

The Gut Microbiota and Short-Chain Fatty Acids in Association With Glycemia and Adiposity in Young Adults With Type 1 Diabetes: The ACTION Ancillary Gut Microbiome Pilot Study

Daria Igudesman,¹ Jamie Crandell,¹ Karen Corbin,² Franklin Muntis,¹ Dessi Zaharieva,³ Joan Thomas,¹ Cynthia Bulik,¹ Ian Carroll,¹ Brian Pence,¹ Richard Pratley,² Michael Kosorok,¹ David Maahs,³ and Elizabeth Mayer-Davis¹

¹University of North Carolina at Chapel Hill; ²Stanford School of Medicine; and ³AdventHealth Translational Research Institute

Objectives: Co-managing glycemia and adiposity is the cornerstone of cardiometabolic risk reduction among people with type 1 diabetes (T1D) but targets are often not met. The gut microbiota and microbiota-derived short-chain fatty acids (SCFA) influence glycemia and adiposity but have not been sufficiently investigated in longstanding T1D. We hypothesized that an increased abundance of SCFA-producing gut microbes, fecal SCFA, and gut microbial diversity were associated with improved glycemia but increased adiposity among young adults with longstanding T1D.

Methods: Participants provided stool samples at up to four time points. 16S rRNA gene sequencing determined the abundance of SCFA-producing gut microbes. Gas-chromatography mass-spectrometry determined total and specific SCFA (acetate, butyrate, and propionate). Dual-energy x-ray absorptiometry (% body fat or lean mass) and

anthropometrics (body mass index [BMI]) measured adiposity. Continuous glucose monitoring (time in range [70–180 mg/dl], above range [>180 mg/dl], and below range [54–69 mg/dl]) and hemoglobin A1c assessed glycemia. Adjusted and Bonferroni-corrected generalized estimating equations modeled the associations of SCFA-producing gut microbes, fecal SCFA, and gut microbial diversity with glycemia and adiposity. COVID-19 interrupted data collection, so models were repeated with restriction to pre-COVID visits.

Results: Data were available for up to 45 participants at 101 visits, including 40 participants at 54 visits pre-COVID. The abundance of *Eubacterium hallii* was associated inversely with BMI (all data). Pre-COVID, increased fecal propionate was associated with increased time above range and reduced time in target and below range; and the increased abundance of four SCFA-producing intestinal microbes (*Ruminococcus gnavus*, *Ruminococcus 2*, *Eubacterium ventriosum*, and *Lachnospira*) was associated with reduced adiposity (% body fat or BMI), of which two microbes were also associated with increased % lean mass.

Conclusions: Unexpectedly, fecal propionate was associated with detriment to glycemia, while several SCFA-producing gut microbes were associated with benefit to adiposity. Future mechanistic studies may determine whether these associations have causal linkages in T1D.

Funding Sources: National Institute of Diabetes and Digestive and Kidney Diseases.