

# Air Pollution Exposure is Associated with the Gut Microbiome as Revealed by Shotgun Metagenomic Sequencing

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Fouladi F, Bailey MJ, Patterson WB, Sioda M, Blakely IC, Fodor AA, Jones RB, Chen Z, Kim J, Lurmann F, Martino C, Knight R, Gilliland FD, Alderete TL.  
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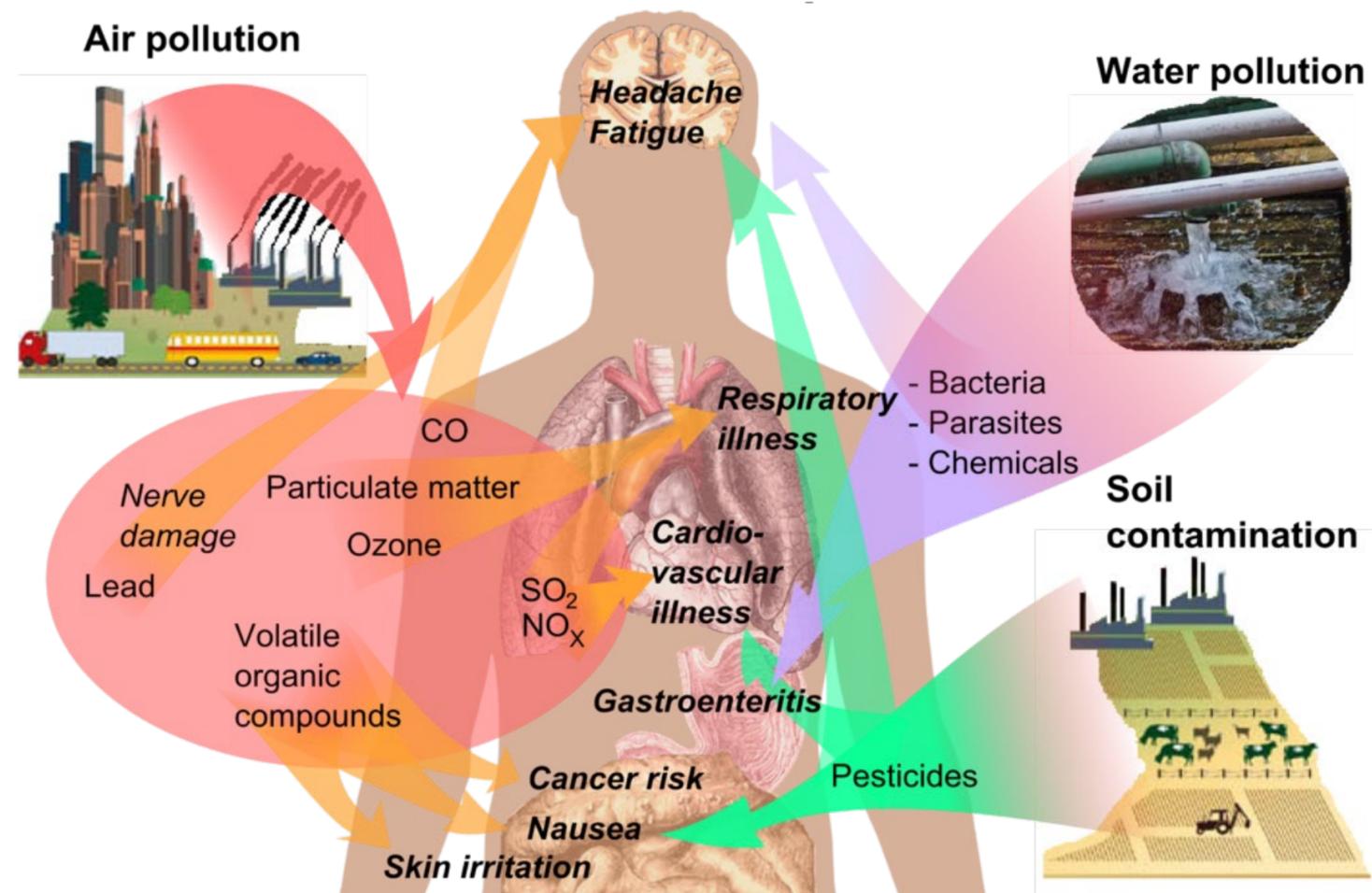


University of Colorado  
Boulder



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# Health Effects of Air Pollution



# Air Pollution Exposure is Associated With Obesity and Type 2 Diabetes

## ADULTS

- ↑Air pollution exposure ( $\text{NO}_x$ ,  $\text{NO}_2$ , and  $\text{PM}_{2.5}$ ) associated with greater risk for **obesity** and **type 2 diabetes**<sup>1-3</sup>
- ↑Annual and shorter-term exposure to  $\text{NO}_2$  and  $\text{PM}_{2.5}$  had adverse effects on **fasting glucose** and **insulin sensitivity**<sup>4</sup>

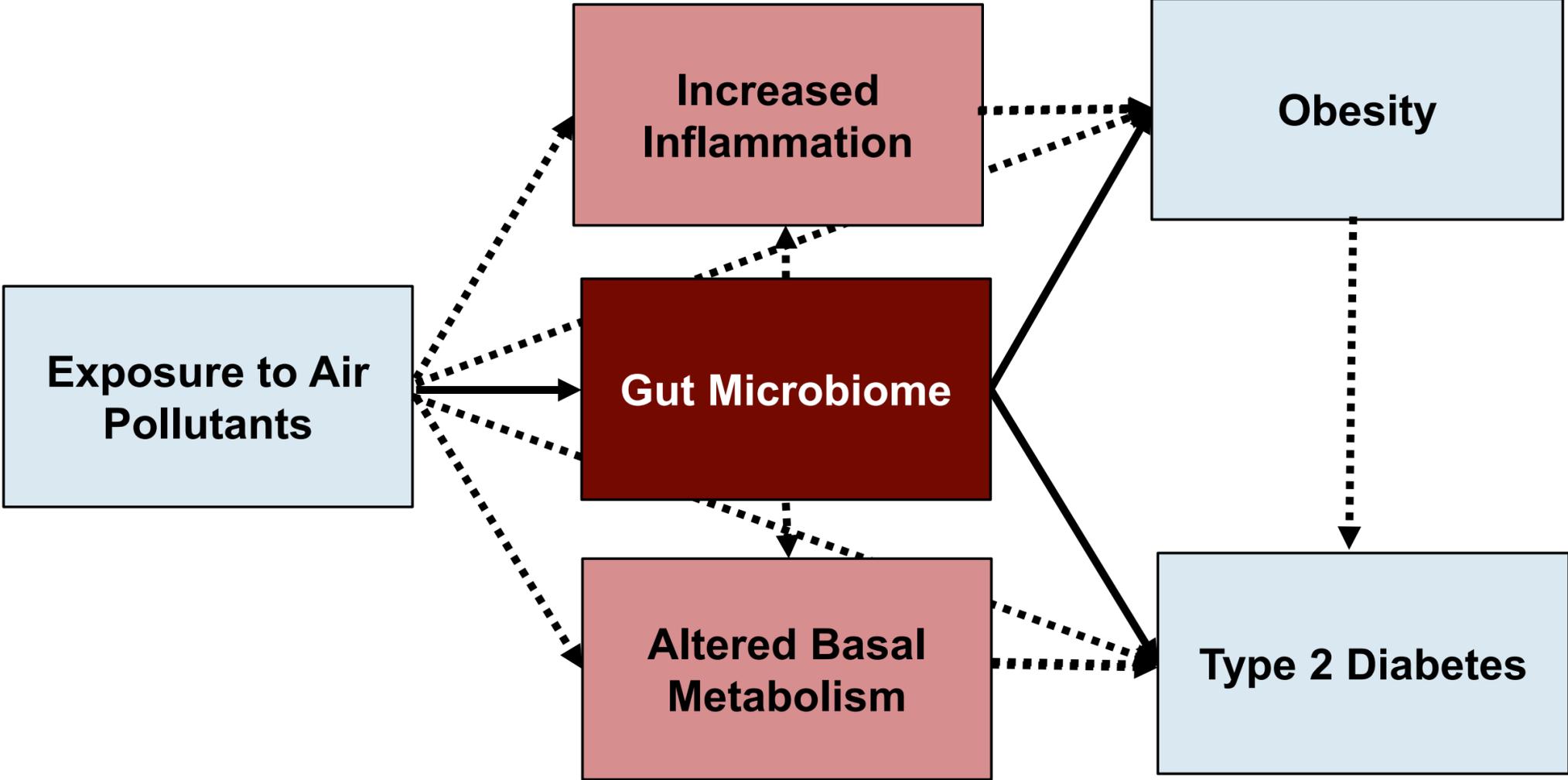
## CHILDREN

- ↑NRAP exposure associated with increased annual **BMI**<sup>5,6</sup>
- ↑ $\text{NO}_2$  and  $\text{PM}_{2.5}$  exposure associated with increased **insulin resistance** (HOMA-IR)<sup>7,8</sup>
- ↑ $\text{NO}_2$  and  $\text{PM}_{2.5}$  exposure associated with declined **insulin sensitivity** and  **$\beta$ -cell function**<sup>9</sup>

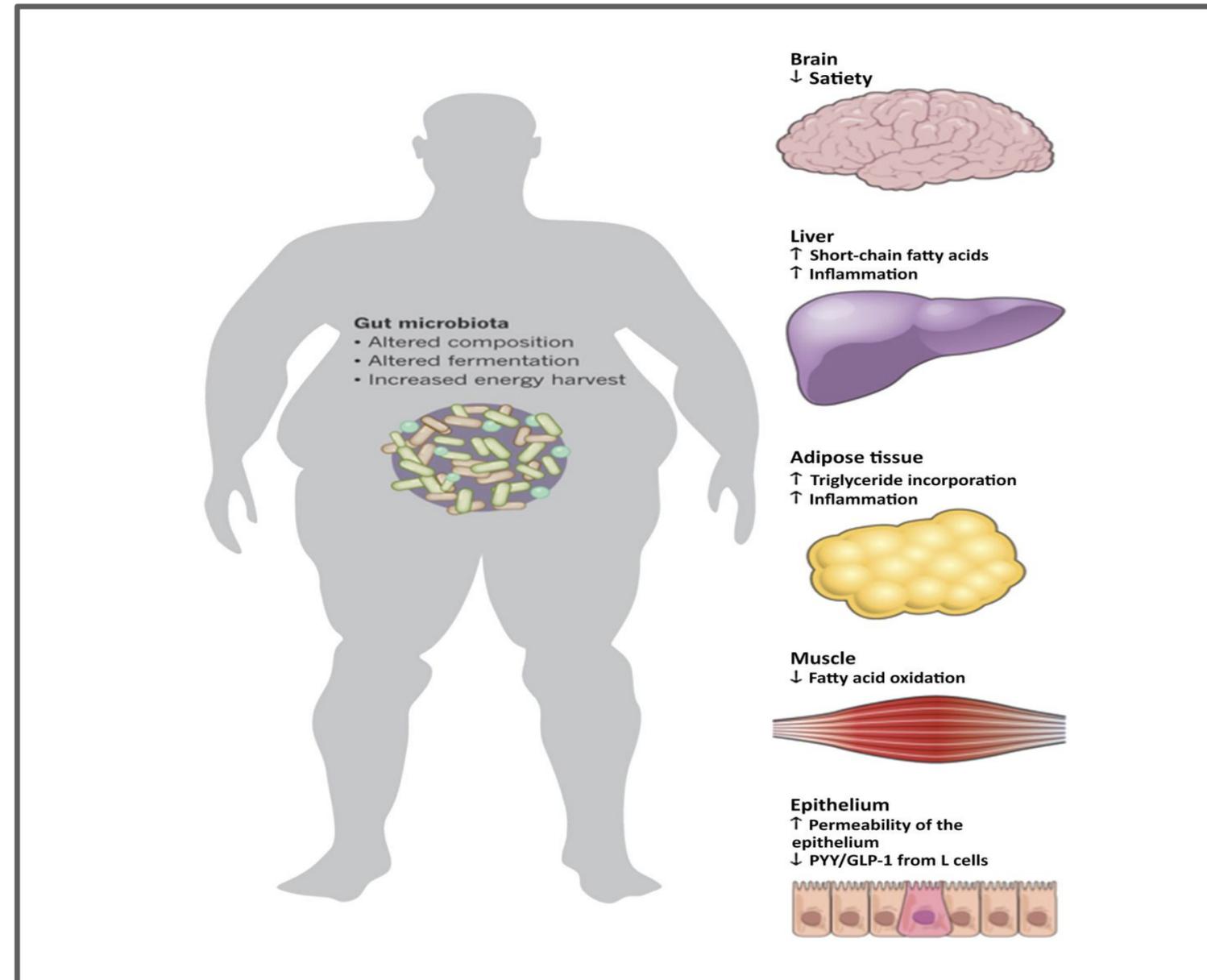
<sup>1</sup>Chen et al., 2013; <sup>2</sup>Weinmayr et al., 2015; <sup>3</sup>Li et al., 2016; <sup>4</sup>Chen et al., 2016;

<sup>5</sup>Jerrett et al., 2014; <sup>6</sup>McConnell et al., 2014; <sup>7</sup>Kelishadi et al., 2009; <sup>8</sup>Thiering et al., 2013 and 2016; <sup>9</sup>Alderete et al., 2017

# Overarching Hypothesis: Air Pollution Contributes to Obesity/Type 2 Diabetes via the Gut Microbiome

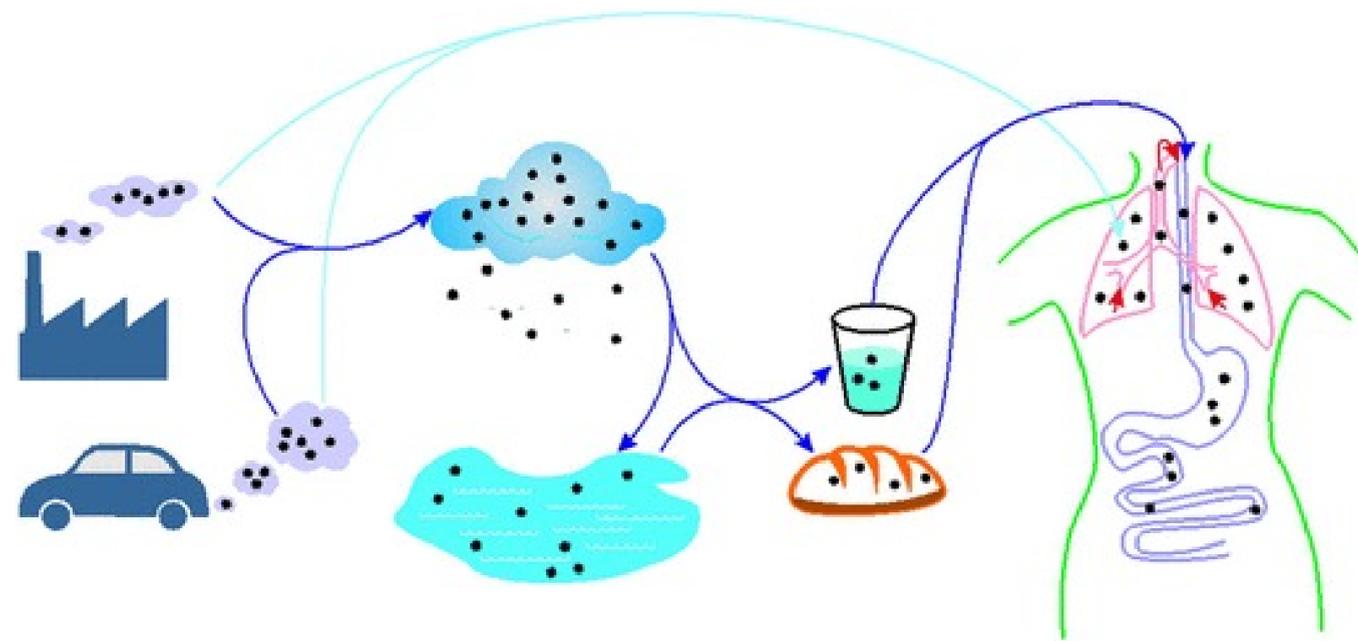


# The Gut Microbiome and Obesity



# Exposure to Air Pollutants and the Gut Microbiome

- **Inhalation and diffusion** from lungs, absorbed into systemic circulation and delivered to gut via the blood stream
- **Cleared** from the airways by cilia and then ingested
- **Ingestion** of contaminated food/water



# Does Air Pollution Exposure Alter the Gut Microbiome (Composition/Function) in Young Adults?

- Exposure data in overweight and obese young adults
- Detailed assessment of the gut microbiome using WGS

**Hypothesis:** Higher exposure to air pollutants would be associated with:

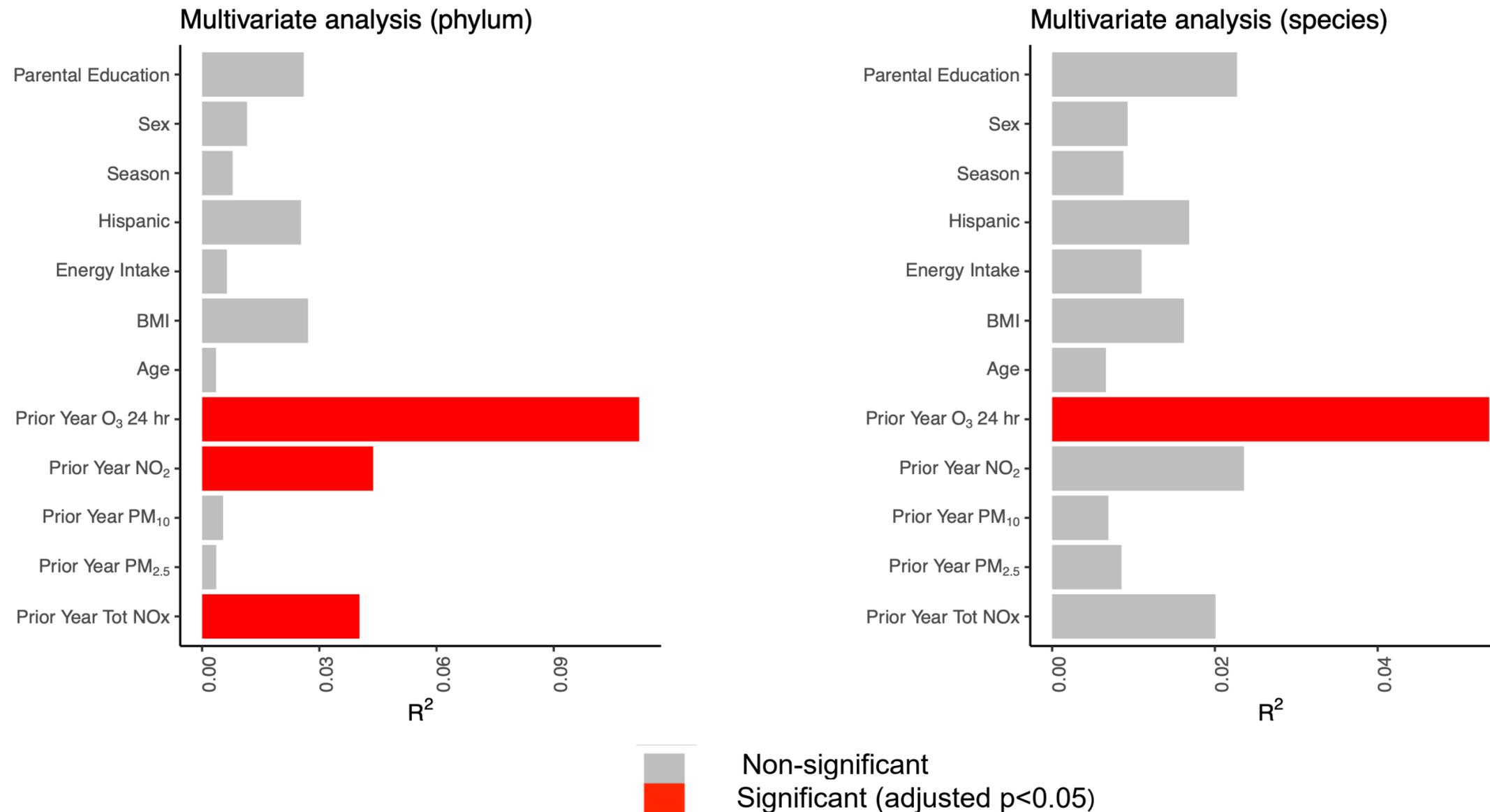
- 1) Specific gut bacteria (species)
- 2) Gut bacteria function (genes/pathways)



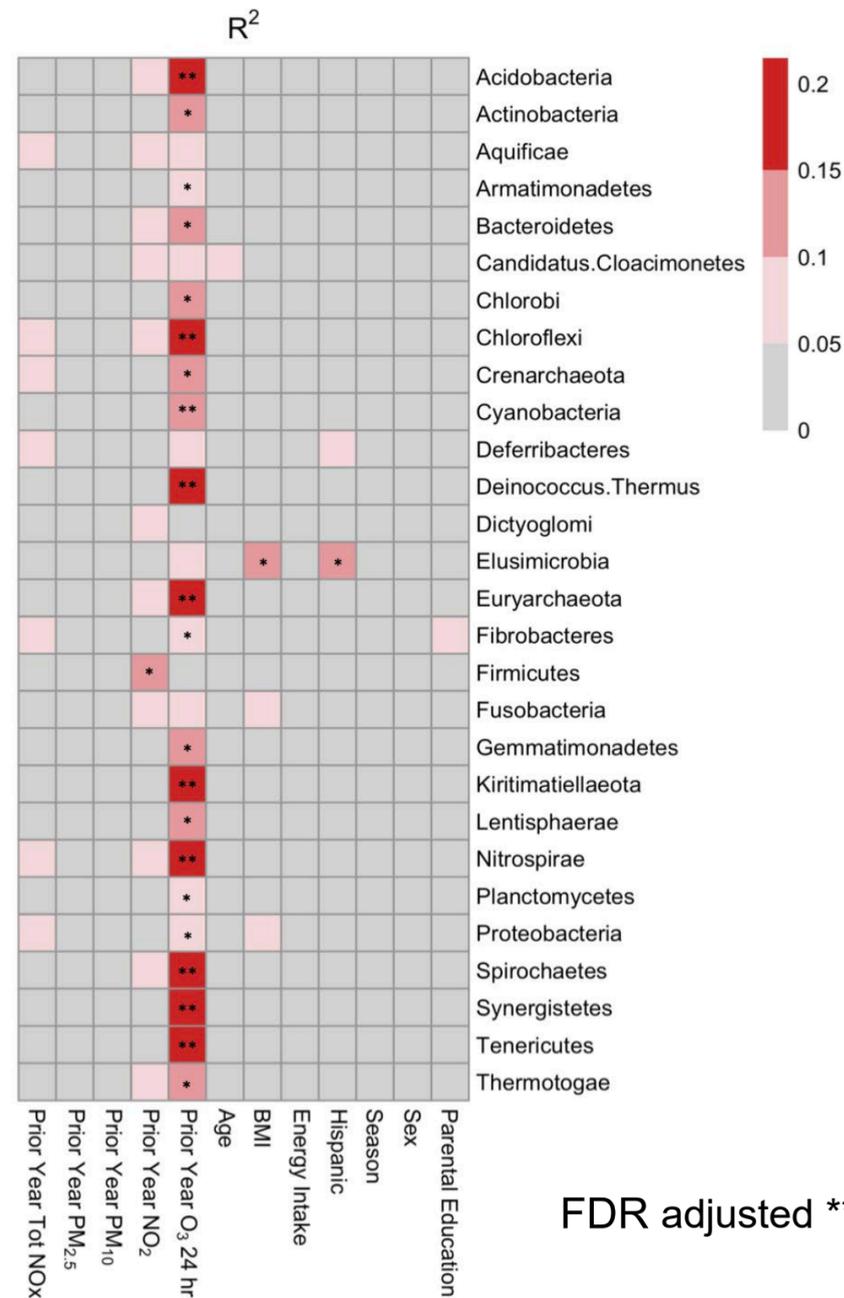
# Cross-Sectional Study

- **Inclusion criteria at study entry**
  - Young adults from Southern California (2014-2017)
  - 17-21 years of age (n=101)
- **Exposure assessments (Sonoma Technologies, Inc.)**
  - **Individual residential ambient air pollution**
    - Air quality stations (AQS) using inverse-distance squared weighting
  - **Individual residential near roadway air pollution (NO<sub>x</sub>)**
    - California-line dispersion model (CALINE4)
- **The gut microbiome**
  - Whole genome sequencing
  - Multivariate and univariate linear models

# Exposure to Air Pollutants was Associated with the Gut Microbiota and Phylum and Species Level Using WGS



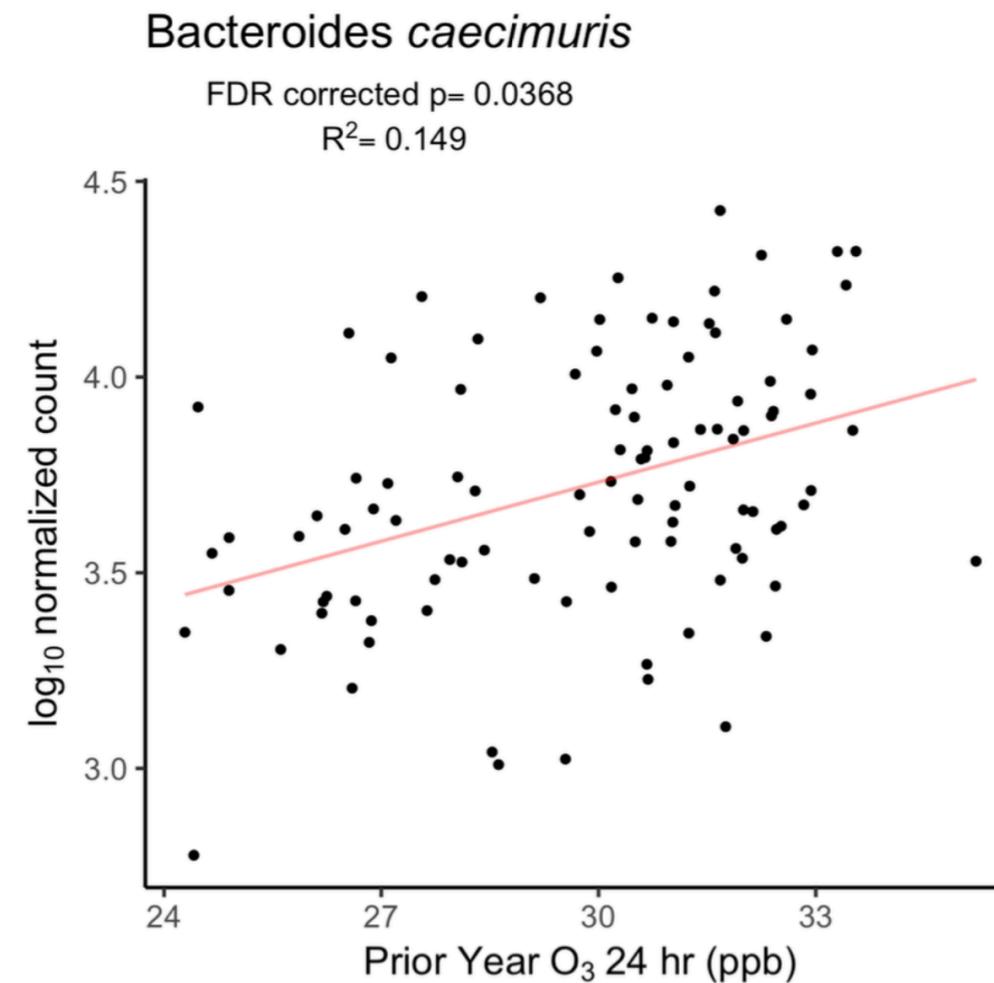
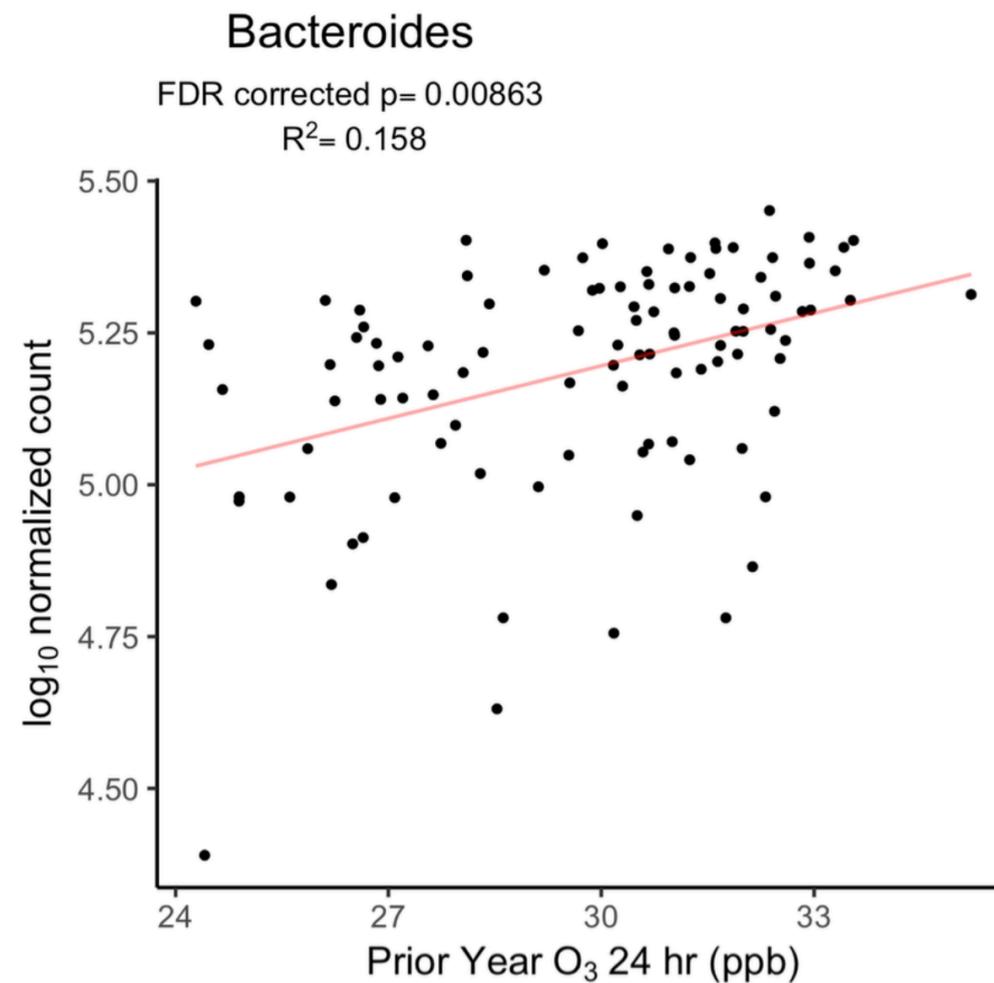
# Ozone was Associated with the Relative Abundance of Gut Bacteria (Phylum Level) using WGS



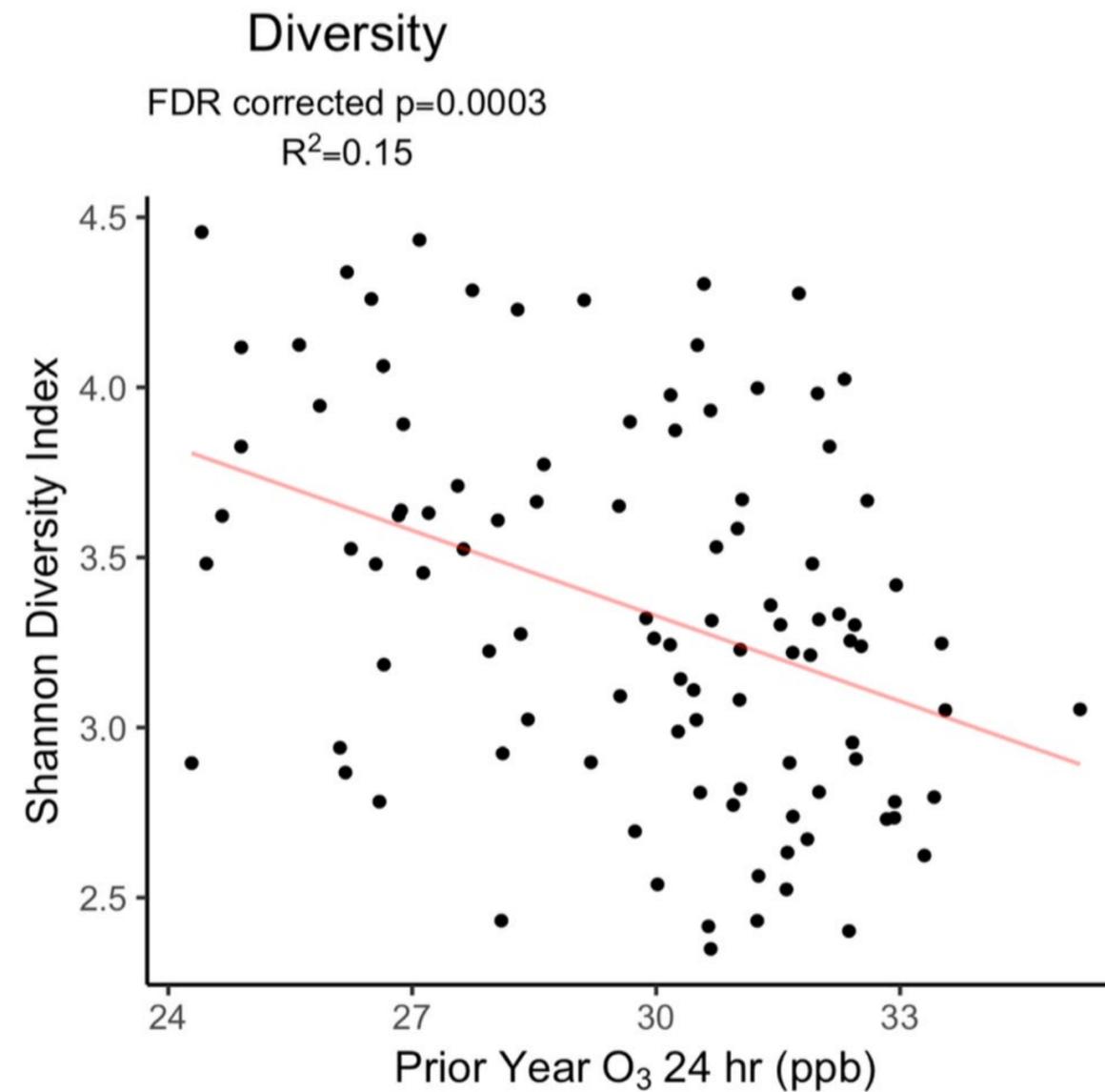
*Associations also seen at species level...*

FDR adjusted \*\* $p < 0.01$  and \* $p < 0.05$

# Exposure to O<sub>3</sub> was Positively Associated with the Relative Abundance of Taxa Belonging to the Bacteroides Genus using WGS

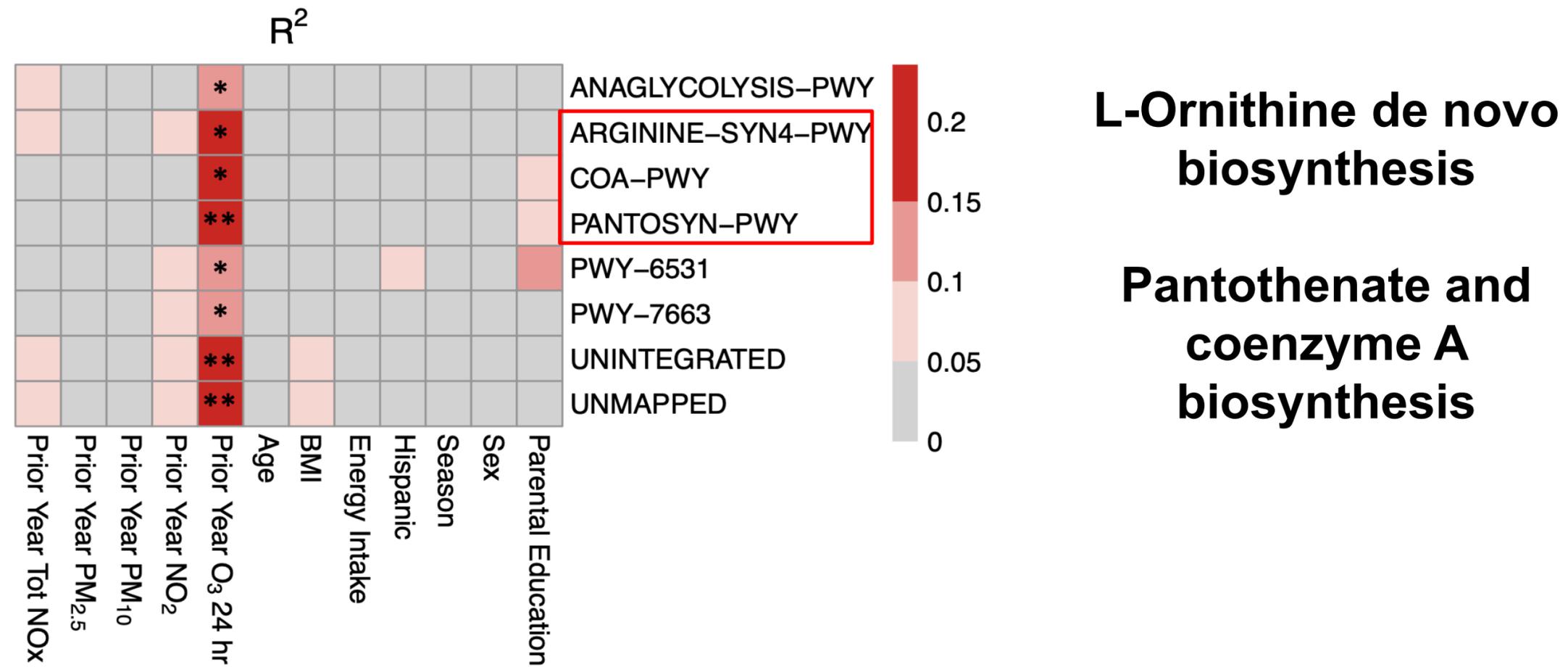


# Exposure to O<sub>3</sub> was Negatively Associated with Gut Bacterial Diversity using WGS



*# of bacteria and how abundant*

# Exposure to O<sub>3</sub> was Significantly Associated with Multiple Gene Pathways Using WGS

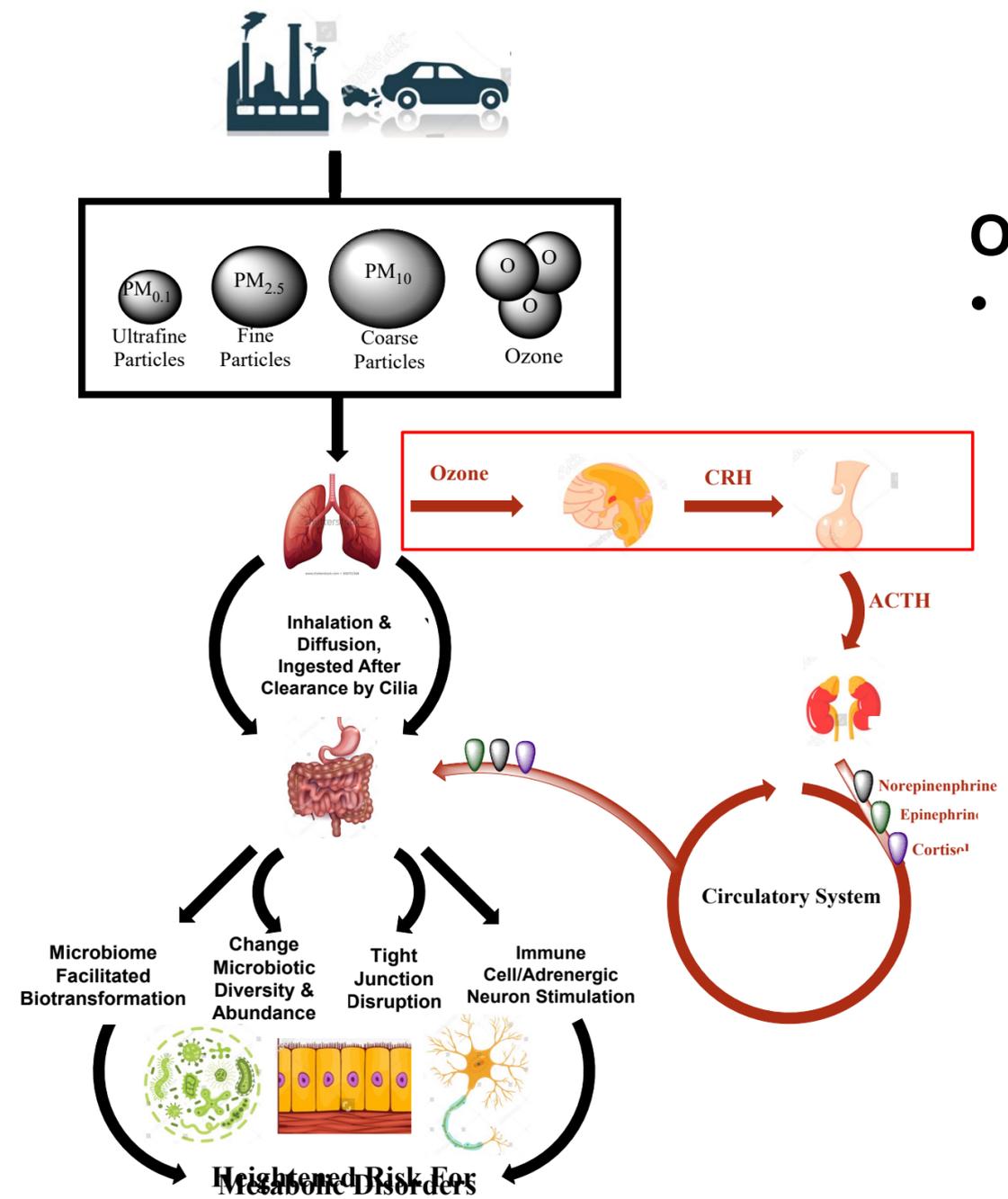


# Gene Pathways Associated with O<sub>3</sub> have the Potential to Impact the Gut Permeability

- **L-ornithine de novo biosynthesis:**
  - **Polyamines:** necessary for cell growth<sup>1,2</sup>
  - **Nitric Acid:** antiproliferative properties (cytotoxicity)<sup>3</sup>
- **Pantothenate (Vit. B) and coenzyme A (CoA) biosynthesis:**
  - **Pantothenate and CoA biosynthesis:** role in fatty acid synthesis/degradation<sup>4</sup>
  - **CoA Derivatives:** inhibit insulin release,<sup>5,6</sup> elevated in T2D / obesity<sup>7</sup>

<sup>1</sup>Selamnia et al., 1998; <sup>2</sup>Hölttä et al., 1993; <sup>3</sup>Kumar et al., 2015; <sup>4</sup>Leonardi et al., 2007; <sup>5</sup>Davaapil et al., 2014; <sup>6</sup>Webster et al., 2008; <sup>7</sup>Bandyopadhyay et al., 2006

# Exposure to Air Pollutants may Alter the Composition of the Gut Microbiome and Gut Permeability



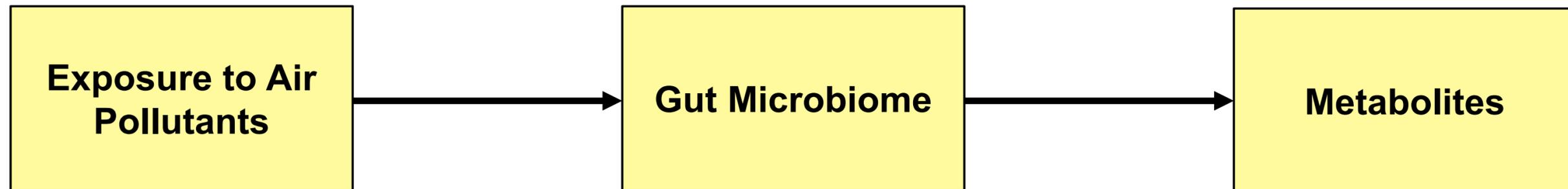
## Ozone:

- Known to stimulate HPA axis → release of catecholamines and steroid hormones
- Alter gut bacteria via adrenergic neuron stimulation (gut lamina propria)
- Damage gut barrier through immune activation

# Ongoing Research

- **Metabolomics**

- Association between targeted and untargeted metabolites and air pollution exposure



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**Thank You!**

**Questions?**

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