SUPPLEMENTARY MATERIAL

Probiotic-mediated modulation of gut microbiome in students exposed to academic stress: a randomized controlled trial

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Supplementary Figure 5. Effect of *L. rhamnosus* CNCM I-3690 on overall gut microbiome composition (genus level) by 16S rRNA gene amplicon sequencing with exclusion of subjects with baseline calprotectin >100 ug/g. **A.** Change of alpha-diversity indices for each subject versus baseline for the placebo and the probiotic group (Wilcoxon test) **B.** Linear mixed-effect models of the effect of the probiotic in the diversity; the model takes as the baseline the “Placebo” and the “Visit 1” as the reference levels for Group and Visit variables. The coefficients and interaction terms are the differences from the baselines. **C.** Within-subject Bray-Curtis dissimilarity to baseline in both groups with lower distance indicating less changes (Wilcoxon test).

Supplementary Figure 6. Topological metrics of microbial interaction networks. **A**. Differences across timepoints in Degree centrality (number of direct connections per node), Closeness centrality (how easily a node can reach all other nodes), Betweenness centrality (how often a node lies on the shortest path between other nodes, indicating its role as a connector), and Eigenvector centrality (a measure of a node's influence based on the connectivity of its neighbors). Significant differences between the placebo and probiotic groups at each timepoint were assessed using the Wilcoxon test. **B**. Centrality values of *Lactobacillus rhamnosus* over time in the probiotic arm. *L. rhamnosus* shows an increase in centrality between timepoints 2 and 3, suggesting a growing influence within the microbial network.

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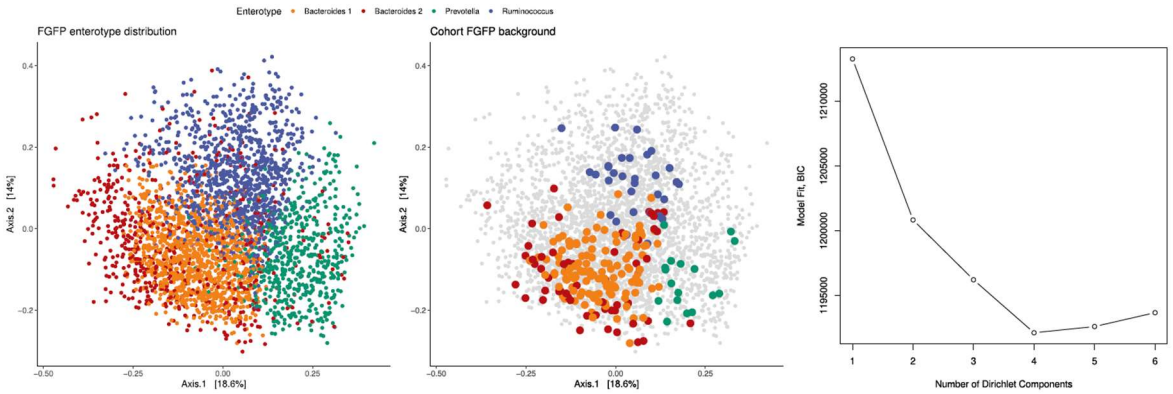
Supplementary Table 11 ANOVA model comparisons of the delta microbiome confounders and clinical variables

Supplementary Table 12 Delta association between species/GMM and host variables



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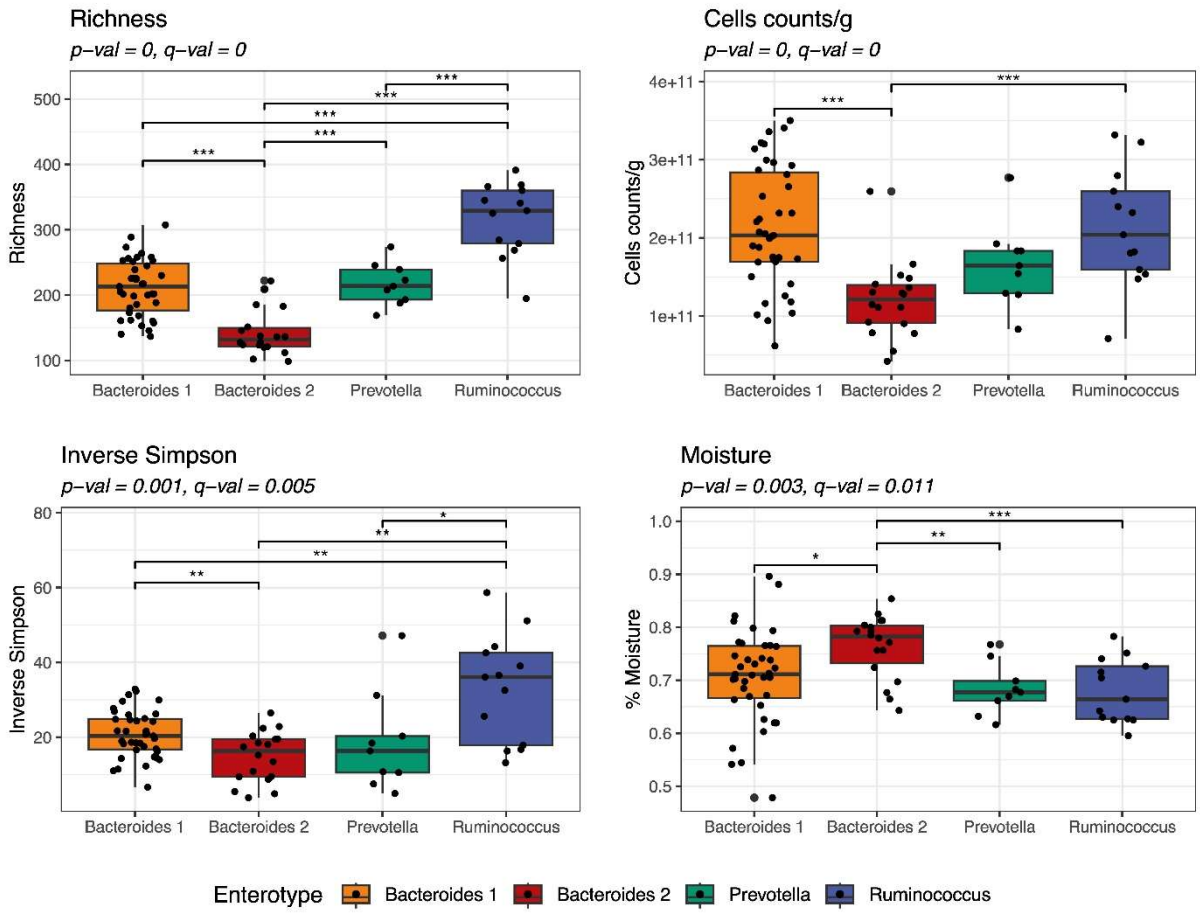

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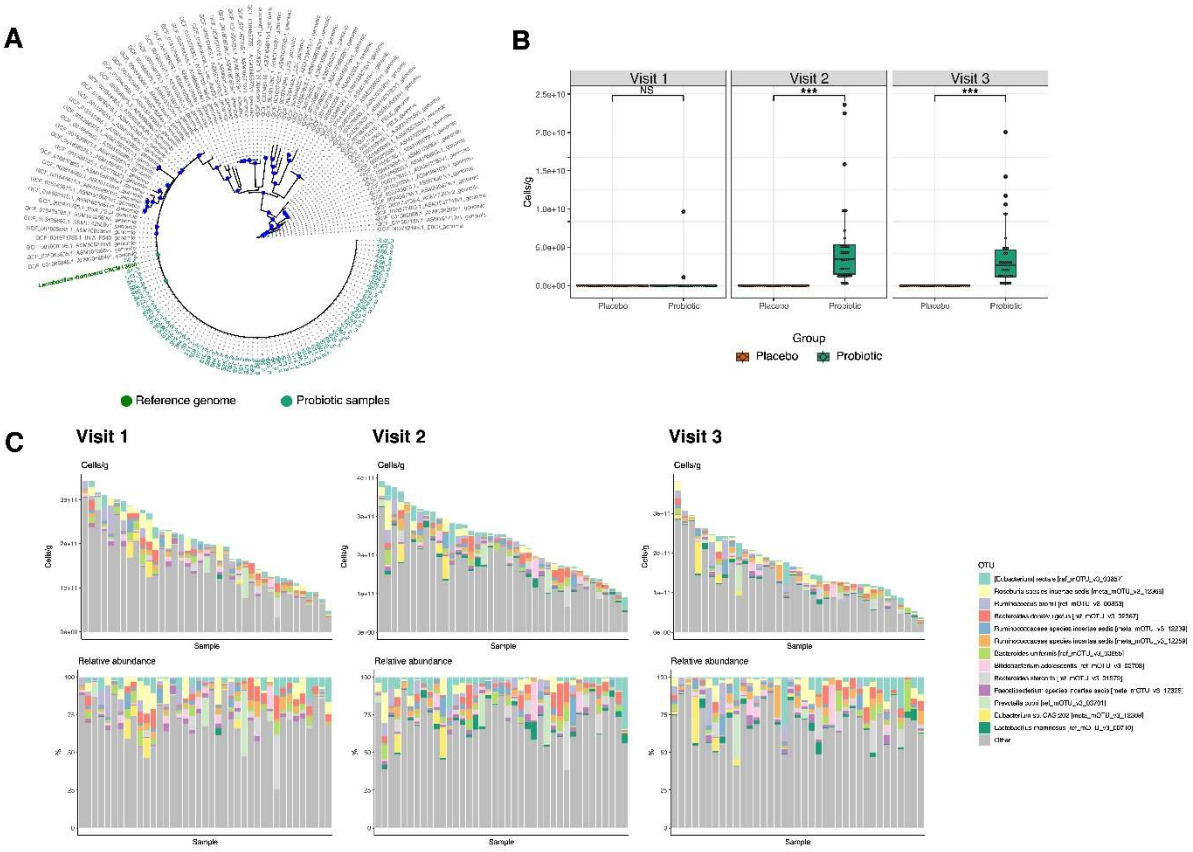

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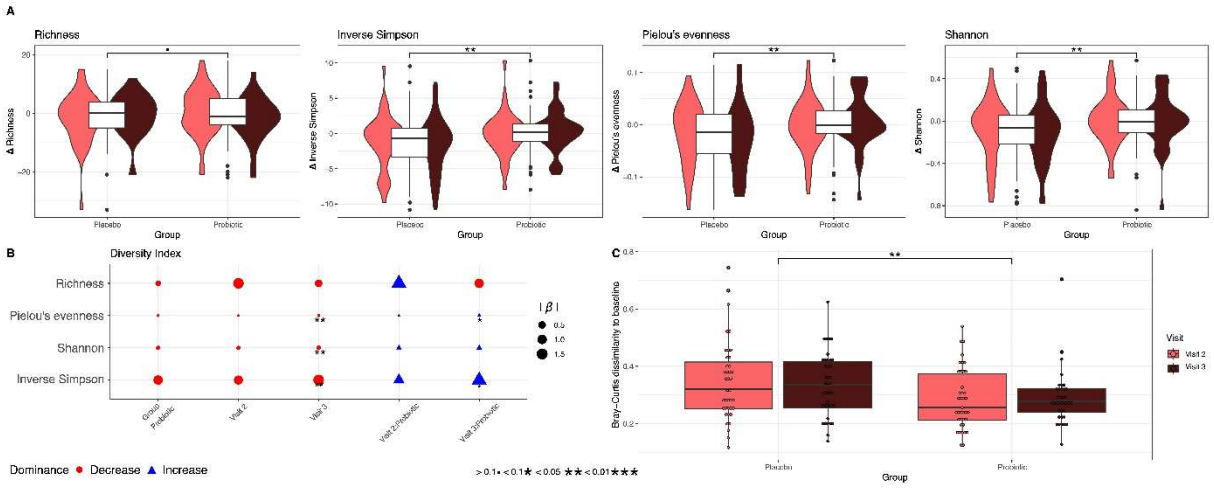

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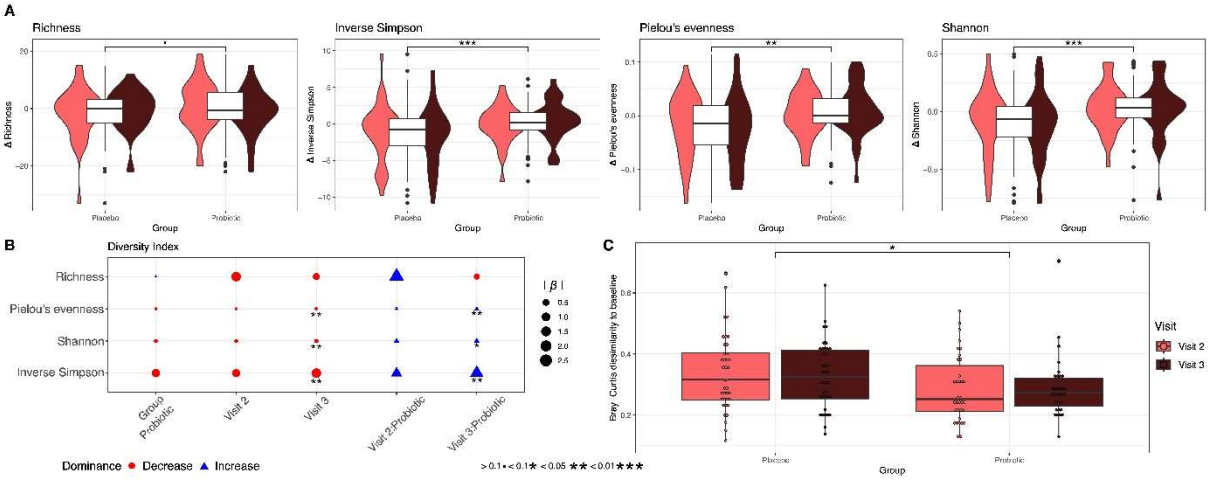

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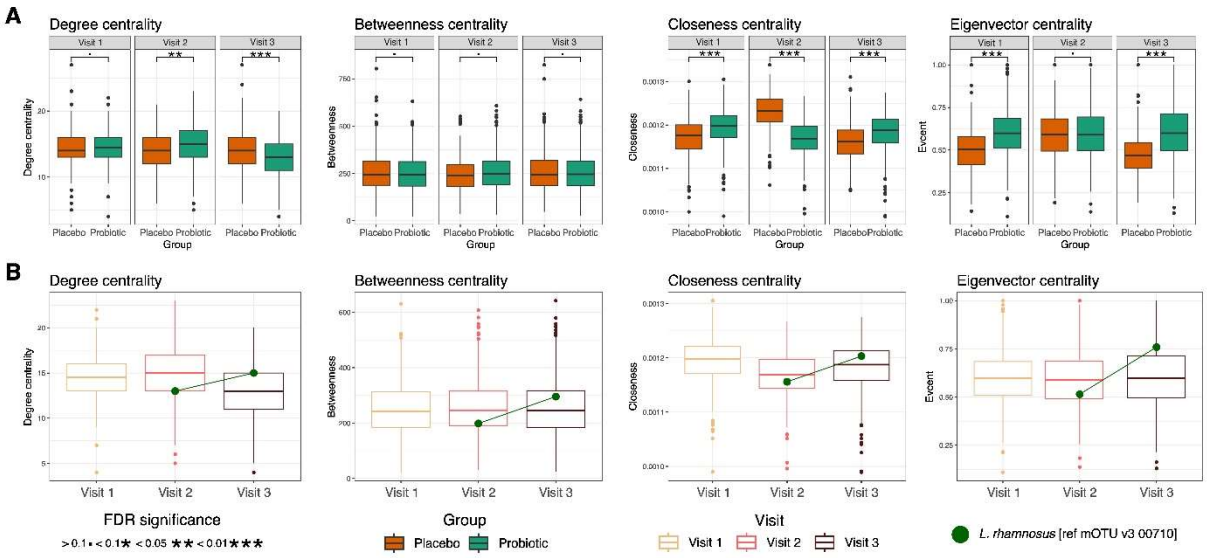

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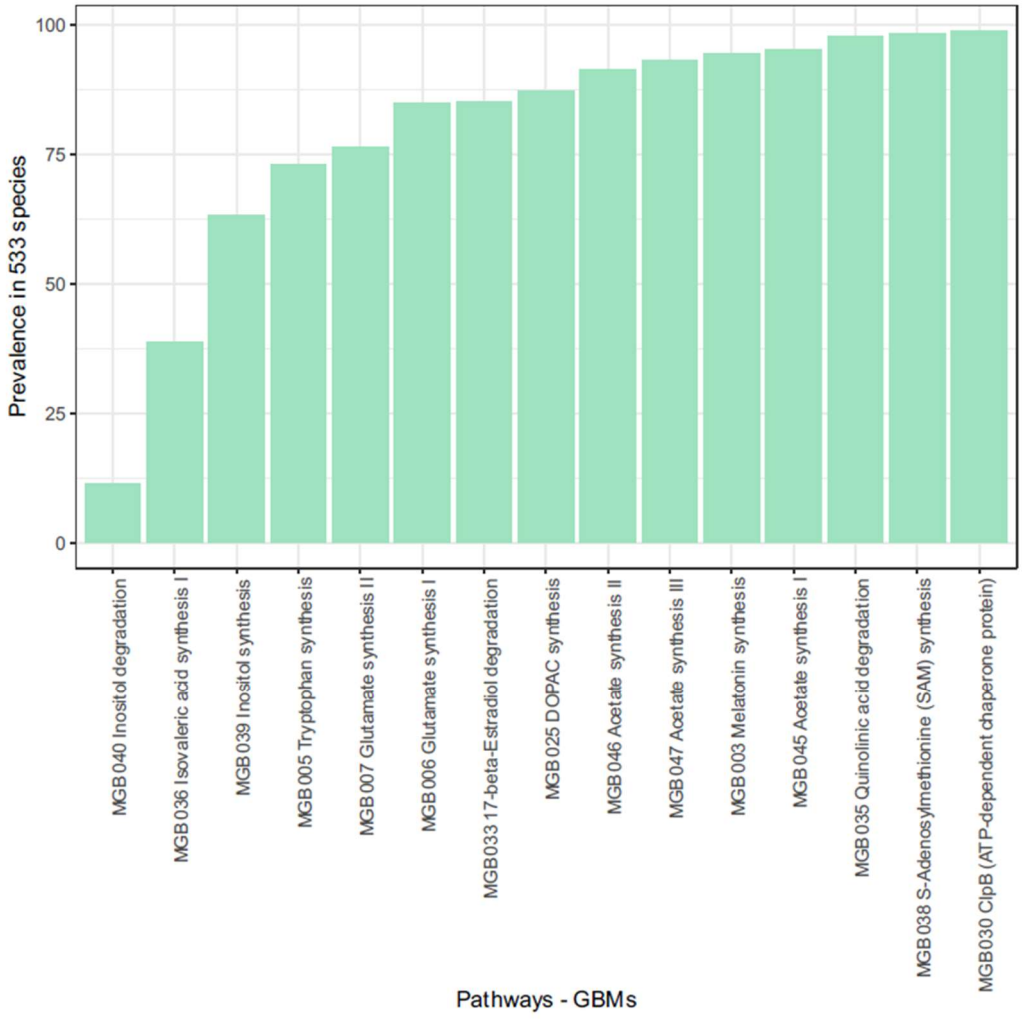

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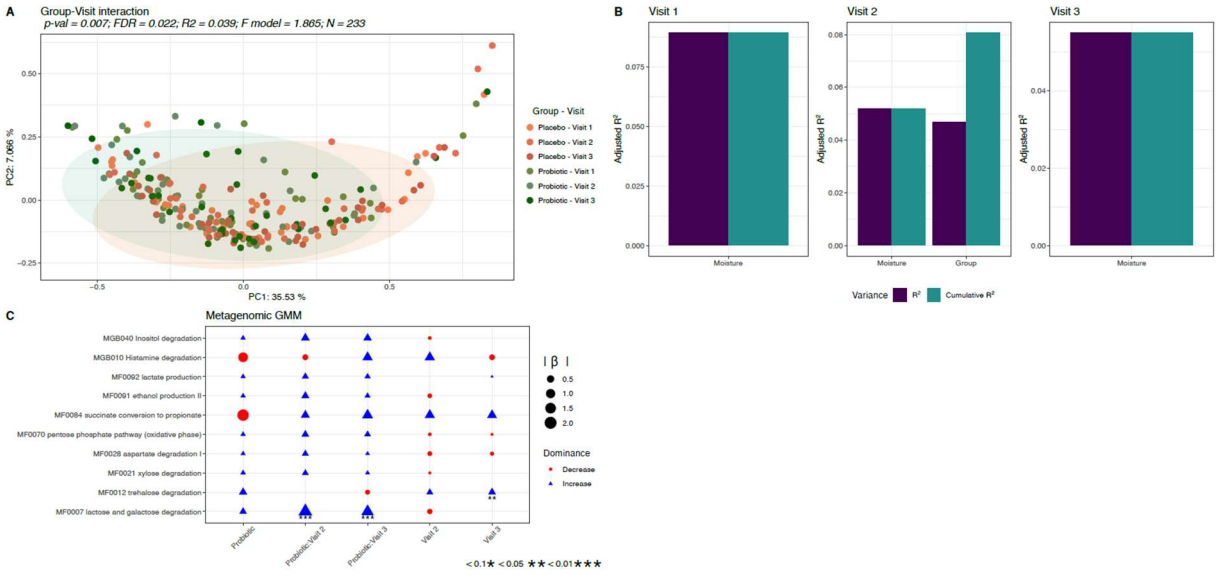

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