Personalized Gut Mucosal Colonization Resistance to Empiric Probiotics Is Associated with Unique Host and Microbiome Features (*Cell*, September 6, 2018)

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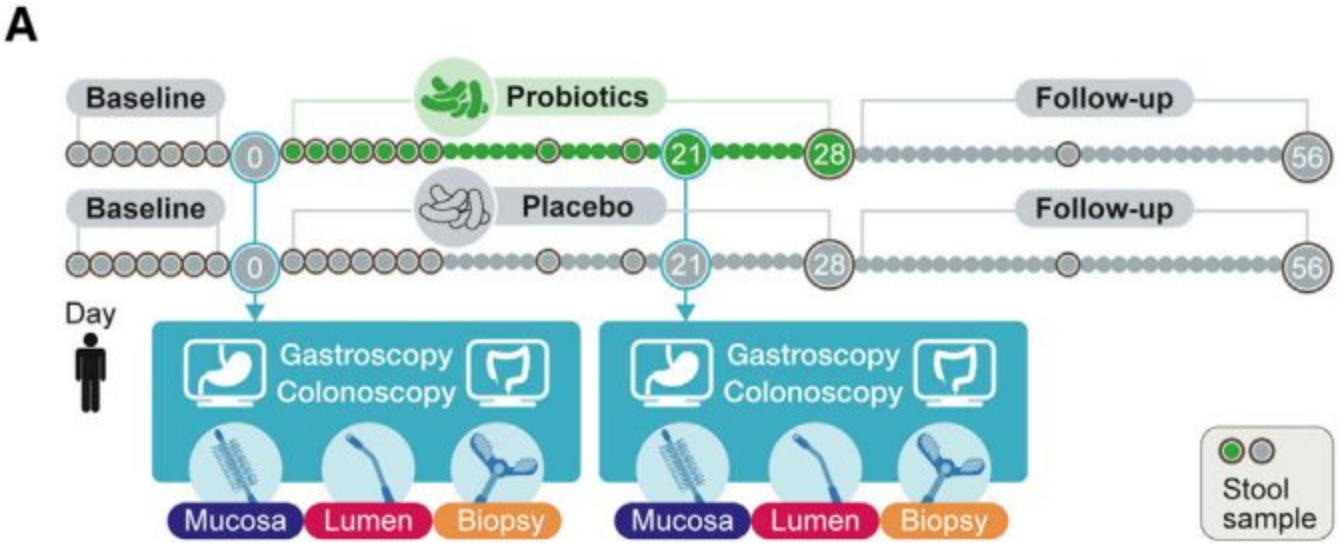
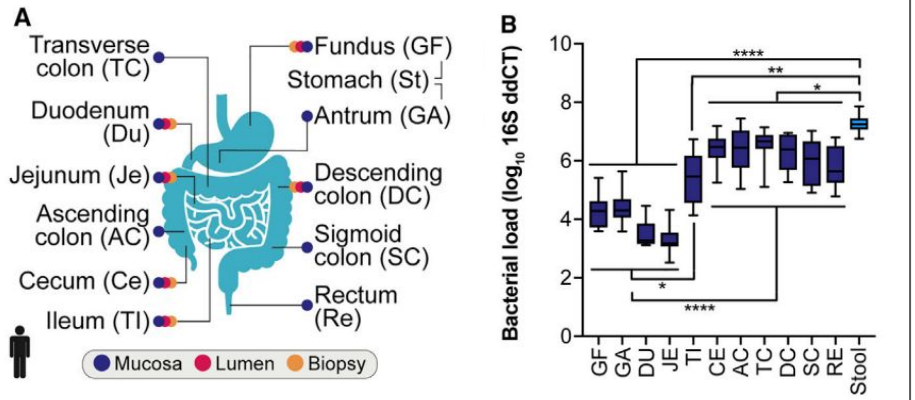
Motivation: Evidence of **probiotic gut mucosal colonization efficacy** remains sparse and controversial.
Experiment: Assessed murine and 15 human GI microbiome (2 endoscopy procedures along with fecal sampling) before and after 11-strain probiotic treatment.
Conclusions:

1. Metagenomically characterized the murine and human mucosal-associated gastrointestinal microbiome and found it to **only partially correlate with stool microbiome**.
2. A sequential invasive multi-omics measurement at baseline and during consumption of an 11-strain probiotic combination or placebo **demonstrated that probiotics remain viable upon gastrointestinal passage.**
3. Probiotics induced a **transient, individualized impact** on mucosal community structure and gut transcriptome. Collectively, empiric probiotics supplementation may be limited in universally and persistently impacting the gut mucosa, **meriting development of new personalized probiotic approaches**.

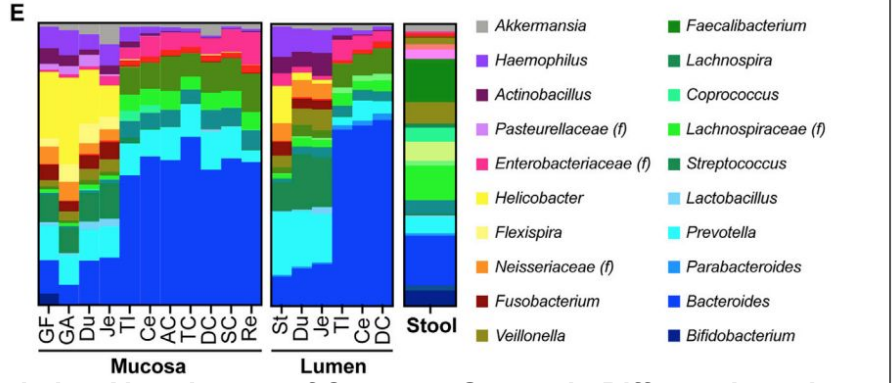
Experimental Outline in Humans



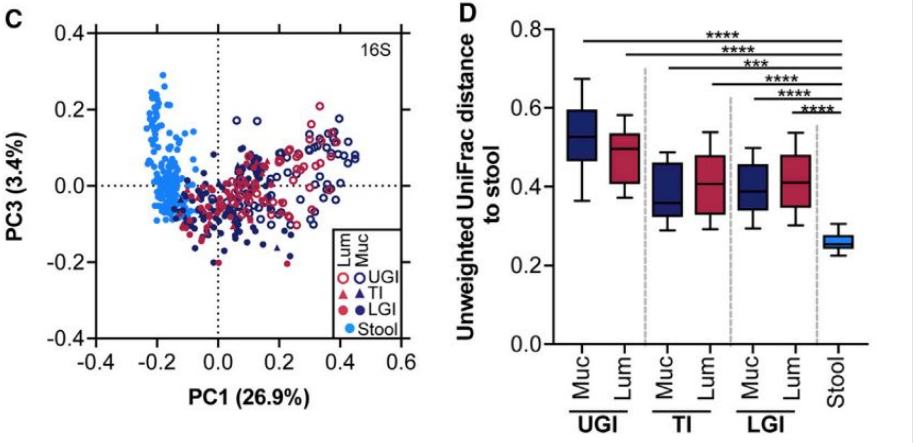
Human Stool ≠ GI Bacteria



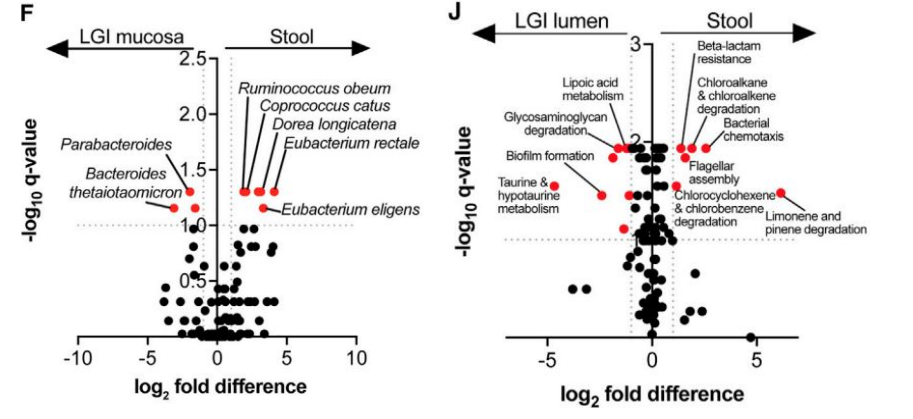
Locations of endoscopic sampling + corresponding bacterial load
(Quantified with qPCR normalized to detection threshold)



Relative Abundances of Common Genera in Different Locations

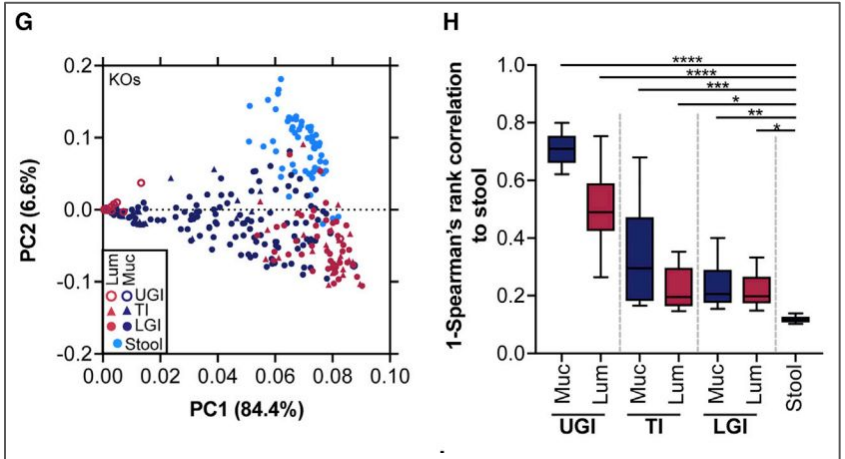


Distance from GI Microbiome to Stool
(16S rDNA sequencing-based Unweighted UniFrac distances)

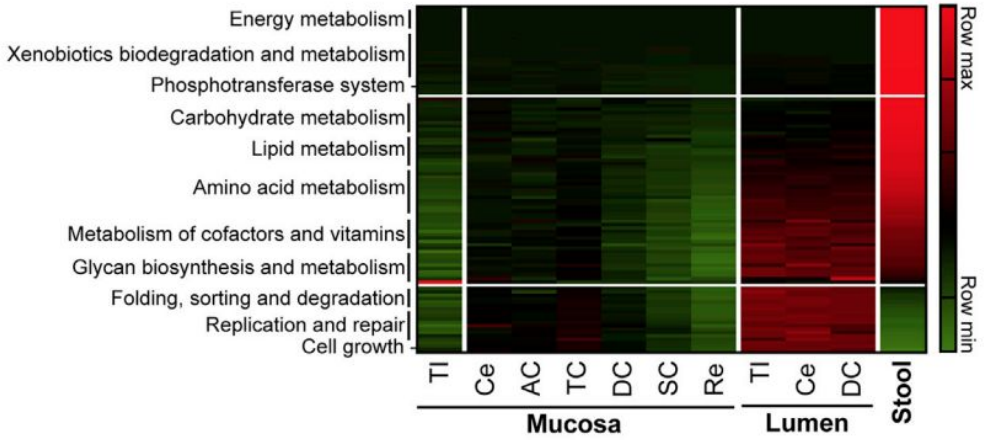


LGI mucosa and lumen species significant from stool
(Significance: Wilcoxon rank sum with FDR correction)

Human Stool ≠ GI Bacteria: Functional Orthologs

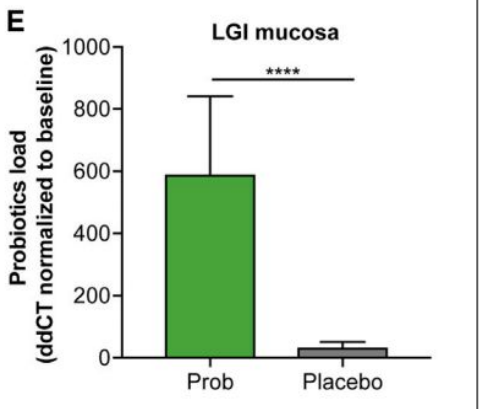


Kegg Orthology (KO) relative abundances
(Based on metagenomic shotgun sequencing data, significance= Kruskal-Wallis & Dunn's)

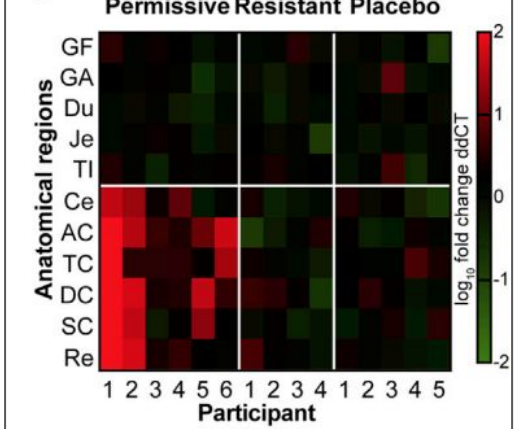


Specific KO pathway differences

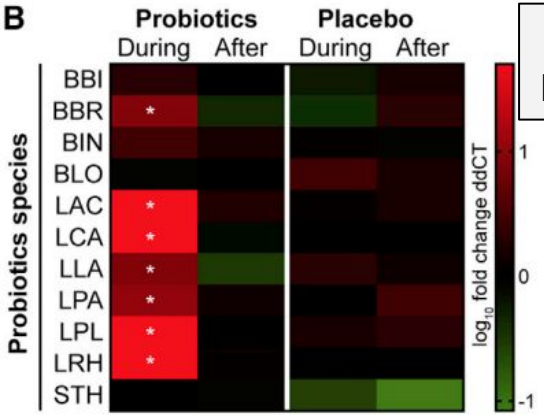
Probiotic Treatment in Humans



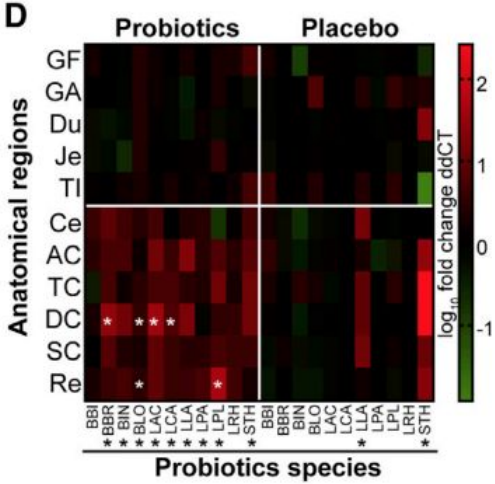
LGI Mucosa Probiotic Load Does Increase In Treatment



Some patients are resistant to probiotic therapy



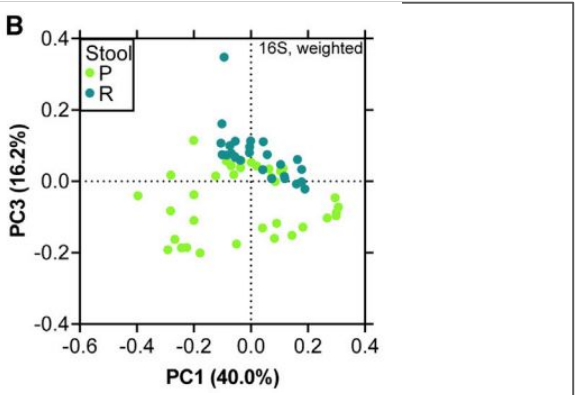
Fecal Day 0 and 28

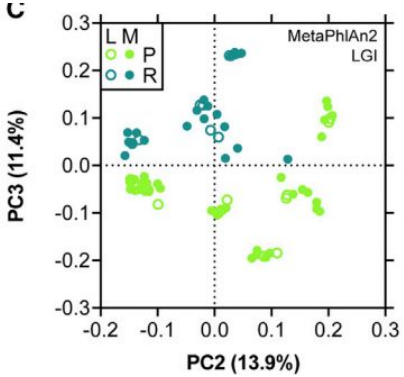


Invasive Day 21

Probiotics act in a spatially-specific and transient manner

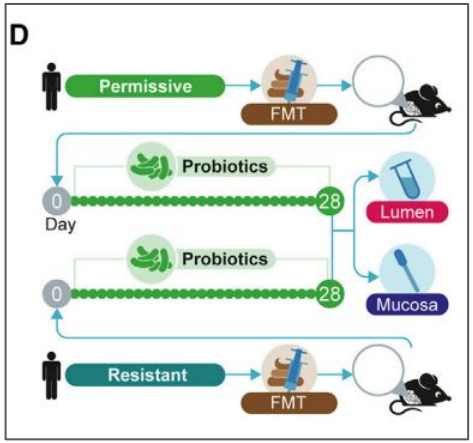
Permissive vs. Resistant

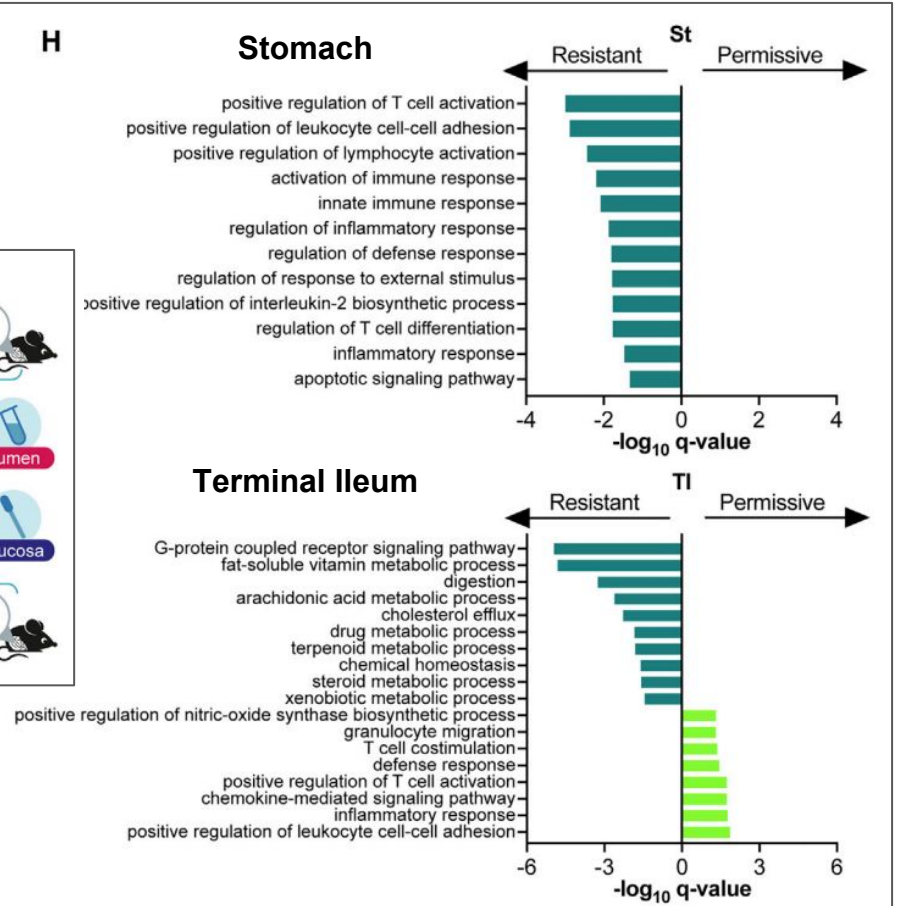




PCoA of 16S-based weighted UniFrac distances of permissive vs resistant individuals prior to probiotics supplementation

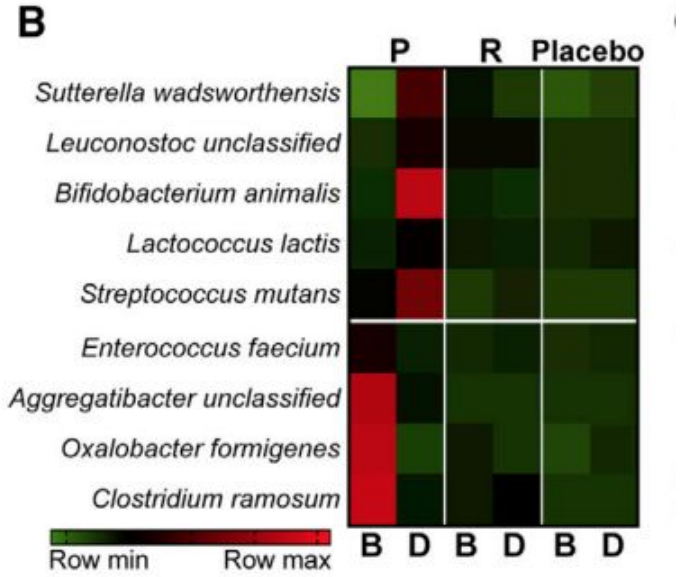
Validation in Mice



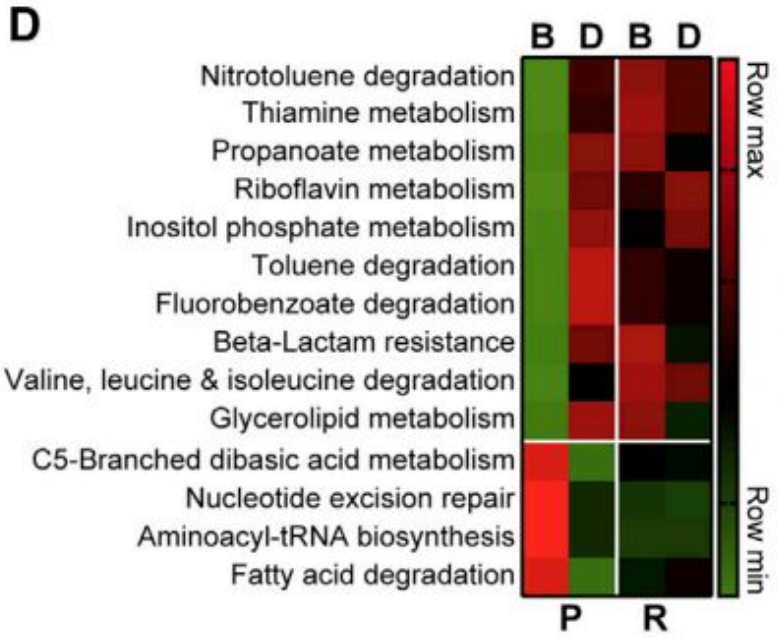


Permissive vs. Resistant Stool

B = Baseline and D = During Treatment



16S-based genera that bloomed or diminished in probiotics, but not in placebo



Kegg Pathways