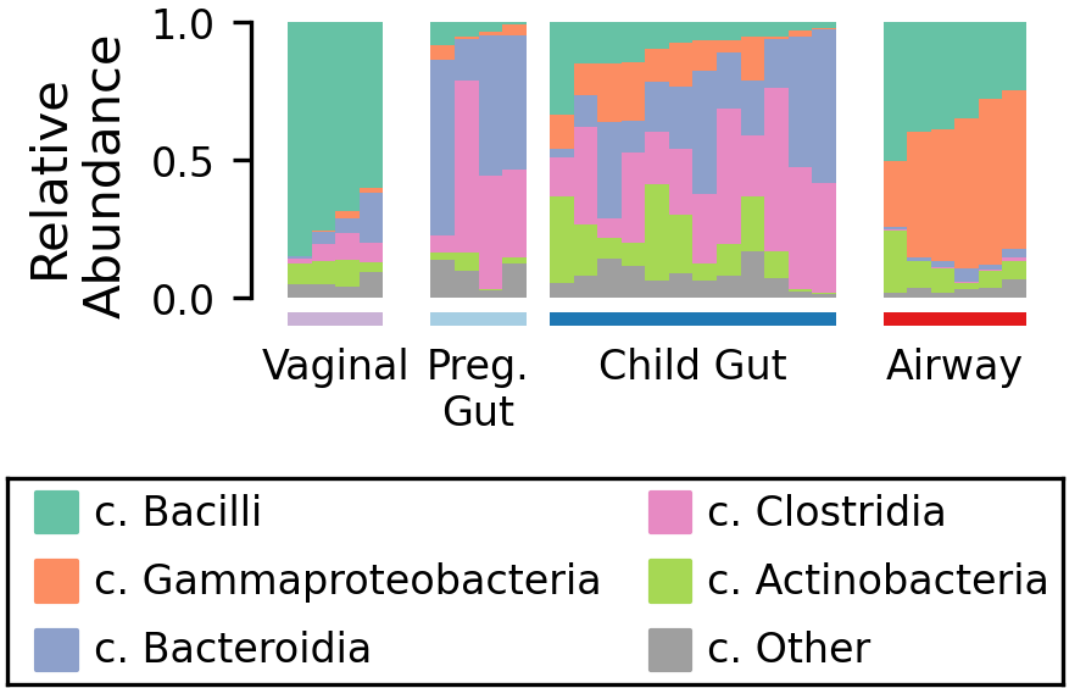


Noel Mueller
Tiange Liu



Microbiota Community Composition Differs by Body Site





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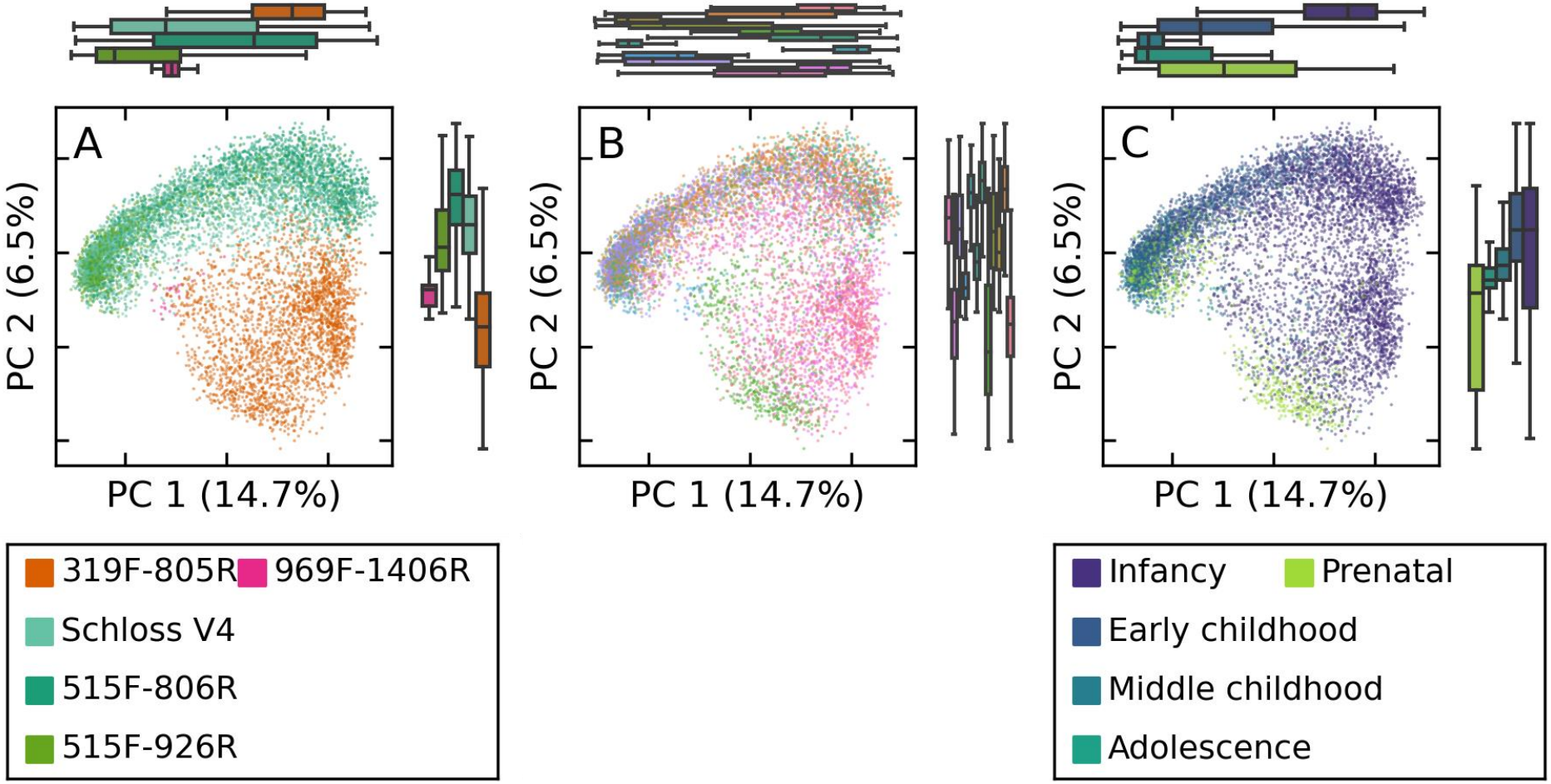
Primer Pair and Lifestage are Associated with Fecal Bacterial Communities



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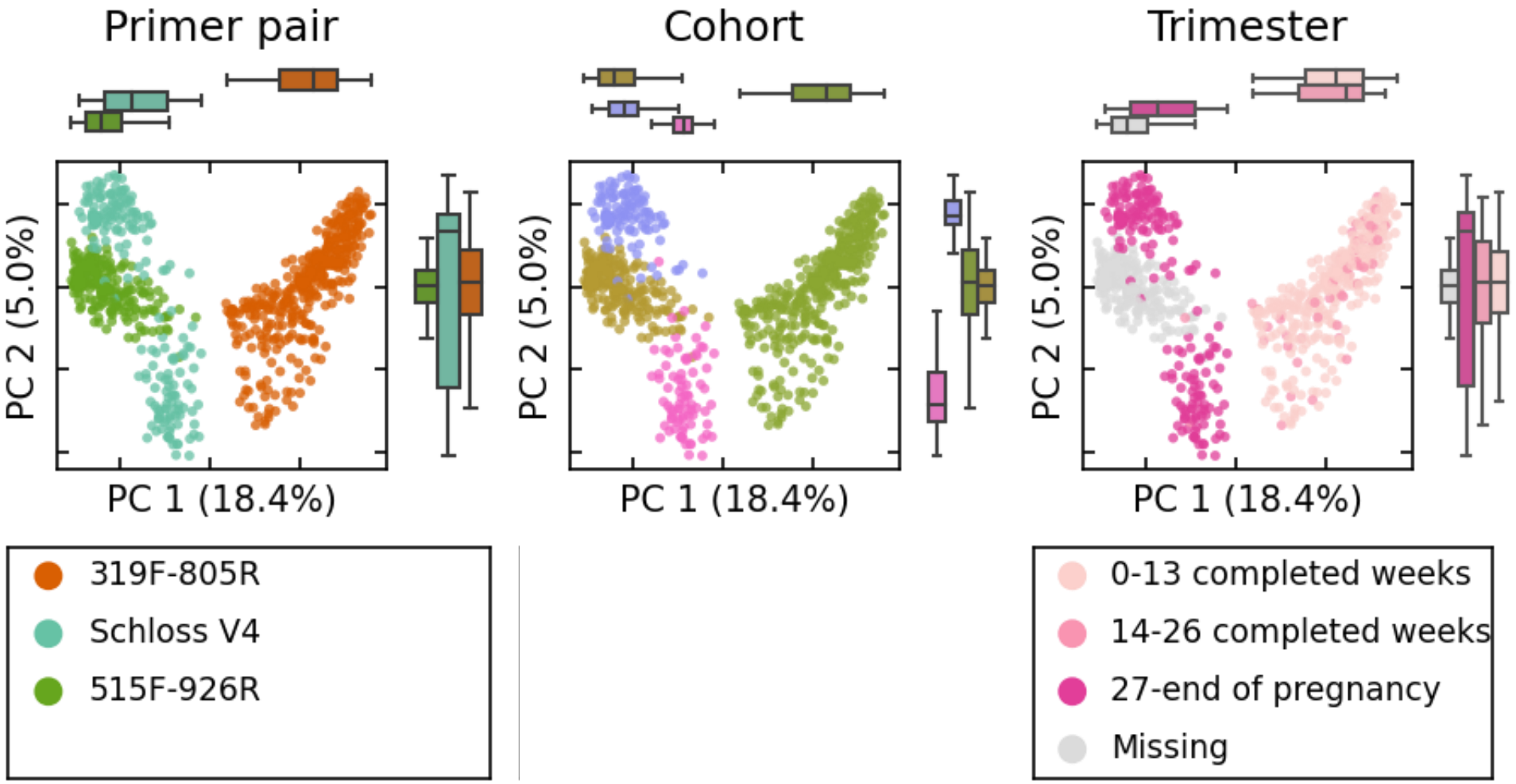
Unweighted UniFrac PCoA of Fecal samples in the Silva 97% OTU table with at least 1,000 sequences

Primer Pair and Trimester are Associated with Prenatal Fecal Bacterial Communities



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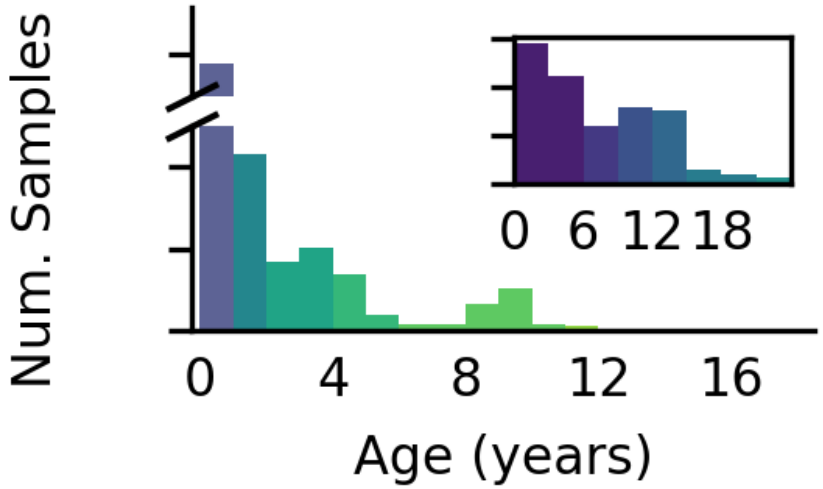
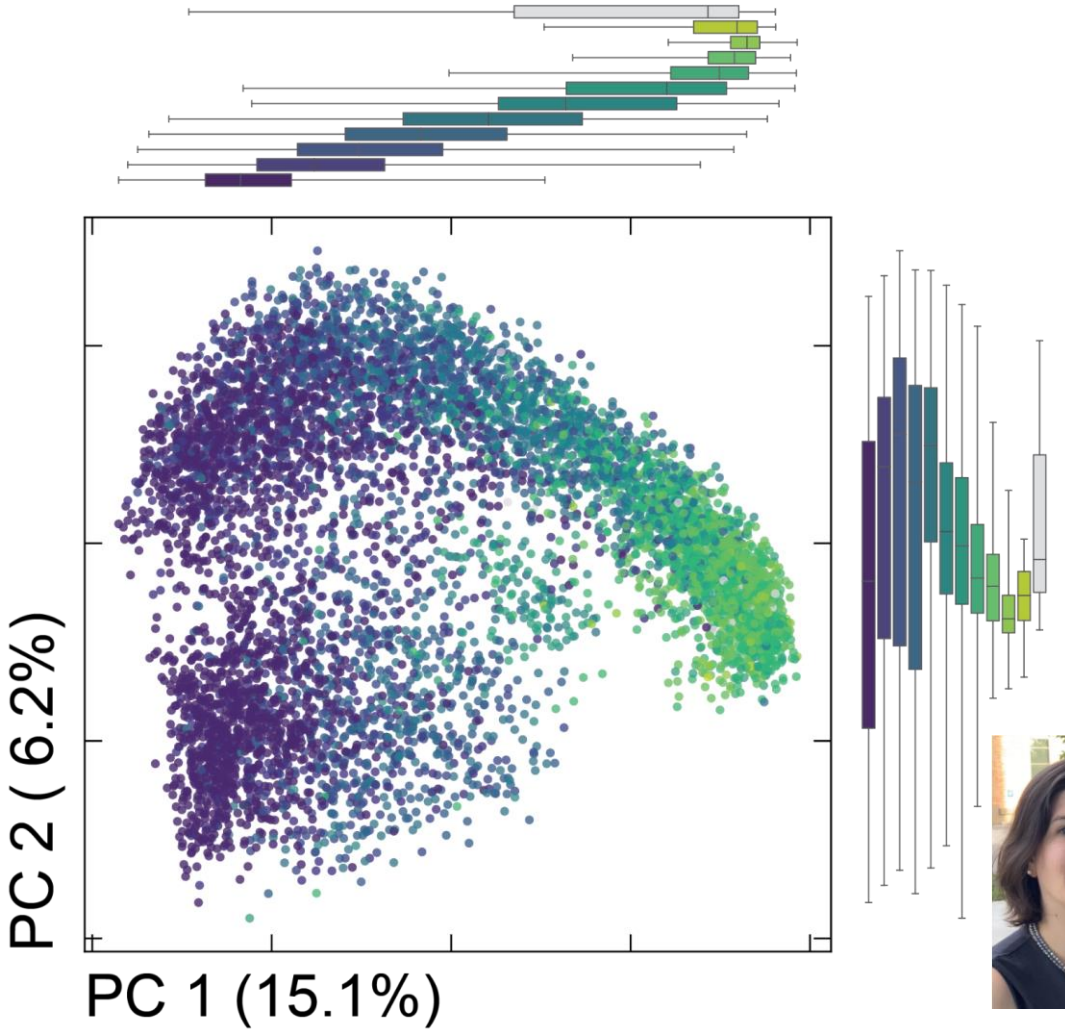
The Bacterial Composition of Fecal Samples Differs by Child Age



- 0-3 months
- 3-6 months
- 6-9 months
- 9-12 months
- 12-18 months
- 18-24 months
- 24-36 months
- 3-5 years
- 6-10 years
- 10-13 years
- 13-18 years
- missing



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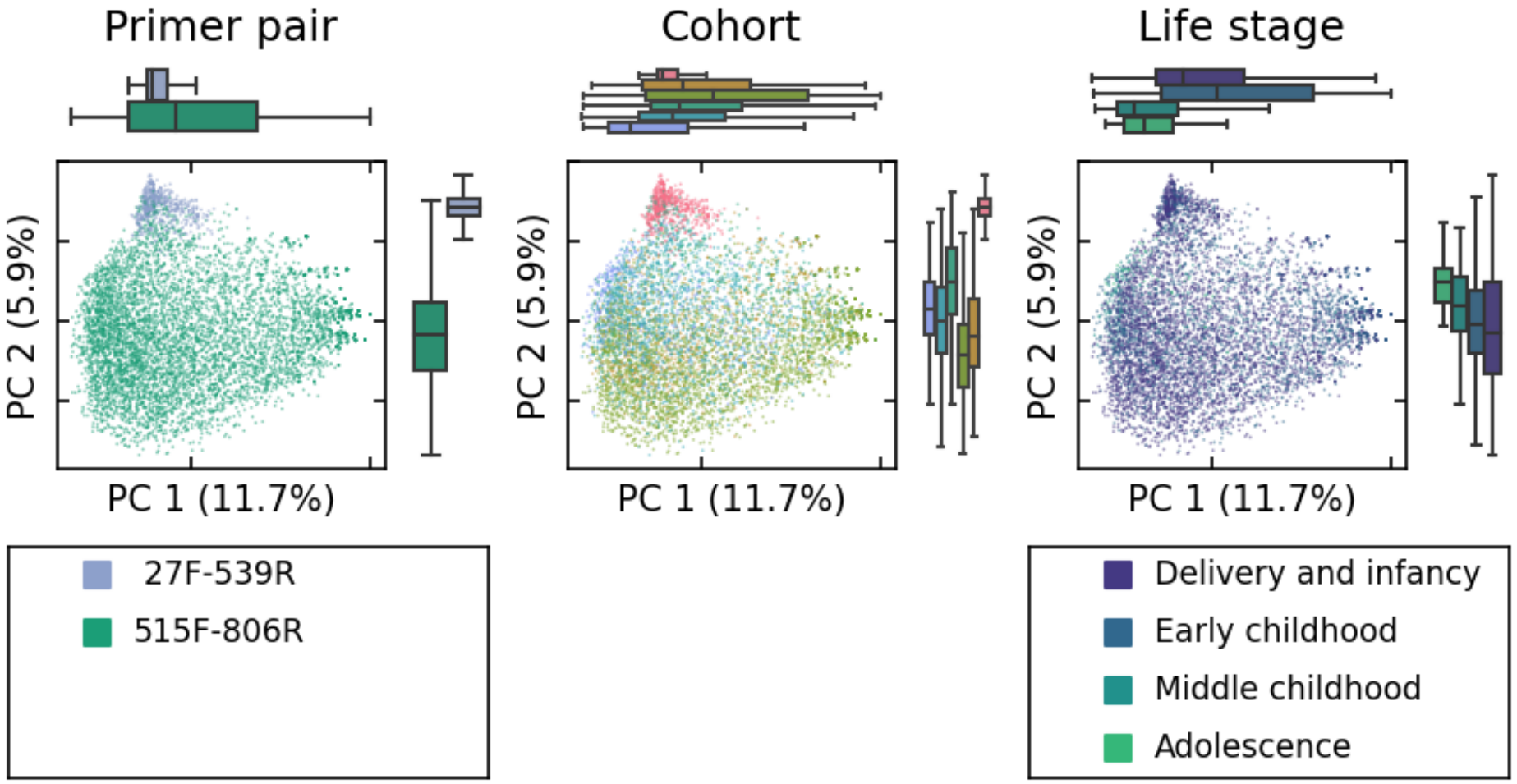
The Bacterial Composition of Airway Samples Differs by Primer Pair and Lifestage



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DAC

Unique child nasal or nasopharyngeal samples in the Silva 97% OTU table with at least 1,000 sequences

Why study infants?

- Defined diets
  - Especially early in life
- No autonomy regarding diet
- Immune system isn’t fully developed
- Gut microbiota isn’t fully developed – or, rather, is still in a dynamic state

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At this point in development, more than at many other points in time across the lifespan, we have the chance to alter the microbiome through diet, and the immune system, and other systems, through the microbiome.

Child Health Advances *from* Research *with* Mothers

Pregnancy Cohorts
- **-ARCH**
- **-MARCH**

Primary Funding Sources
- **-Michigan Health Endowment Fund**
- **-NIH ECHO Program**

Nigel Paneth

Jean Kerver

ECHO
Environmental influences on Child Health Outcomes

A research program supported by the National Institutes of Health

CHARM Microbiome Collaboration

Andrea Cassidy-Bushrow

Kim McKee

Michael Petriello

Sara Santarossa

Sarah Comstock

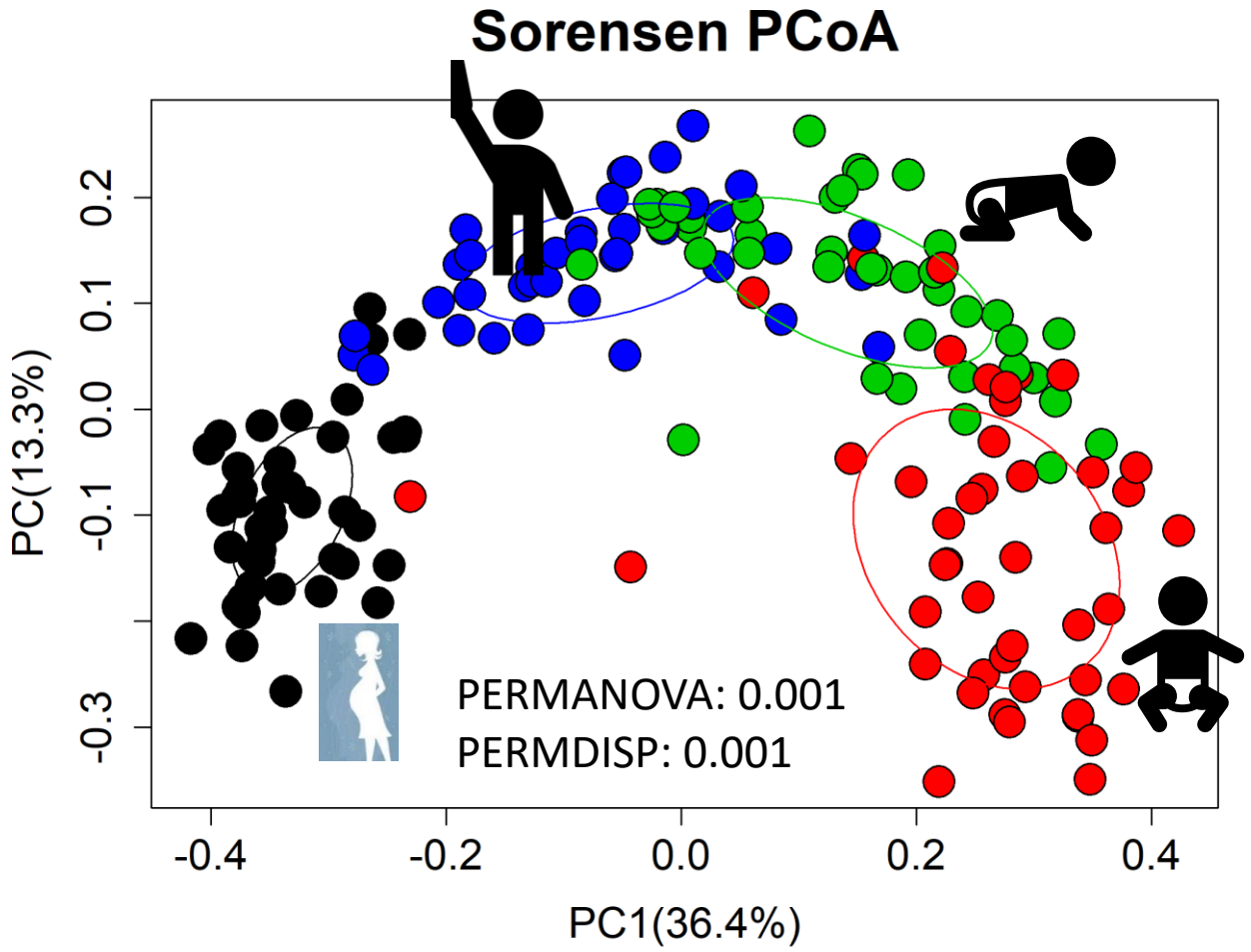
Rebecca Knickmeyer

Tengfei Ma

Lixin Zhang

CHARM

Members of Fecal Microbial Communities Differ by Time Point Across the Lifespan

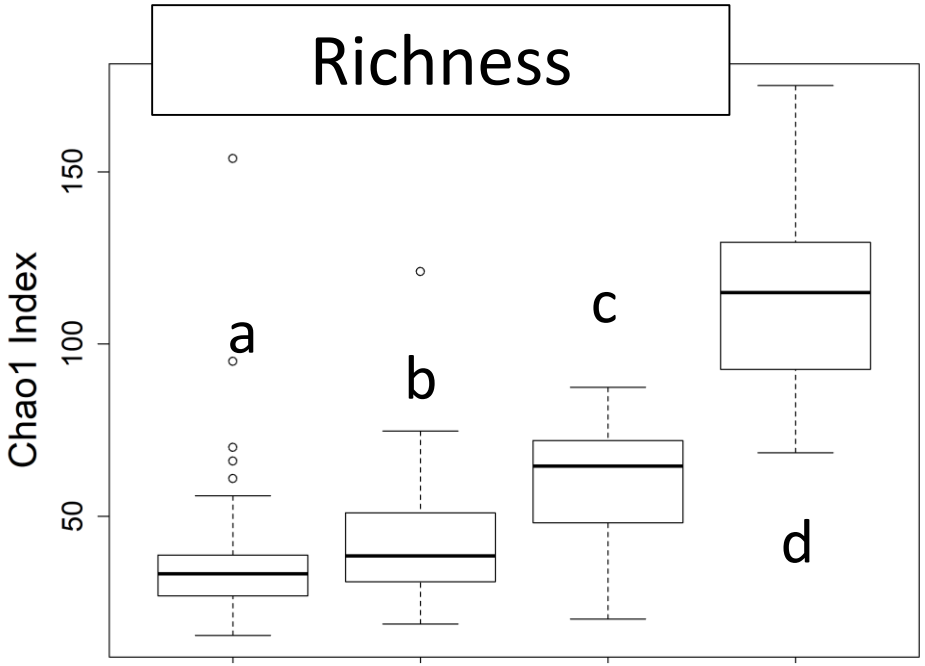


- Pregnancy
- 1 week old infants
- 6 month old infants
- 12 month old infants

Genus

Kameron Sugino

Alpha Diversity is Greatest in Pregnancy Fecal Microbial Communities



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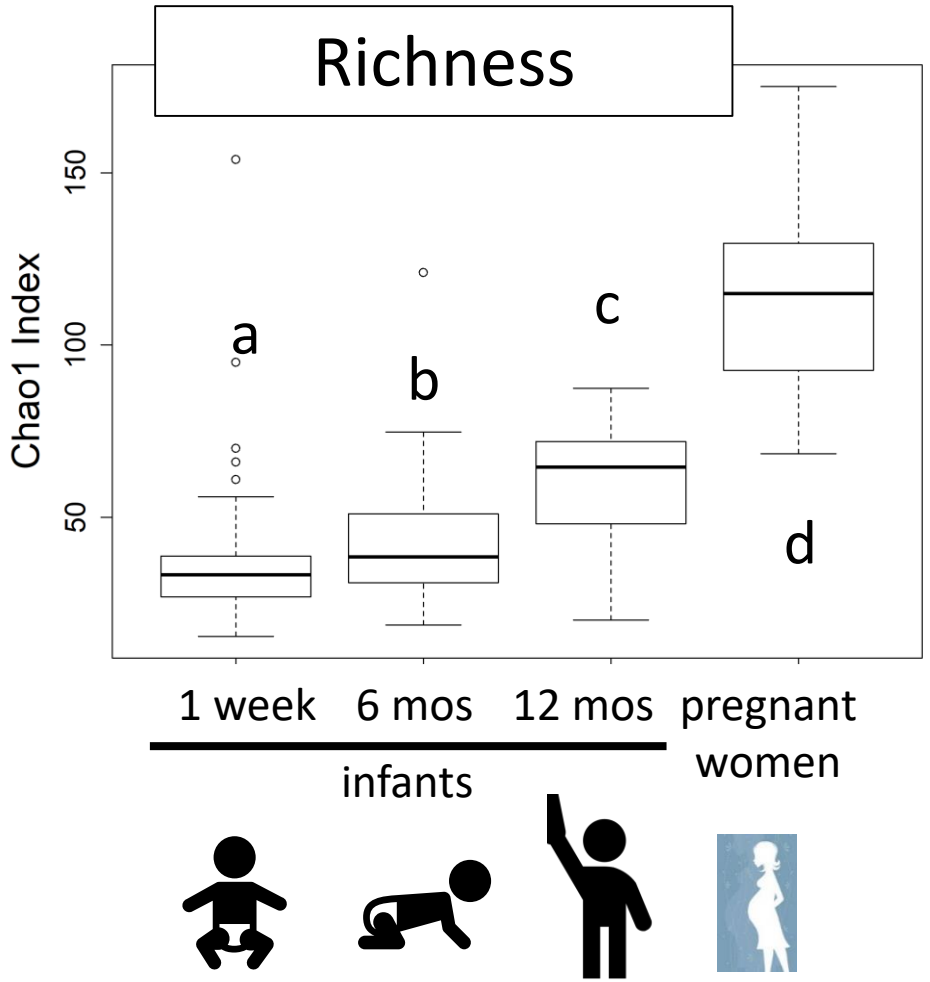
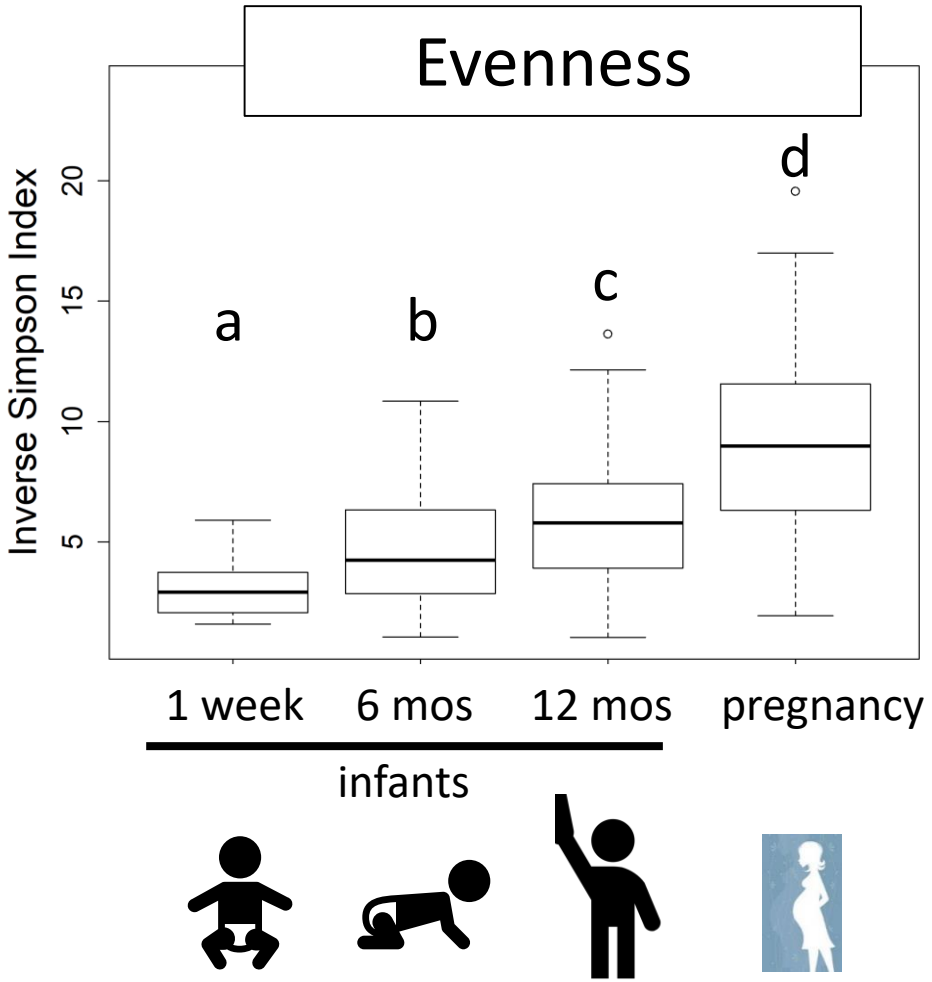
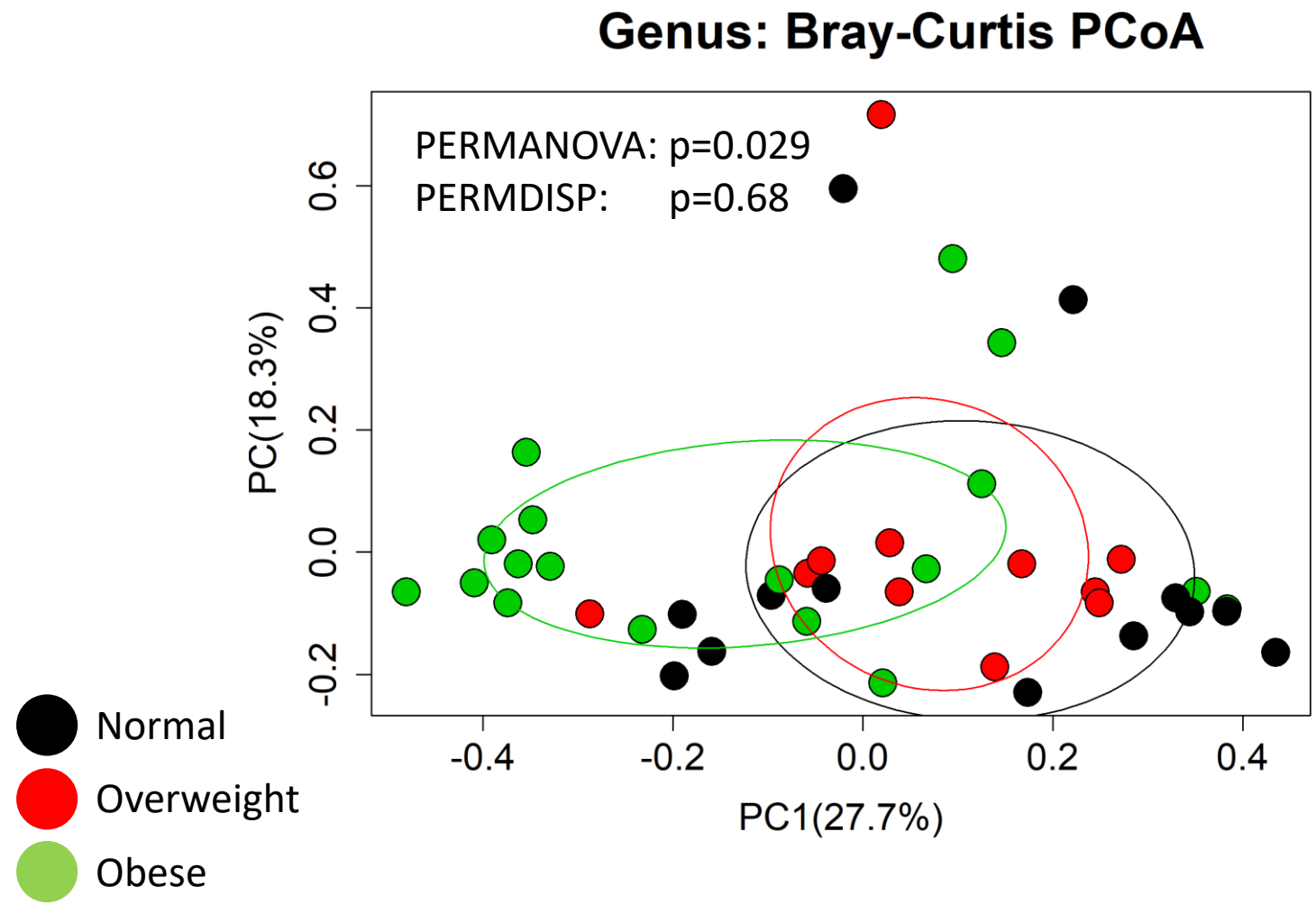




Genus

The Fecal Microbial Communities of 6 month old Infants Born to Women who were of Normal Weight Prior to becoming Pregnant are Different from those of Infants Born to Women with Pre-Pregnancy Obesity



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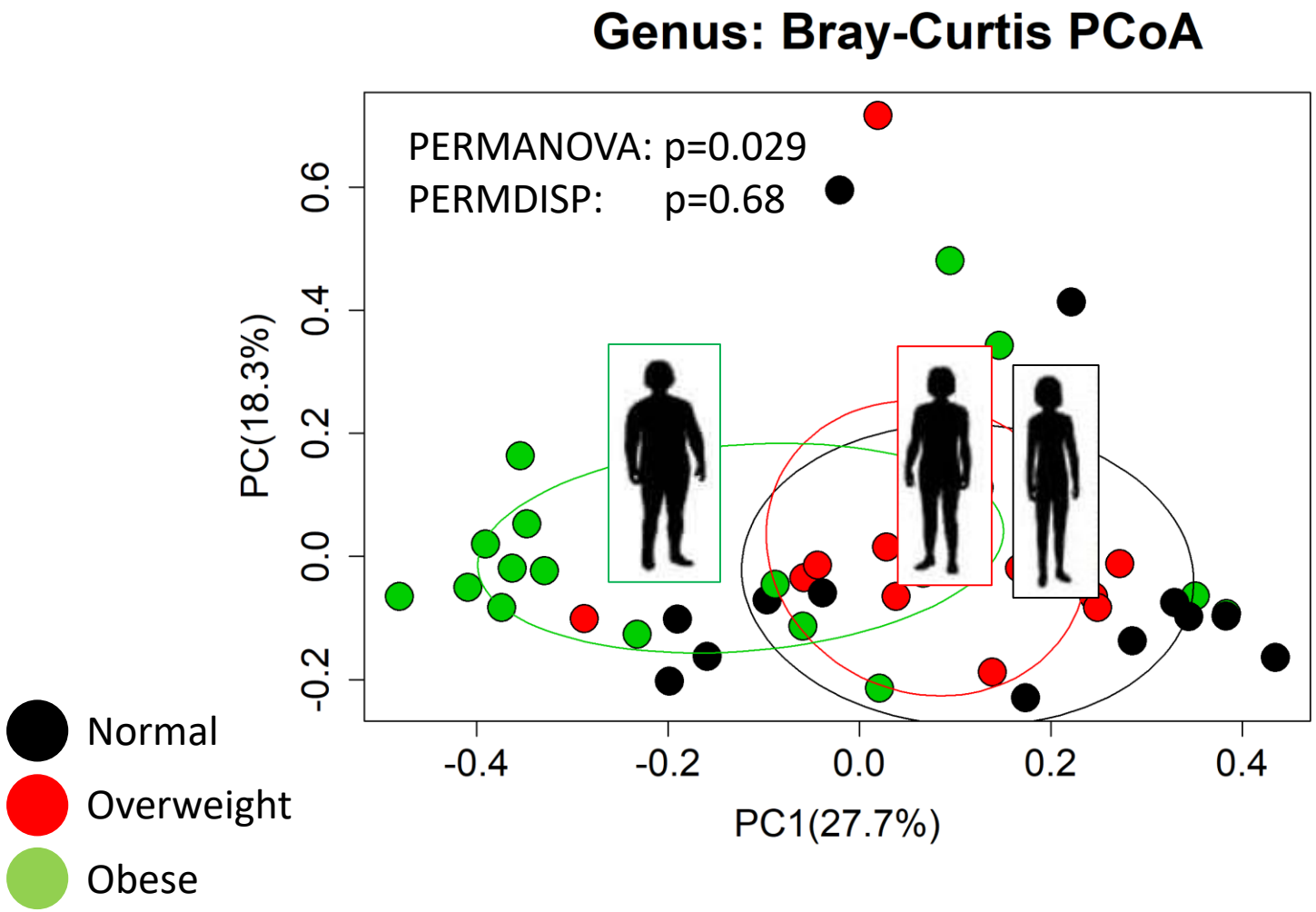
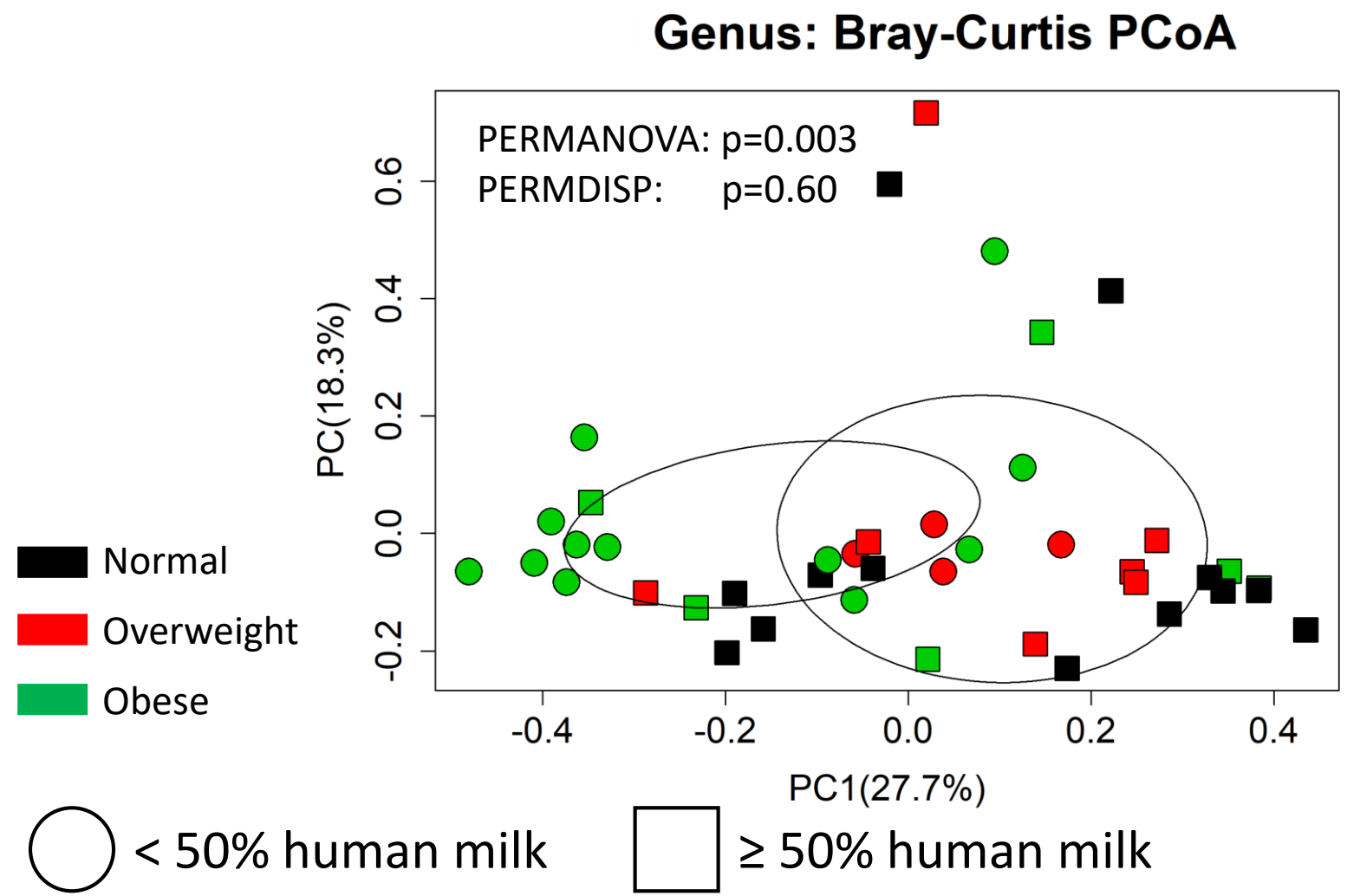


However, this Association is Significantly Confounded by Human Milk Exposure



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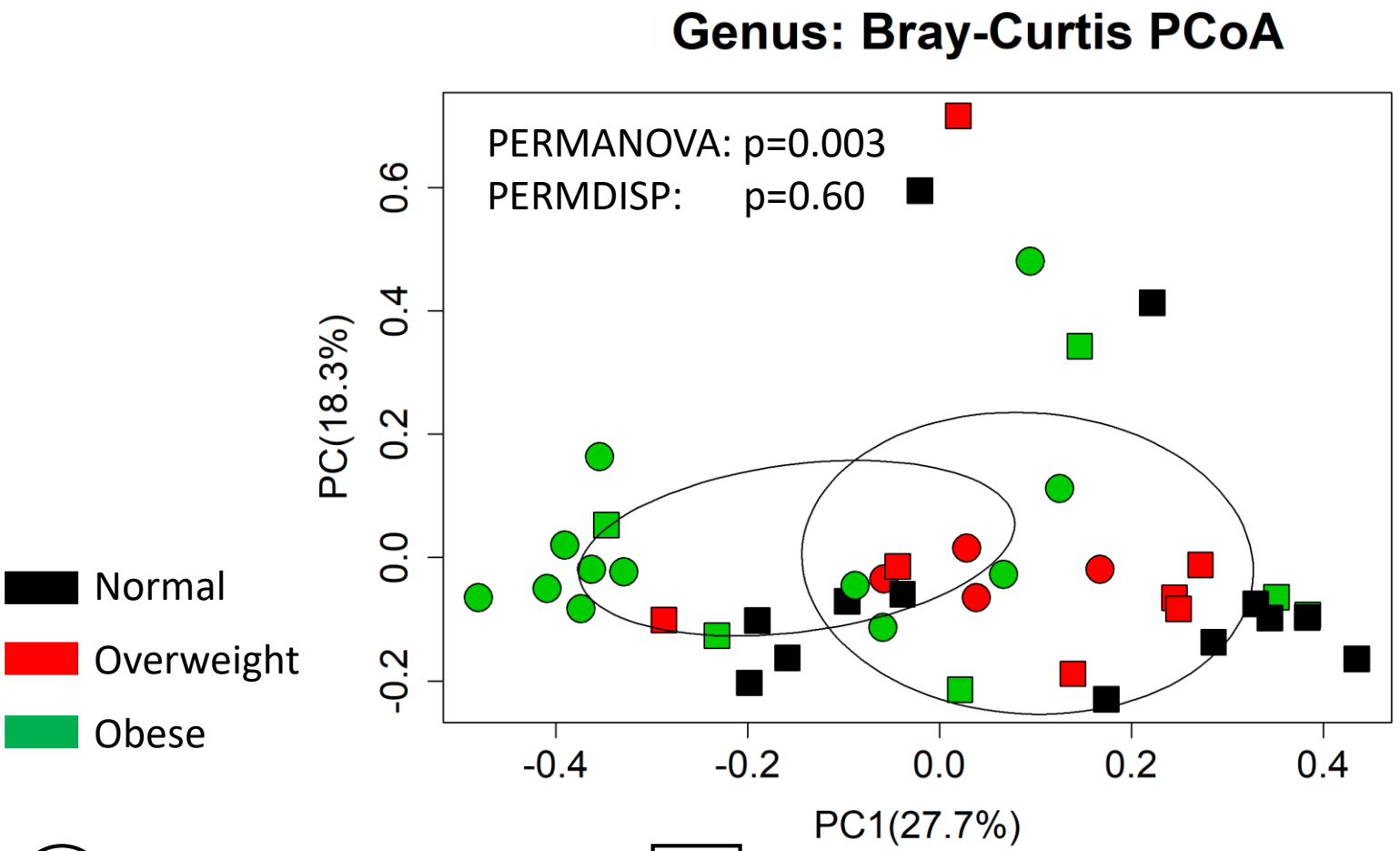
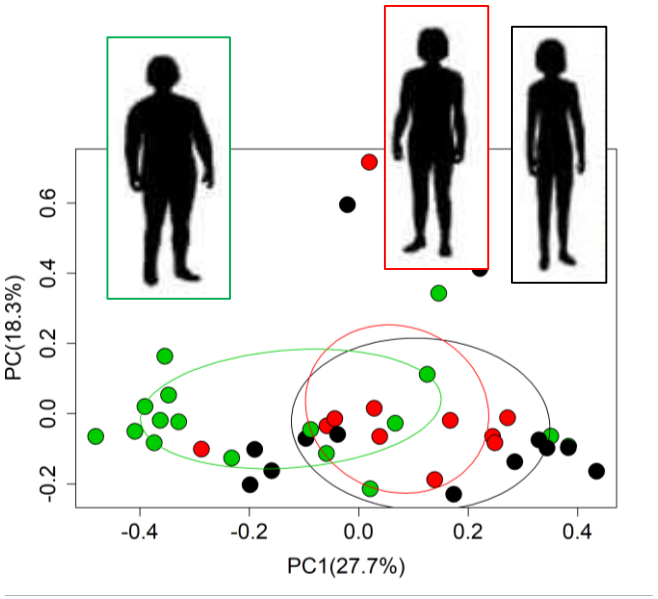
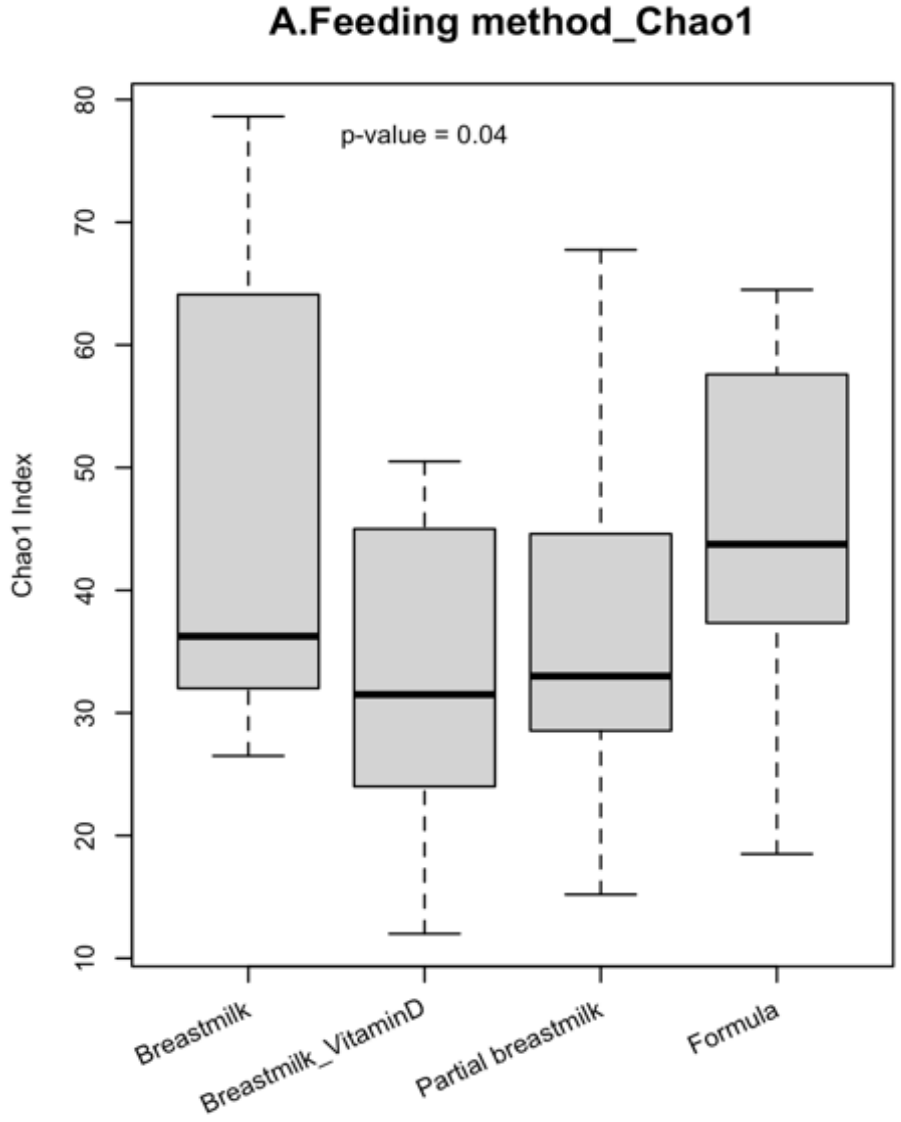
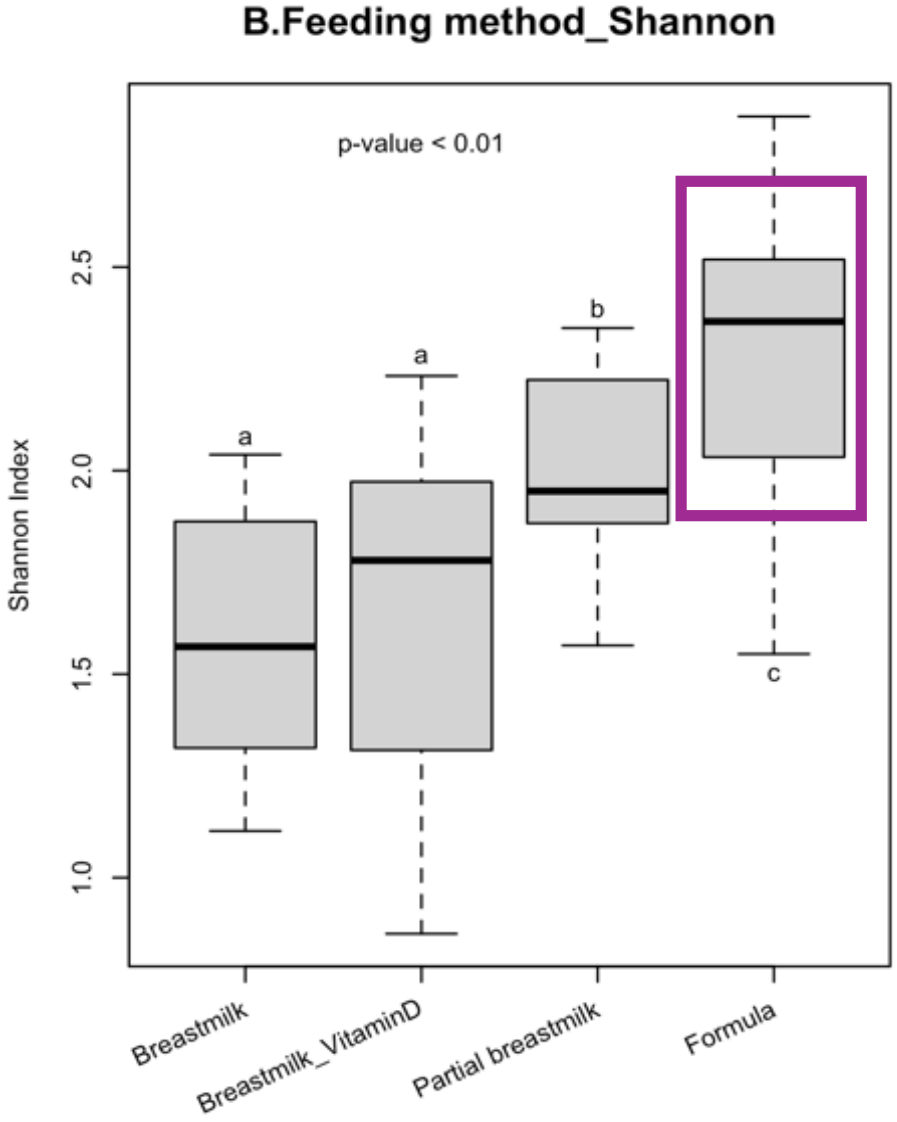
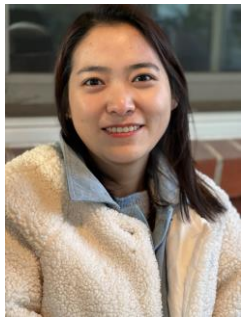




3 Month Old Infants Fed Formula had Greater Shannon Alpha Diversity Compared to Infants Fed any Human Milk in the 24 Hours Prior to Sample Collection

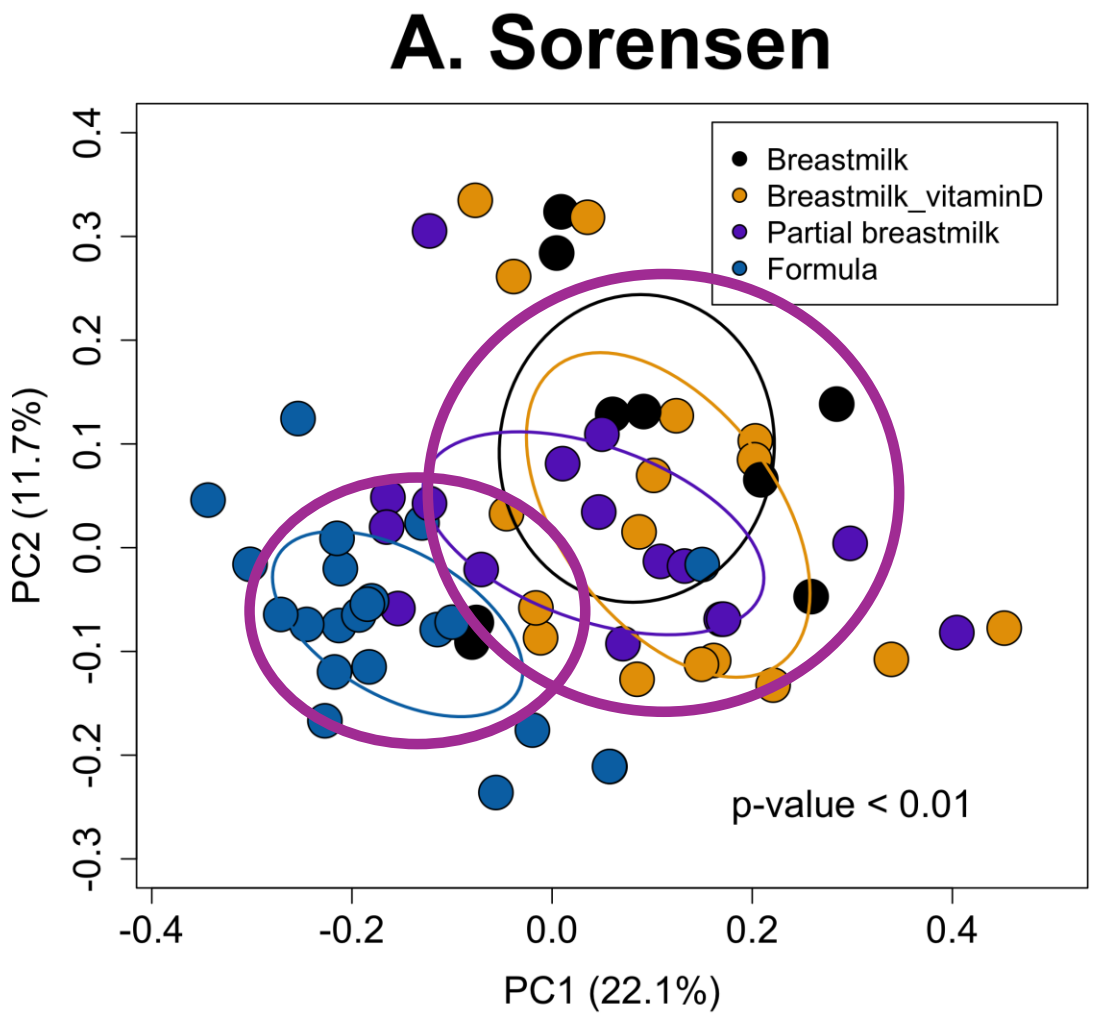


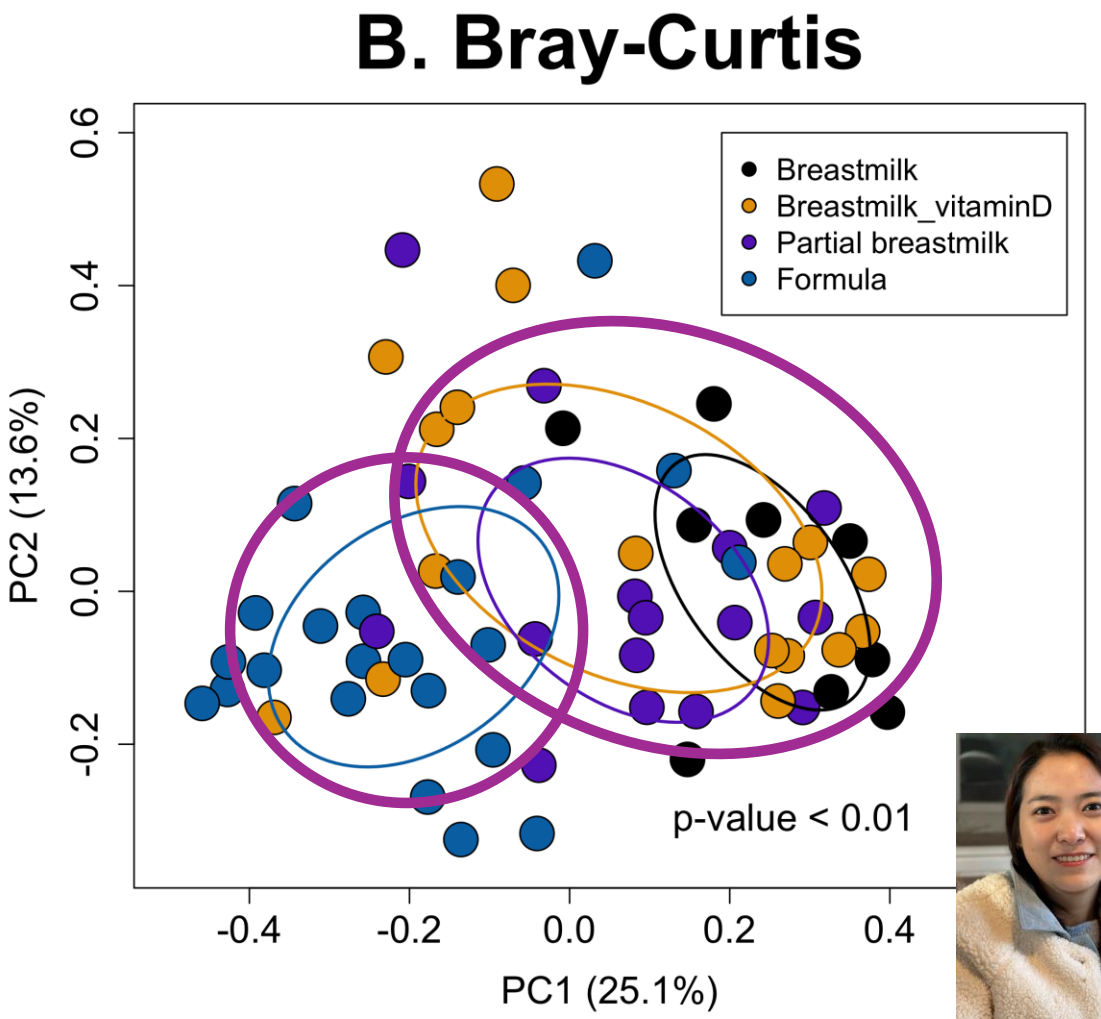




Sihan Bu

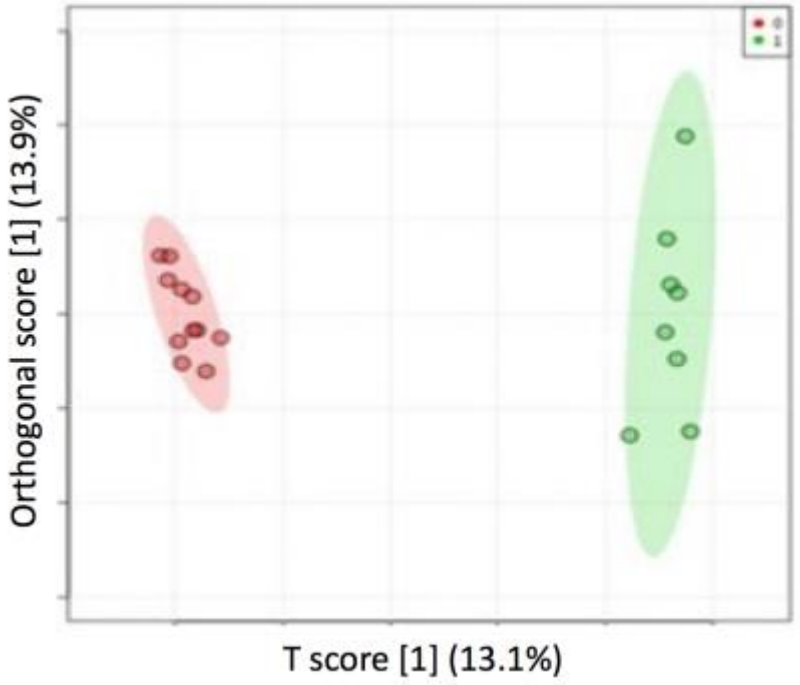
3 Month Old Infants Exclusively Fed Formula had Distinct Gut Microbiotas from those Exclusively Fed Human Milk, with Mixed Fed Infants having Microbiotas More Similar to those Infants Exclusively Fed Human Milk





Sihan Bu

Metabolites in the Stool of 6 Month Old Infants Differ by Diet



Human Milk Fed

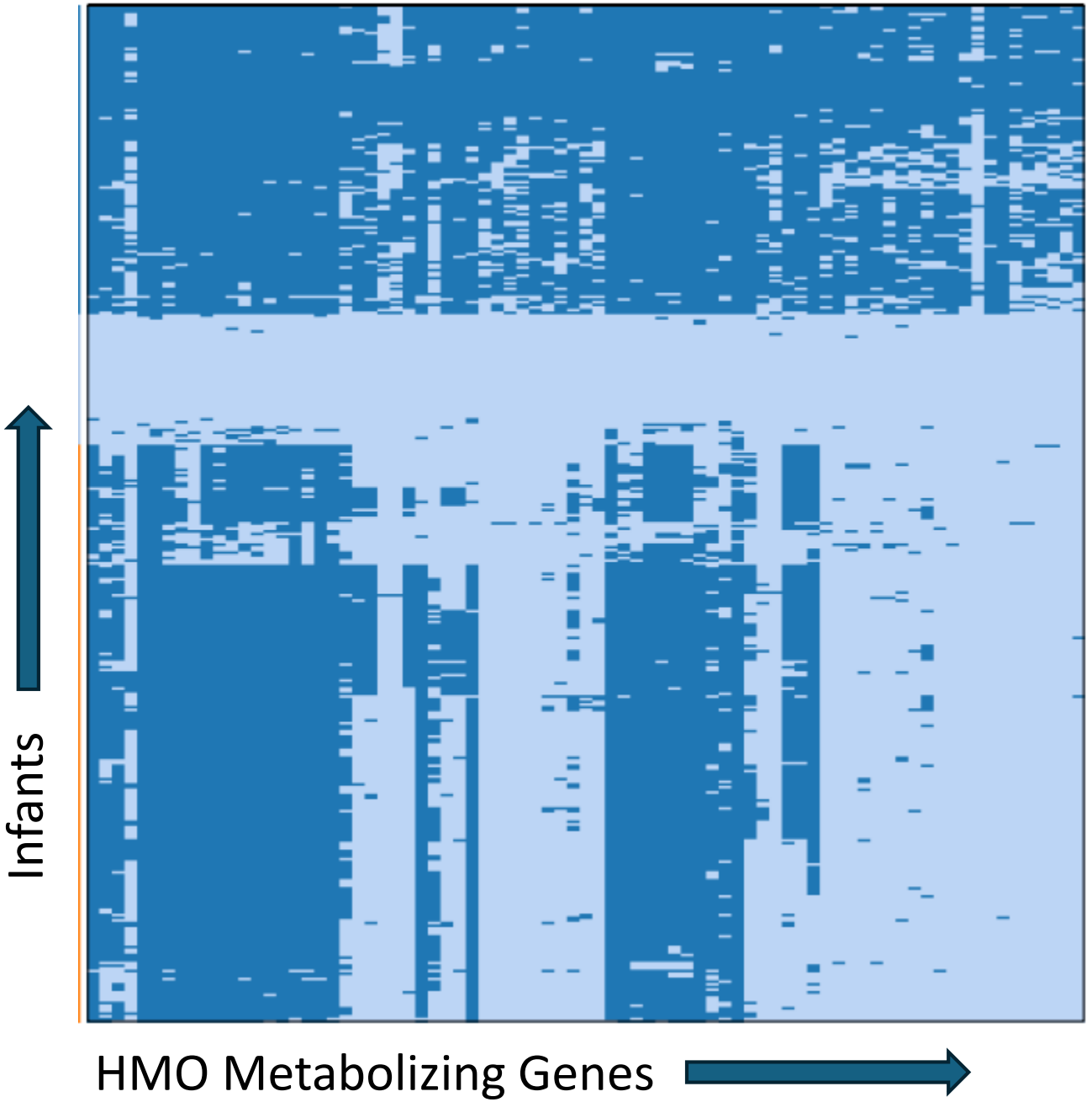
Formula Fed

HHEAR Human Health Exposure Analysis Resource

Unpublished, NIH CHEAR lab (Susan Sumner, Susan McRitchie), Dan Rajasinghe (Pestka Lab)

Leimanis Laurens & Comstock 2020 *Nutrients*, review article

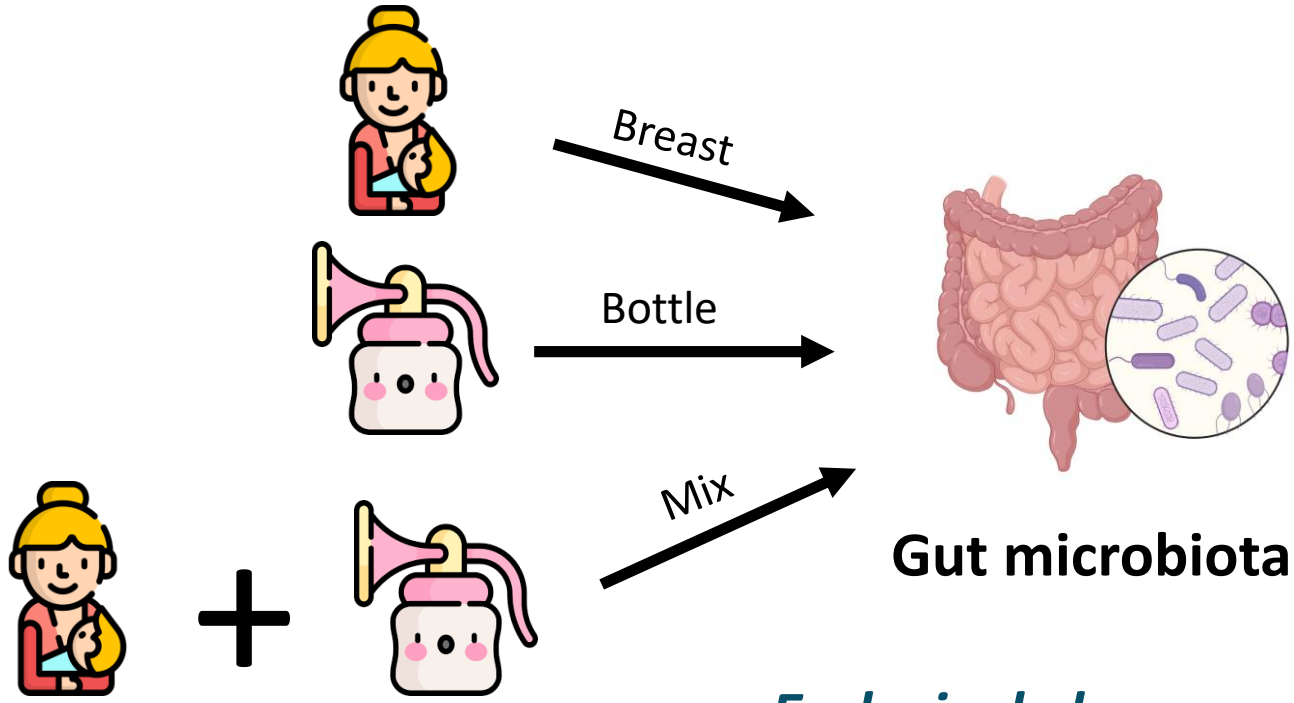
Infant Stool Samples have Unique Human Milk Oligosaccharide Metabolizing Gene Repertoires



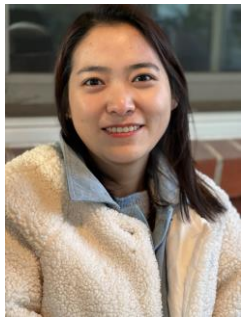
Vanja Klepac-Ceraj

Guilherme Fahur Bottino

Associations Between Breastfeeding Modality and the Infant Gut Microbiota

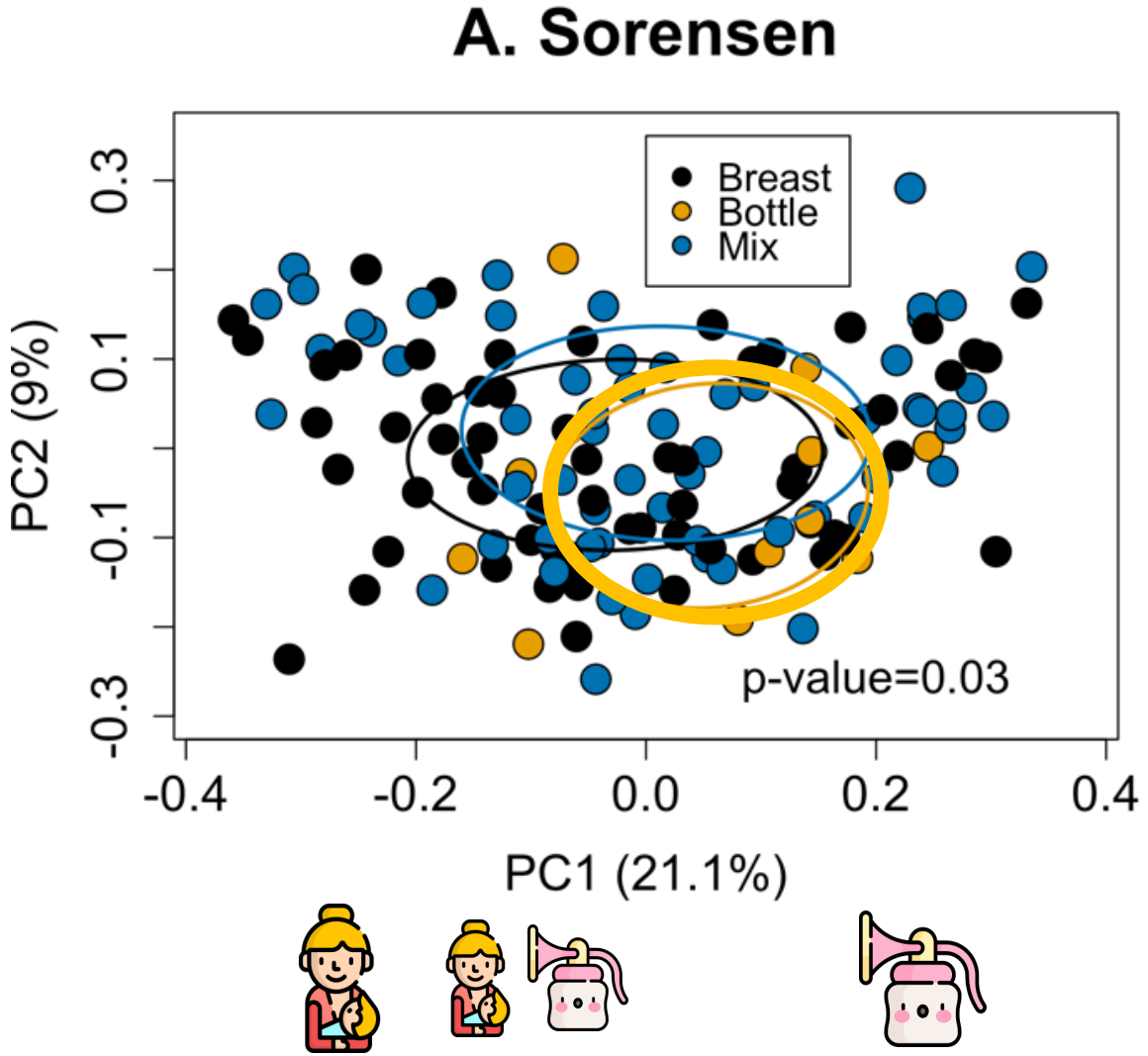


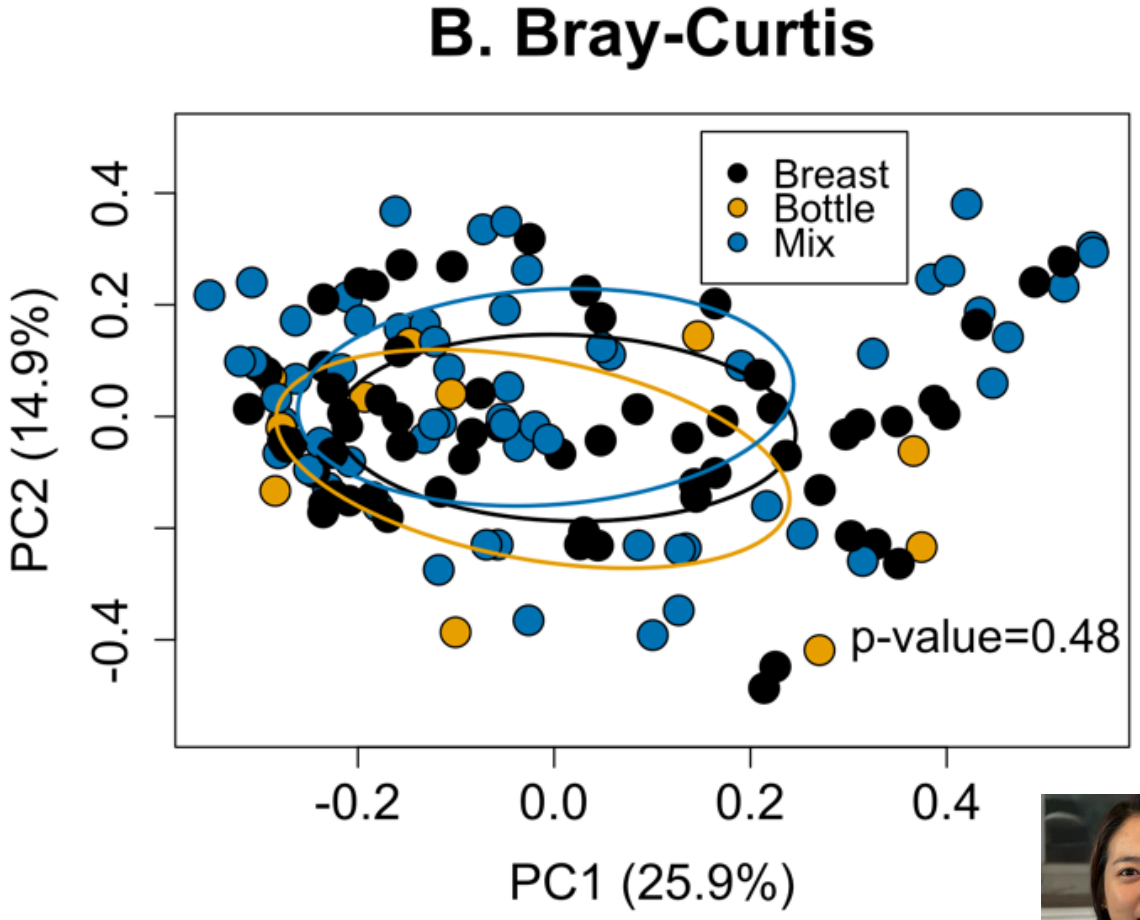
Exclusively human milk fed infants only

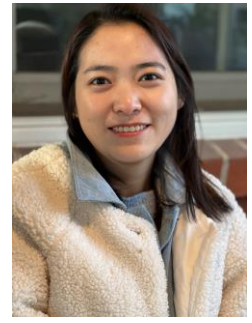


Sihan Bu

The Gut Microbiotas of Exclusively human Milk Fed 3 Month Old Infants had Distinct Gut Microbial Community Membership According to Breastfeeding Modality

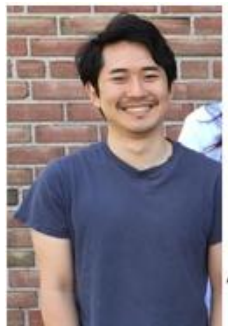






Sihan Bu

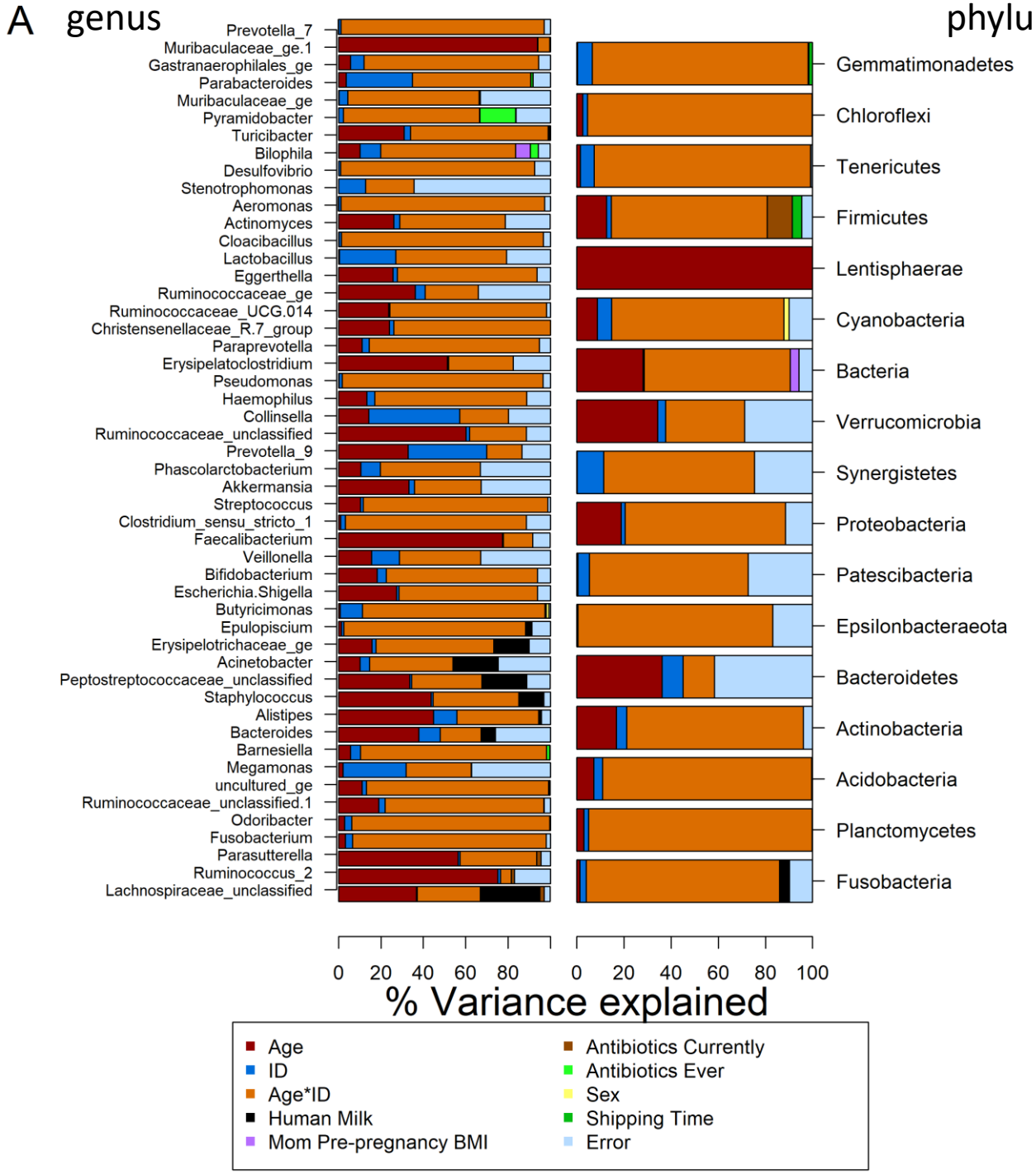
Exposures Contributing to the Longitudinal Development of the Infant Gut Microbiome



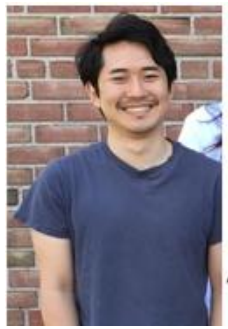
Kameron Sugino

Tengfei Ma

Sugino, Ma 2021 *Microorganisms*



Exposures Contributing to the Longitudinal Development of the Infant Gut Microbiome



Kameron Sugino

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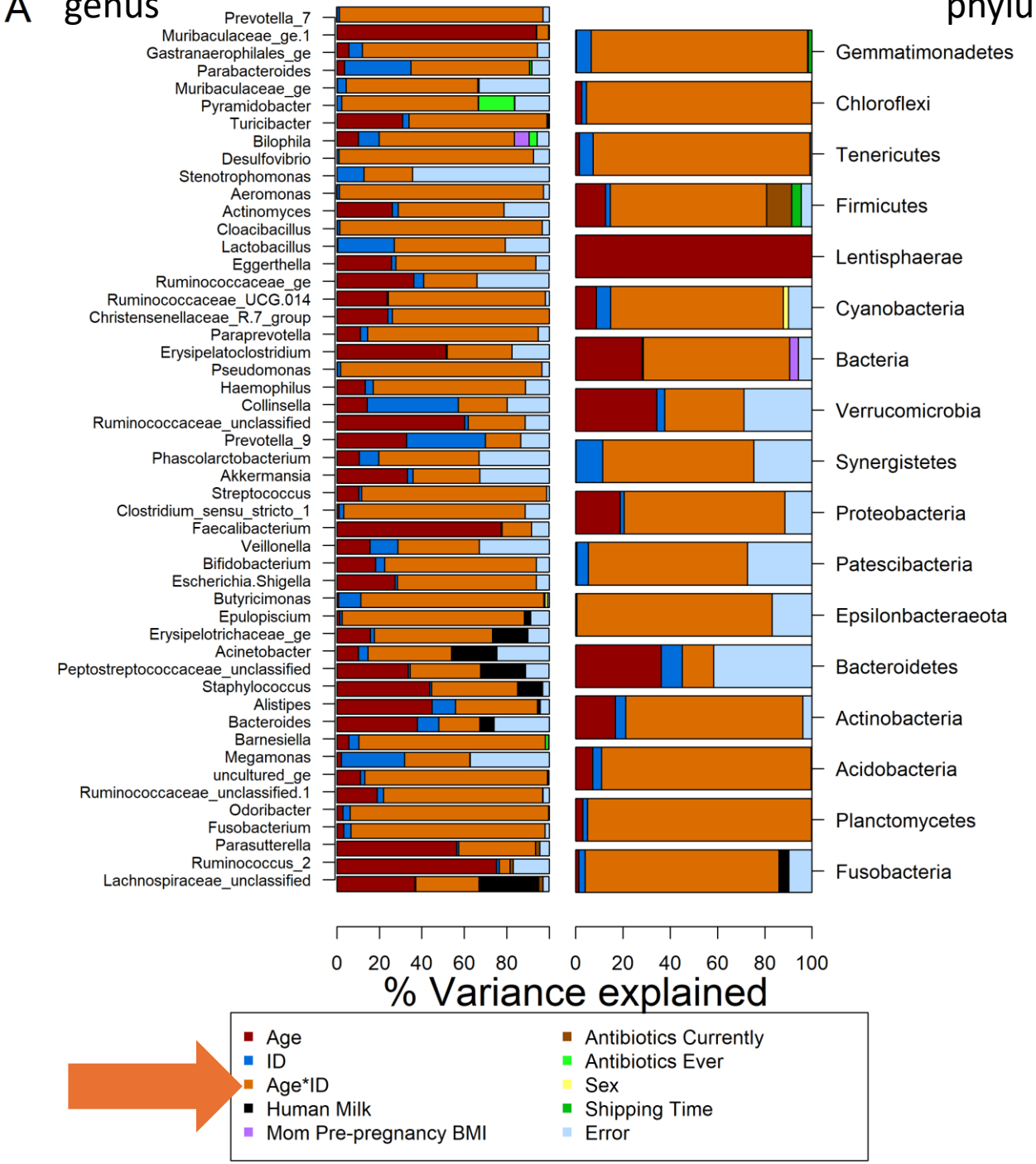

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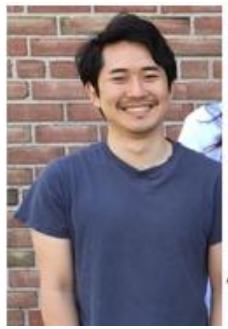

Kameron Sugino

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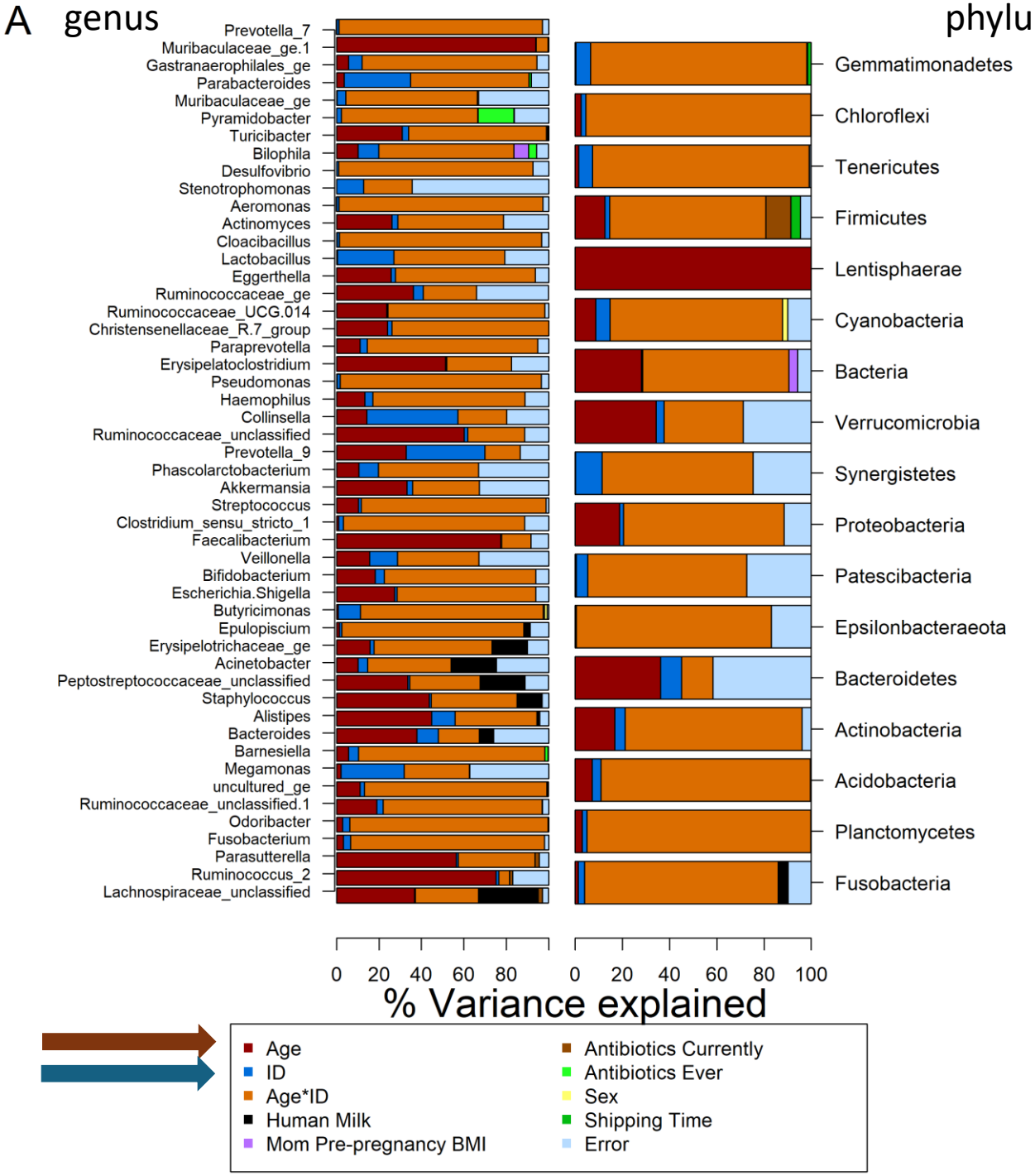
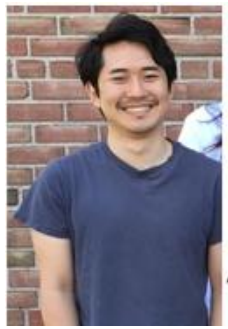


Exposures Contributing to the Longitudinal Development of the Infant Gut Microbiome



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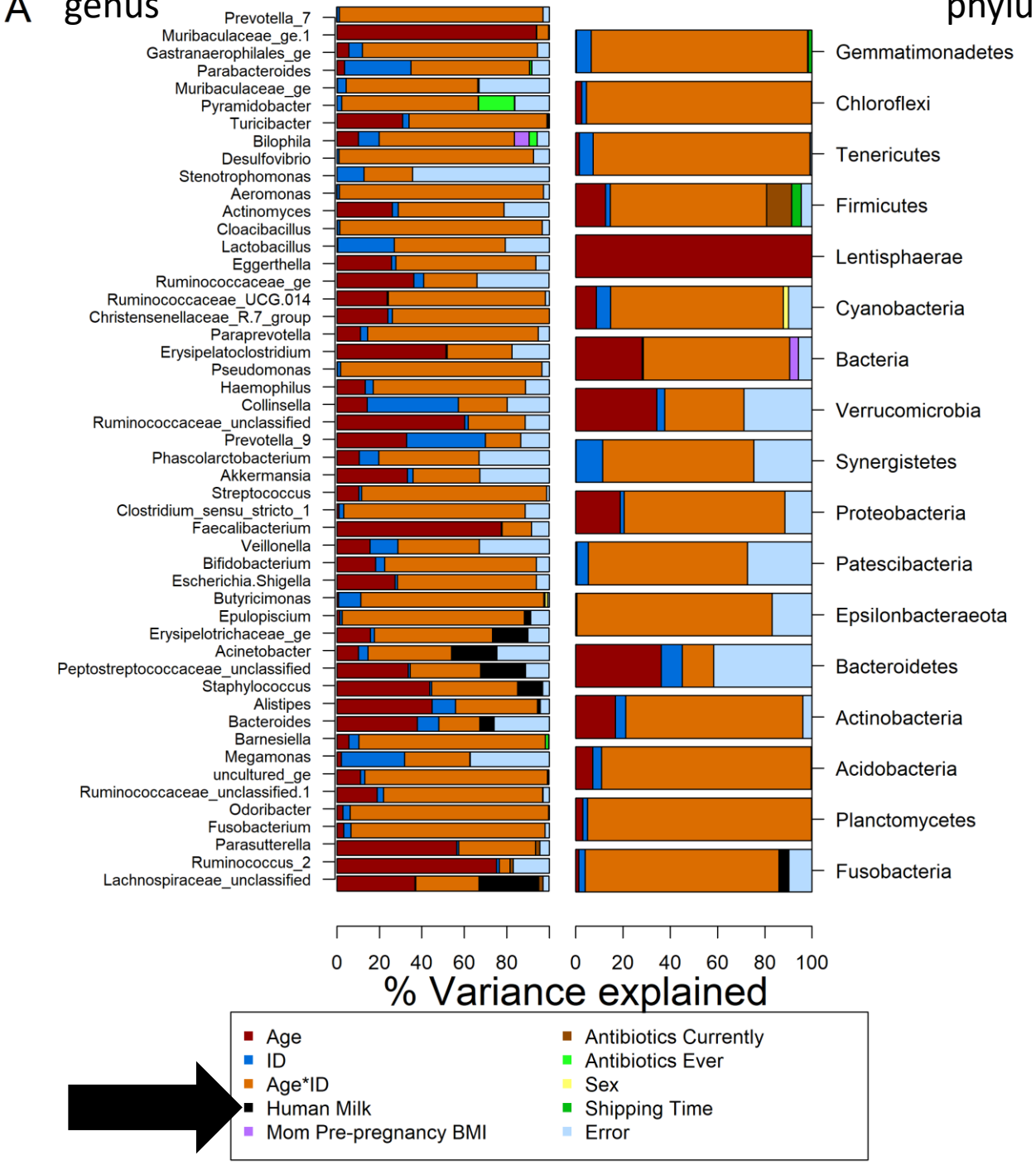
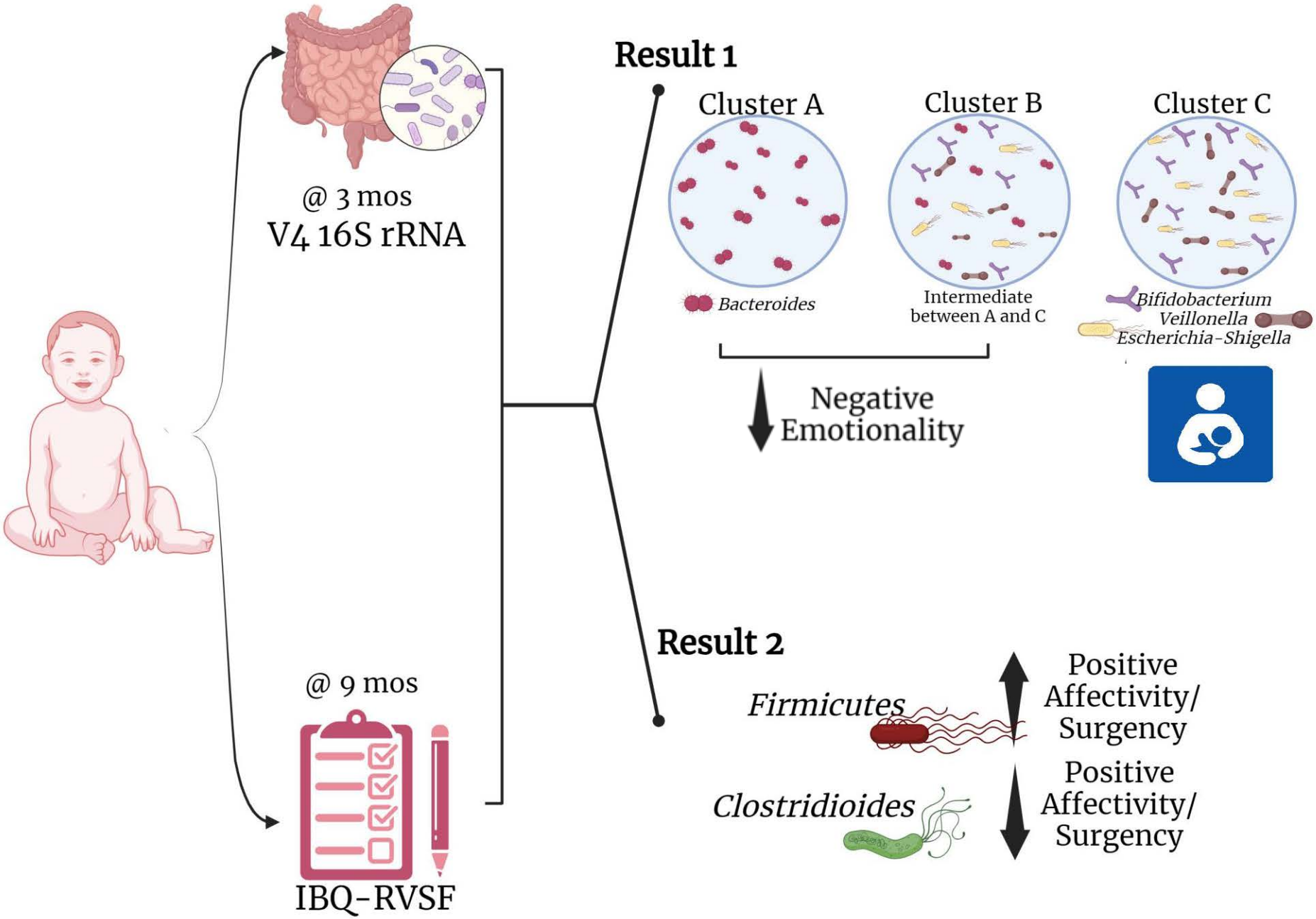




Dana Nzerem

Ma 2024
Microorganisms

Ongoing ECHO-Wide Analyses are Assessing Associations between the Various Microbiotas and these Child Health Outcomes

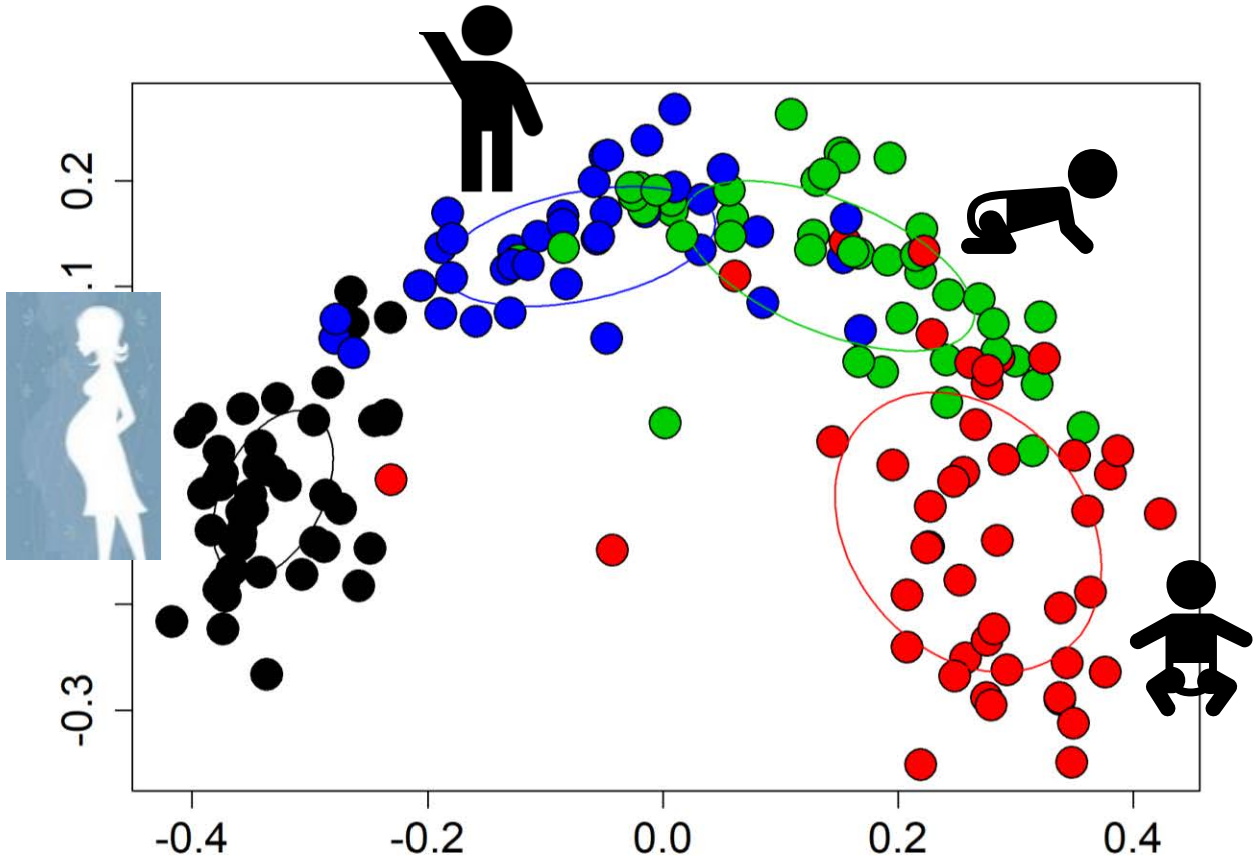
- Allergic Rhinitis
- Asthma
- Food Allergy
- Anxiety and Depression

- Child Development (ASQ)
- Child Temperament (IBQ)
- Autism-Related Behaviors
- Obesity
- Preterm Birth
- Neurodevelopment

Summary & Outlook

- Host-associated microbiomes are important modifiable factors playing key roles in human development and health
- ECHO has both extant data and extant samples that can be used to determine which exposures build host-associated microbiomes that ensure appropriate child development
- Further extant samples could also be analyzed using whole metagenome sequencing or for metabolites
- Ongoing efforts ECHO-wide should generate over a dozen manuscripts by the end of 2025

Thank You!



Comstock SS[au] - PubMed

ECHO

Environmental influences
on Child Health Outcomes

A program supported by the NIH