

Metabolic dysfunction is associated with alterations in gut microbiota in an obese adolescent cohort

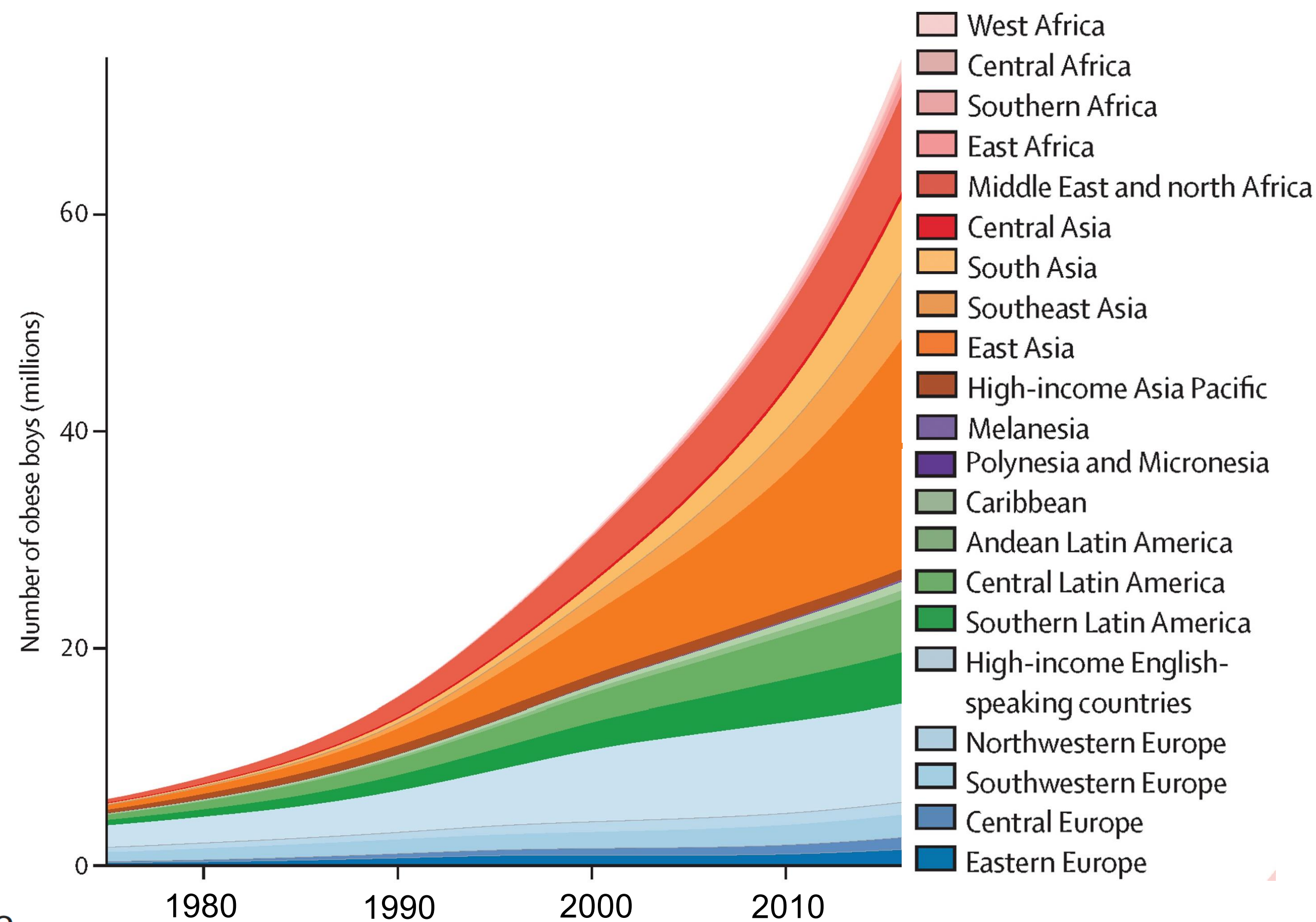
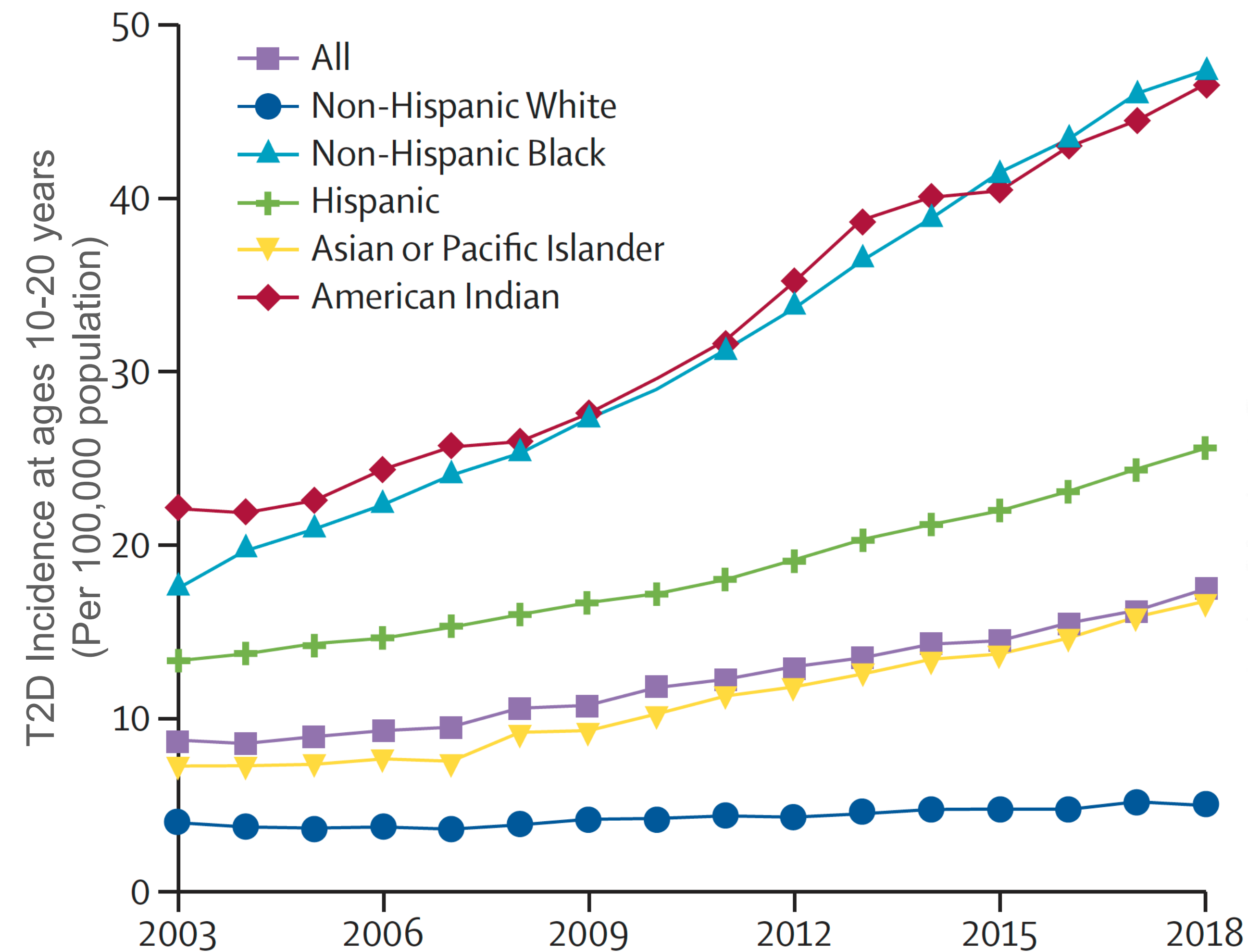
Quin Xie

PhD candidate, Lab of Dr. Jayne Danska

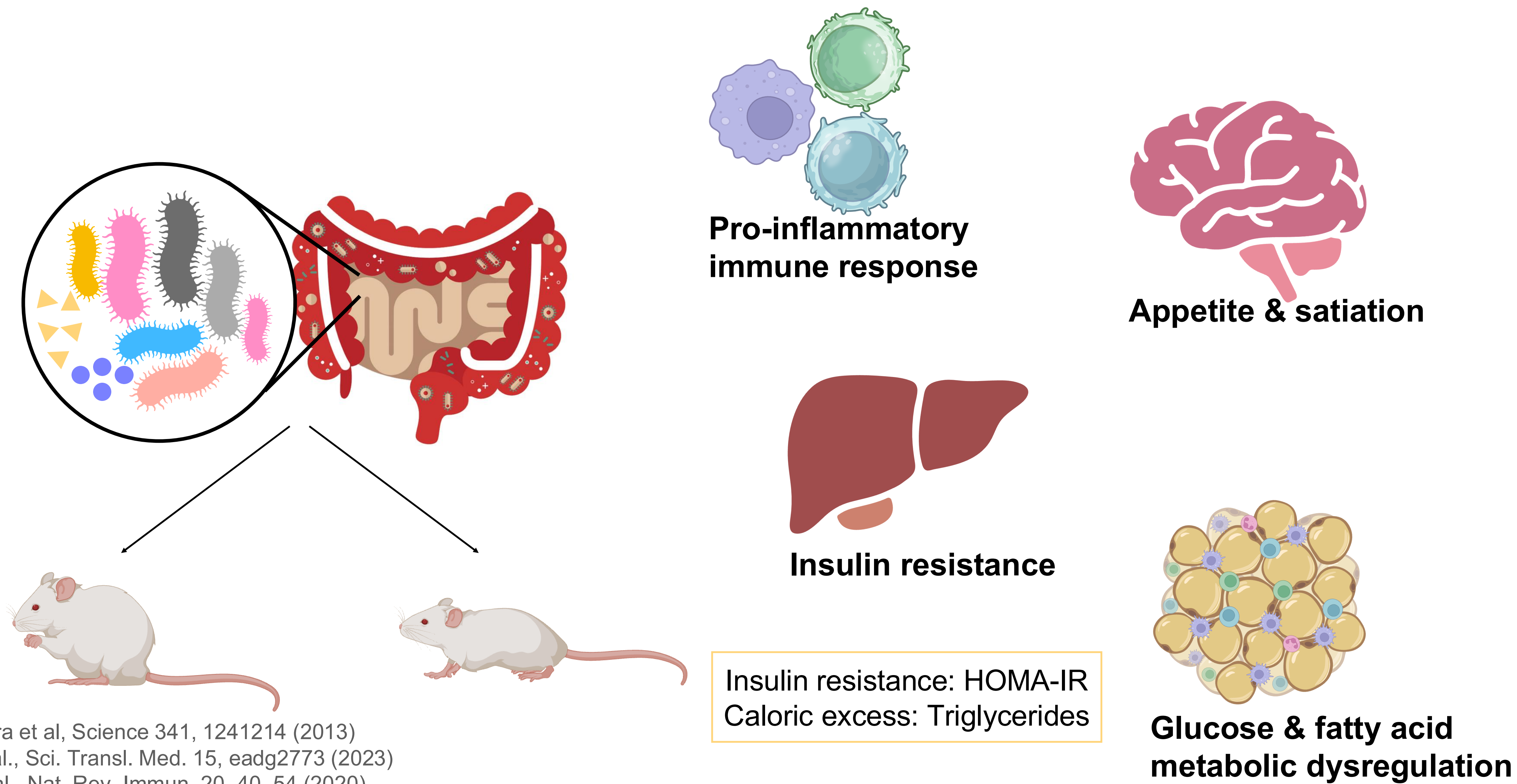
James Lepock Memorial Symposium

2024

Obesity: the emerging epidemic

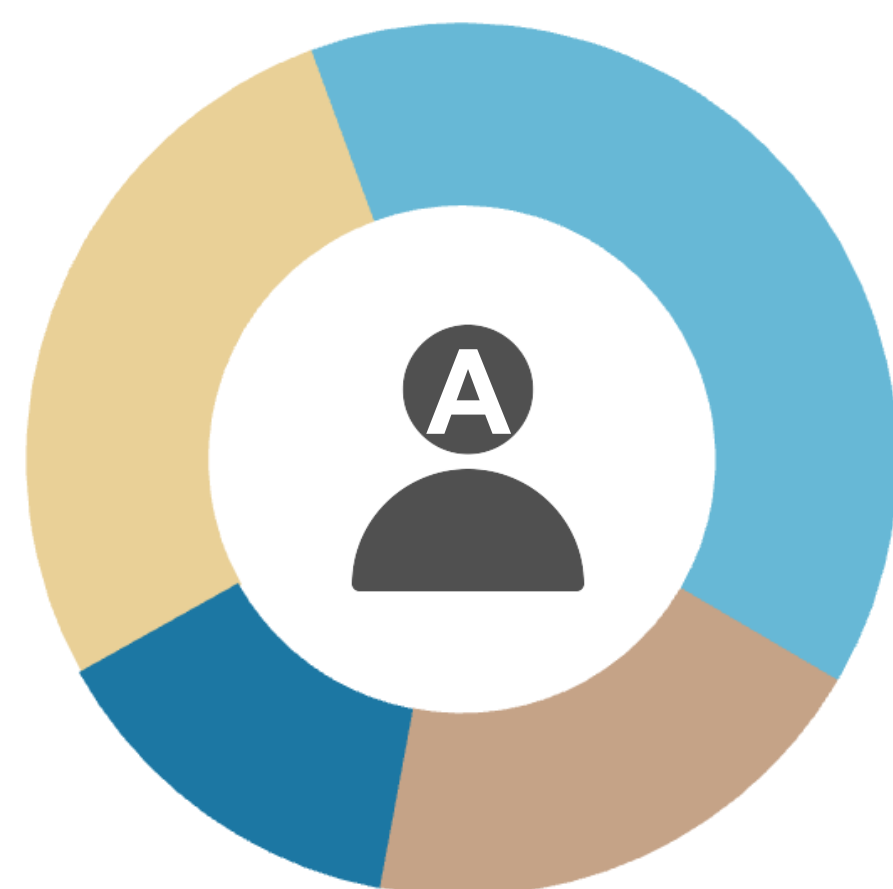
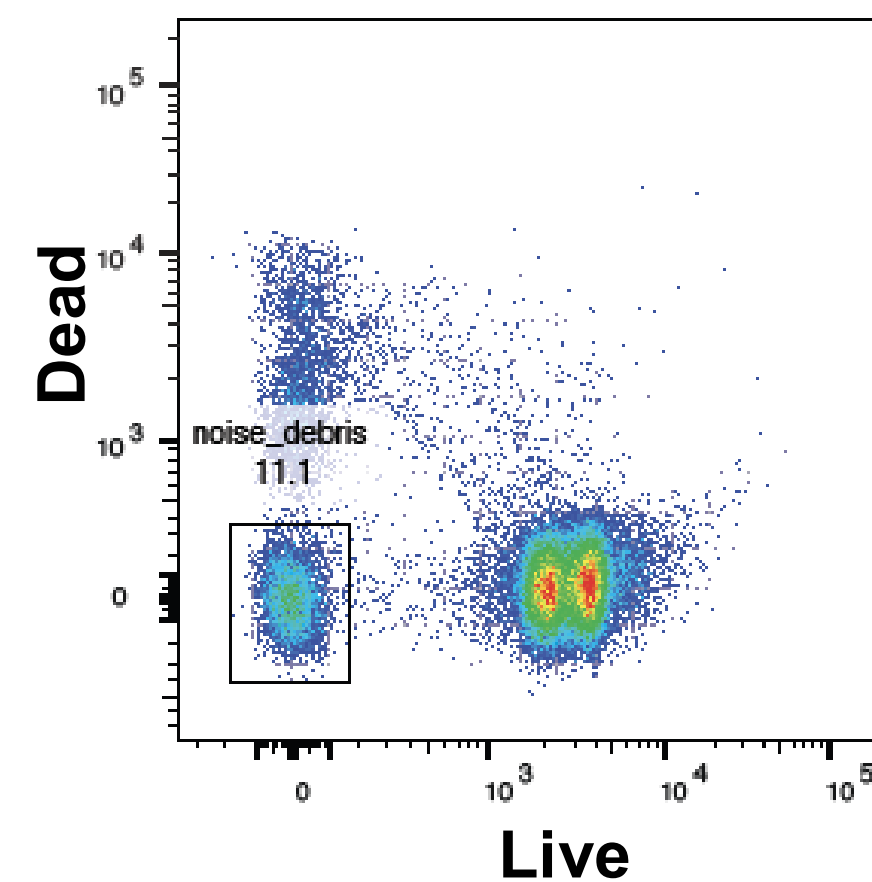
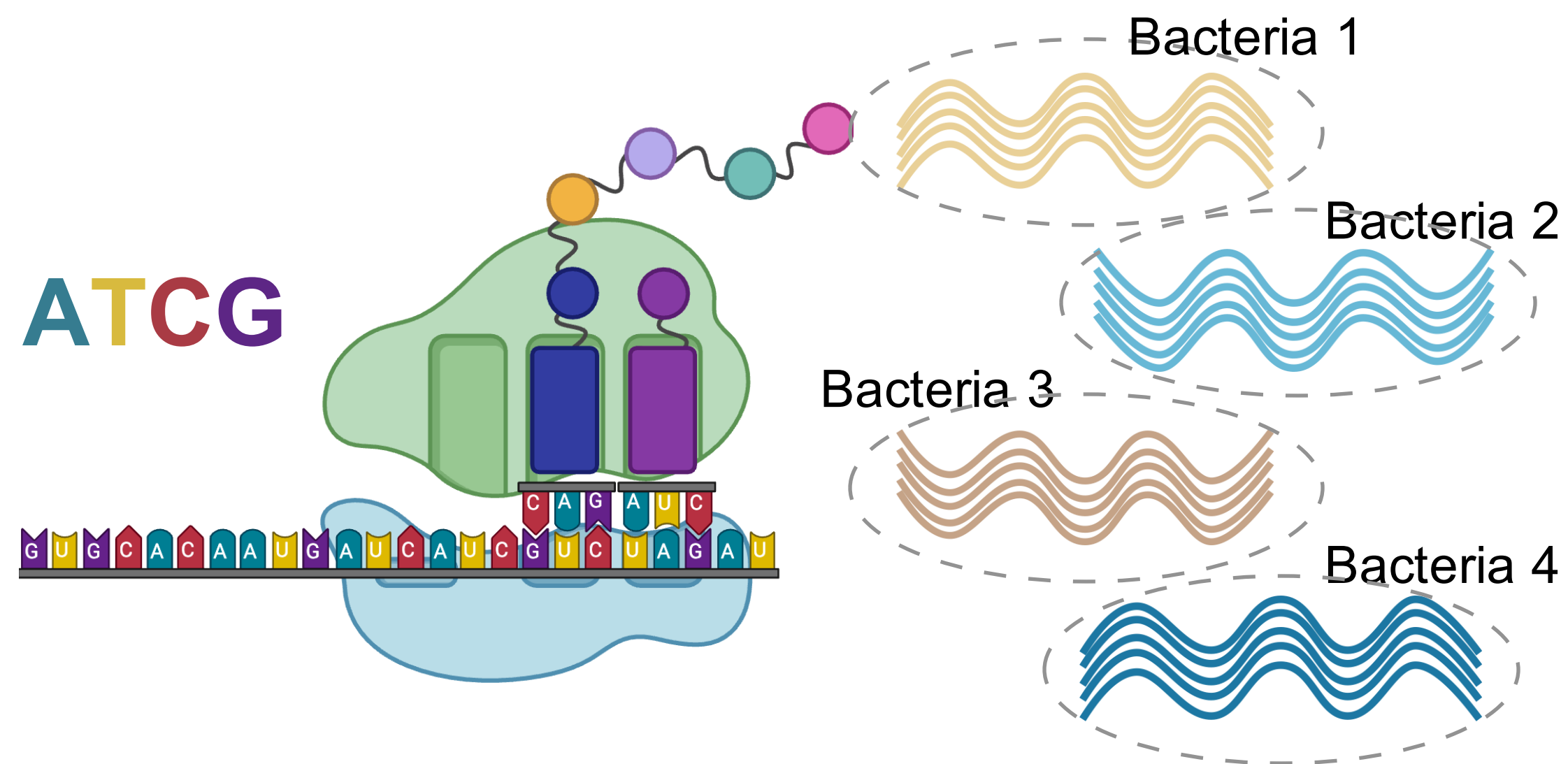


Role of gut microbiota (Mb) in obesity and metabolic dysfunction

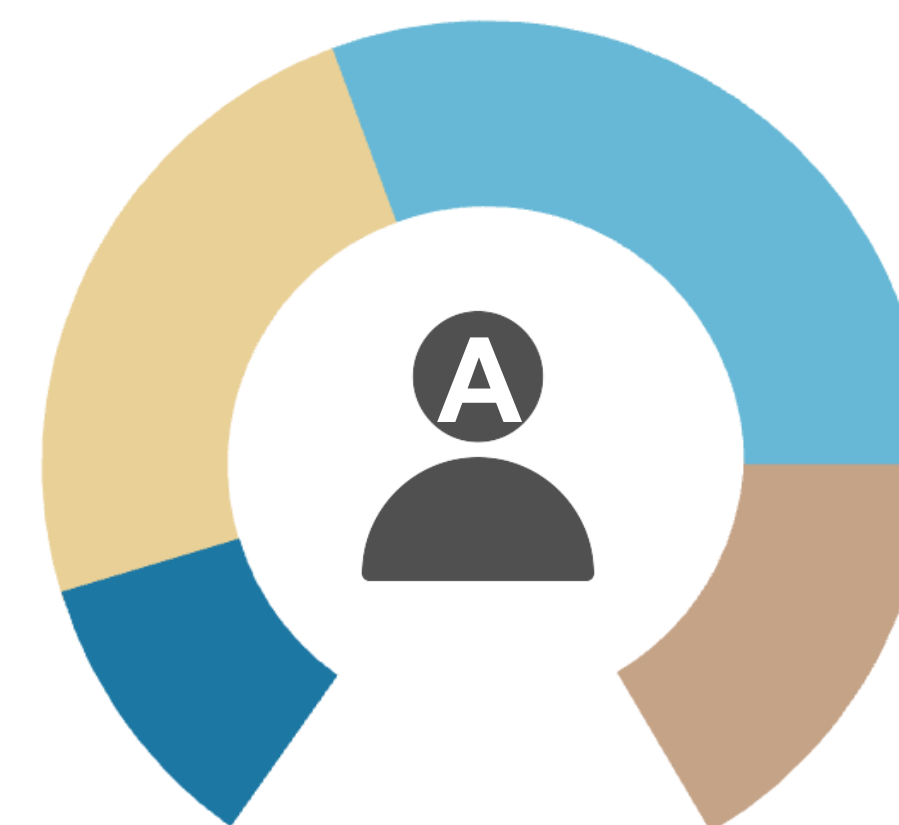
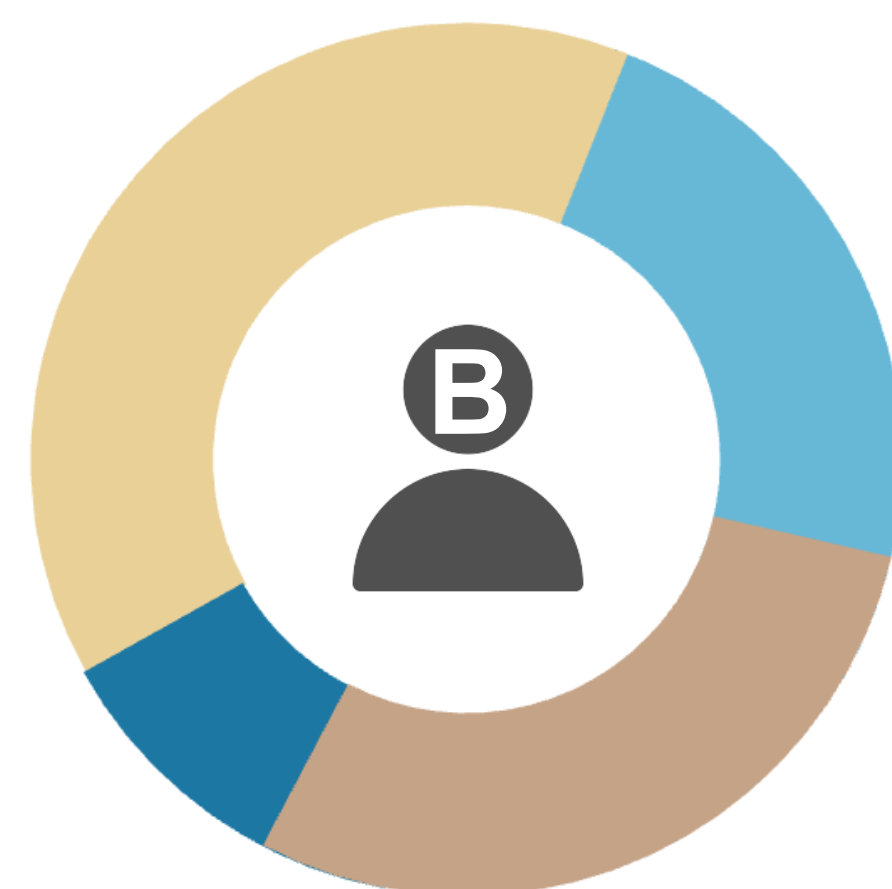


Ridaura et al, Science 341, 1241214 (2013)
de Wit et al., Sci. Transl. Med. 15, eadg2773 (2023)
Tilg et al., Nat. Rev. Immun. 20, 40–54 (2020)

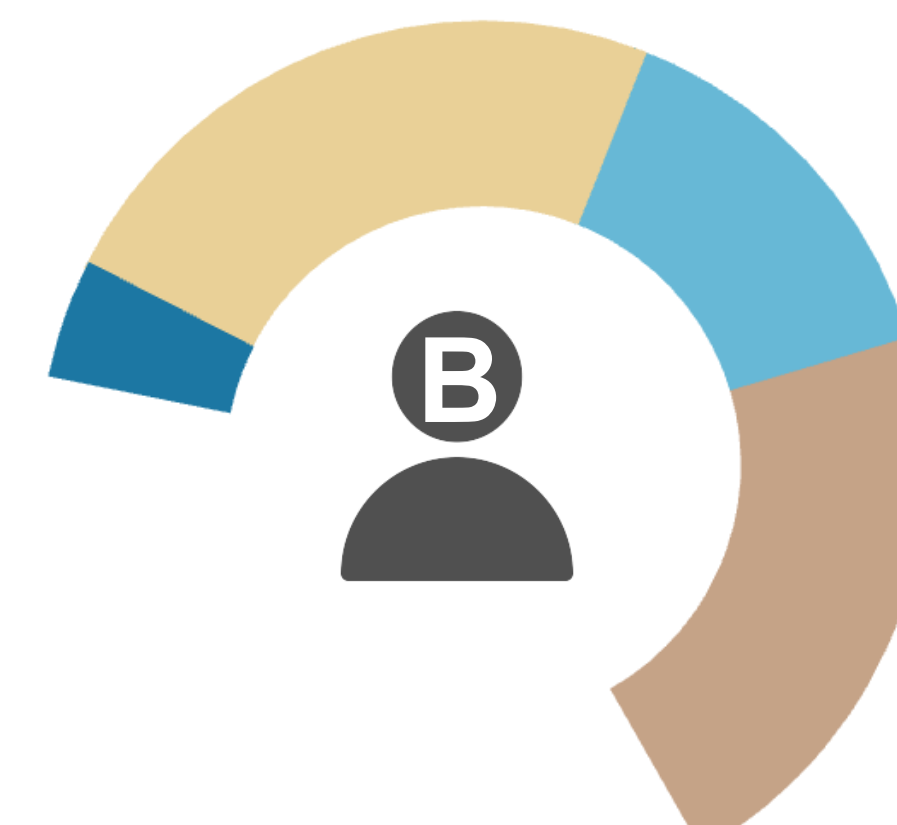
Relative and absolute quantification of microbiome sequencing



Relative abundance: bacteria%



Absolute abundance: # bacteria

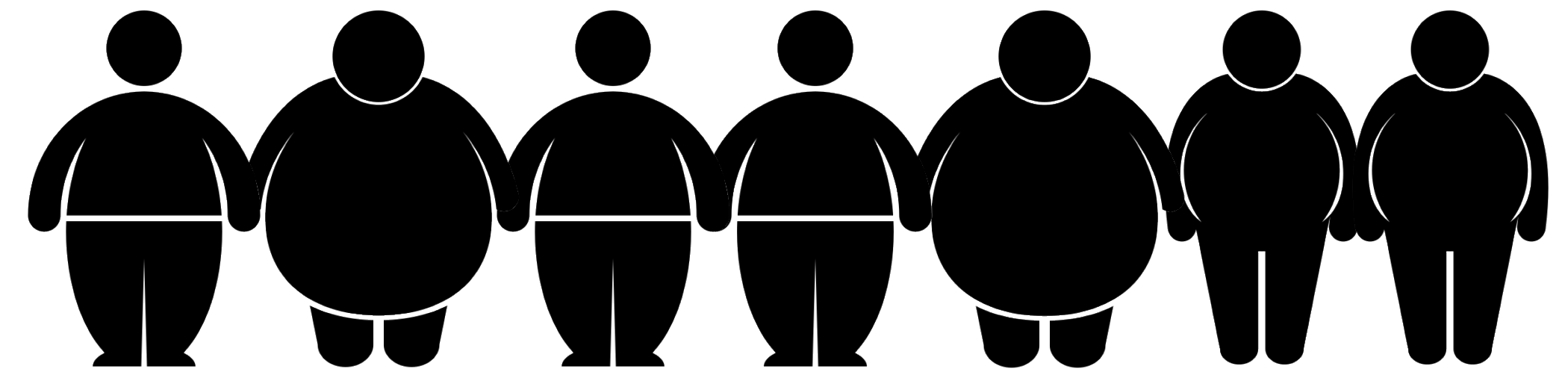


Obese adolescents at risk of Type 2 Diabetes

Inclusion criteria

- Age 12 - 18 years old
- Age- and sex-standardized BMI ≥ 97 th percentile
- Median BMI = 39

Goal: to understand risk factors of metabolic dysfunction in obese adolescents



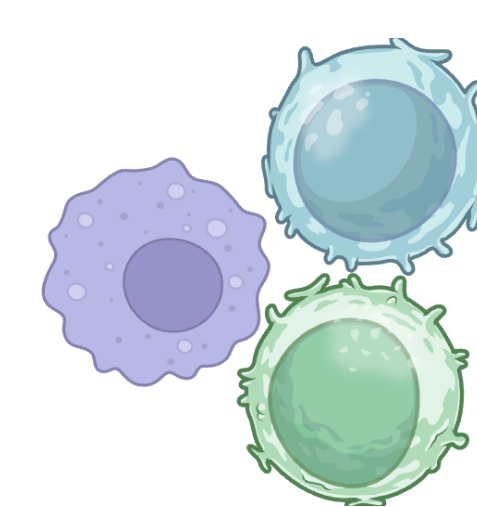
n = 56



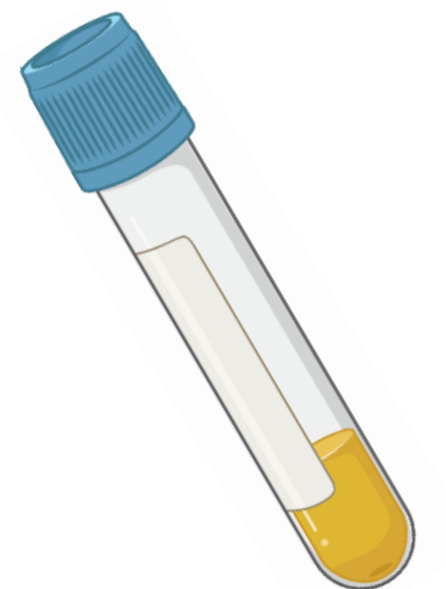
Clinical
Measurements



Stool

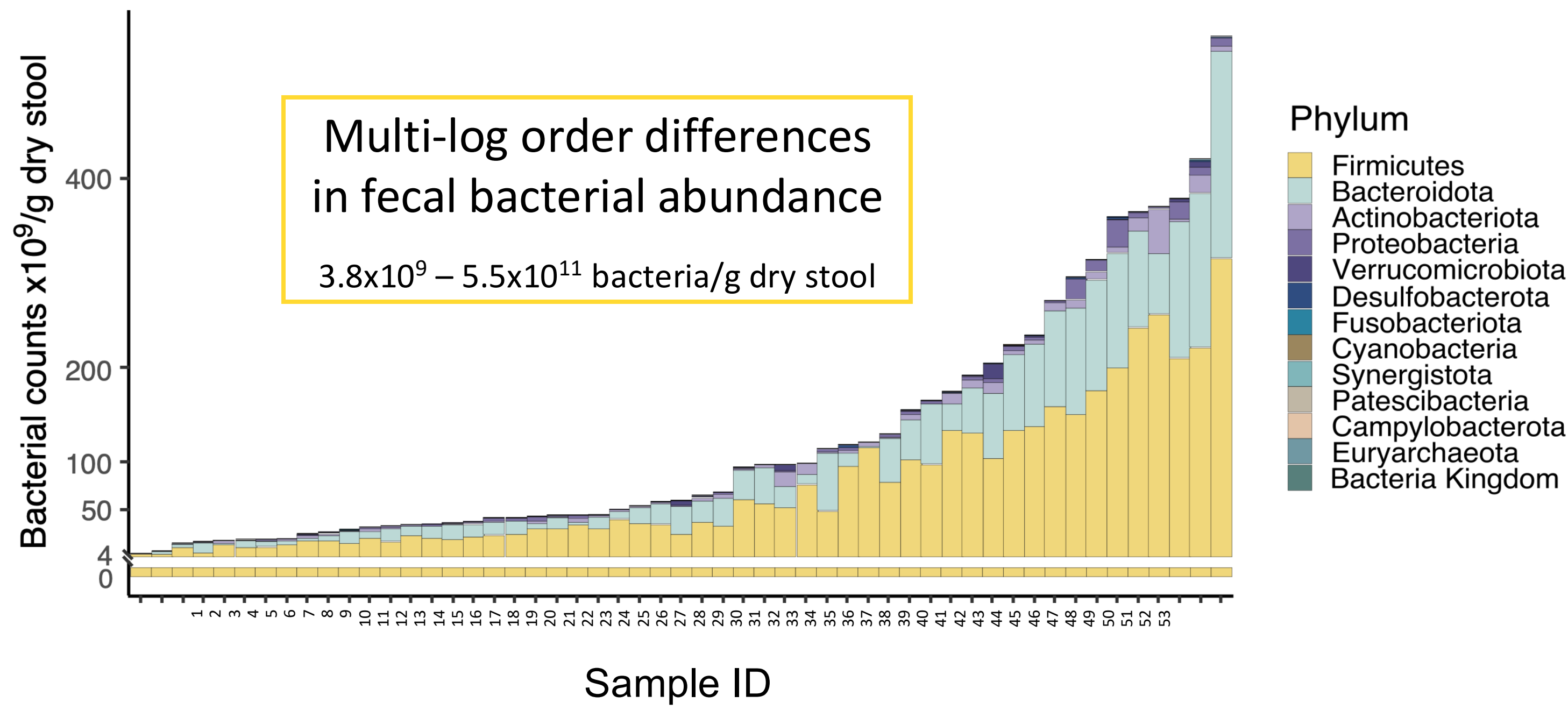
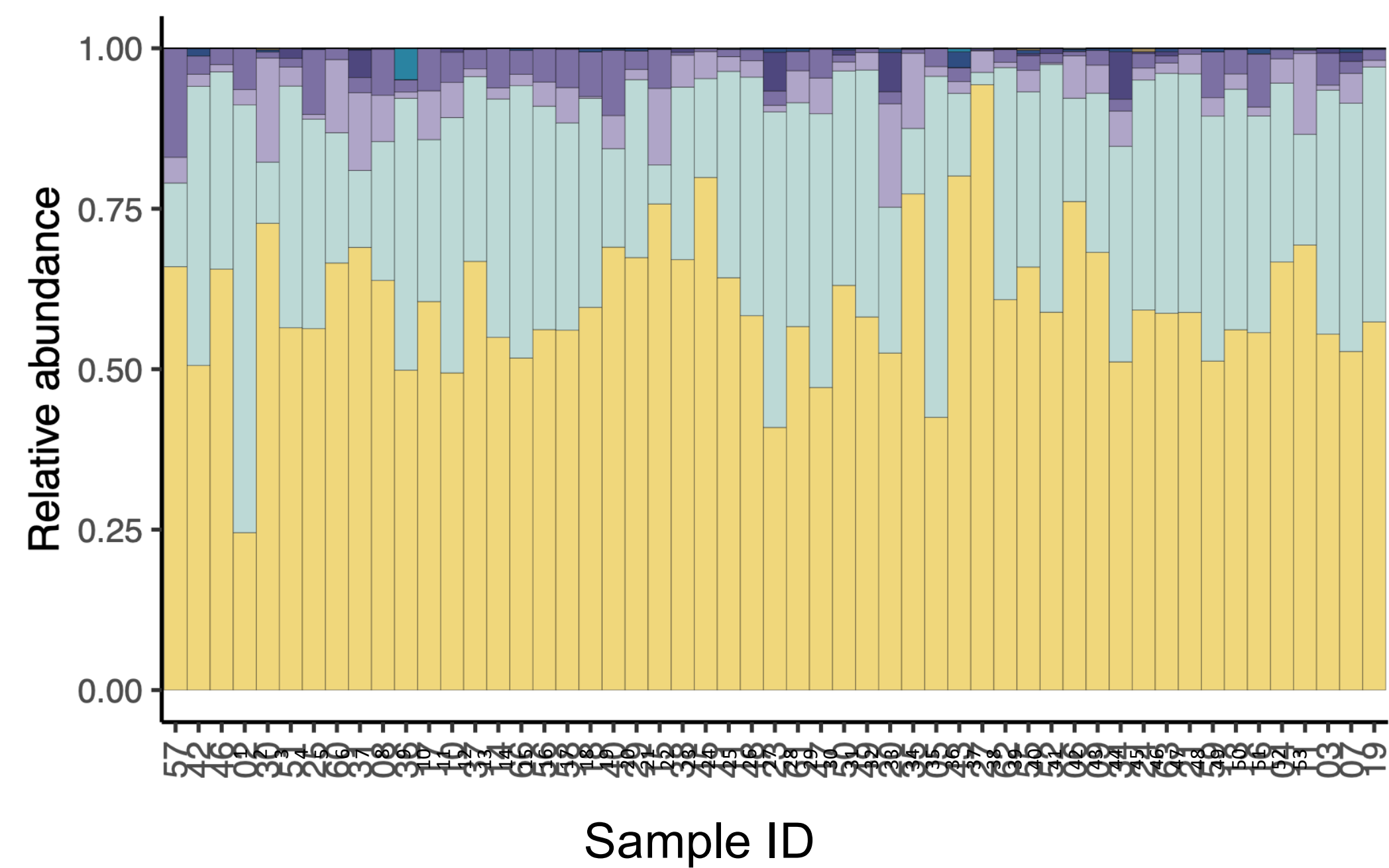


PBMC



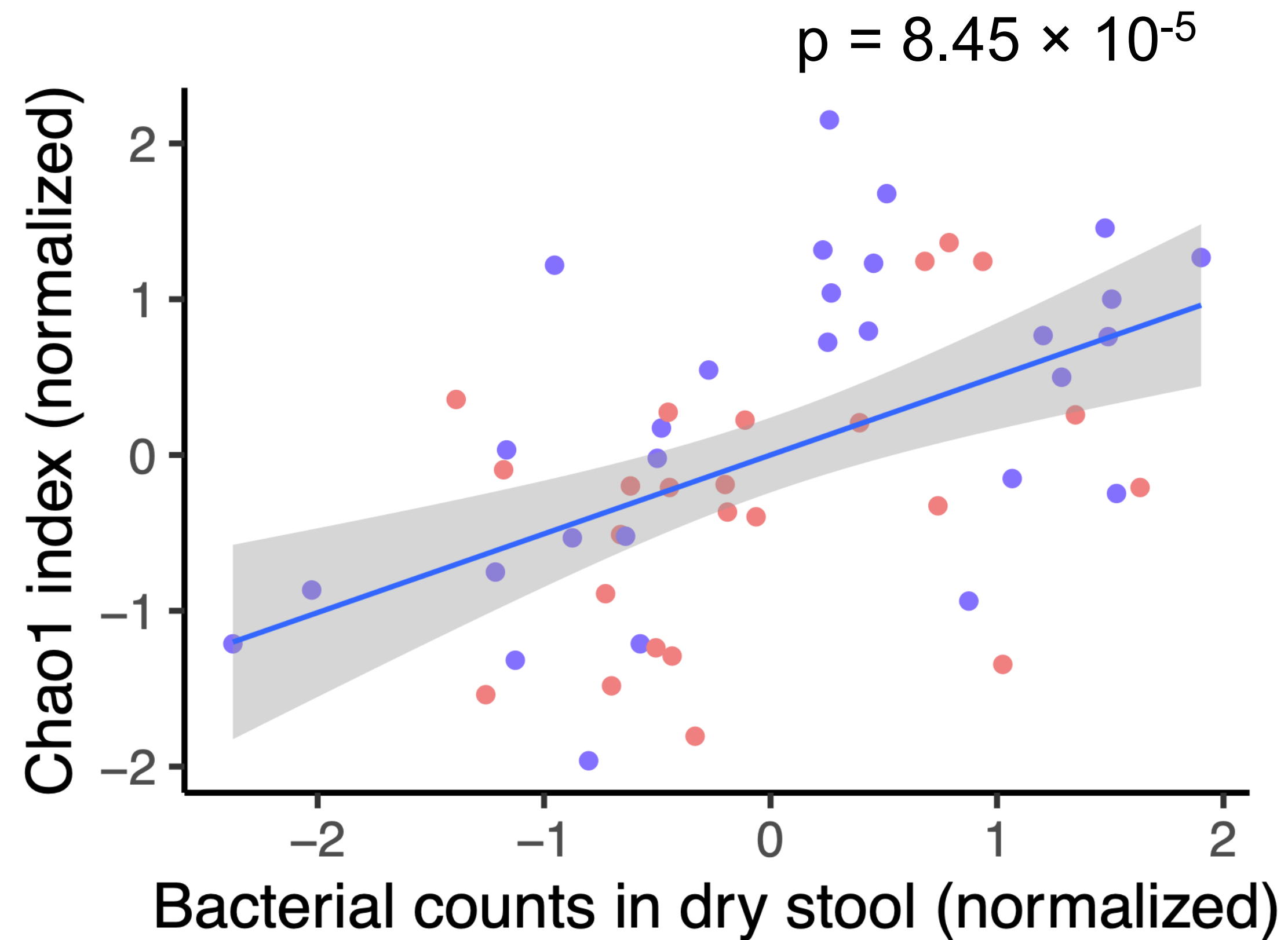
Plasma

Analysis of the gut microbiome of obese adolescents

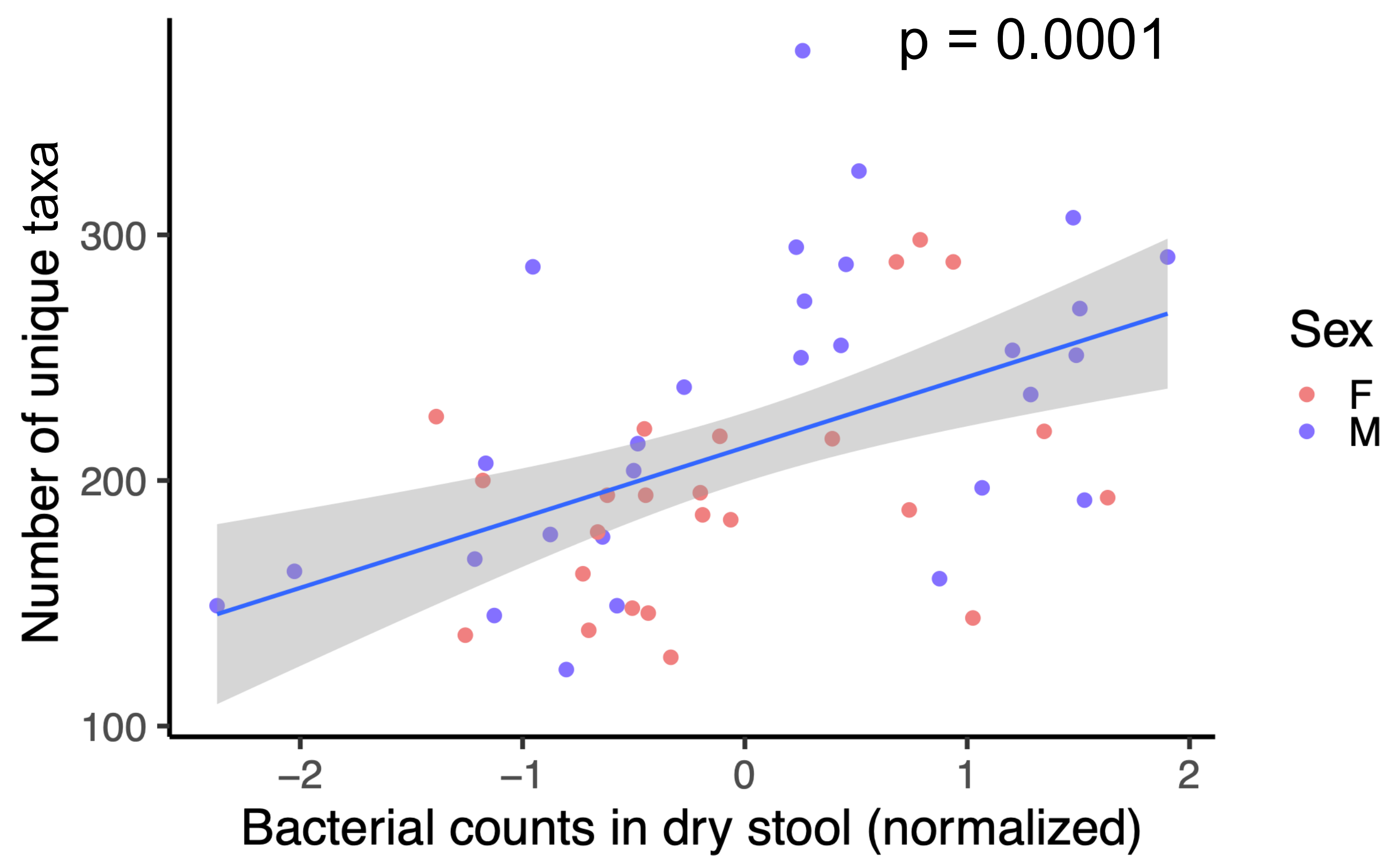


Absolute bacteria abundance associated with gut microbiome diversity

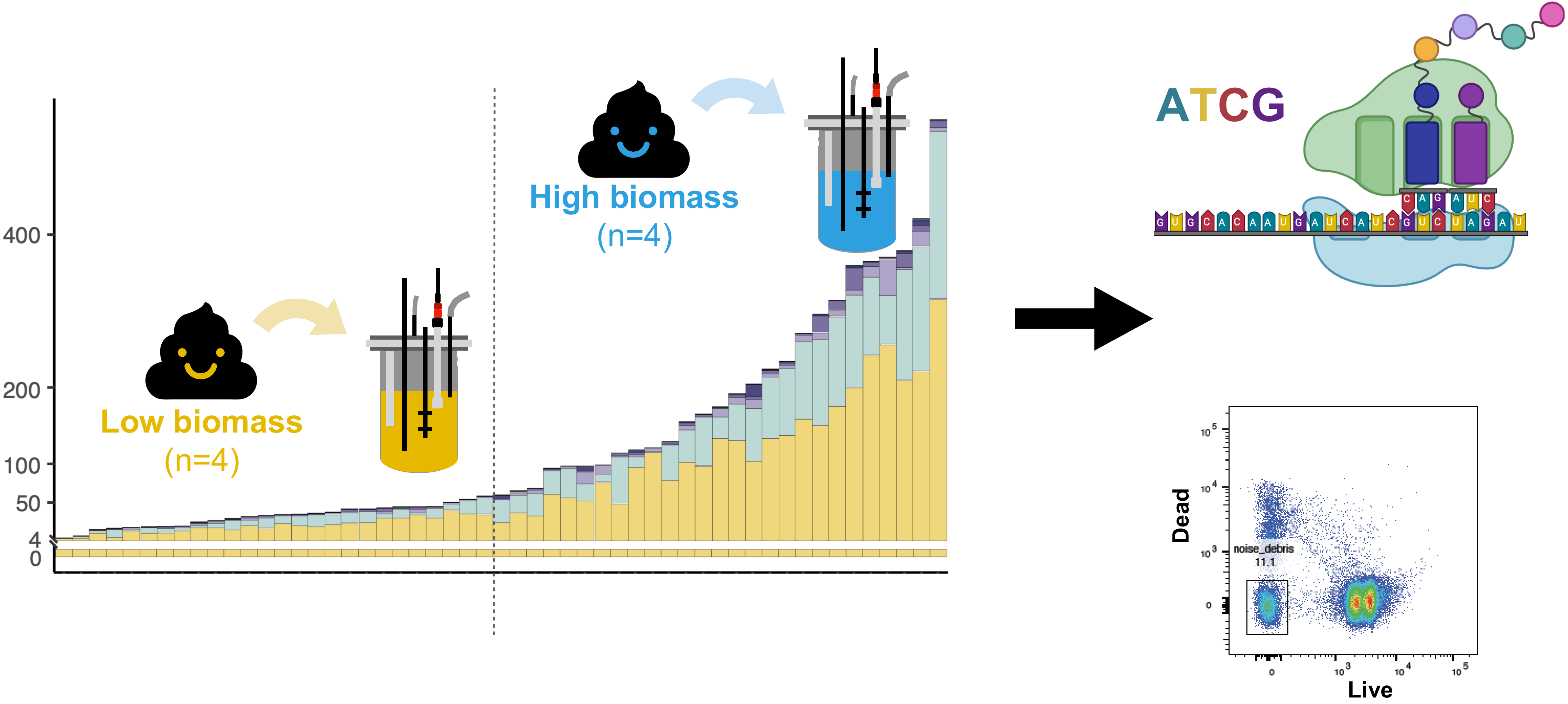
bacterial diversity



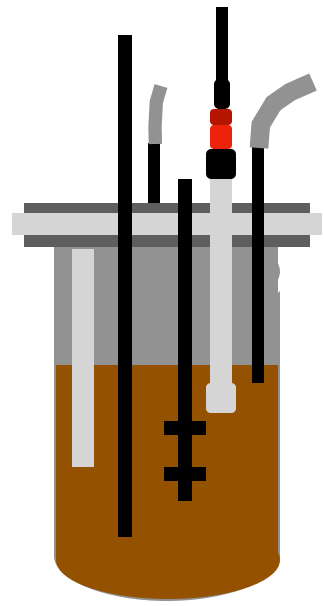
bacteria taxa



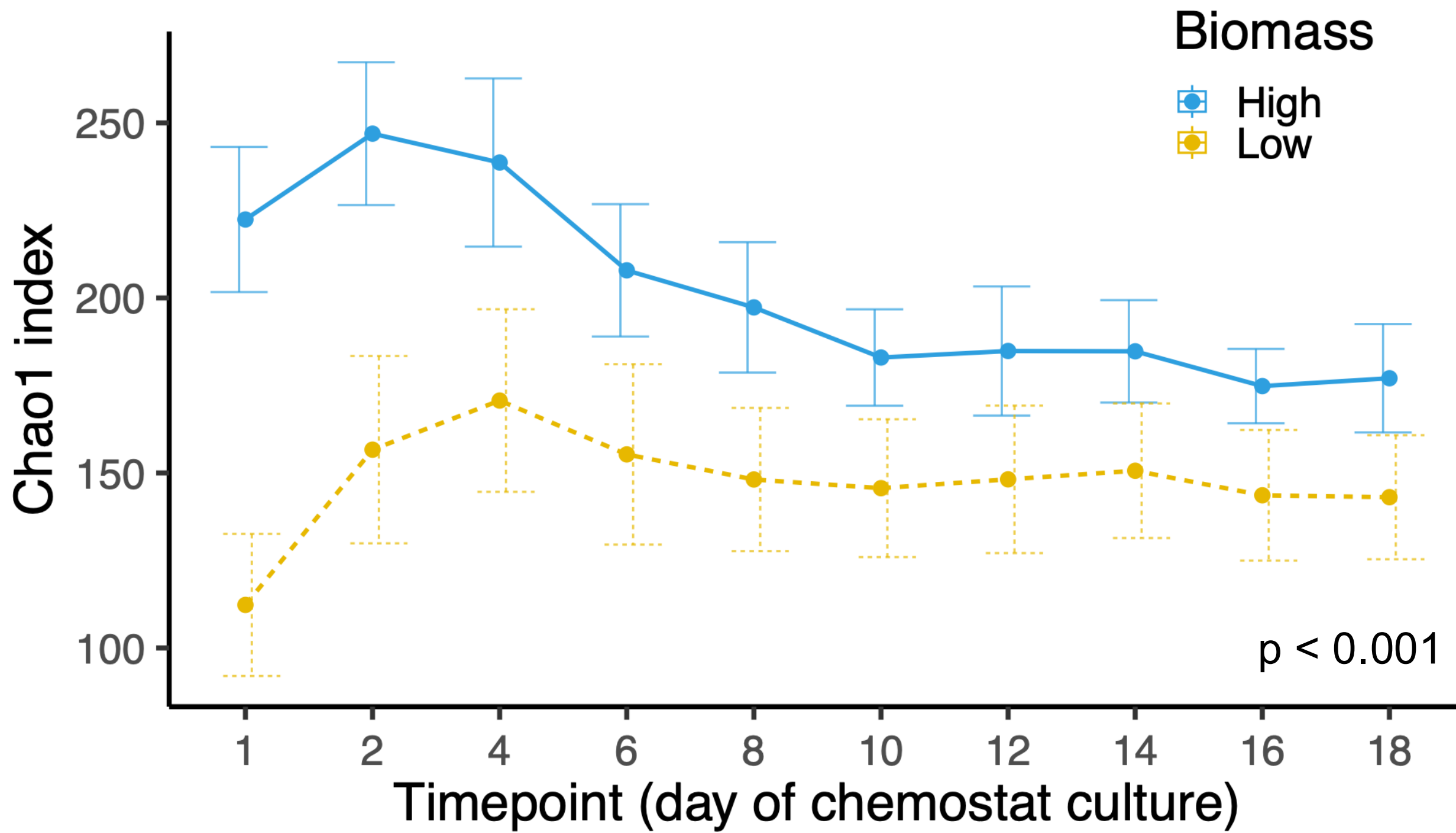
Difference in absolute abundance: intrinsic to gut Mb or host influence



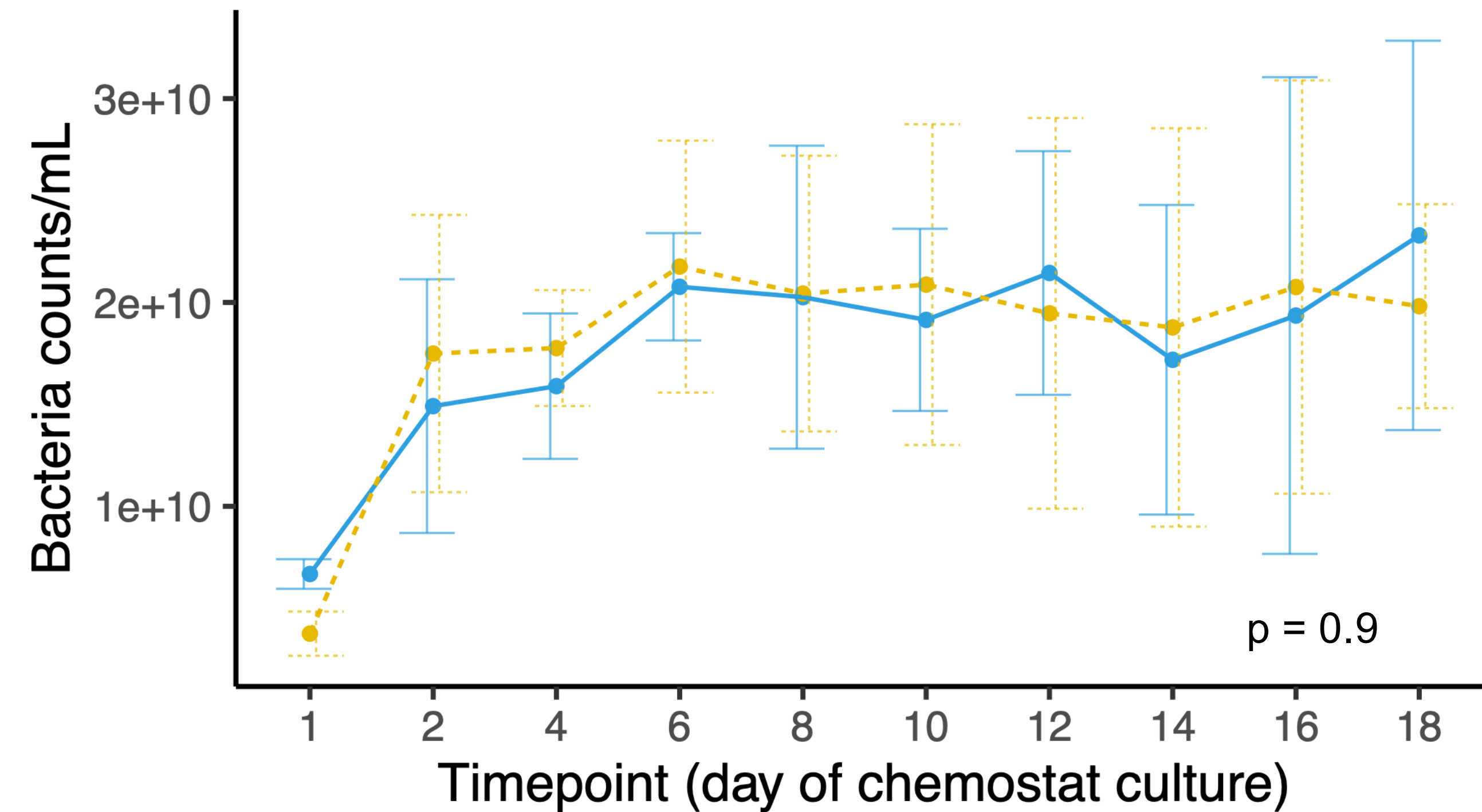
Bacterial biomass is a host-dependent feature



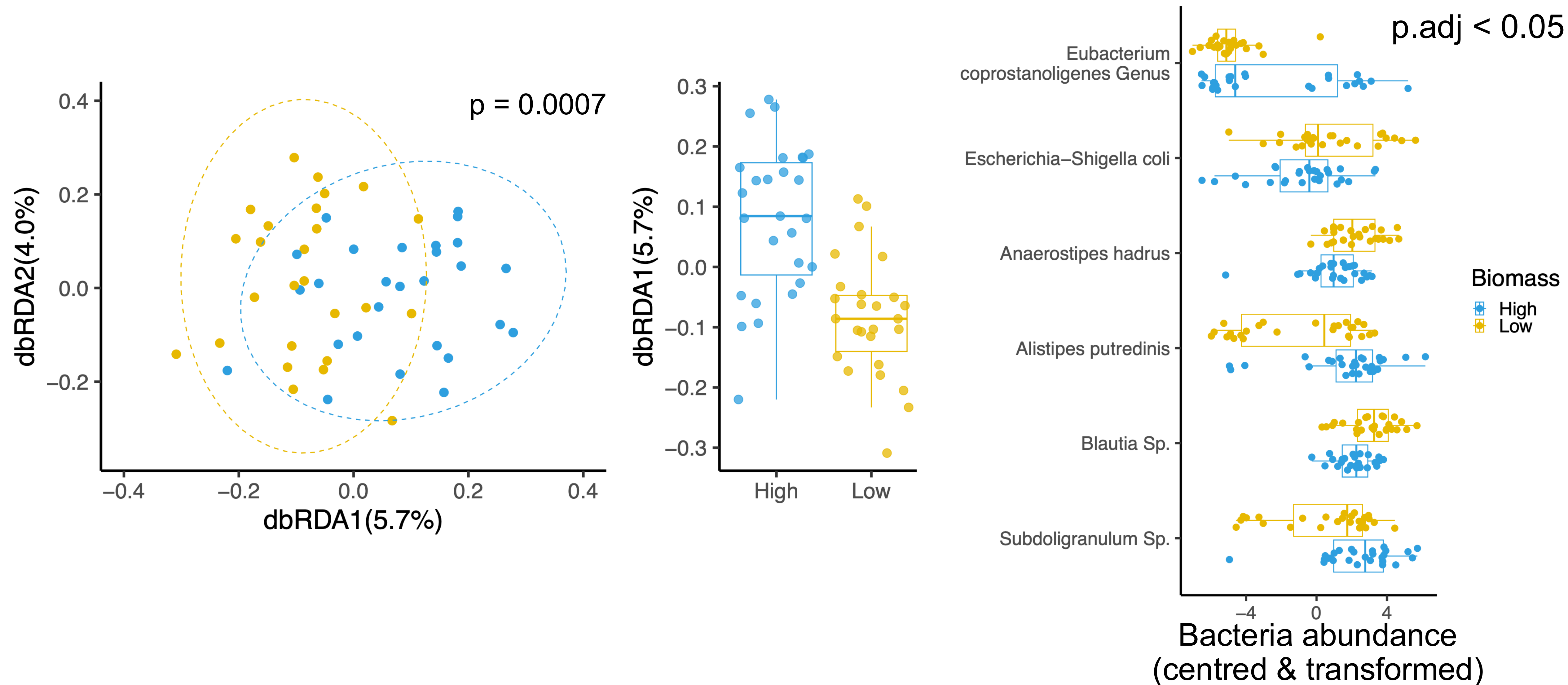
bacterial diversity



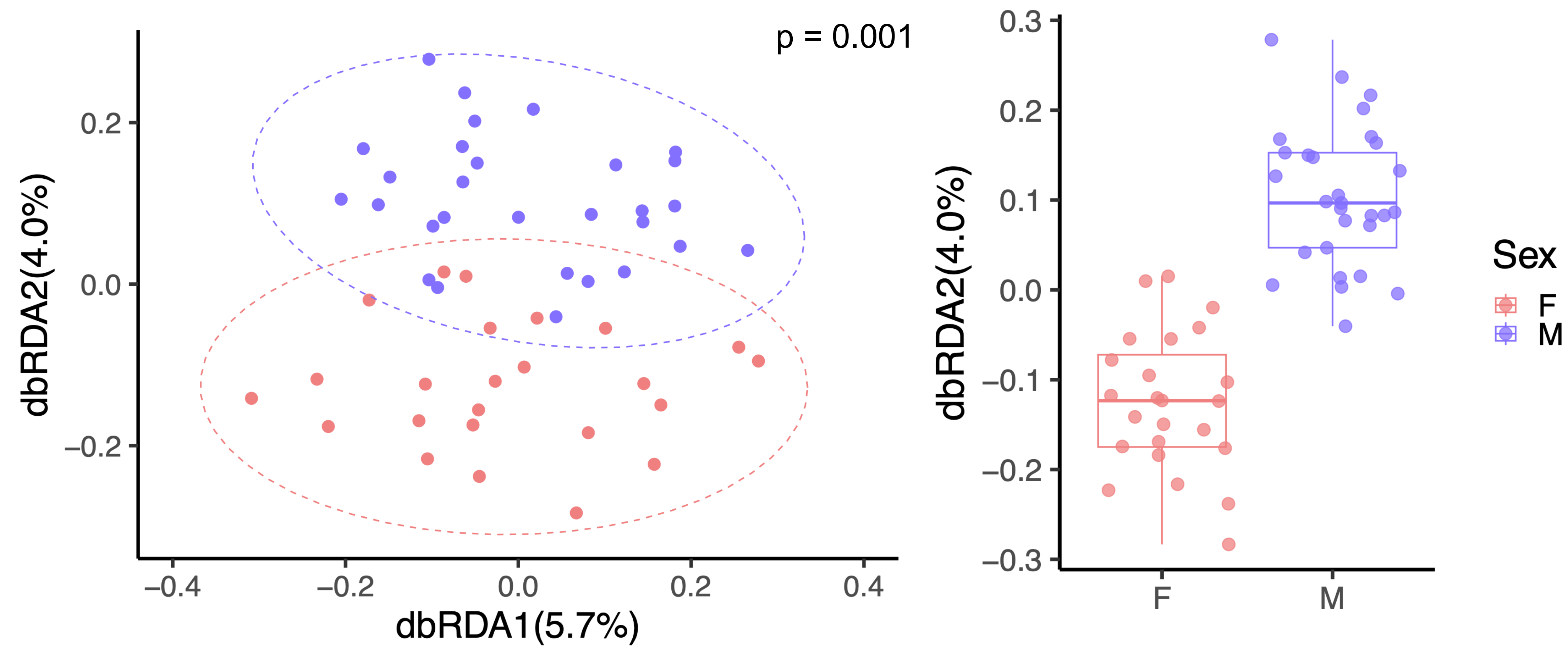
absolute abundance



Fecal biomass associated with gut microbiome variance

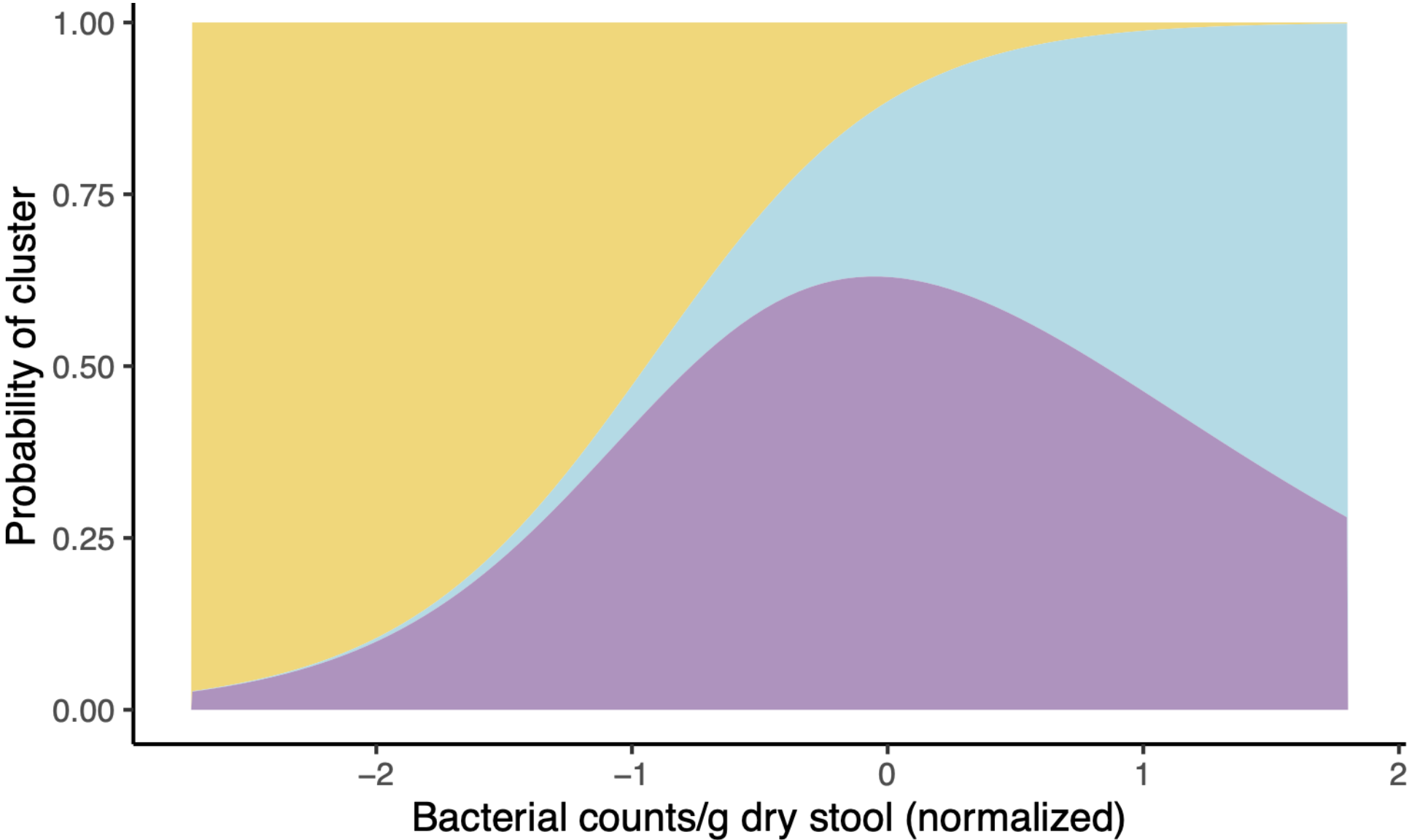
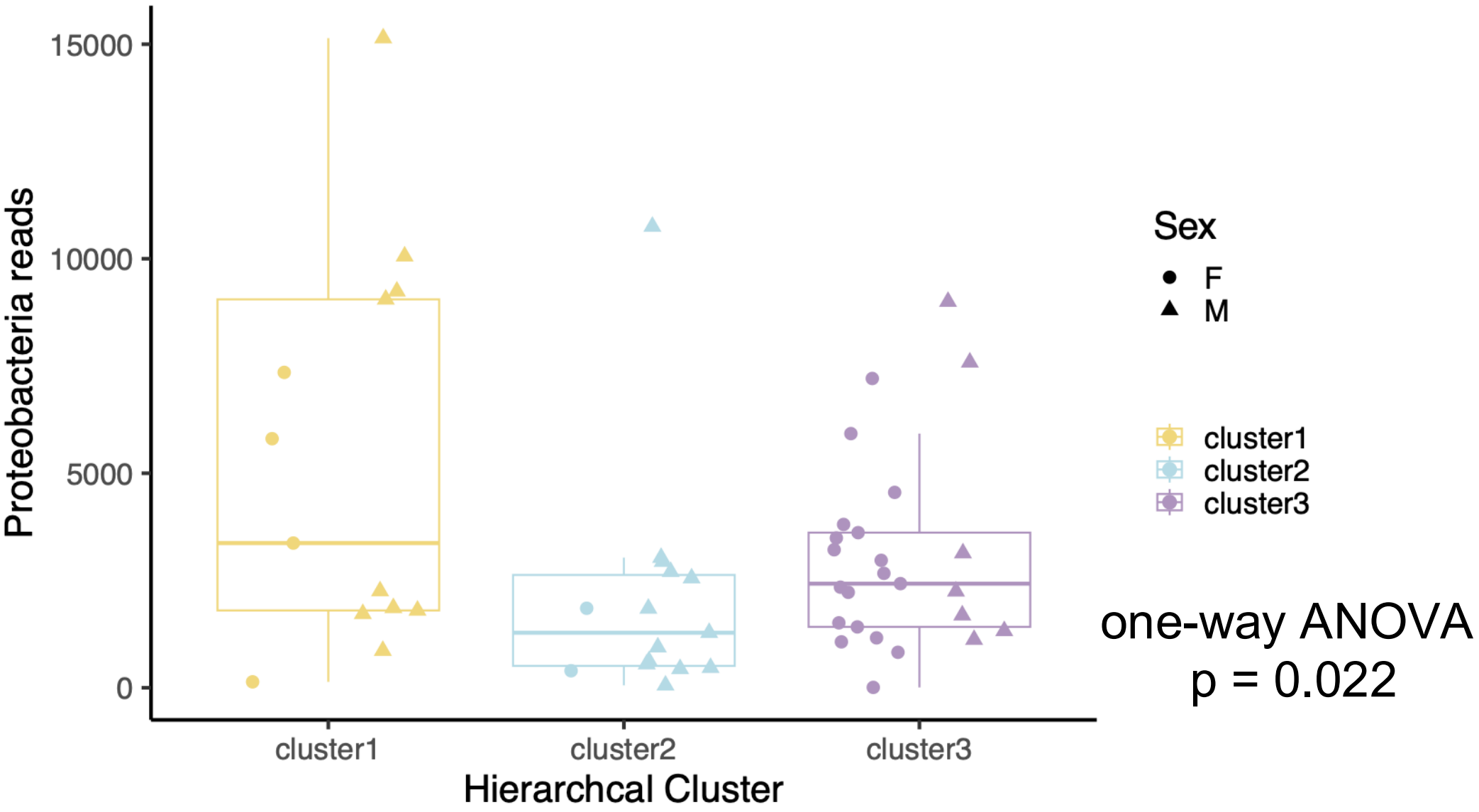
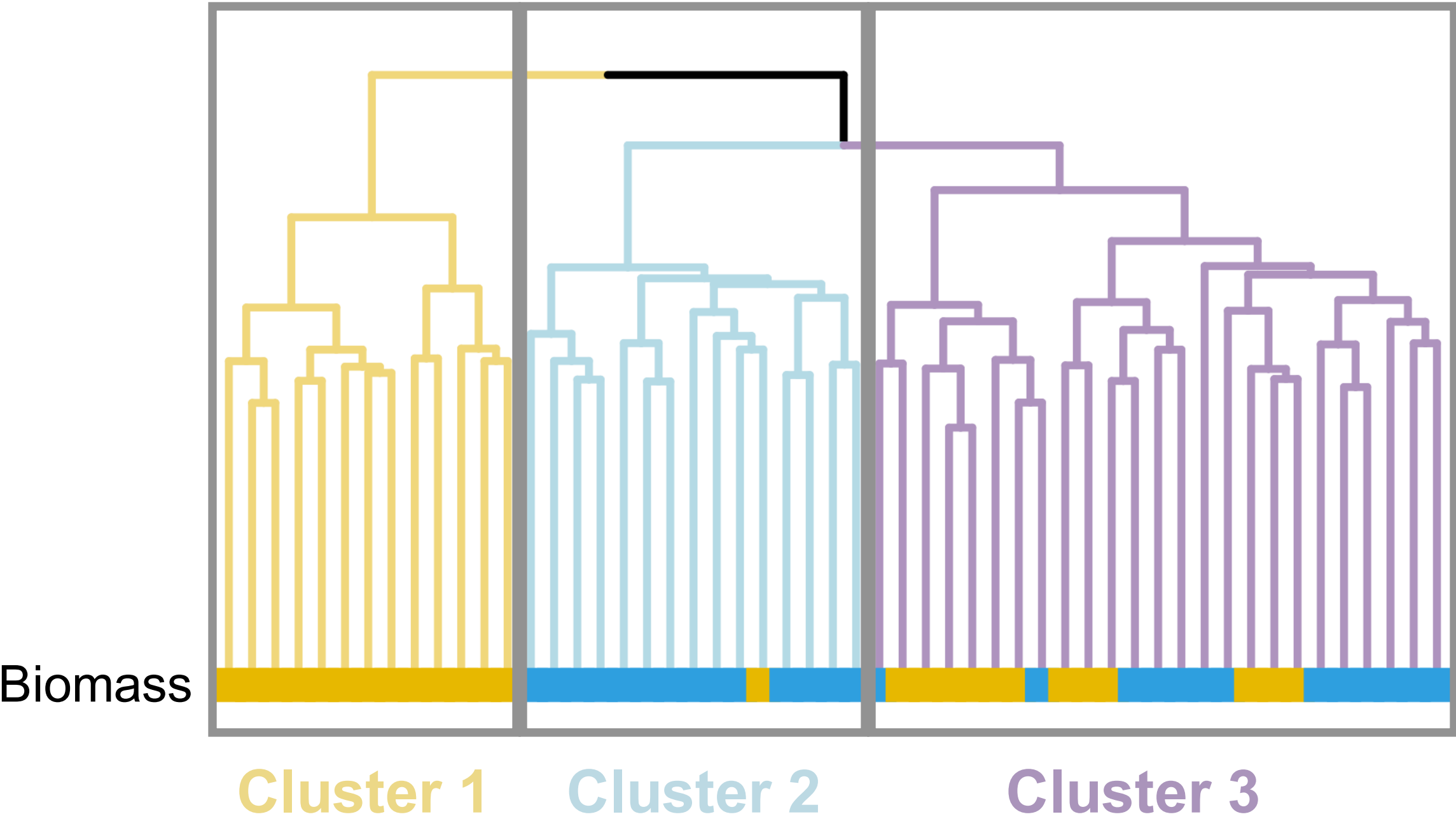


Sex associated with gut microbiome variance



Clustering of gut microbiome correspond to bacterial biomass

Clustering of gut microbiome from all individuals

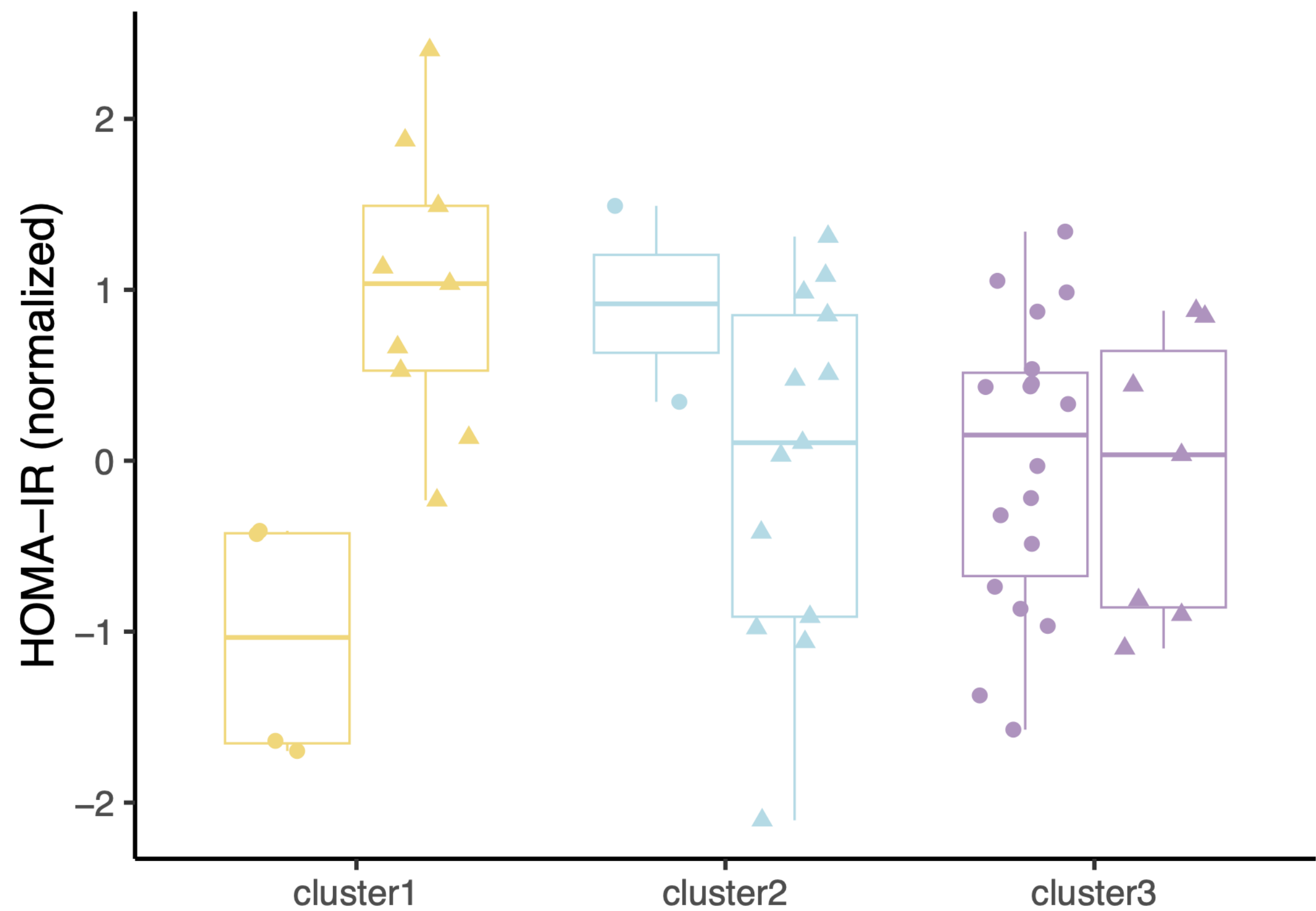


Difference in cardiometabolic measures across microbiome clusters & sex

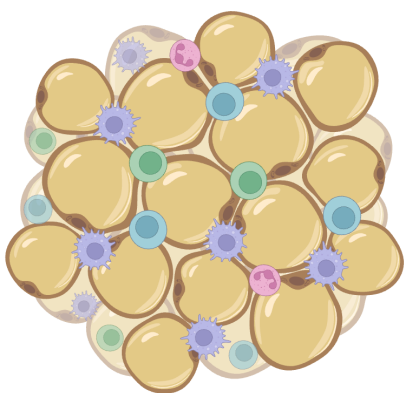
Insulin resistance



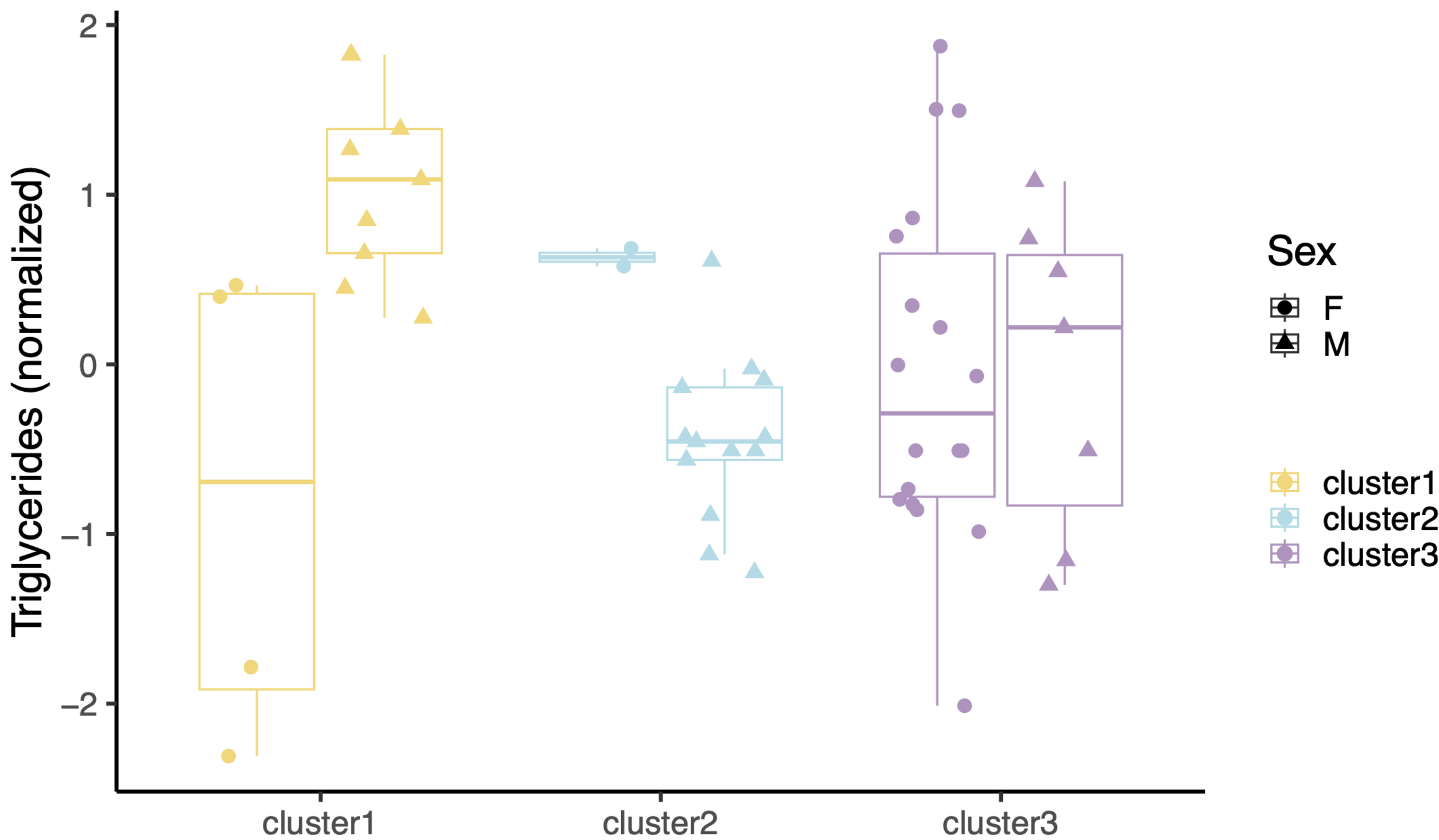
Sex $p=0.0005$,
Cluster 2 $p = 0.024$,
Cluster 3 $p = 0.045$,
Sex-Cluster 2 interaction $p = 0.002$,
Sex-Cluster 3 interaction $p = 0.004$



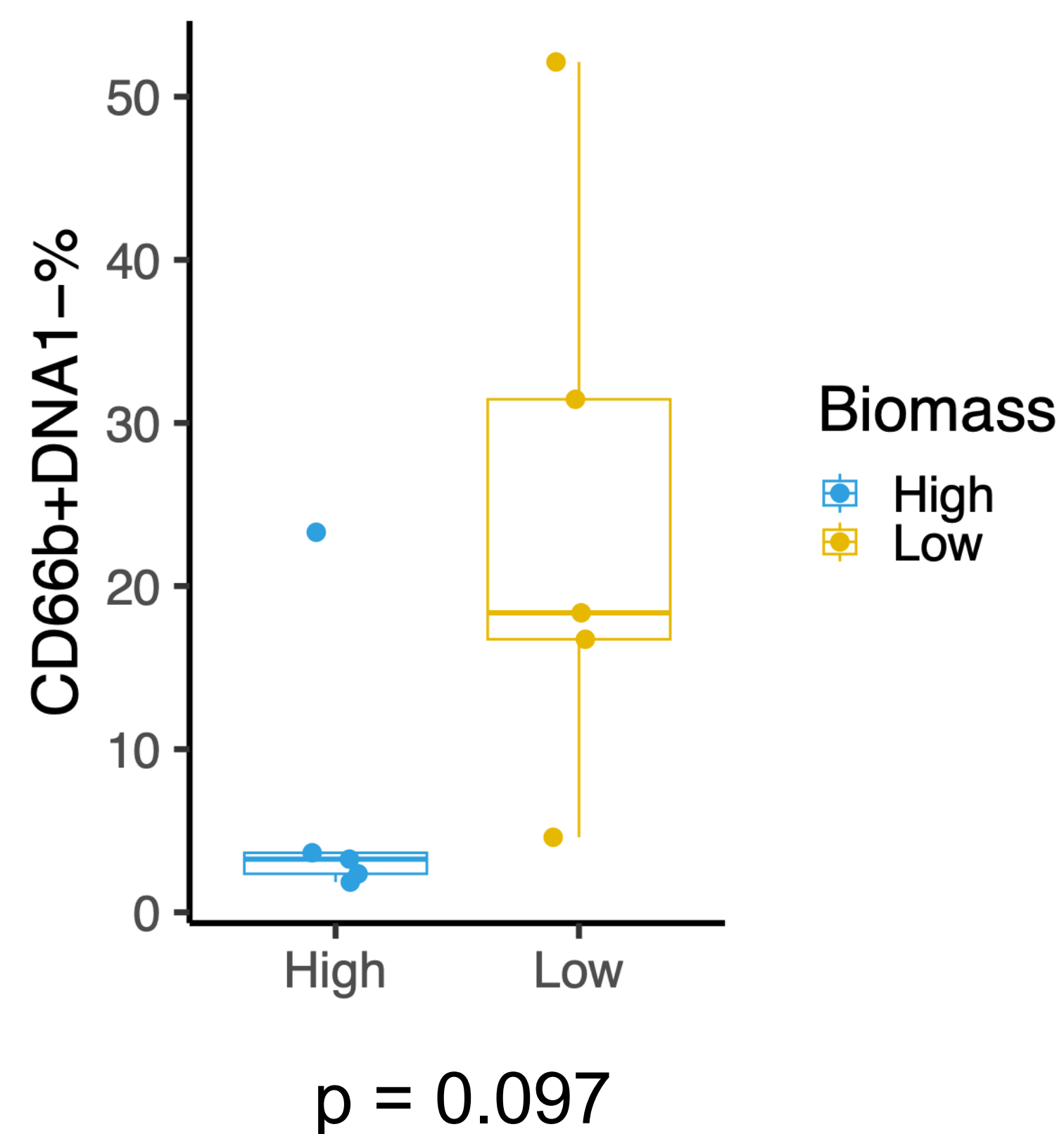
Plasma triglycerides



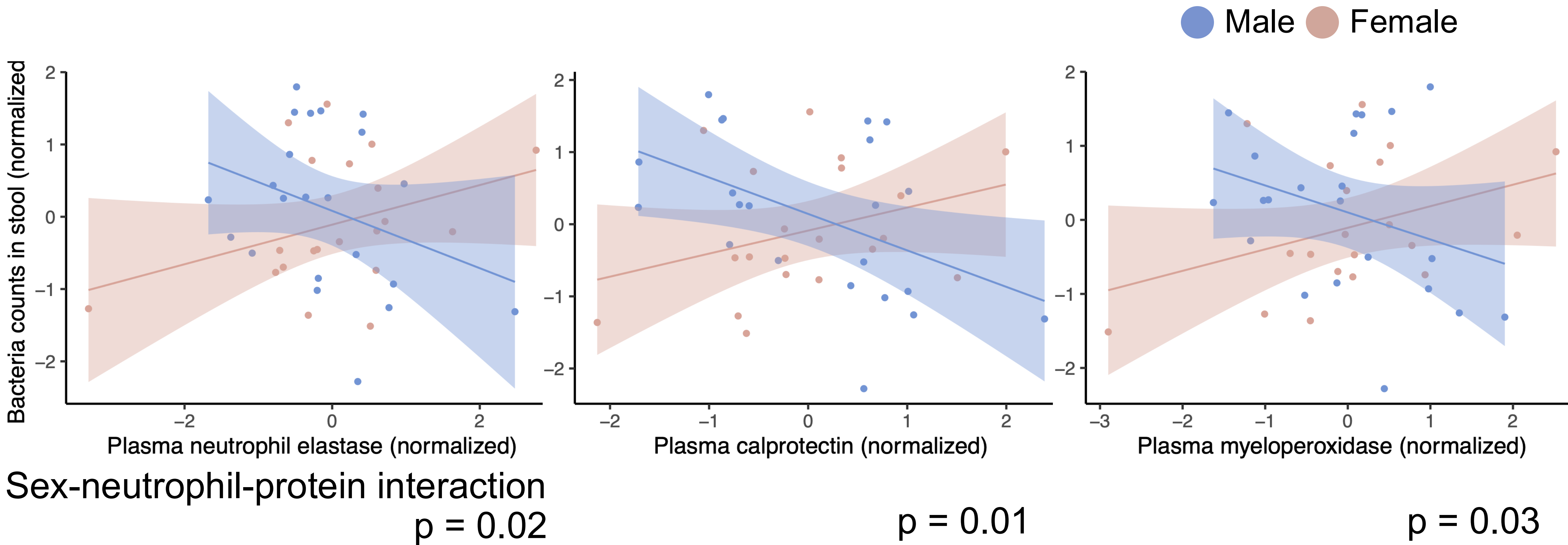
Sex $p=0.0005$,
Cluster 2 $p = 0.030$,
Cluster 3 $p = 0.079$,
Sex-Cluster 2 interaction $p = 0.0007$,
Sex-Cluster 3 interaction $p = 0.004$



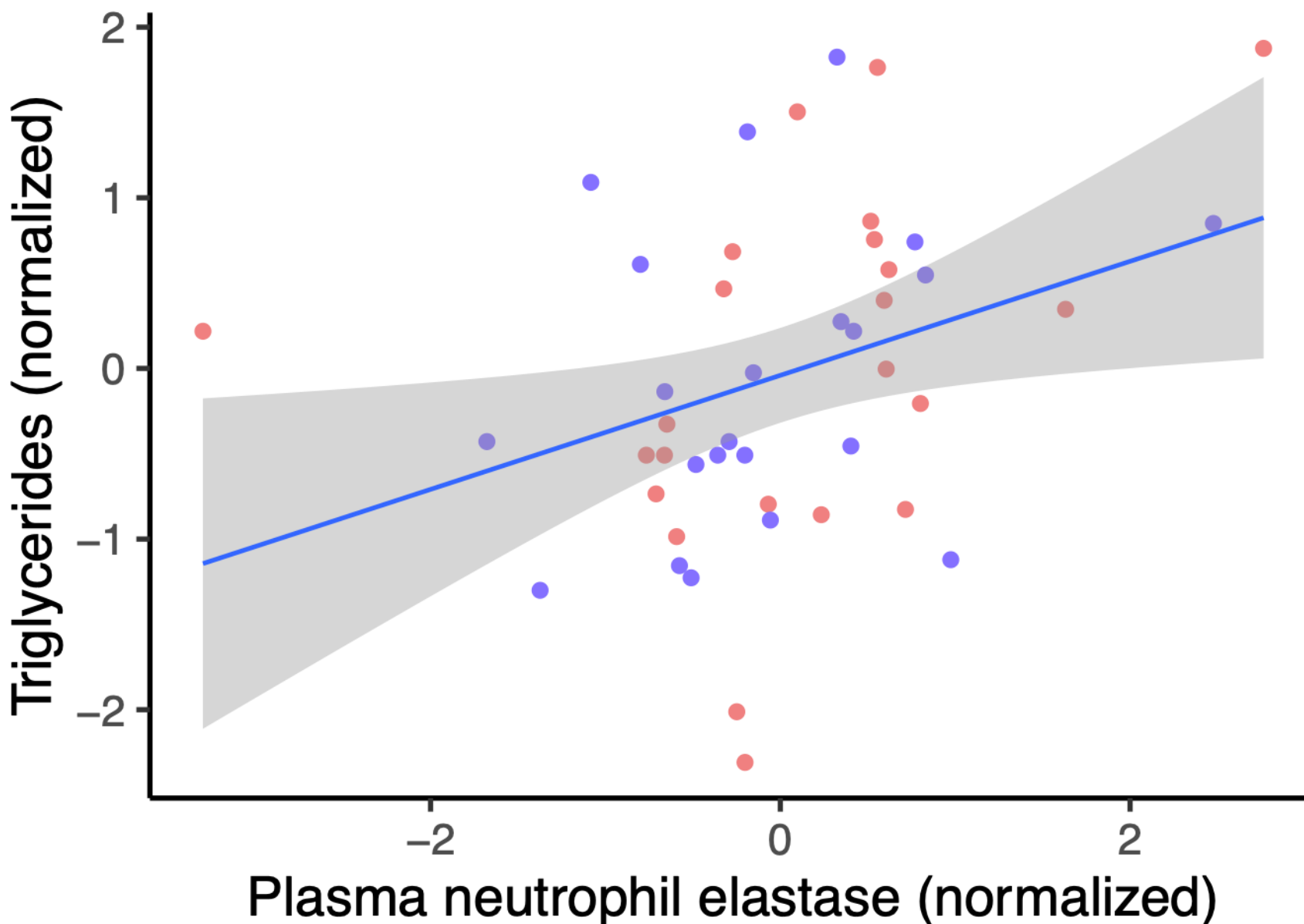
Neutrophil activities associated with bacterial biomass



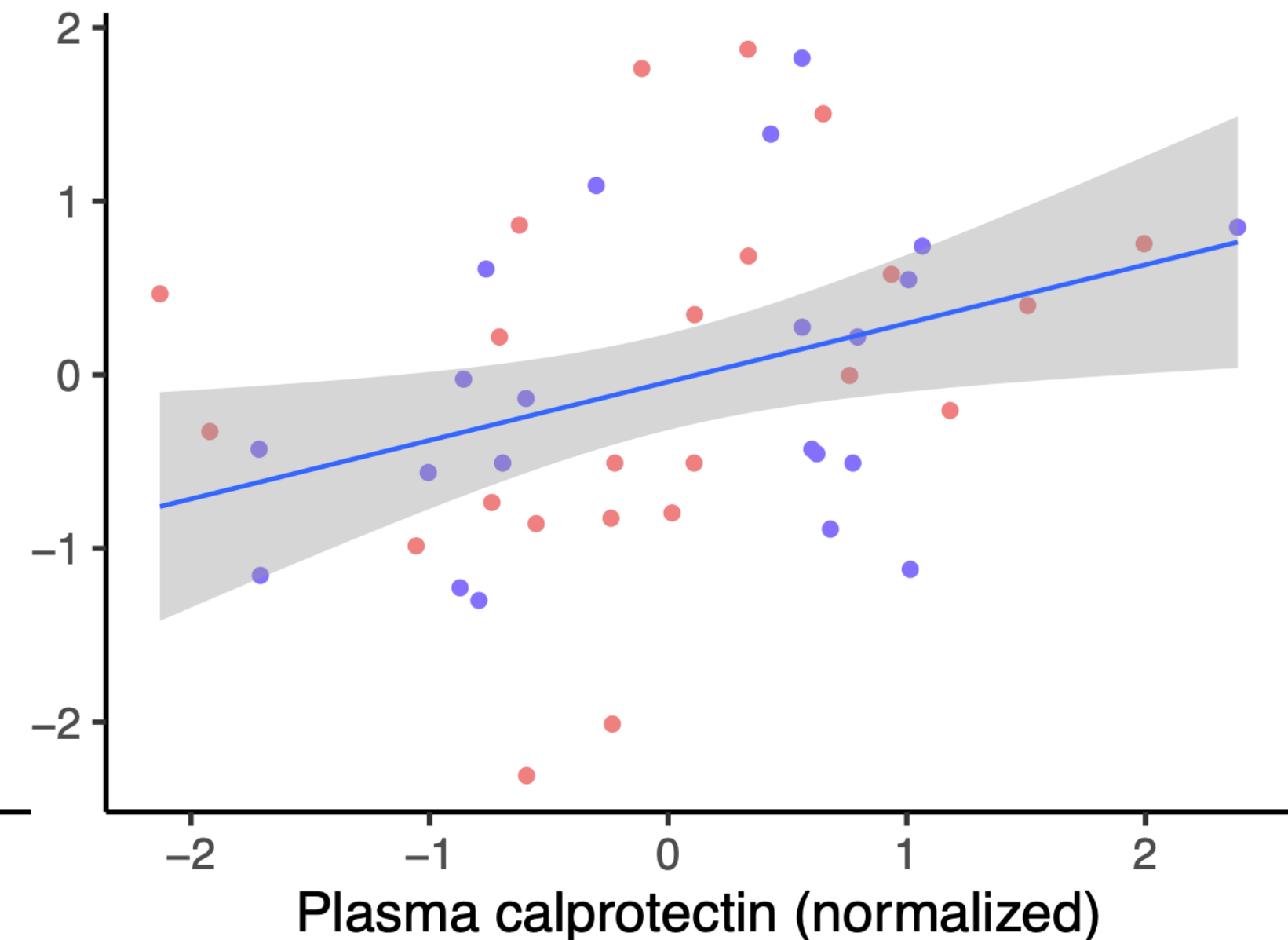
Neutrophil proteins associated with bacterial biomass in a sex-specific manner



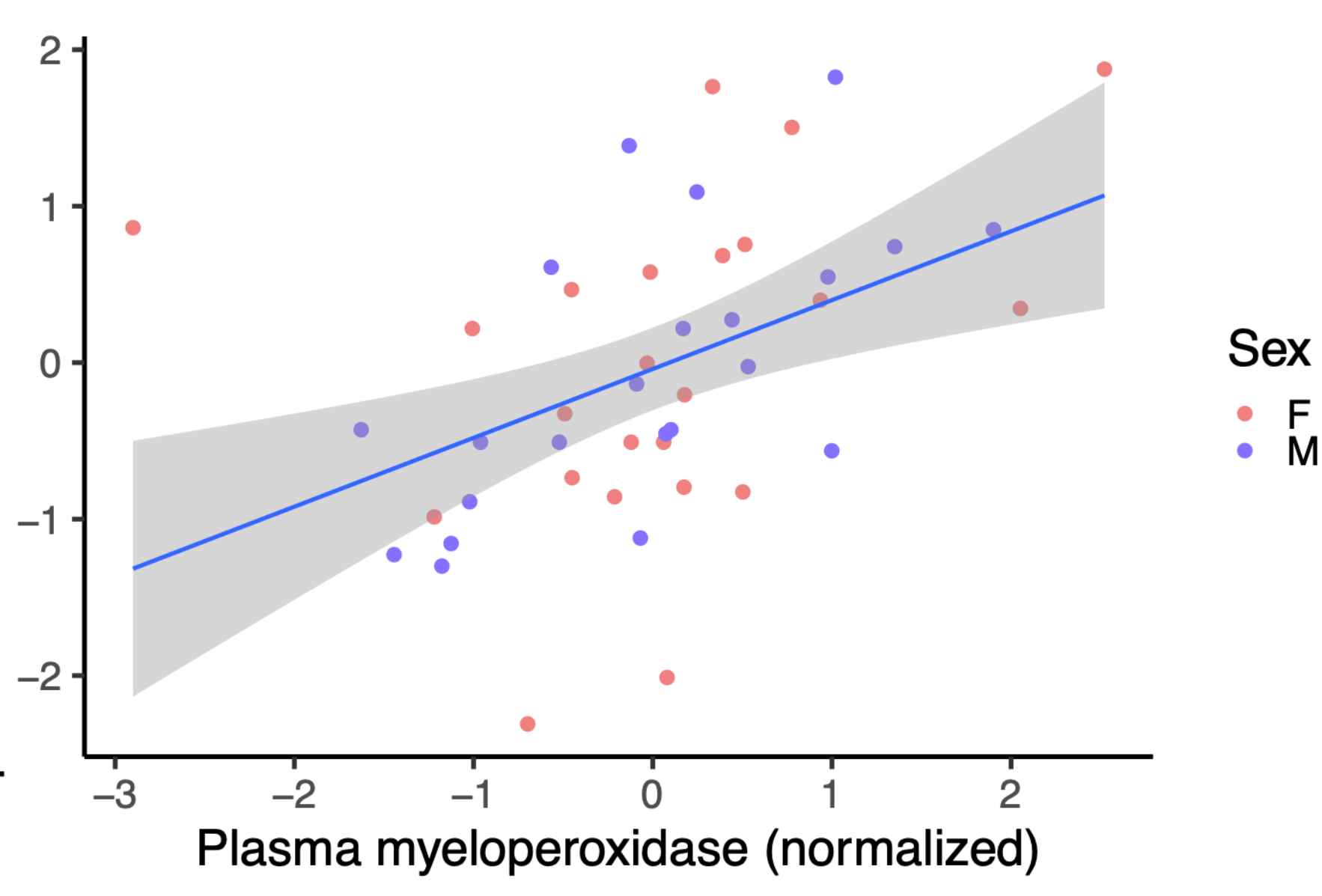
Neutrophil activities associated with higher triglycerides in both sexes



Neutrophil protein $p = 0.02$



$p = 0.02$



$p = 0.004$

Conclusions

- Multi-log order variation in bacterial biomass present in an obese adolescent cohort
- Absolute bacterial biomass revealed significant difference in gut microbiome composition within the cohort, and association of gut microbiota cardiometabolic measures
- Association of bacterial biomass to cardiometabolic dysfunction and immune markers are sex-specific. In male participants, lower bacteria biomass associated with greater metabolic dysregulation & elevated systemic inflammation attributed to neutrophil activities

Acknowledgements

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