Metabolic dysfunction associated with alterations in gut microbiota in obese adolescents

Quin Yuhui Xie[1,2†], Alessandra Granato[1†], Anthony Wong[1], Christopher Yau[1,3], Lisa Chu[4], Shawna Steele[4], Tina Chen[5], Cynthia Guidos[5], Jill K. Hamilton[4], Jayne S. Danska[1,2,3]

[1]Genetics and Genome Biology, The Hospital for Sick Children Research Institute, Toronto, M5G1X8, Canada; [2]Department of Medical Biophysics, University of Toronto, Toronto, M5T2S8, Canada; [3]Department of Immunology, University of Toronto, Toronto, M5T2S8, Canada; [4]Division of Endocrinology, The Hospital for Sick Children, Toronto, Ontario, Canada; [5]Cell Biology, The Hospital for Sick Children Research Institute, Toronto, M5G1X8, Canada †contributed equally to this work

Background: The increasing prevalence of obesity and metabolic dysfunction, and the origins of these conditions in childhood, have become a worldwide public health concern. The human gut microbiota has been implicated in metabolic dysfunction given alterations of microbial composition and function in obesity and type 2 diabetes. However, clear causal relationships between altered gut microbiota and chronic inflammation in obesity have not been elucidated in humans. Despite the importance of child health in disease prevention, few studies have investigated relationships between cardiometabolic fitness, inflammation and the gut microbiota in children and adolescents, where these connections likely originate.

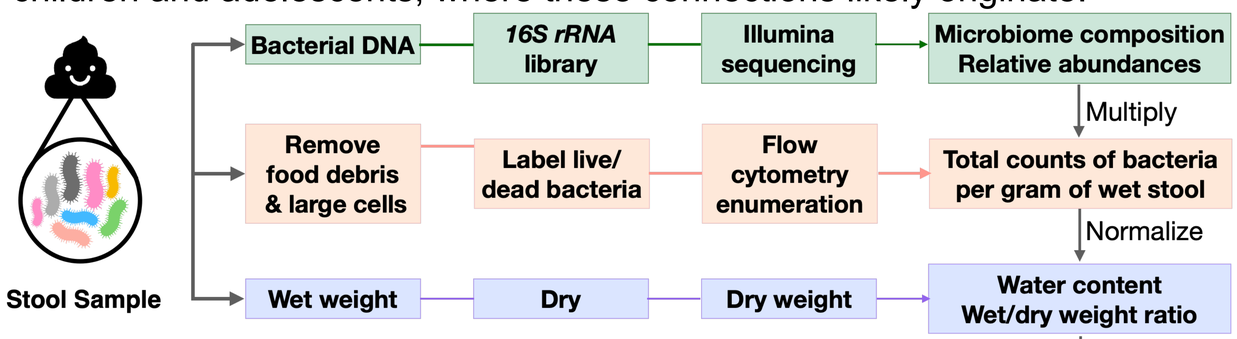

Figure 1. Approach to relative and absolute abundance quantification of microbiome sequence data

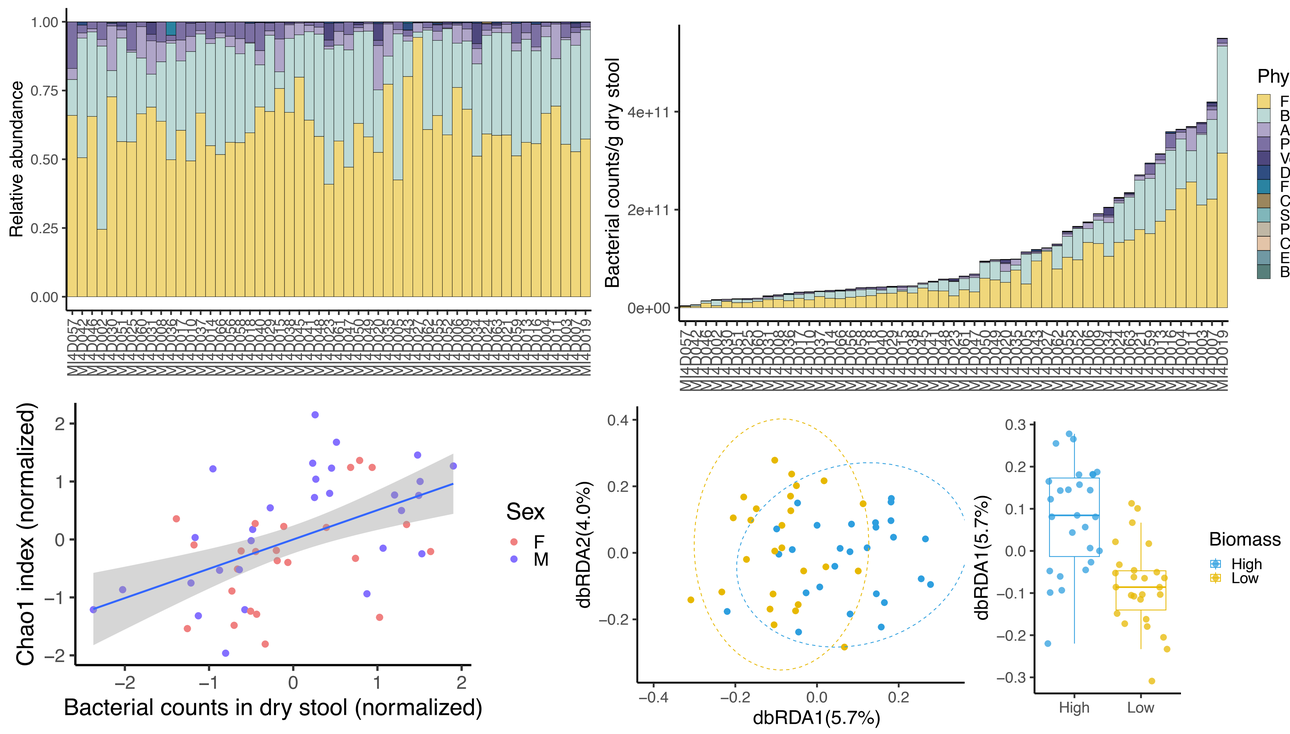

Figure 2. Multi-log differences present in fecal biomass of MI4D participants

The observed multi-log order differences in stool bacterial biomass were correlated with stool water content, bacterial taxonomic composition and diversity. The MI4D participants had not been exposed to antibiotics or other medications with known affects on the microbiota.

Significance: This study expands the understanding of sex-specific mechanisms driving metabolic dysfunction in the obese youth and suggests that intestinal bacterial biomass and composition contribute to their metabolic and inflammatory dysregulation prior to diabetes diagnosis.

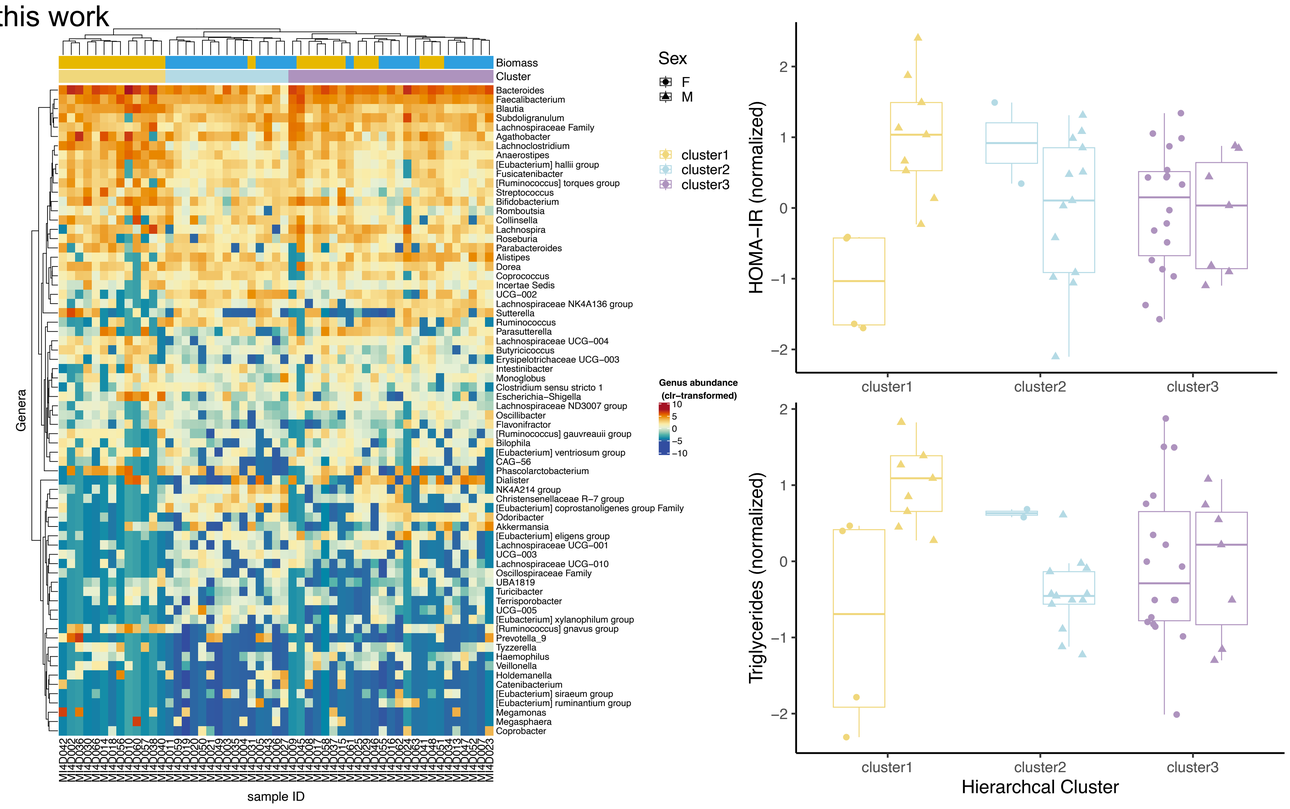

Figure 3. Fecal biomass is a major determinant of gut microbiome composition and is associated with lipid and glucose metabolism

In male participants, clusters of predominantly low biomass individuals had the highest HOMA-IR scores and plasma triglyceride levels, suggesting a sex-specific association between fecal biomass and metabolic dysfunction

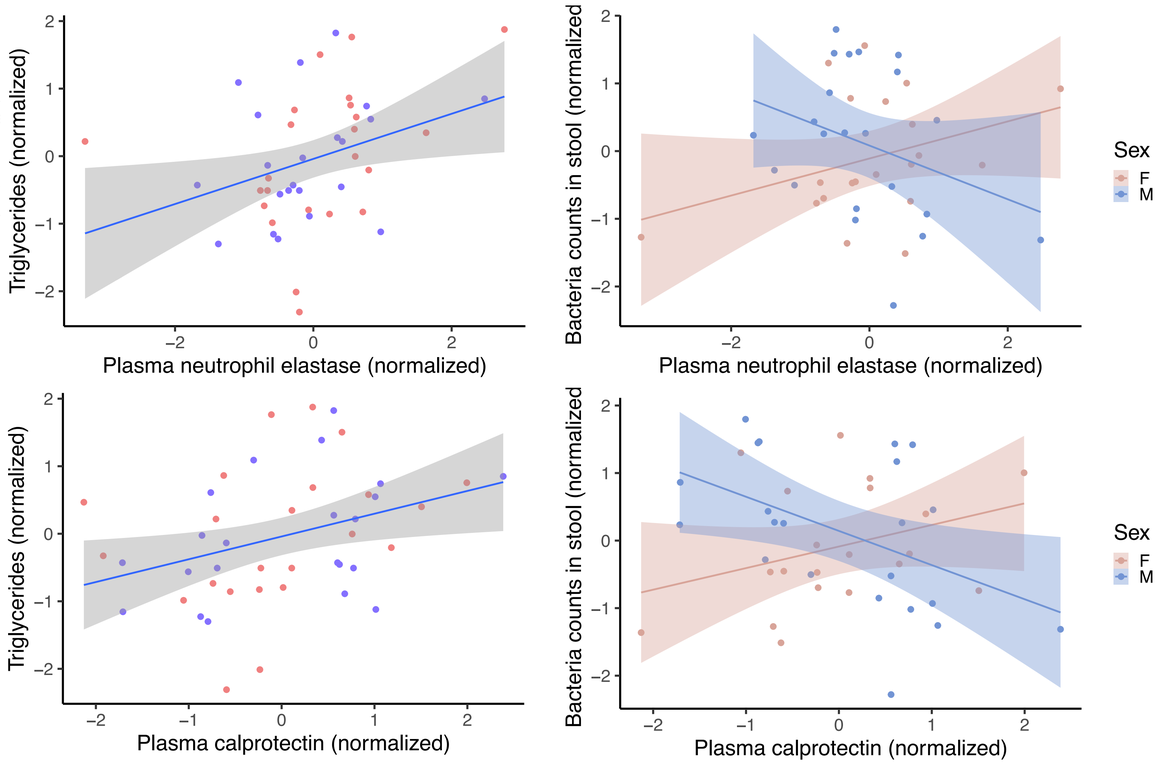

Figure 4. Associations between neutrophil activity, triglycerides, and biomass

To evaluate systemic inflammation, neutrophil elastase and calprotectin were quantified in the plasma of MI4D participants. A sex-dependent association was observed between neutrophil protein abundances and fecal biomass, suggesting that this is a feature associated with elevated systemic inflammation, especially in obese adolescent males.

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