# Exploring bacterial β-glucuronidase diversity in the human gut

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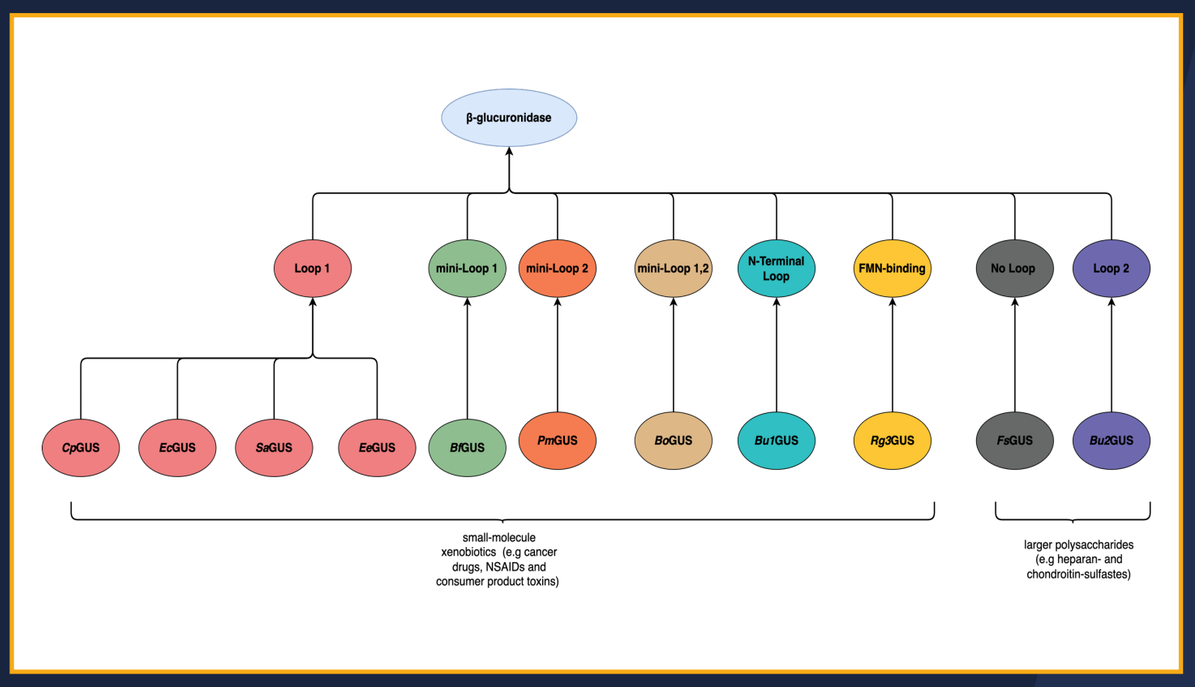
## Identified 11 GUS enyzmes from *Streptococcaceae* that may metabolize small molecules.




## 1. Introduction

- Bacteria that contribute to the metabolism of administered drugs, also convert drug metabolites, which include drug conjugates from the liver
- Bacterial β-glucuronidase (GUS) genes encode enzymes that convert most parent drug metabolites or prodrugs

## 2. Methods

- We developed an ontology-centric database to catalogue all reported drug-metabolizing genes systematically, termed the Human Microbiome Drug Metabolism (HMDM) database (Figure 1)
- We used sequence similarity networks (SSNs) to compare the homologs and modelled each enzyme using ColabFold to predict the structure (Figure 2)
- The predicted structures were aligned using PDB's pairwise structure aligner

## 3. Results

- Catalogued 50 bacterial genes and 42 gene variants to the β-glucuronidase (*uidA* gene) into the HMDM database
- 29 *uidA* variants from the HMDM belongs to Loop 1 category
- Identified 11 variants from *Streptococcaceae with* N-Terminal loop and sugar acid-recognizing NxK motif (Figure 2)
- 2 from *Pasteurellaceae* and *Dictyoglomaceae* and 1 from *Propionibacteriaceae* of unknown function


Figure 1. (a) The drug metabolizing genes predicted from bacterial isolates from healthy volunteers; (b) The topology of the HMDM ontology used to organize the terms used to describe bacterial drug metabolism in the human gut microbiome.

## 4. Discussion

- Biochemical tests are required to determine which small molecules will be affected by the 11 *Streptococcaceae* GUS and 29 Loop 1 GUS
- Perform docking experiments to identify substrates for these enzymes

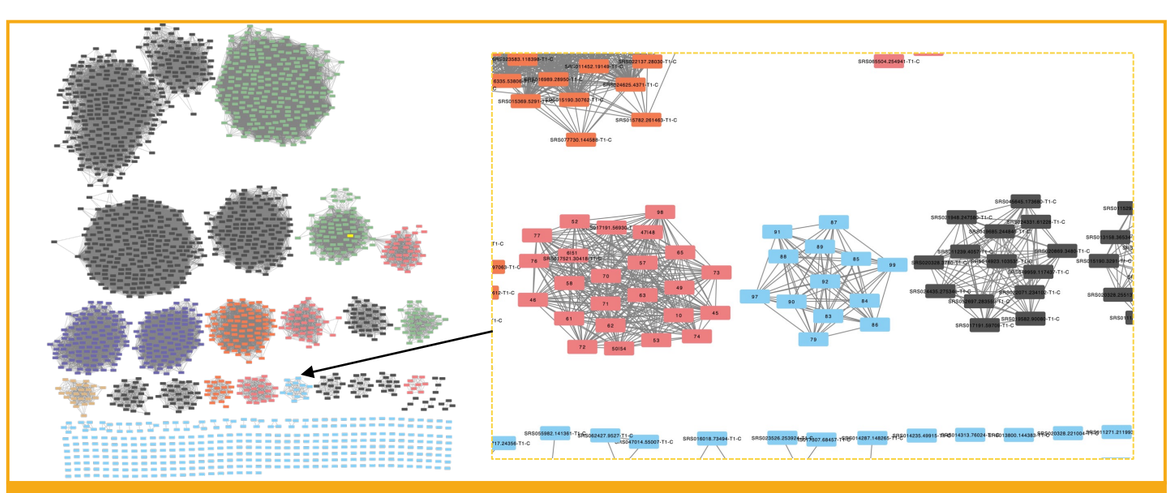


Figure 2. HMDM's GUS and published GUS (Pollet *et al.* 2017) SSN results on the left and *Streptococcaceae* cluster with N-Terminal loop on the right in blue.

### References

1. Pollet *et al.* (2017). An atlas of β-glucuronidases in the human intestinal microbiome. Structure. 2017;25(7):967-977.e5
2. Simpson *et al.* (2024). Gut microbial β-glucuronidases influence endobiotic homeostasis and are modulated by diverse therapeutics. Cell Host Microbe. 2024;32(6):925-944.e10
3. Raphenya *et al.* (2024). The human microbiome drug metabolism database. http://hdl.handle.net/11375/28823

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https://github.com/raphenya/csm-2024