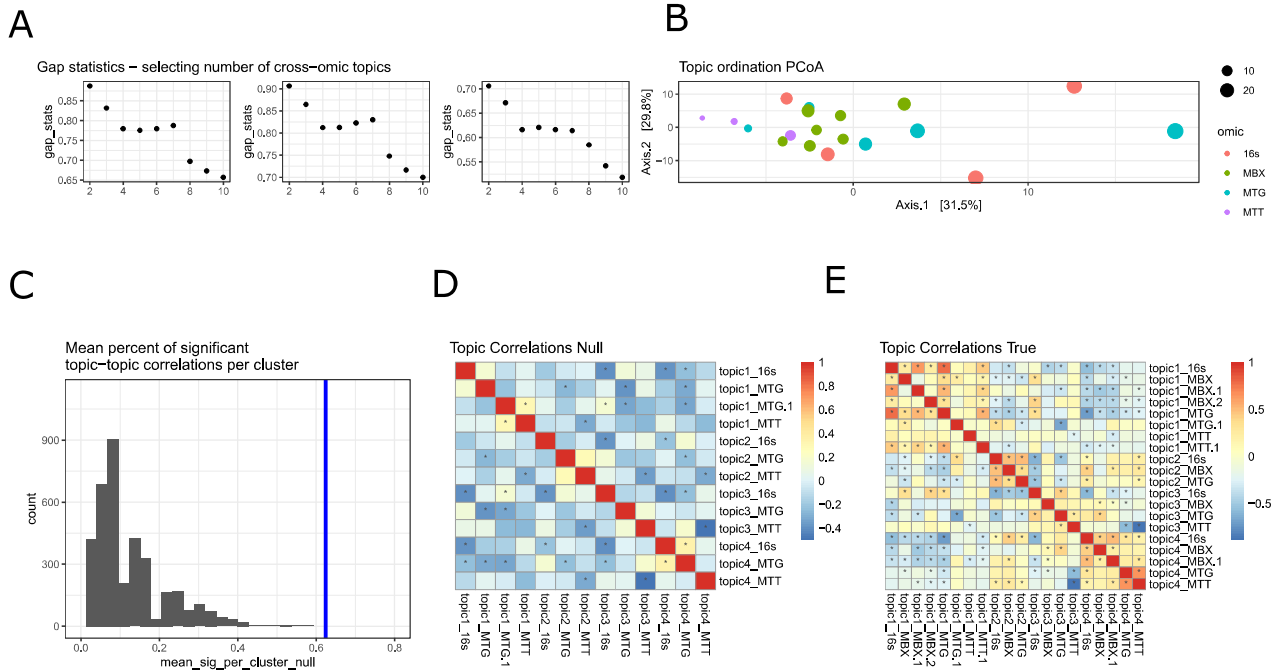
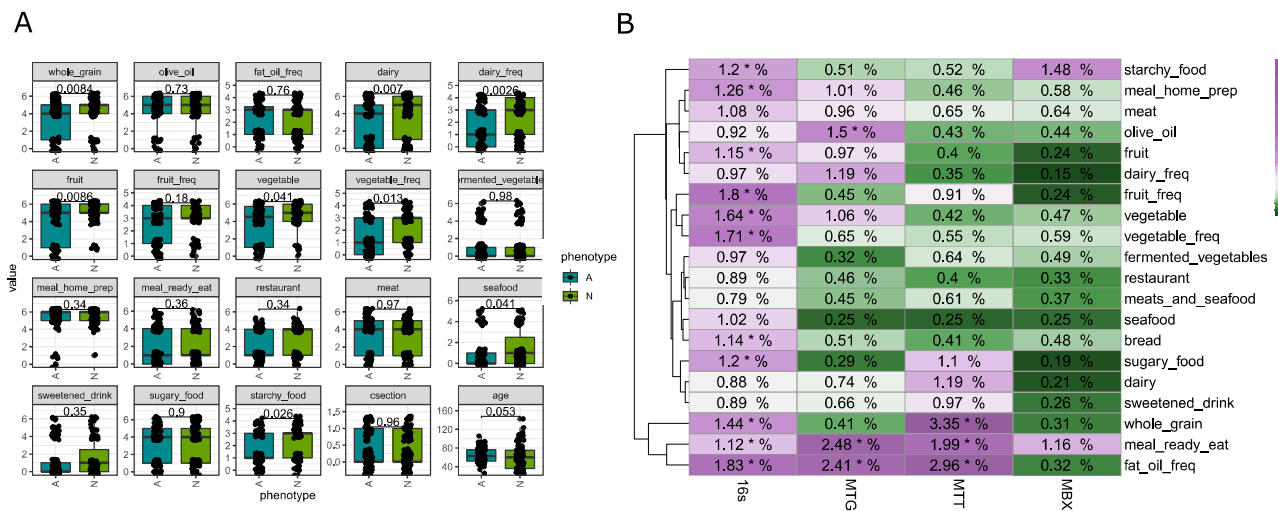


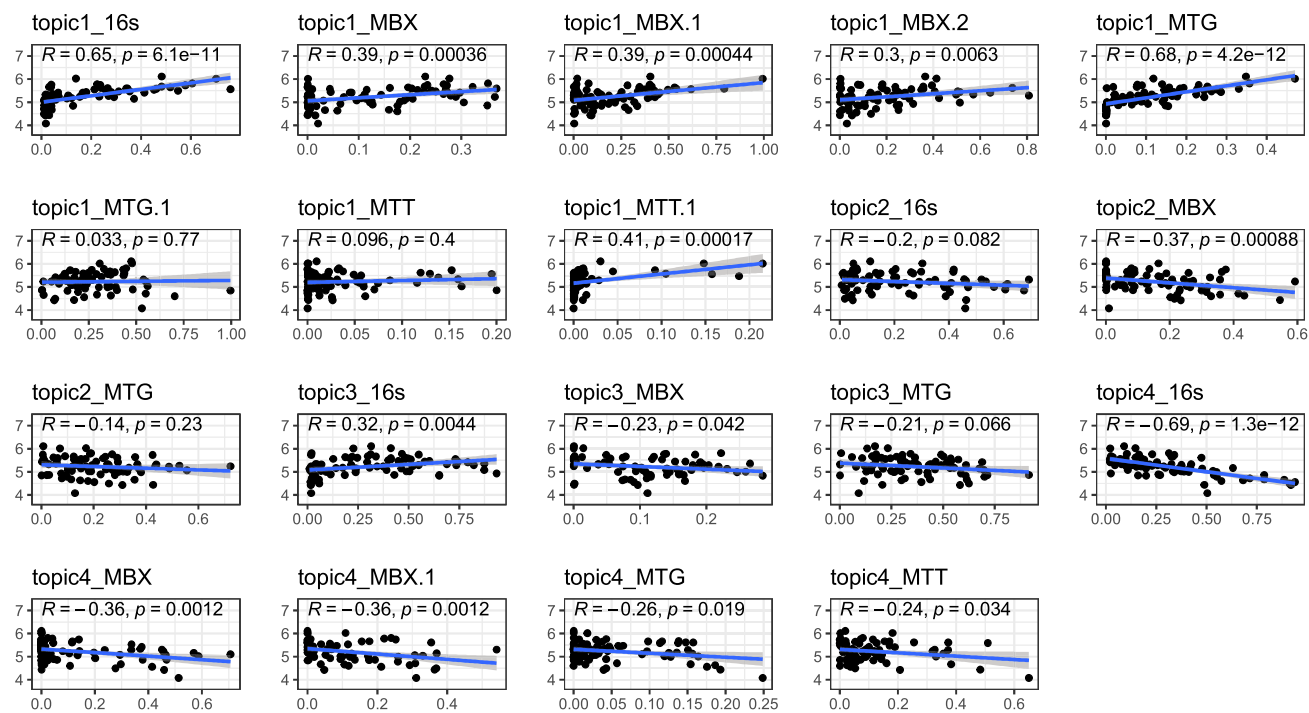


Supplementary Figure 1 Cross-omic topic evaluation

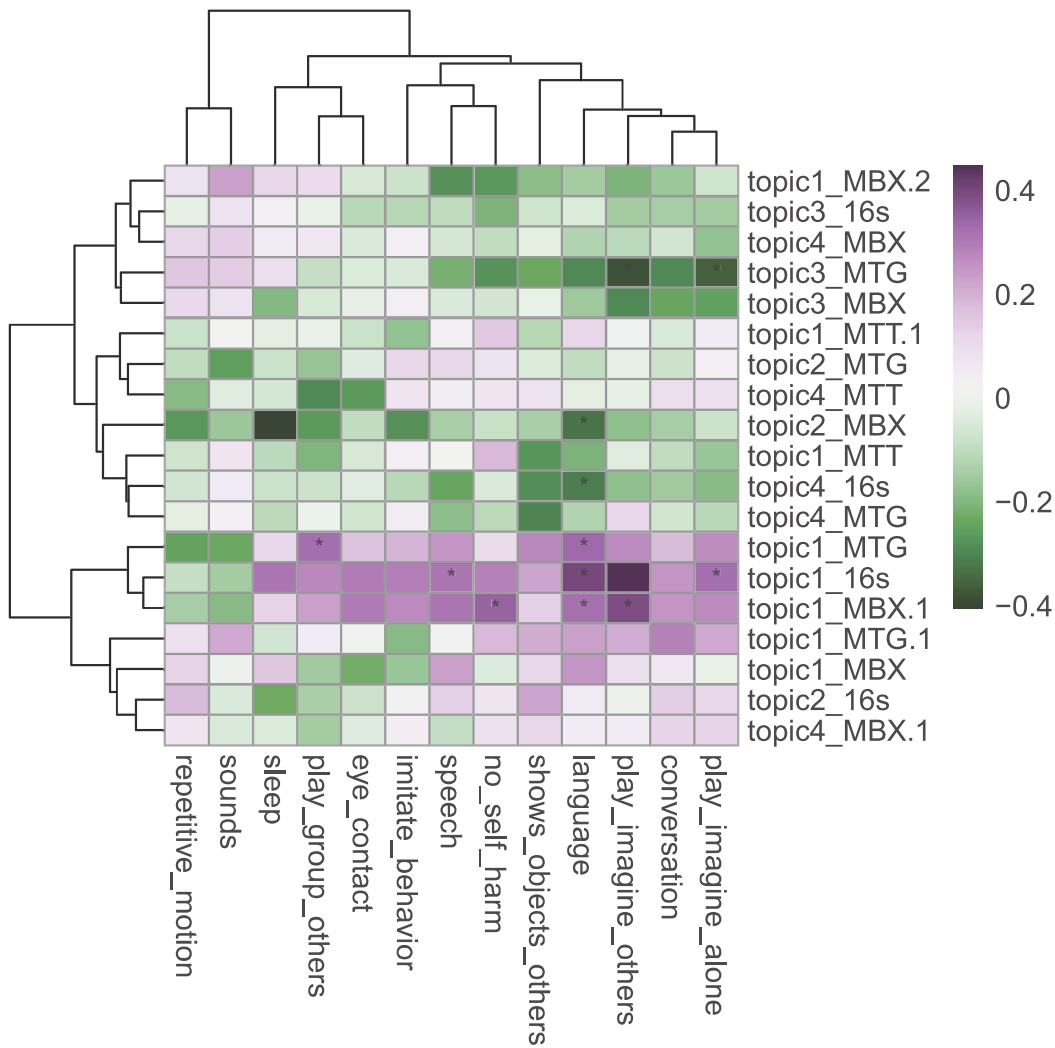
Gap statistics (within/between cluster distances) were calculated using manhattan, euclidean, and inverse correlation distance metrics for 2-10 cross-omic topics. The elbow method was used to select 4 cross-omic topics (A). Topics were visualized by PCoA on the topic distribution across samples using manhattan distance. Size of points represents the total weight attributed to a topic across all samples (how common the topic is) and color represents omic of origin (B). Topic-topic correlations within a cross-omic topic cluster are significantly more correlated than would be expected by random chance. The mean number of significant (spearman correlation $p < 0.05$) topic-topic correlations within a cluster using null simulated data (15 permutations) is between 0 and 0.4. The true number mean of significant correlations is over 0.6 (C). Topic-Topic correlation matrix using null simulated data (D). Topic-Topic correlation matrix using true data (E). Cells are colored by spearman correlation coefficient and star indicates significant ($p < 0.05$). Multiple topics from the same omic dataset may be in the same cross-omic topic, denoted by “.1” or “.2”, etc.



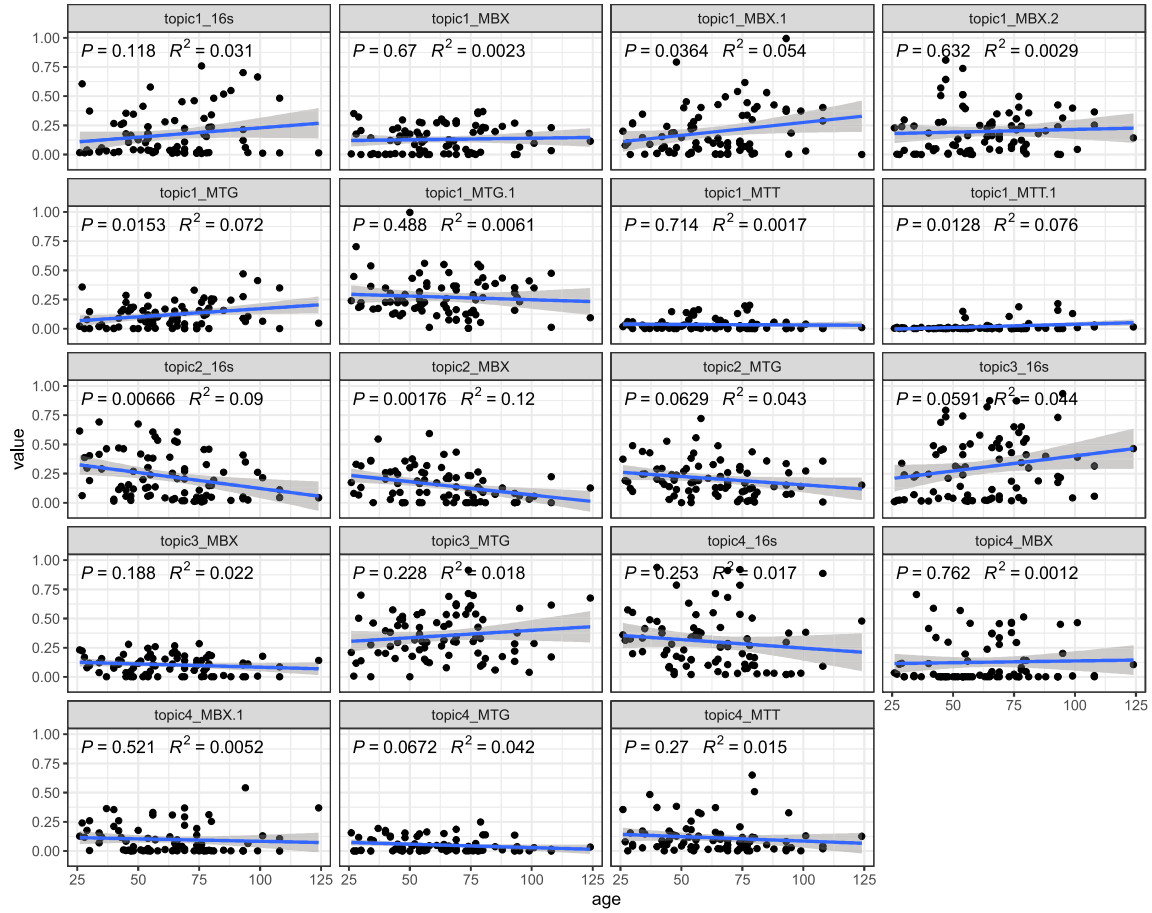
Supplementary Figure 2 Dietary and lifestyle characteristics between autistic and typically developing children compared using a Wilcoxon rank sum test (A). Association between individual dietary variables and omic data (B). Omic data was normalized using relative log expression (RLE), numbers in the cell are R^2 values as percents, and a star indicates a significant association by a permanova test



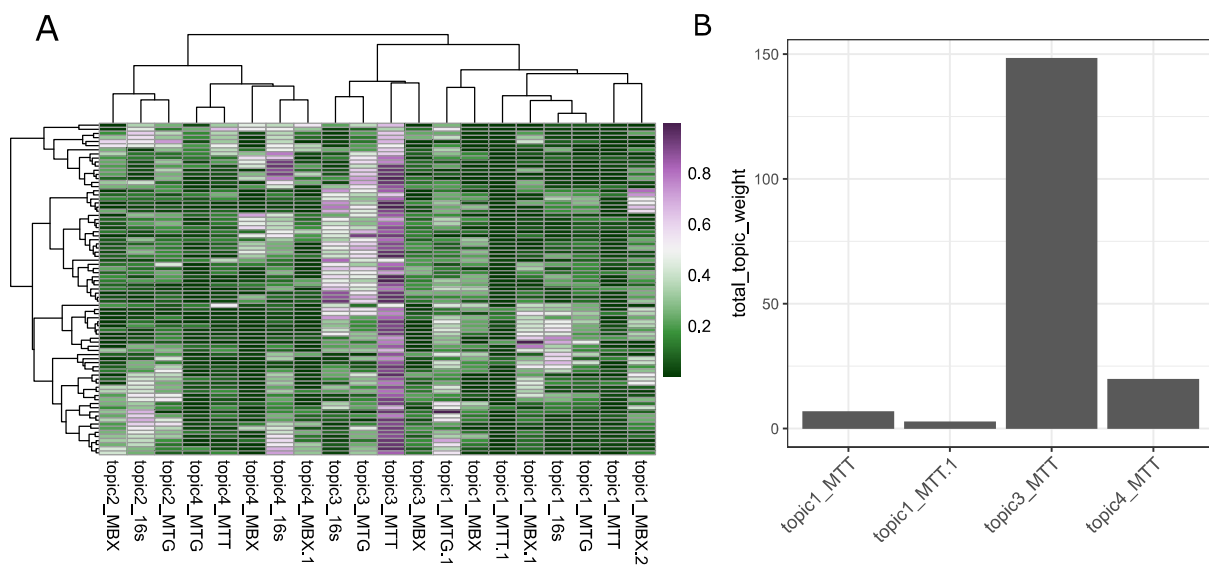
Supplementary Figure 3 Correlation between topic values and 16S Shannon diversity. Lines and confidence intervals are linear regression fits, while R and p values are spearman correlations.



Supplementary Figure 4 Correlations between topics and specific Autism-related behaviors, as determined by parent-completed questionnaire. Questionnaire was only completed for autistic children. Cells are colored by the spearman correlation test R^2 value, and a star indicates significant ($p < 0.05$).

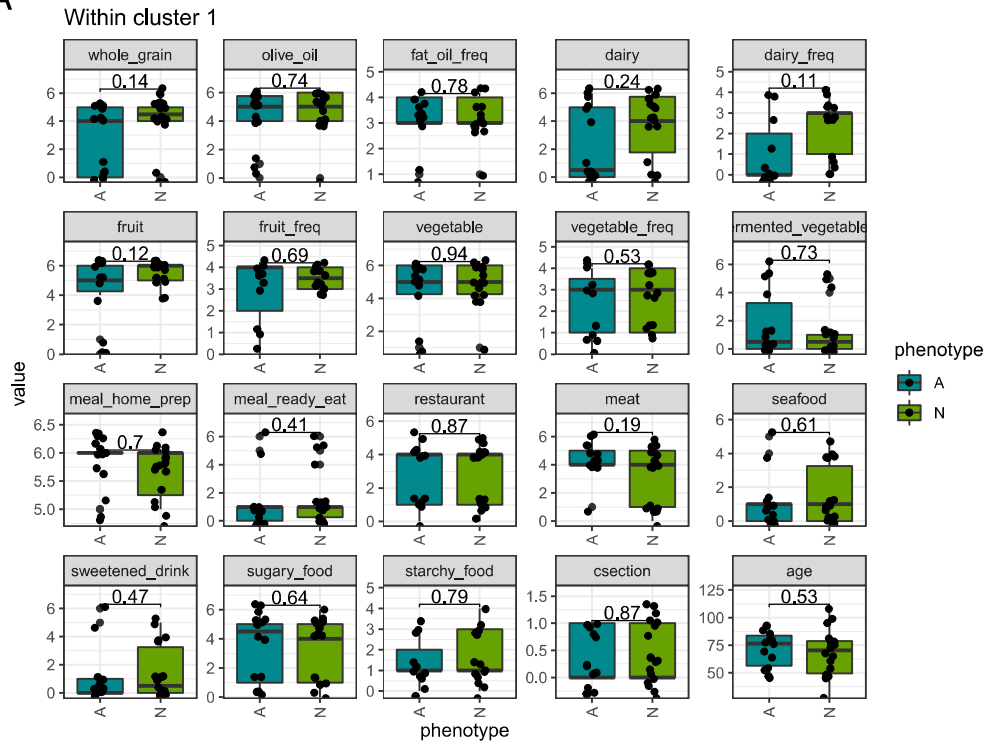


Supplementary Figure 5 Spearman correlation between age (in months) and topic values. Topic 2 most consistently correlates inversely with age, and Topic 1 correlates with age in some omics.

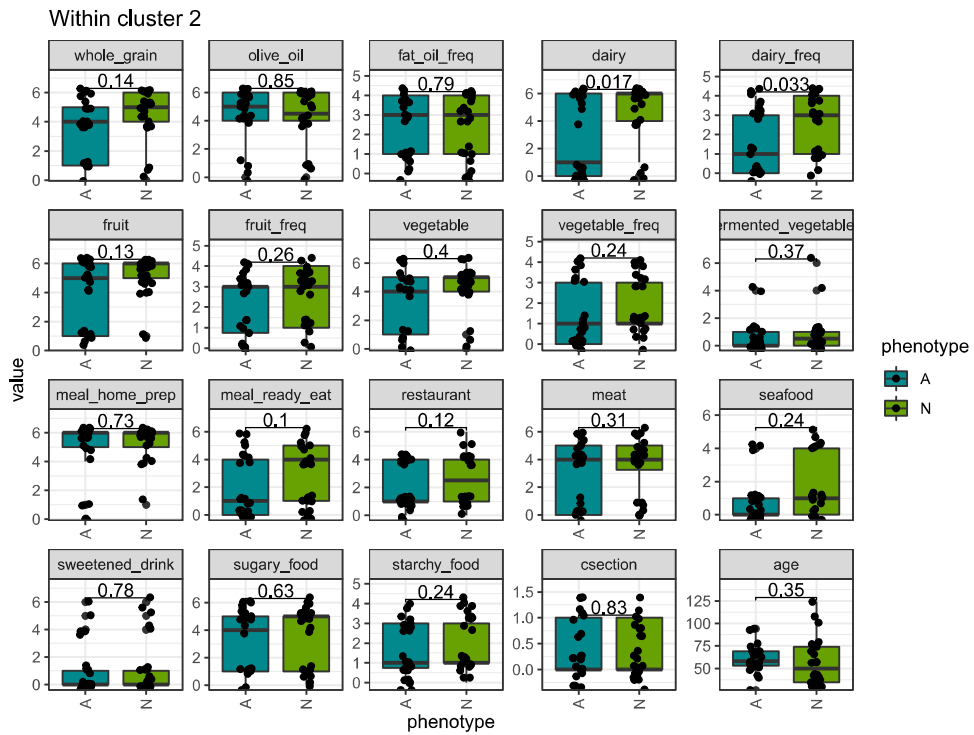


Supplementary Figure 6 MTT topic 3 was removed due to failure to low variability across samples and excessively high topic attribution across samples. MTT topic 3 has high topic values across nearly all samples, and far exceeds all other topic value magnitudes (A). MTT topic 3 has orders of magnitude higher topic attribution across samples compared with other MTT topics (B).

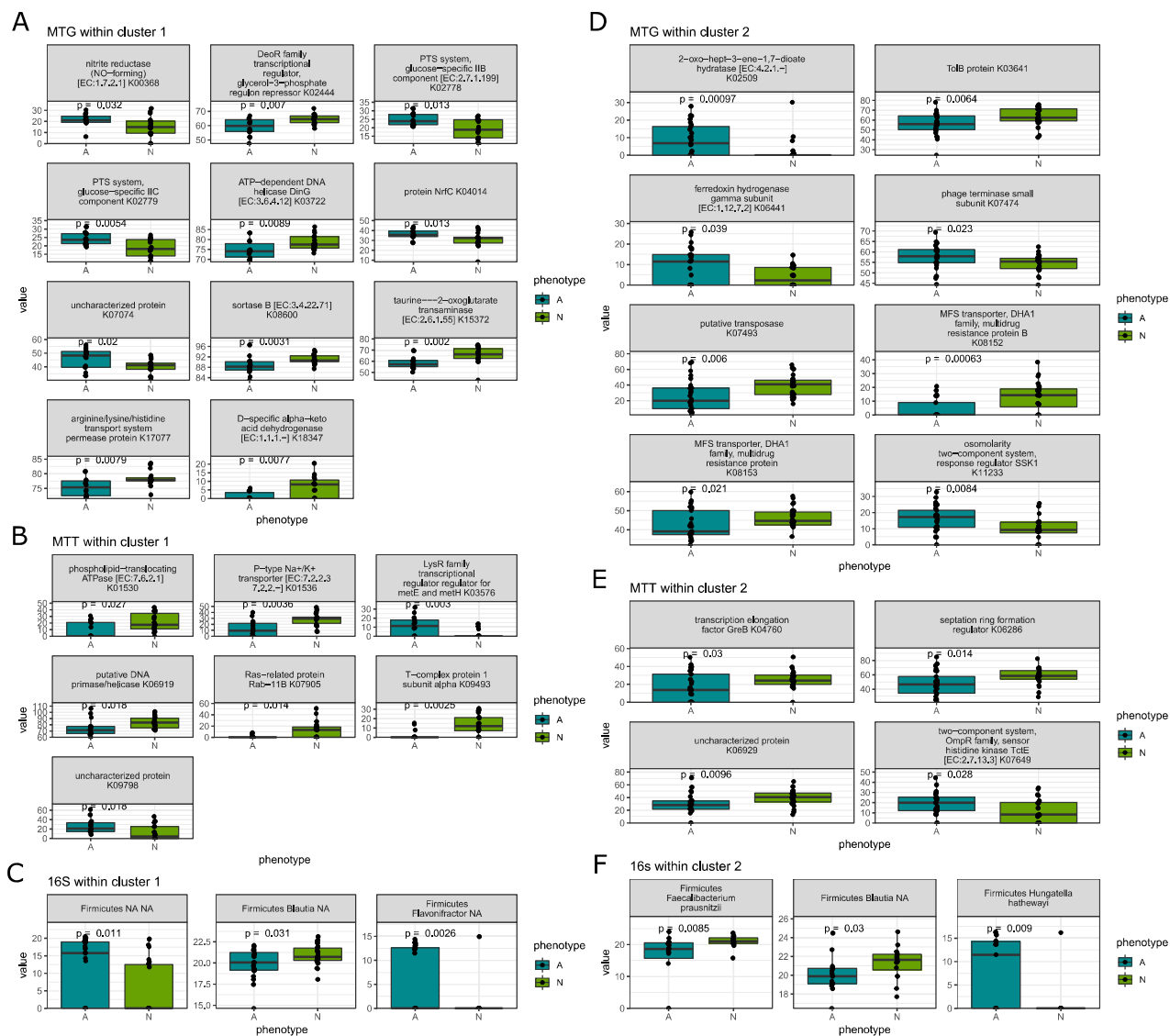
A



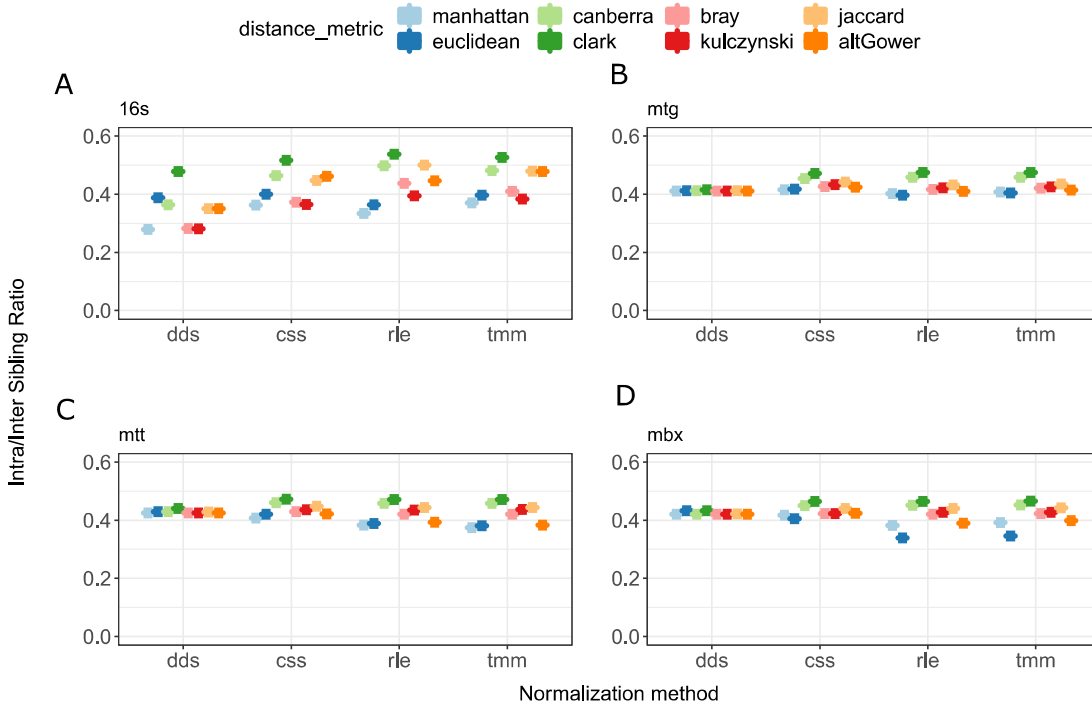
B



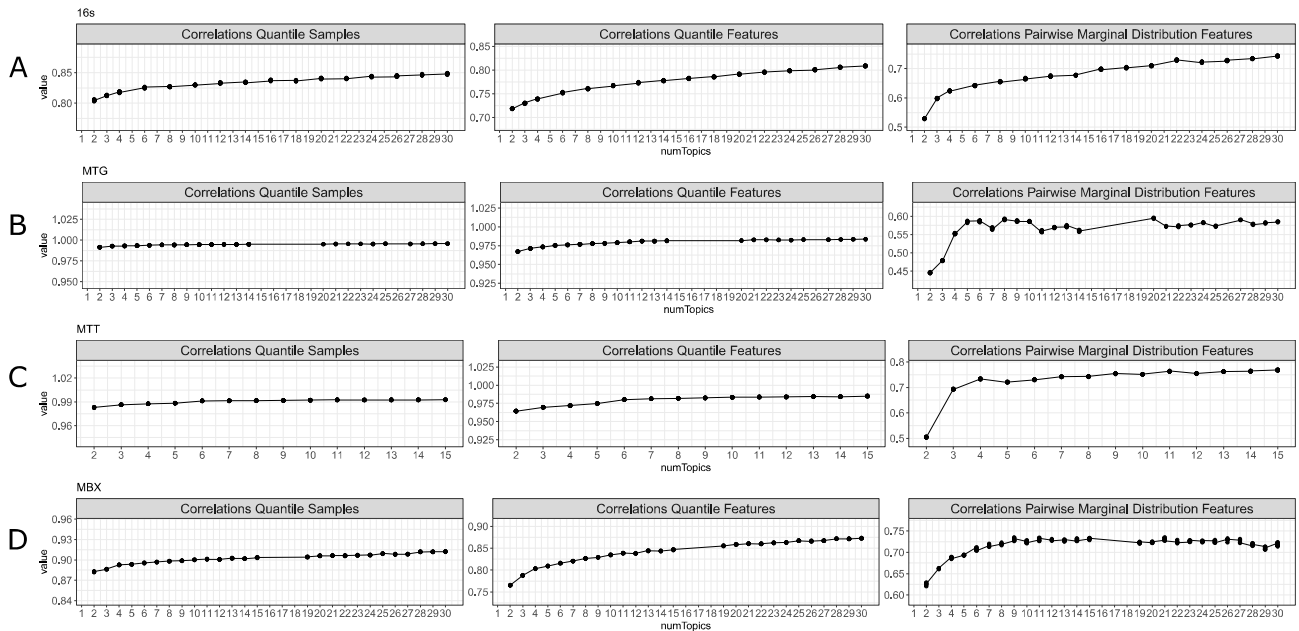
Supplementary Figure 7 Wilcoxon rank sum test on dietary variable differences between Autistic and typically developing participants per sample cluster.



Supplementary Figure 8 Differential analysis of MTG, MTT, and 16S features between autistic and typically developing children within sample clusters as determined by topics. Within cluster 1, MTG features (A), MTT features (B), 16S features (C). Within cluster 2, MTG features (D), MTT features (E), 16s features (F). Features are first filtered using the Boruta package, and then p values are reported using Wilcox rank sum test.



Supplementary Figure 9 Choosing a normalization method per omic datasets. Normalization methods that minimized the distance between siblings vs. the distance between all unrelated samples there selected. When differences in normalization performance were negligible, the majority method was used. 16S DeSeq2 (A), MTG RLE (B), MTT RLE (C), MBX RLE (D)



Supplementary Figure 10 Selecting number of topics per model. To evaluate model fit, sample data was simulated using each model, and simulated and true data were compared using three metrics: correlation of sample quantiles, correlation of feature quantiles, and marginal pairwise distribution of features. Number of topics was selected using the elbow method. The final number of topics selected were 4 for 16s data (A), 5 for MTG data (B), 4 for MTT data (C), and 7 for MBX data (D).