

**Farnaz Fouladi**

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

**\*Background.\*** Studies have shown that increased exposure to air pollutants is associated with increased obesity and dysregulated glucose metabolism. One of the potential underlying mechanisms could be attributed to changes in the gut microbiome since animal studies suggest exposure to air pollutants may alter the composition of the gut microbiome. The objective of this study was to examine relationships between air pollutants and the gut microbiome in adolescents residing in Southern California.

**\*Methods.\*** Adolescents (18-22 years, n=101) residing in Southern California were enrolled between 2014–2017. Individual residential exposure to prior year NO<sub>2</sub>, PM<sub>10</sub>, PM<sub>2.5</sub>, and 24-hour O<sub>3</sub> was estimated from central site monitors. The gut microbiome was characterized using whole genome sequences. Univariate linear regression and multivariate models were used to examine the associations between the relative abundance of microbes and their functional genes with exposure to air pollutants.

**\*Results.\*** Our results demonstrate significant associations between exposure to air pollutants and the composition and function of the gut microbiome. Higher exposure to 24-hour O<sub>3</sub> was associated with lower bacterial diversity ( $p < 0.001$ ;  $R^2 = 0.15$ ), higher *Bacteroides caecimuris* ( $p = 0.034$ ,  $R^2 = 0.15$ ) and multiple gene pathways, including L-ornithine de novo biosynthesis and pantothenate and coenzyme A biosynthesis I ( $p < 0.05$ ,  $R^2 = 0.14-0.18$ ). While fewer taxa were associated with other pollutants, higher NO<sub>2</sub> exposure was associated with higher Firmicutes. The percent variation in gut bacterial composition that was explained by air pollution exposure was up to 11.2% for O<sub>3</sub> concentrations, which was the largest effect compared to other covariates. Furthermore, associations between O<sub>3</sub> and composition and function of the microbiome remained significant after controlling for potential confounders, including body mass index, sex, energy intake, season, Hispanic ethnicity, and dietary macronutrients.

**\*Conclusions.\*** This study provides the first evidence of significant associations between exposure to air pollutants and the compositional and functional profile of the human gut microbiome. These results identify O<sub>3</sub> as an important pollutant that may alter the gut microbiome. Future mechanistic studies are warranted to determine if the effect of air pollutants on the gut microbiome mediate the adverse effect of air pollutants on human health.