Early-Life Exposures, Lasting Imprints: Gut Microbiota-Metabolite Alterations Linking Prenatal Alcohol and Cannabinoids to Adult Addiction Risk

MEDICINE
TEXAS A&M HEALTH SCIENCE CENTER

Deepa Upreti, PhD

FASD 2026, April 18-21

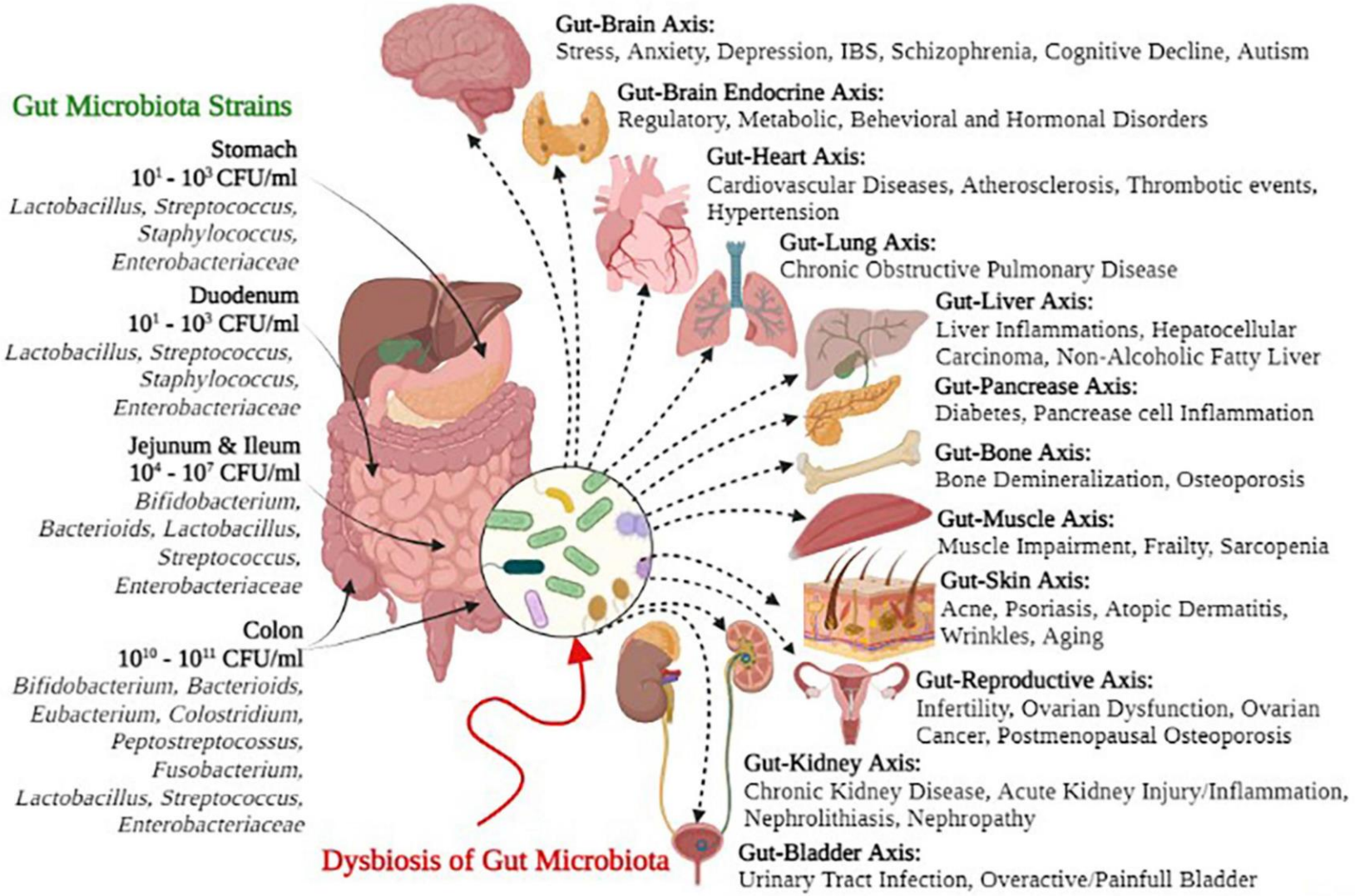
Texas A&M School of Medicine
deepa.upreti@tamu.edu

Prenatal Alcohol and Cannabinoid Exposure: Implications for Long-Term Health

- Alcohol exposure during pregnancy leads to lifelong developmental effects
- Cannabis use is increasingly co-used with alcohol (20–30% in young adults)

  (Patrick et al., 2020, Alcohol Clin Exp Res)
- Combined exposure may worsen outcomes
- Effects extend beyond the brain to gut, immune, and metabolic systems
- Long-term consequences may include increased addiction vulnerability

Gut Microbiota Drives System-Wide Health Effects



Adil et al., 2022 (Frontiers in Microbiology)

Study Questions:

1. **Does prenatal exposures alter the adult gut microbiota and metabolome?**
2. **Are these changes associated with neurobehavioral outcomes, including alcohol-seeking behavior?**

Prenatal Exposure Model and Study Design

Four Groups (16-17 mice/group)
1. Control
2. Alcohol Only (PAE)
3. Cannabinoid Only (CBD)
4. Alcohol + Cannabinoid (SAC)

G12-15 (Drug Exposure)

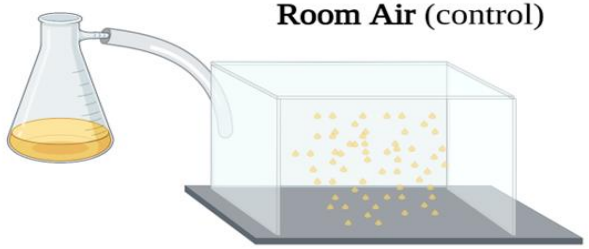
Gestational Day 0 (G0)

~G19-20 (Birth)

C57Bl/6J Pregnant Mice

I.P Injection: **CP-55940** (Cannabinoid agonist, 0.75mg/kg, in 10% DMSO/Saline) or **10% DMSO in Saline** (control)

95% Vapor Ethanol or **Room Air** (control)



30-min Inhalation period before tail-blood collection for BACs.

~P100-104 — P107-253 — P253+

Habituation & Handling

Adult Behavior Analyses

(Motor activity and alcohol-seeking behavior)

- Rotarod, Open Field Test
- Home cage Drinking
- Progressive Ratio

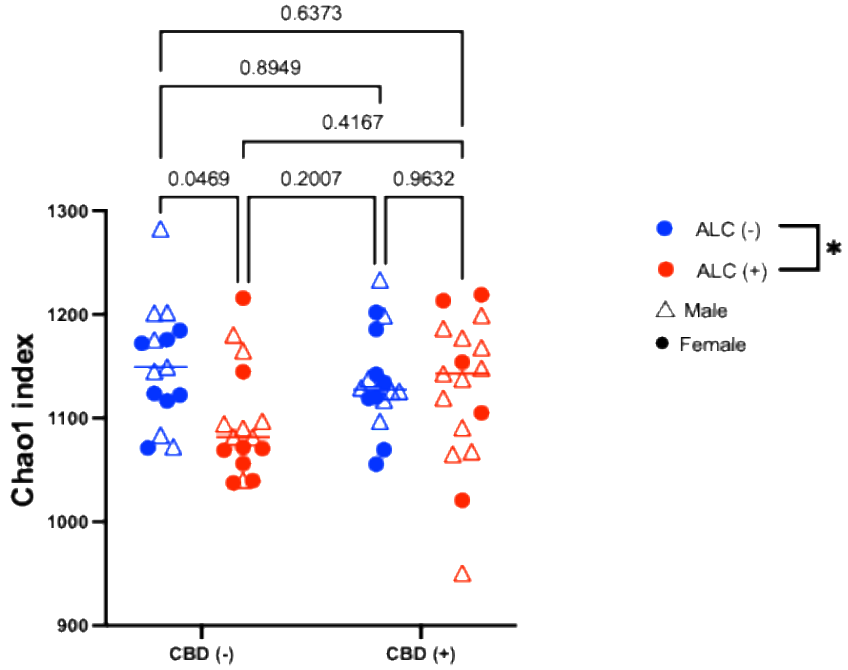
Sample Collection

- Fecal (caecum)
  - Microbiome (Shotgun sequencing)
  - Metabolite analysis (Metabolomics)
- Plasma
  - Metabolomics/LPS analysis

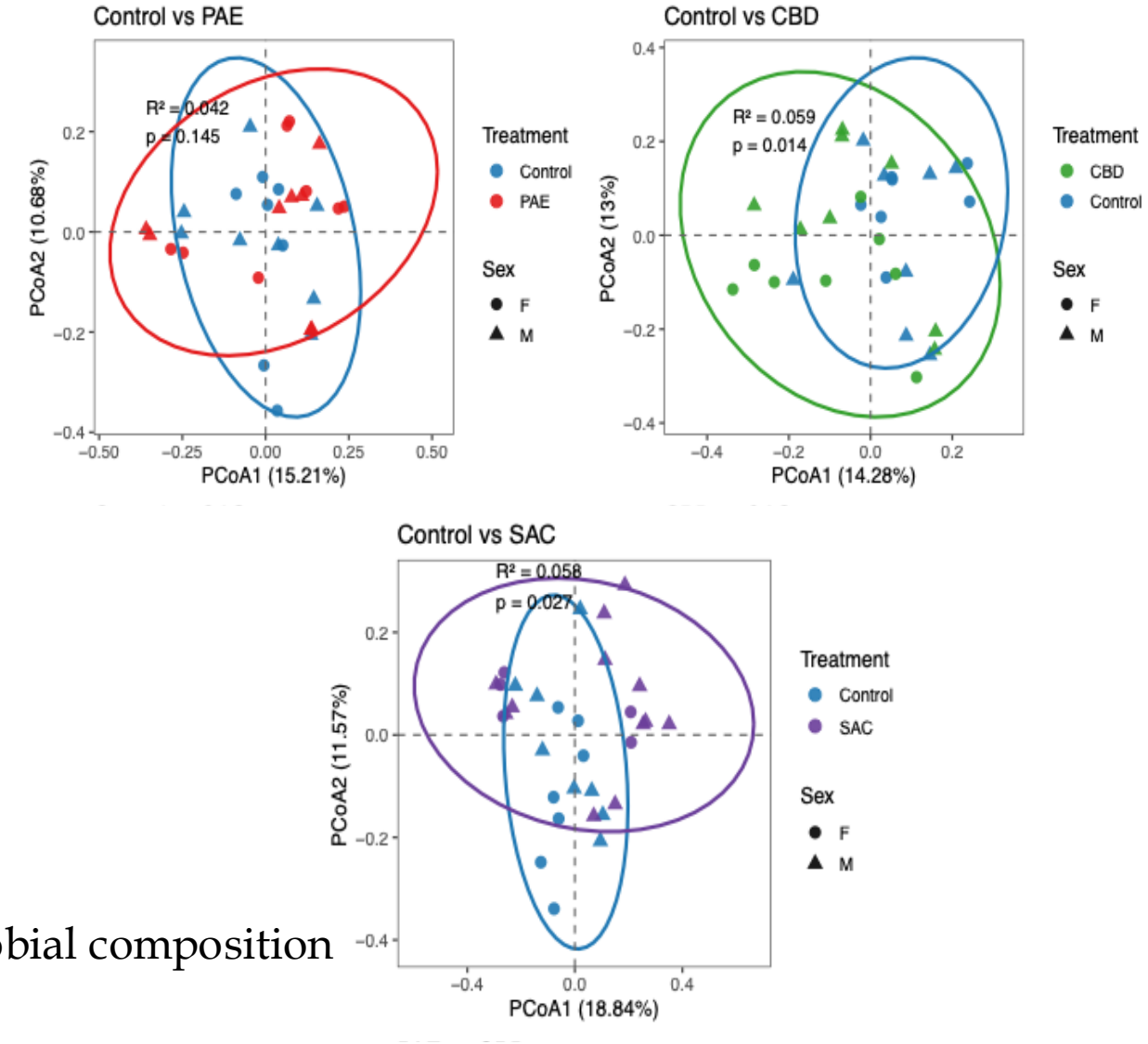
Prenatal Alcohol and Cannabinoid Exposure Alters Gut Microbiota in Adult Mice

Alpha diversity

Two-way ANOVA	Ordinary			
Alpha	0.05			
Source of Variation	% of total variation	P value	P value summary	Significant?
Interaction	3.696	0.1189	ns	No
CBD	0.4803	0.5706	ns	No
ALC	7.478	0.0281	*	Yes

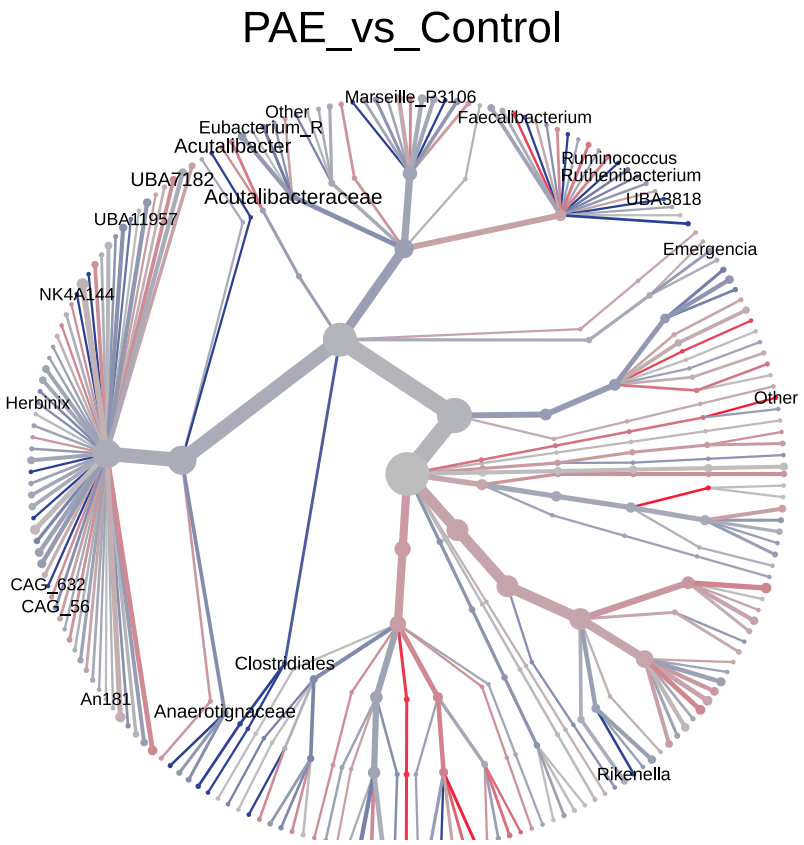


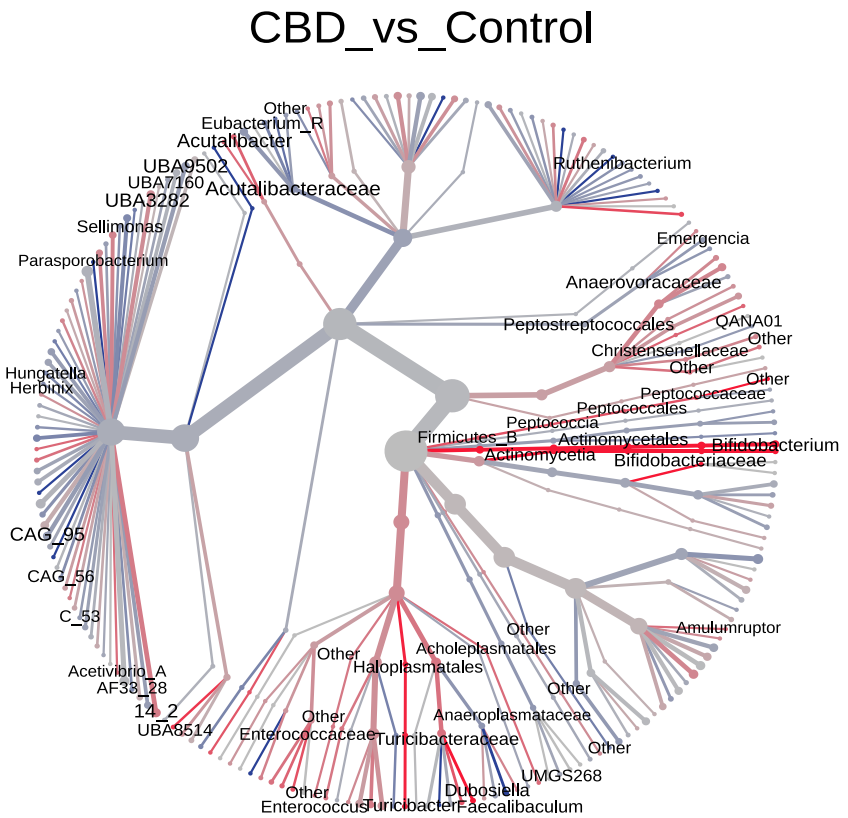
Beta diversity

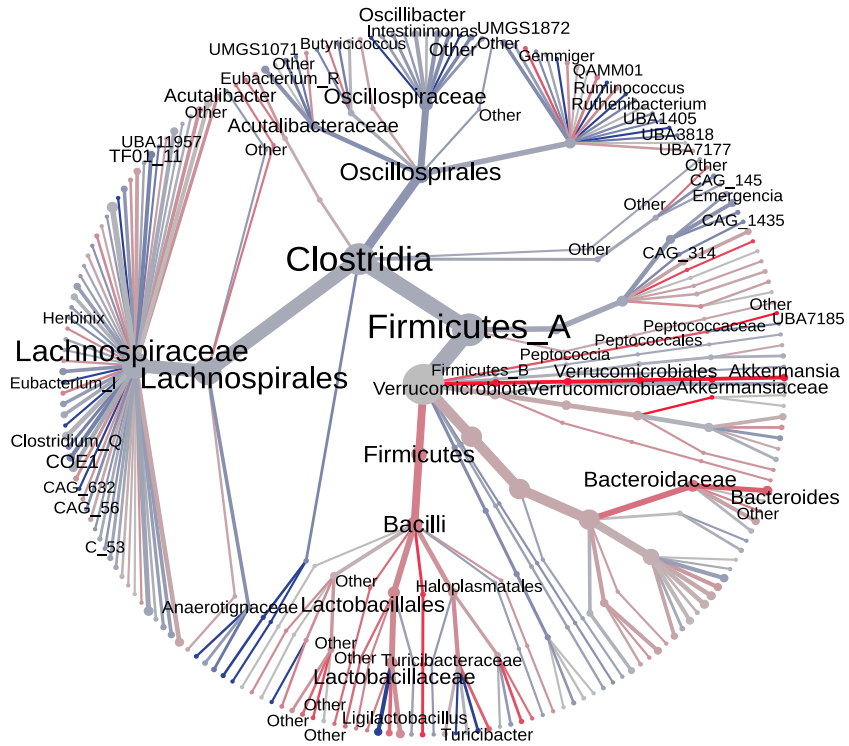


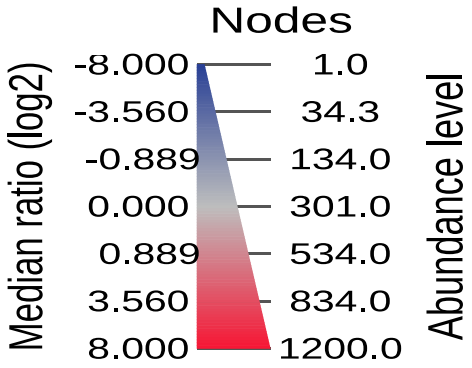
- Prenatal exposure leads to persistent shifts in microbial composition

Prenatal Exposure Alters Specific Microbial Taxa



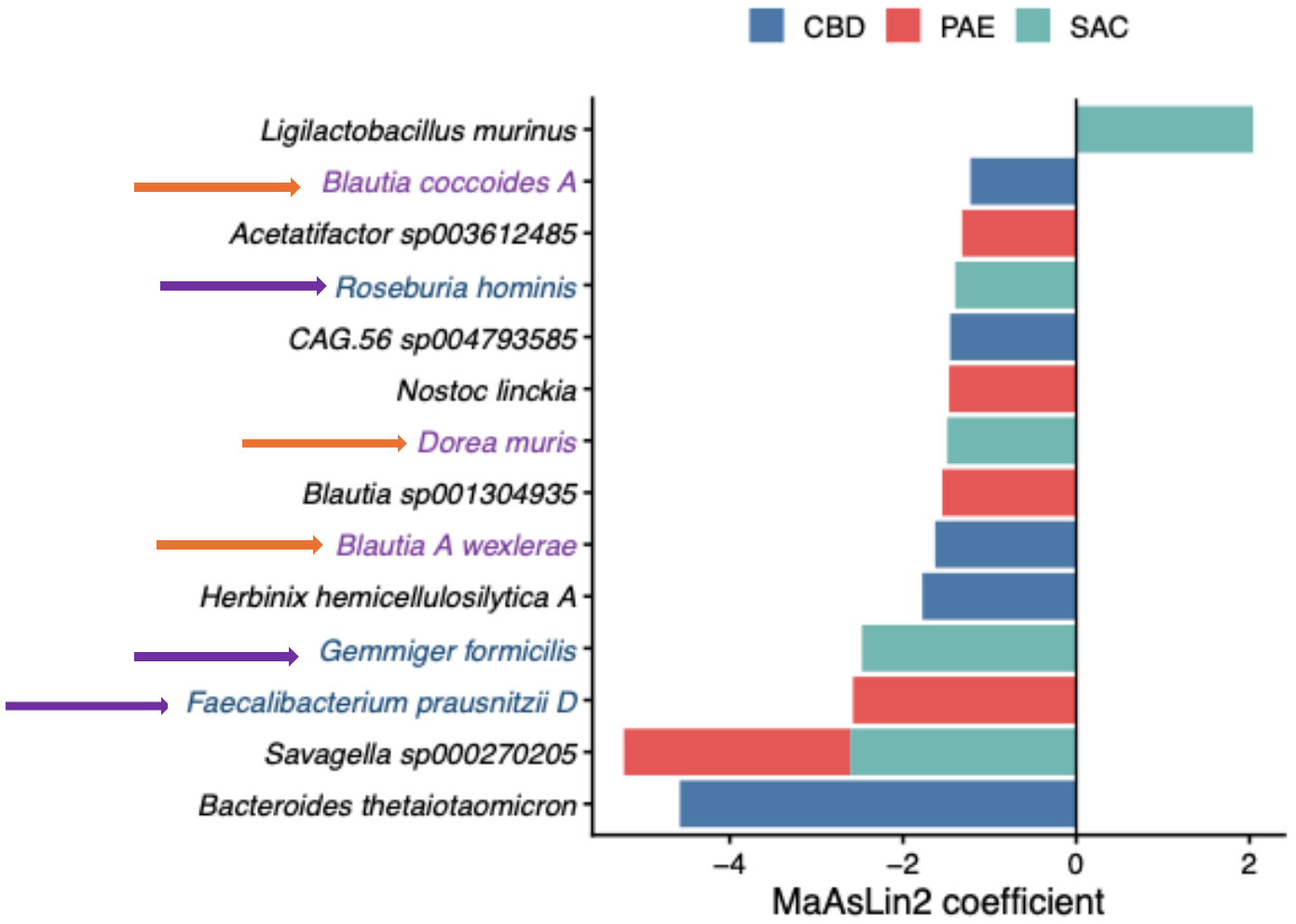






Prenatal Exposure Reduces Short Chain Fatty Acid-Producing Bacteria

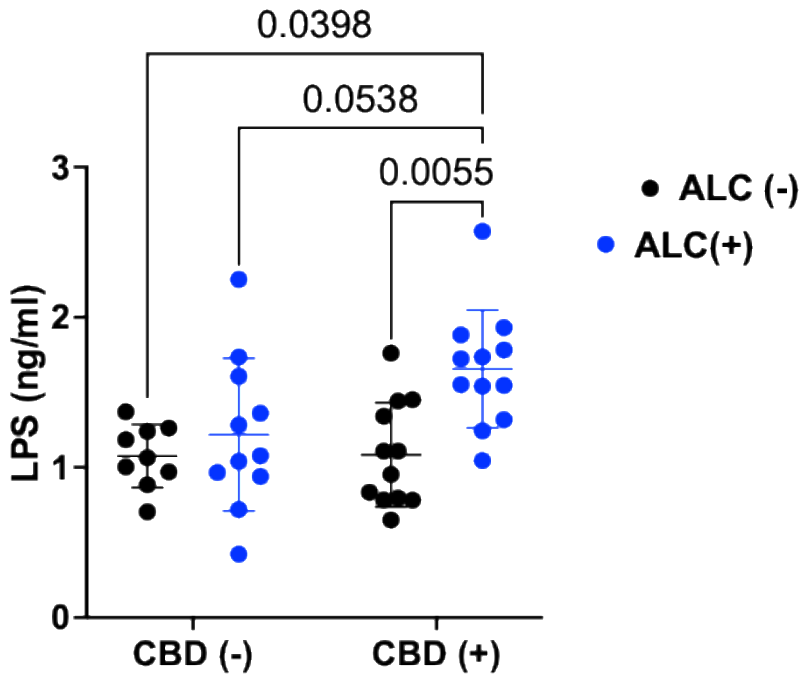
- Loss of SCFA-producing bacteria suggests impaired gut metabolic function



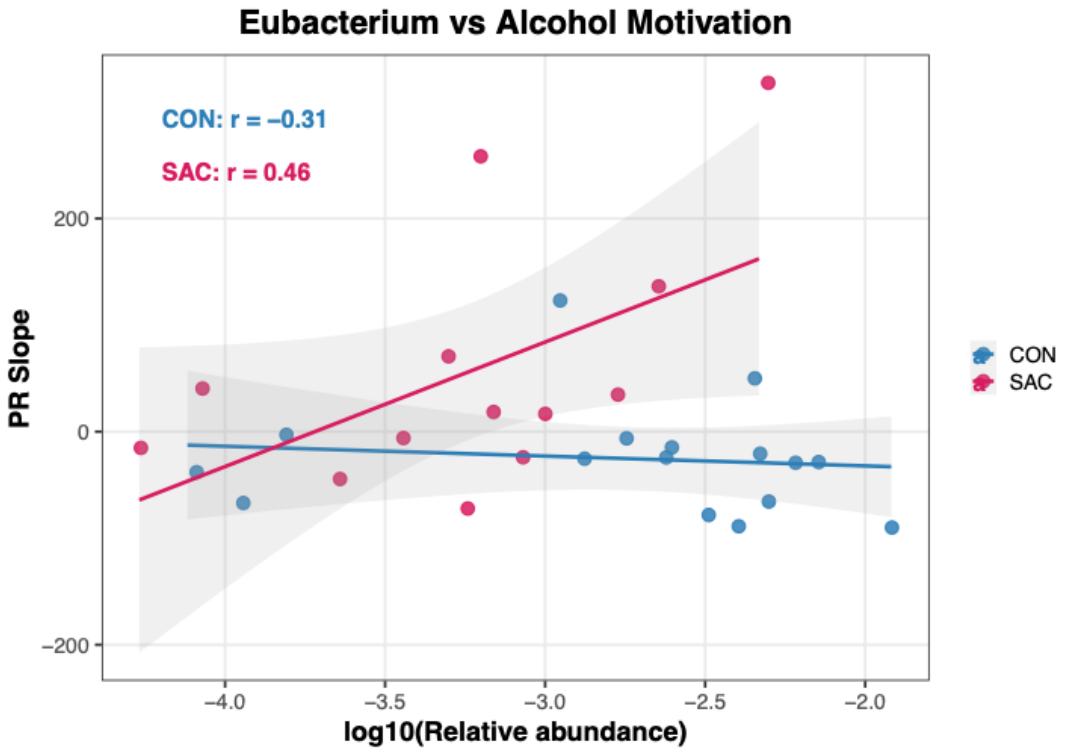
Negative = decreased abundance; Positive = increased abundance

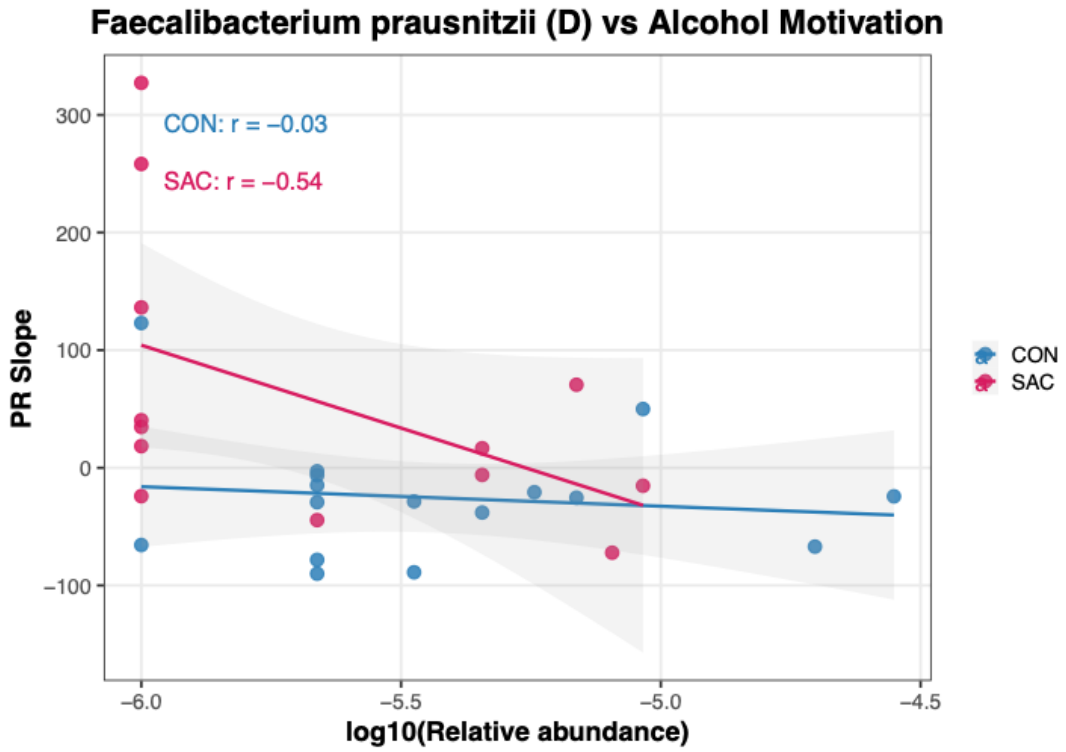
Combined Alcohol and Cannabinoids exposure disrupts gut barrier integrity

Source of Variation	% of total variation	P value	P value summary
Interaction	8.726	0.0348	*
Row Factor	3.883	0.1528	ns
Column Factor	12.14	0.0138	*



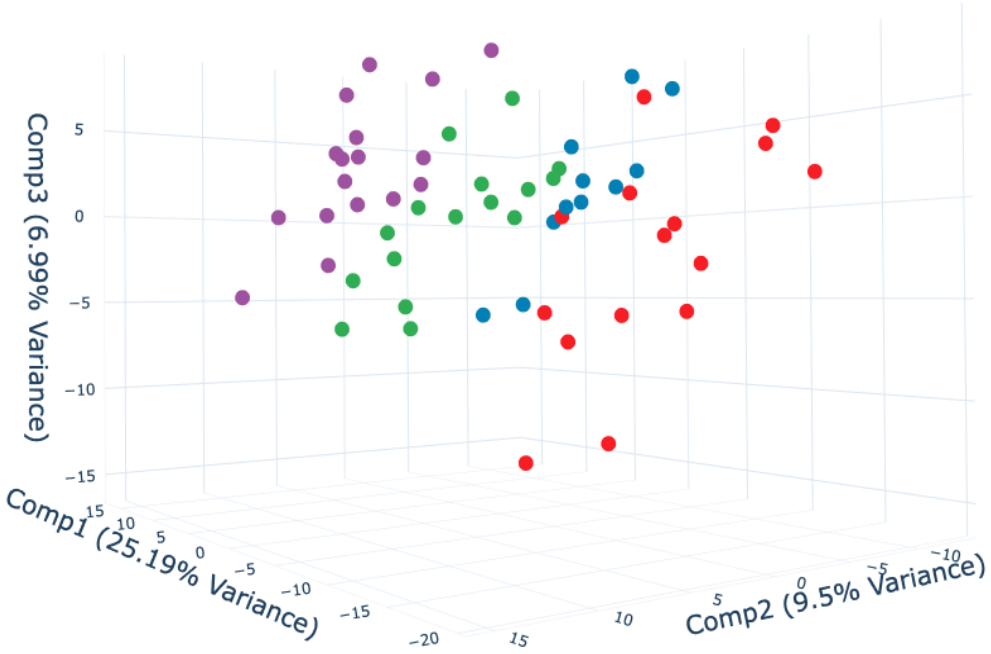
Gut Microbiota Correlates of Alcohol-Seeking Behavior in Alcohol/Cannabinoid Exposure



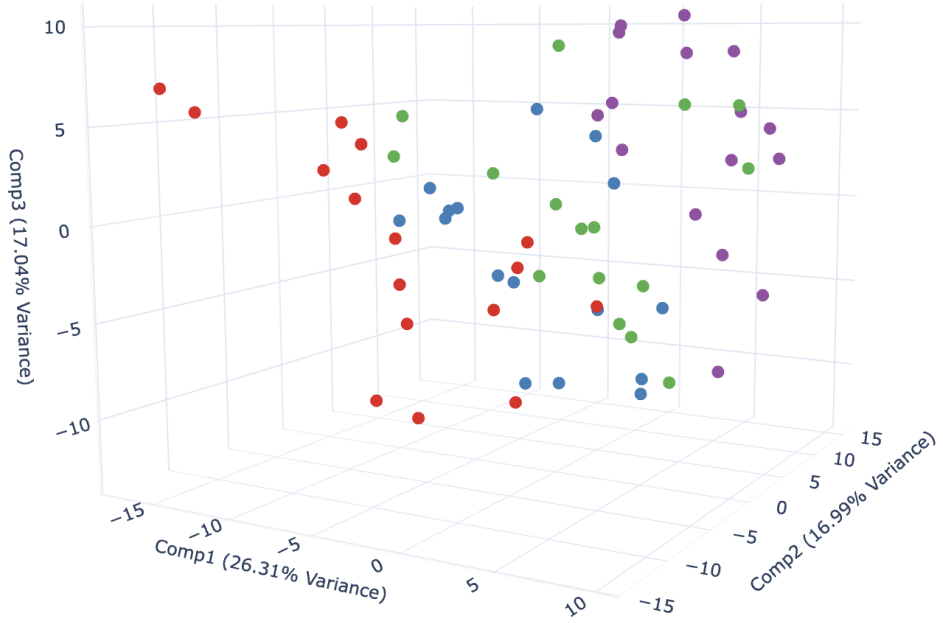


Prenatal Exposure Drives Distinct Metabolomic Signatures

Cecal Samples

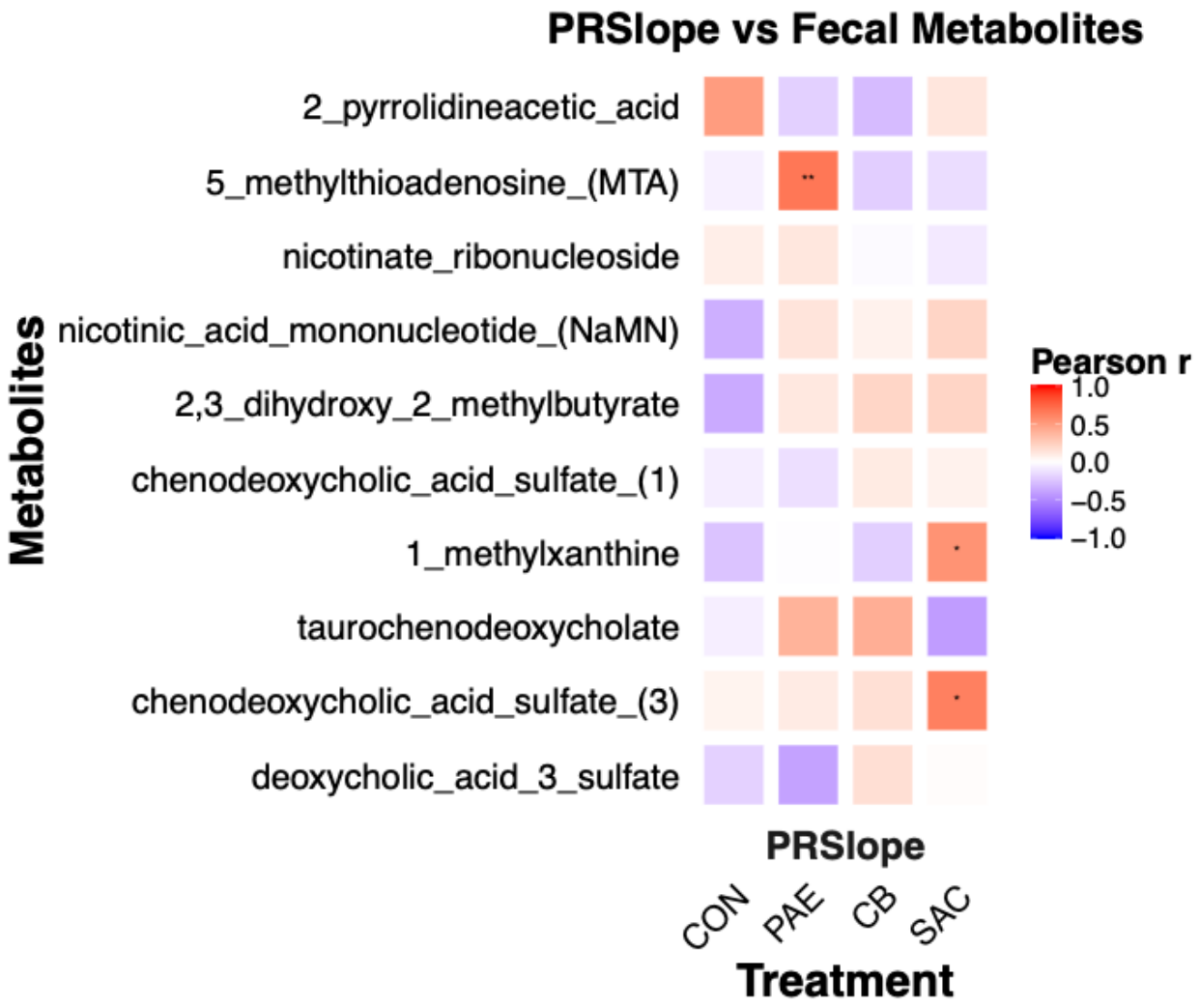


Plasma Samples

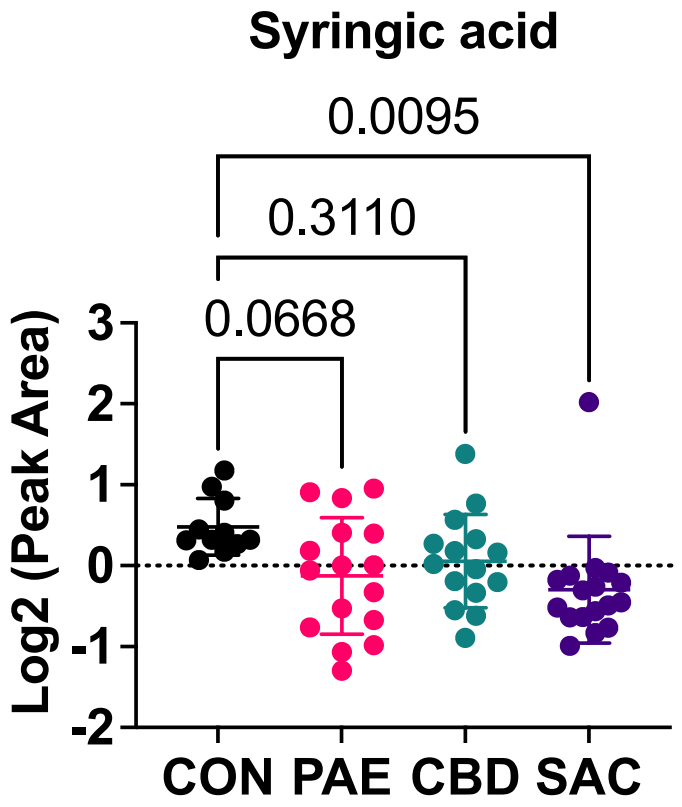


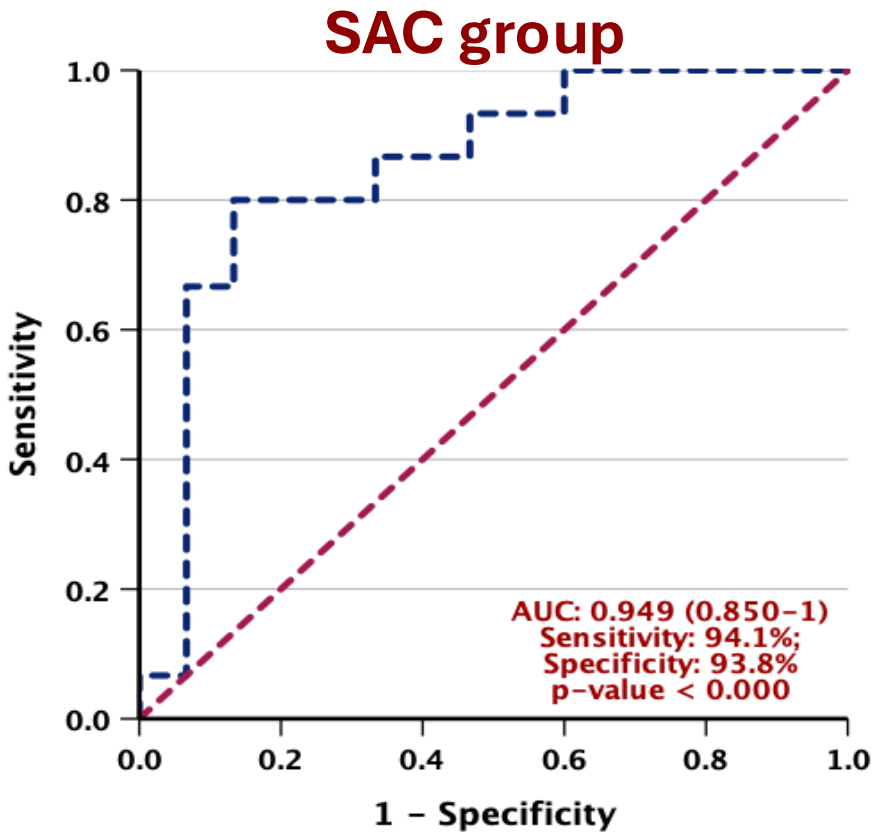
CBD CON PAE SAC

Cecal Metabolites Associate with Behavioral Outcomes Following Prenatal SAC Exposure

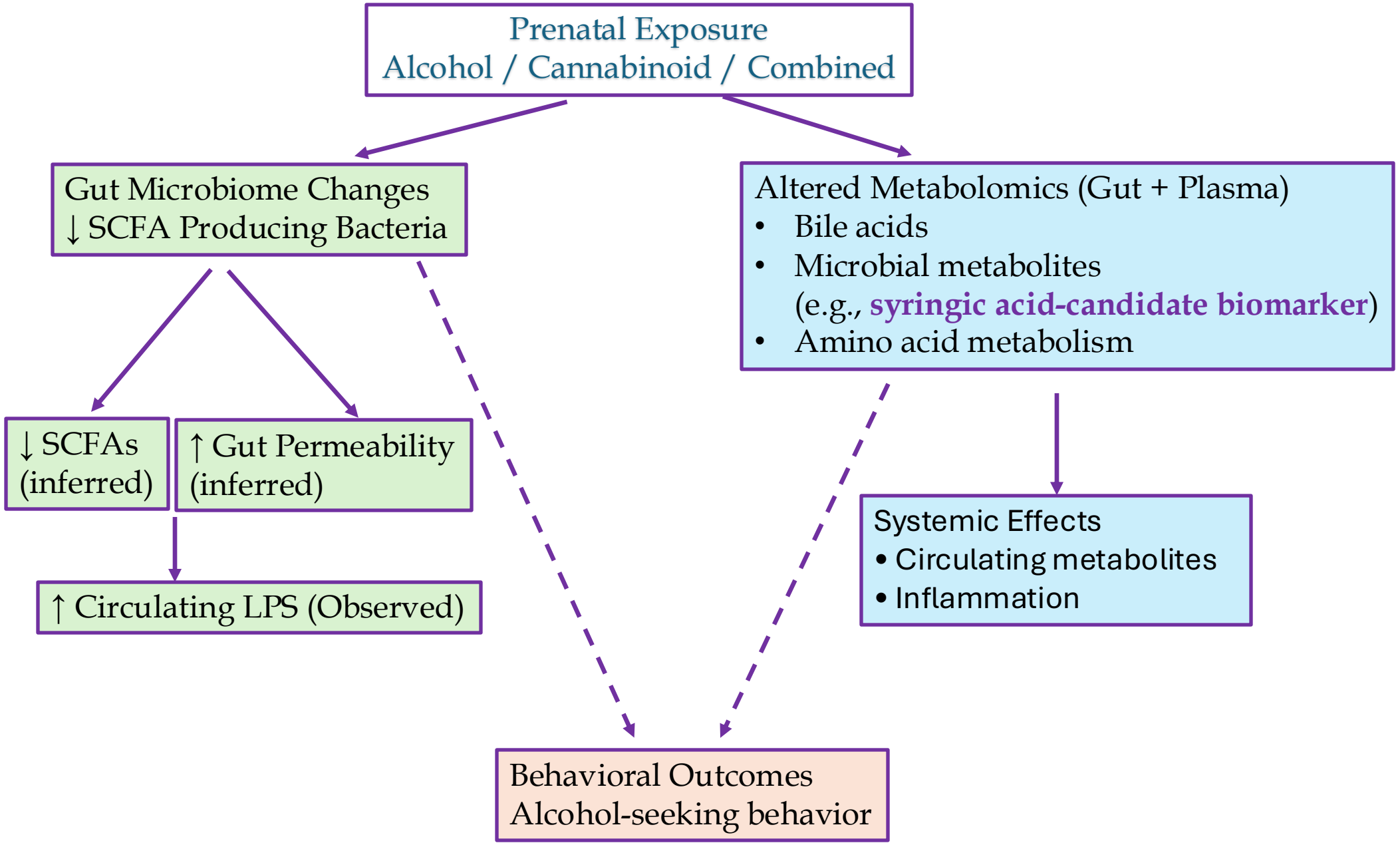


Metabolic Signatures and Candidate Biomarker for Prenatal Alcohol and Cannabinoid Exposure





Model of Prenatal Exposure Effects on Gut, Metabolism, and Behavior



Where we go from here?

- Comparison of the fecal and plasma metabolites
- Transcriptomics analysis in the liver, caecum and spleen
- Investigation of the association of microbiota, metabolites, transcriptomes, cytokines and behavioral outcomes
- Prioritizing candidates for nutritional interventions.

Acknowledgements

PI: Dr. Rajesh Miranda

-Dr. Siara Rouzer

-Rosaline Kumar

-Riley Figueroa

-Nadia Samiya

-Shamika Bhikule

-Aleena Khan

-Rodrigo Aguilar

Neuro-Gut-Immune axis (NGIA) Consortium

-Dr. Farida Sohrabji

Texas A&M Veterinary Medicine & Biomedical Sciences (Gastrointestinal Laboratory)

-Dr. Rachel Pilla

-Jonathan Turck

MEDICINE
TEXAS A&M HEALTH SCIENCE CENTER

WoodNext Foundation

NIH National Institute on Alcohol Abuse and Alcoholism

R01 AA028406

R01AA029594

Early-Life Exposures, Lasting Imprints: Gut Microbiota-Metabolite Alterations Linking Prenatal Alcohol and Cannabinoids to Adult Addiction Risk

MEDICINE
TEXAS A&M HEALTH SCIENCE CENTER

Deepa Upreti, PhD

FASD 2026, April 18-21

Texas A&M School of Medicine
deepa.upreti@tamu.edu