

Introduction

- Inflammation in the gut drives **dysbiosis**, as documented in Inflammatory Bowel Disorder (IBD)
- During inflammation, nitric oxide free radicals oxidize glucose into **glucarate** and **galactarate** (Faber et al. 2016).
- Oxidized sugar metabolism (gud/gar pathway) is a known **pathogenic colonization factor**, giving *Escherichia coli* and *Salmonella enterica* a competitive advantage in an inflamed gut (Winter et al. 2013, Faber et al. 2016).
- Oxidized sugar metabolism is well annotated in *E. coli* and *S. enterica*, but **its full distribution in gut bacteria is unknown** (Santana et al. 2022).
- Understanding the taxonomic distribution of oxidized sugar metabolism can help us understand mechanisms of inflammation-driven dysbiosis.

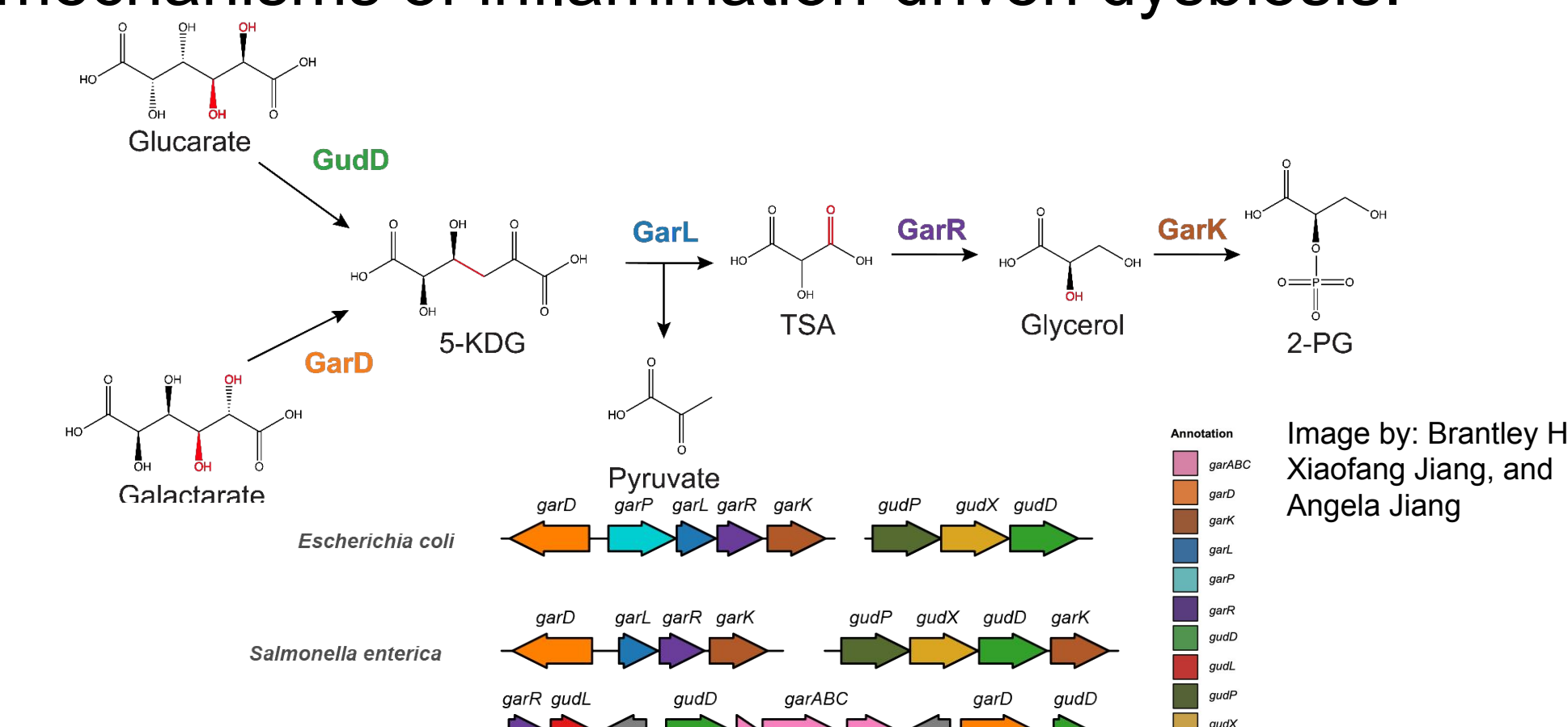



Figure 1: Glucarate and galactarate metabolism pathway and *S. enterica*, *E. coli* and *E. clostridioformis* gud/gar gene organization.

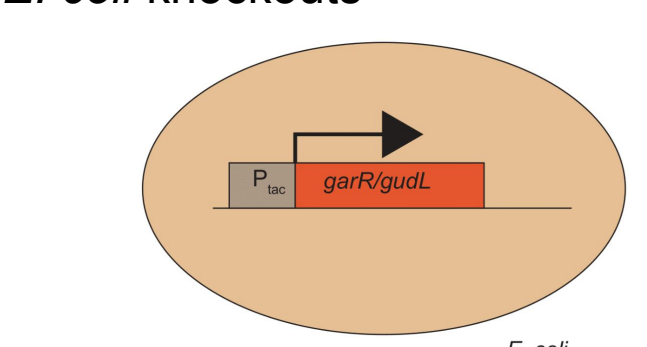
Aim: To characterize the taxonomic distribution and the evolution of oxidized sugar metabolism pathway in gut bacteria

Methods


Screening for gut bacteria that can grow on glucarate/galactarate



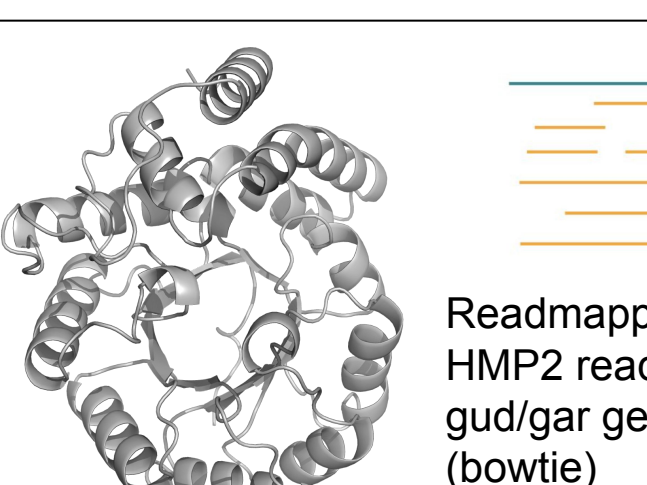
Heterologous expression of *E. clostridioformis* garR and gudL in *E. coli* knockouts



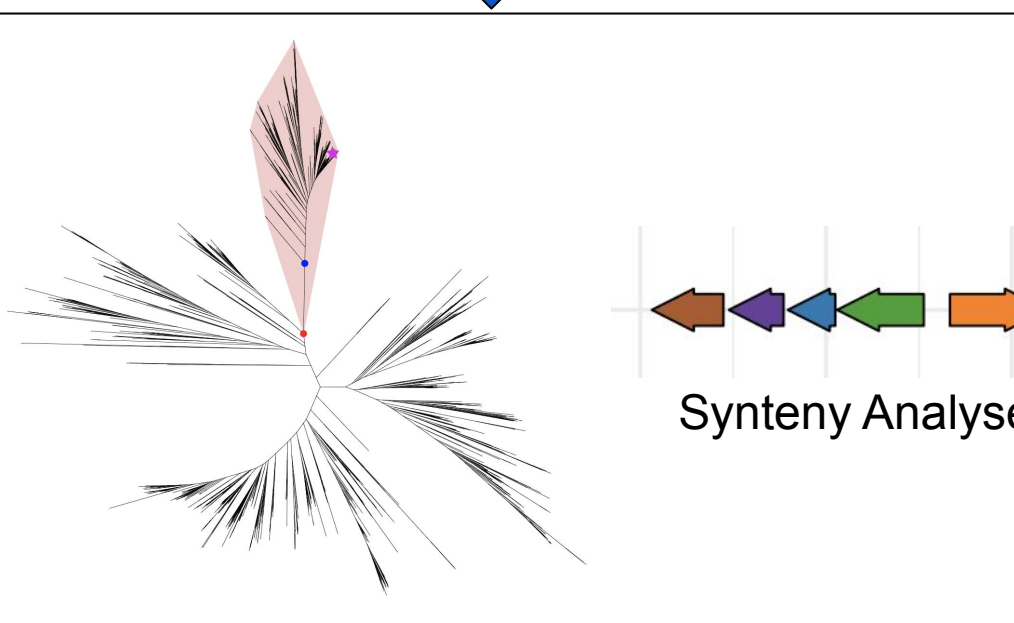
Identification of *E. coli* gud/gar homologs in the Genome Taxonomy Database (GTDB) using the ProkFUnFind pipeline



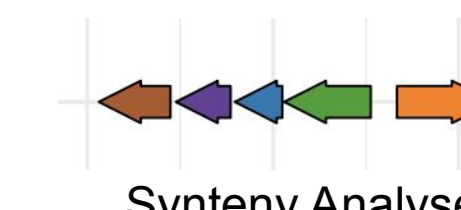
Readmapping of HMP2 reads to gud/gar genes (bowtie)



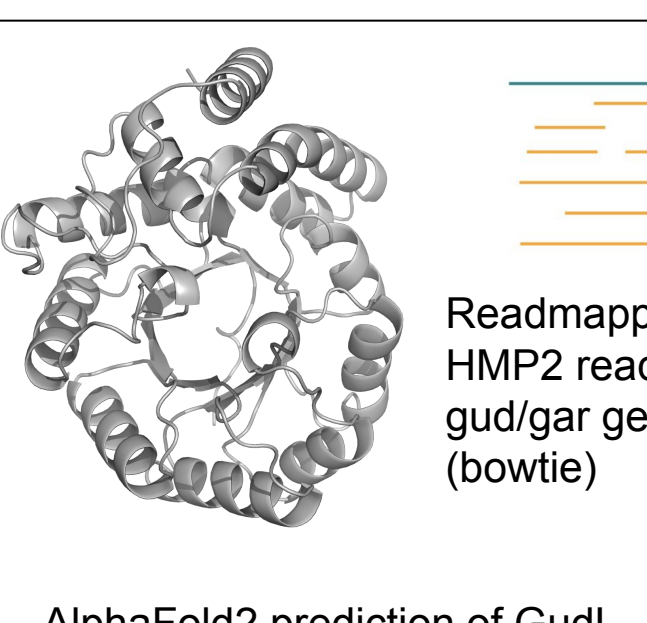
Tree Building using ClustalW, IQ-TREE2



Synteny Analyses



AlphaFold2 prediction of GudL



GudL is a GarL Analog

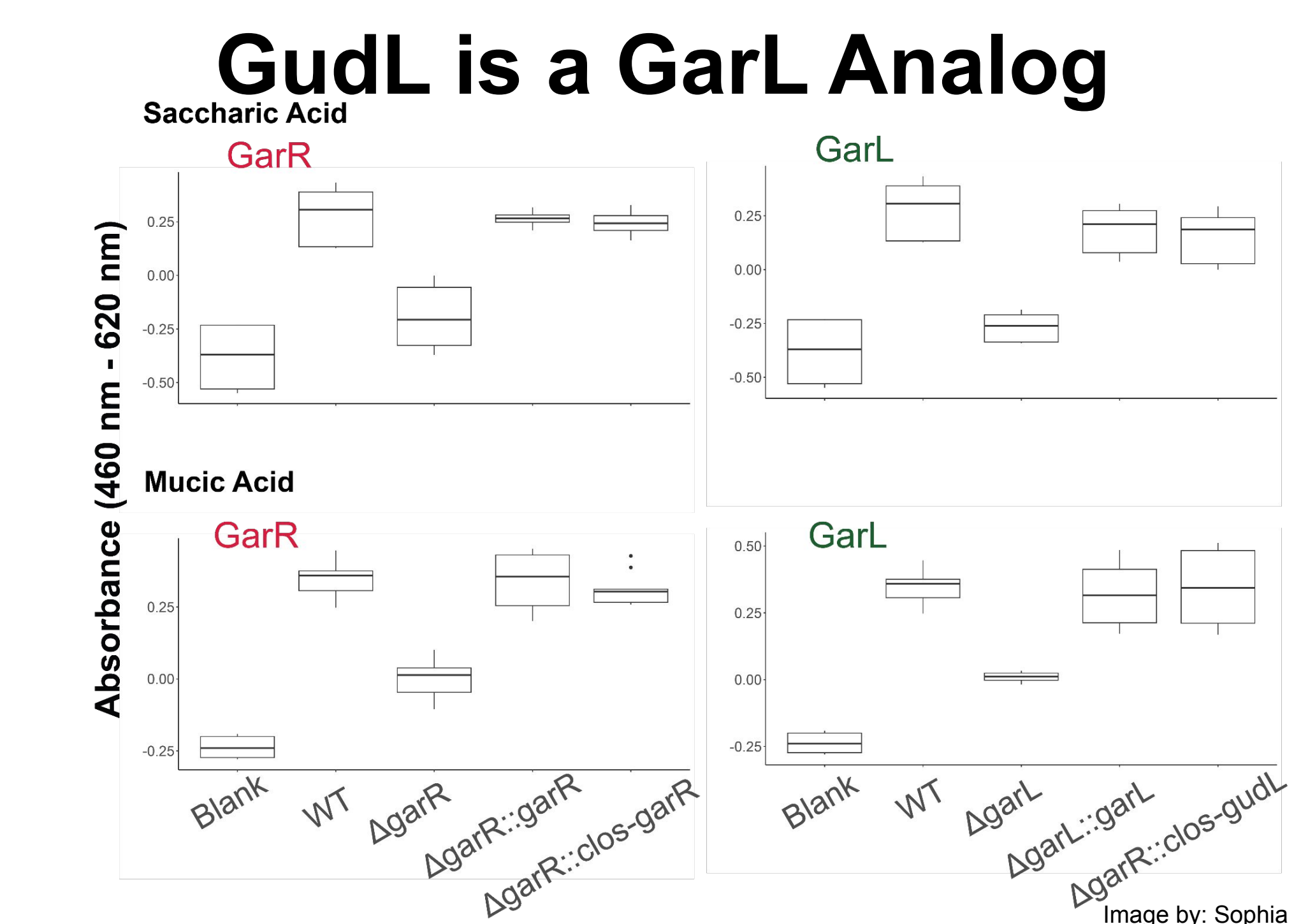


Figure 2: Using *E. coli* knockout and cloning experiments, we demonstrate that the putative *E. clostridioformis* GudL and GarR are functional.

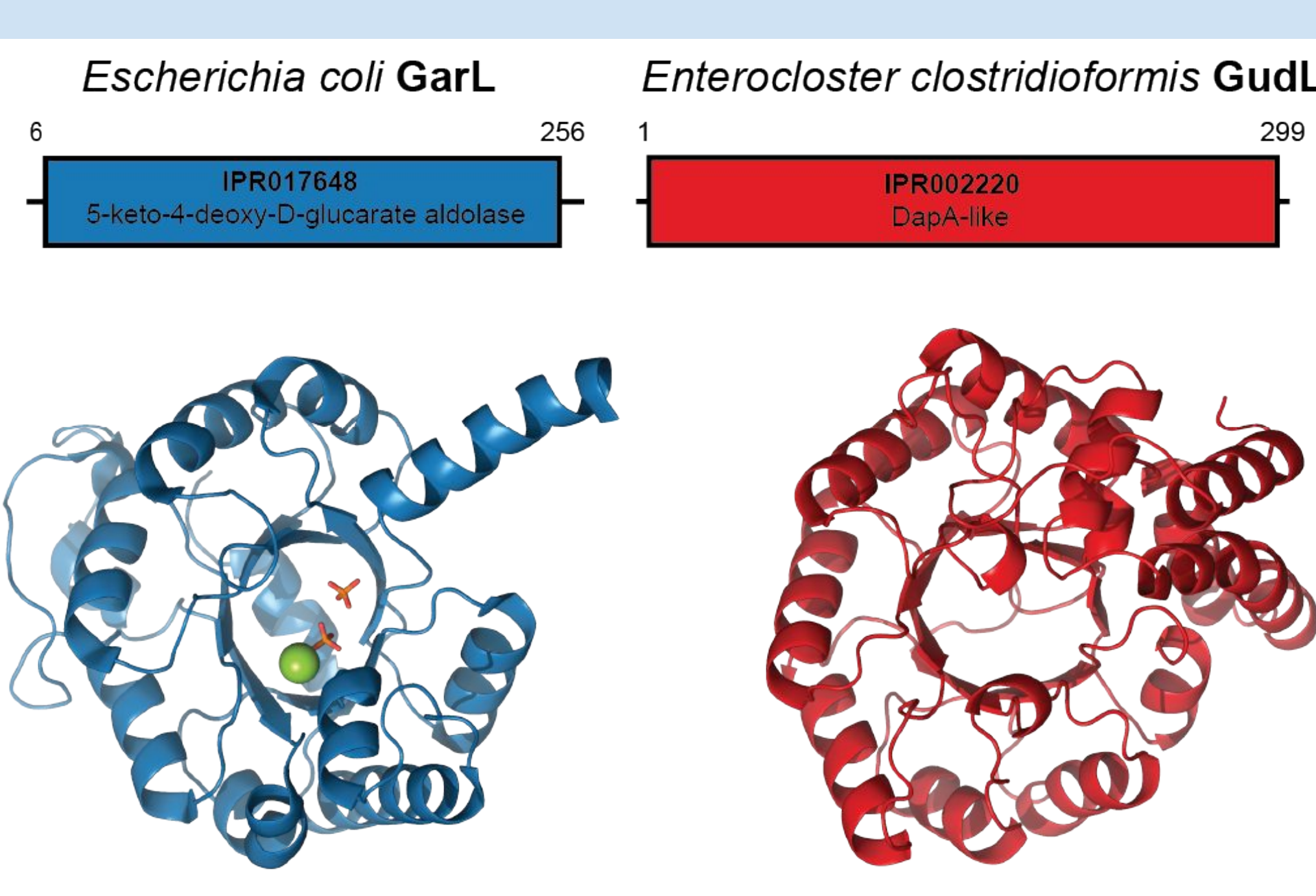


Figure 3: Comparison of *E. clostridioformis* GudL and *E. coli* GarL structures and InterProScan annotations, showing convergent evolution of 5-KDG aldolase.

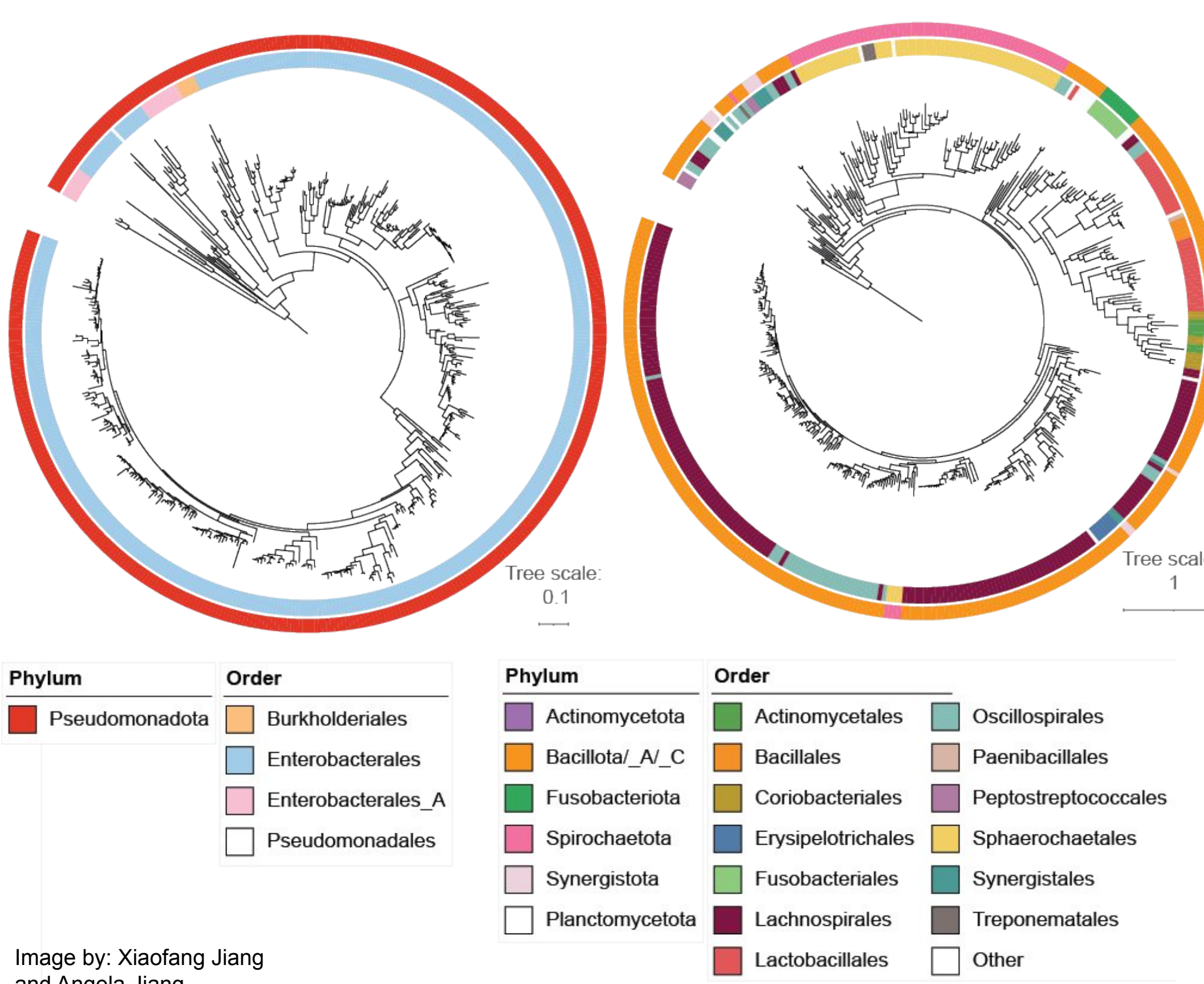


Figure 4: Taxonomic distribution of the gud/gar pathway in GTDB genomes. The gud/gar pathway is mostly present in Bacillota, Fusobacteriota and Pseudomonadota species.

Taxonomic Distribution of Oxidized Sugar Metabolism

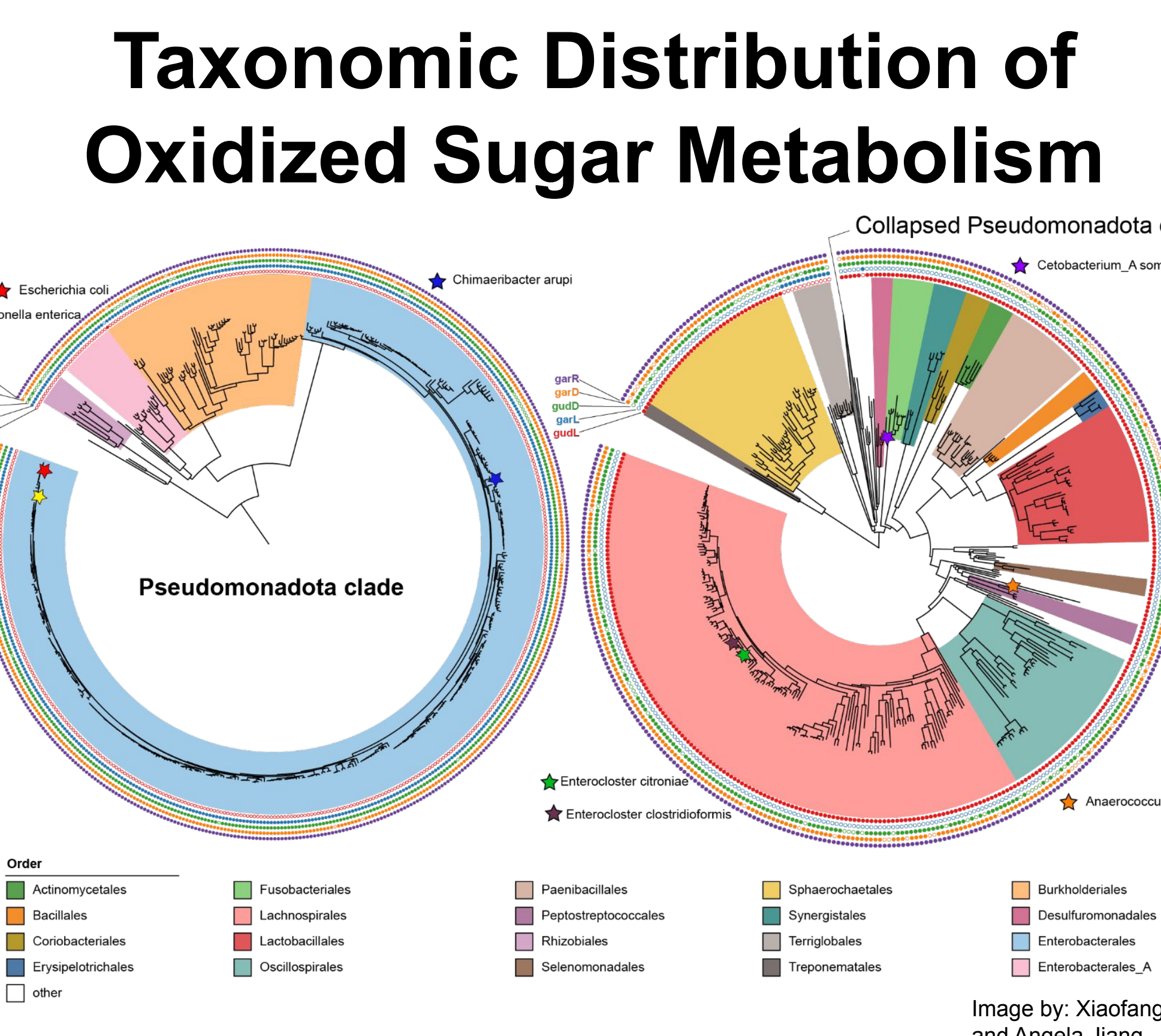


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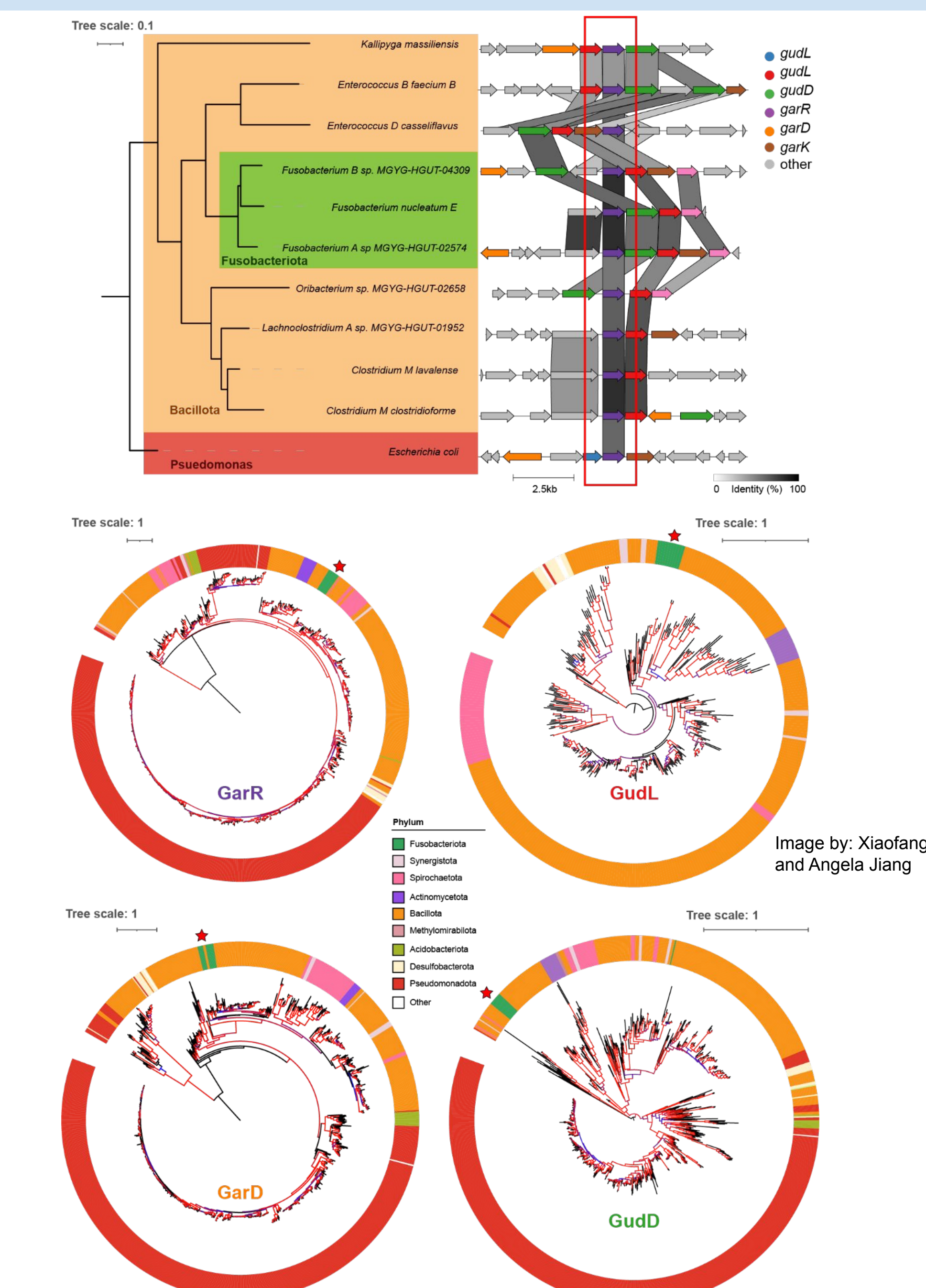


Figure 5: The gud/gar gene trees and the similarity of the clusters show potential HGT of gud/gar from Bacillota to Fusobacteriota.

Oxidized Sugar Metabolism Genes are Increased in IBD

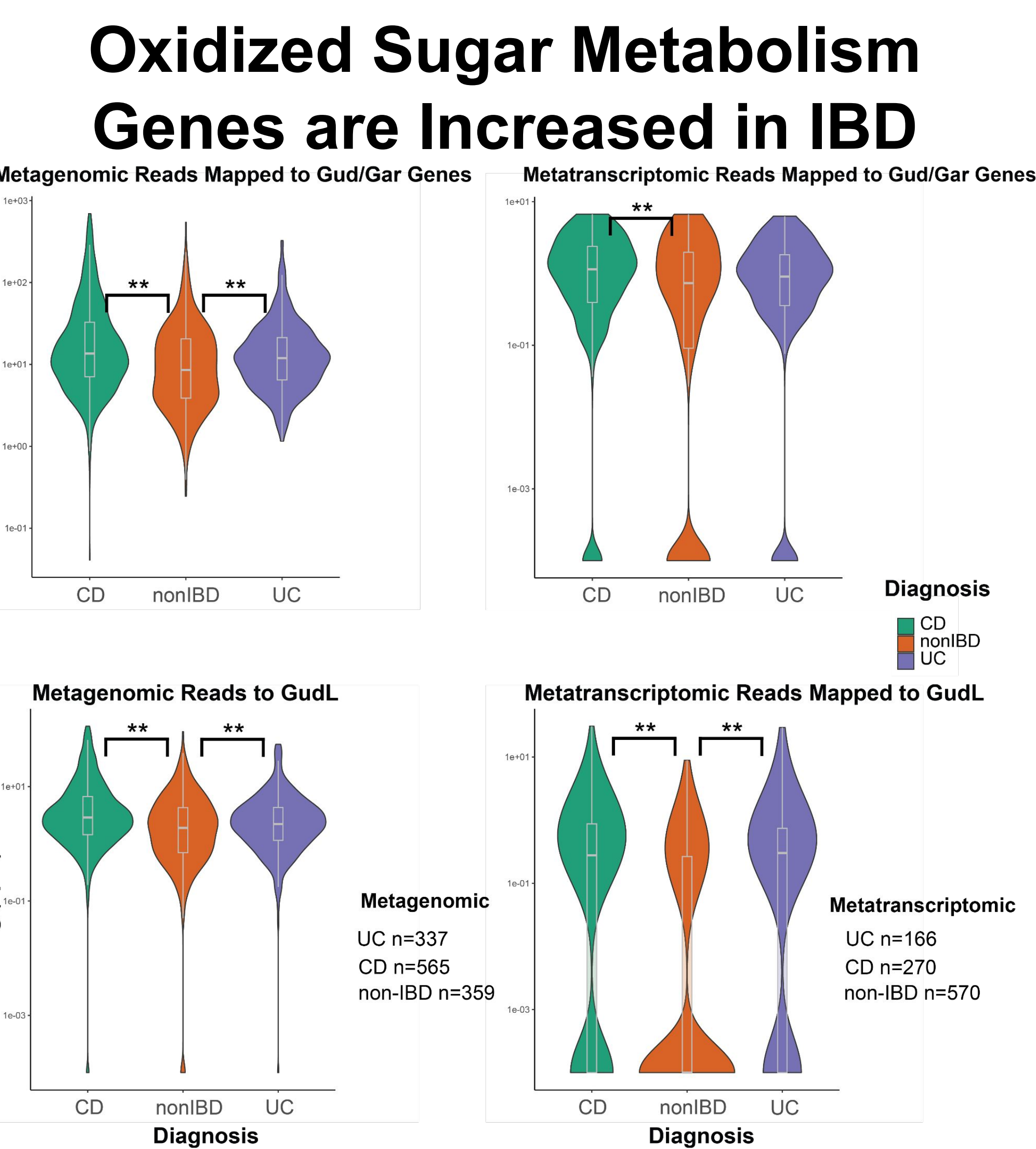


Figure 6: Comparison of mapped reads abundance in CD and UC vs non-IBD. Data from HMP2 and HPFS. ** indicates a statistically significant comparison $p < 0.05$

Gud/gar genes and transcripts are significantly increased in inflammatory bowel disorder patients.

Conclusion:

- We show that the ability to metabolize oxidized sugars is more widespread in gut bacteria than previously known
- We discover a GarL analog in *E. clostridioformis*, GudL
- We show potential spread of the gud/gar pathway to Fusobacteriota through HGT.

Bibliography

Faber, Franziska, et al. "Host-Mediated Sugar Oxidation Promotes Post-Antibiotic Pathogen Expansion." *Nature*, vol. 534, no. 7609, June 2016, pp. 697–99. DOI.org (Crossref), <https://doi.org/10.1038/nature18597>.

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Santana, Patricia Teixeira, et al. "Dysbiosis in Inflammatory Bowel Disease: Pathogenic Role and Potential Therapeutic Targets." *International Journal of Molecular Sciences*, vol. 23, no. 7, Mar. 2022, p. 3464. PubMed Central, <https://doi.org/10.3390/ijms23073464>.

Winter, Sebastian E., et al. "Host-Derived Nitrate Boosts Growth of *E. coli* in the Inflamed Gut." *Science (New York, N.Y.)*, vol. 339, no. 6120, Feb. 2013, pp. 708–11. PubMed, <https://doi.org/10.1126/science.1232467>.