

## Identifying gut bacterial consumers of dietary glycans by metabolic labeling of microbiota samples

Bastien CASTAGNER [1], Lharbi DIRDI [1], Olivia LUI [1], Emmanuel GONZALEZ [1], Corinne MAURICE [1]

[1] McGill University, CANADA

bastien.castagner@mcgill.ca

Diet-derived polysaccharides are an important carbon source for gut bacteria and shape the human gut microbiome.[1] Despite recent advances in our understanding of glycan metabolism by human gut bacteria, we still need efficient methods to link glycans to their consuming bacteria. We used *ex-vivo* metabolic labeling of a human microbiota sample to identify and isolate gut bacteria that take-up fluorescent glycans. The method combines metabolic labeling using fluorescent oligosaccharides with fluorescence-activated cell sorting (FACS), followed by amplicon sequencing or culturomics (Fig. 1).[2] Using this method, bacteria consumers of various glycans were identified, including species not previously known to be consumer. In addition, we have used this method to reveal gut bacteria whose metabolism of maltodextrin is inhibited by  $\alpha$ -amylases inhibitors used in the treatment of type 2 diabetes.[3] Acarbose, a compound used clinically was found to inhibit bacterial metabolism of maltodextrin in 4 species. In contrast, montbretin A, a new drug candidate for the treatment of type 2 diabetes, slowed the growth of only one bacterial species, supporting the fact that it is more selective. By linking bacteria to the glycans they consume, this approach increases our basic understanding of glycan metabolism by gut bacteria. Going forward, it could be used to provide insight into the mechanism of prebiotic approaches, where glycans are used to manipulate the gut microbiota composition.

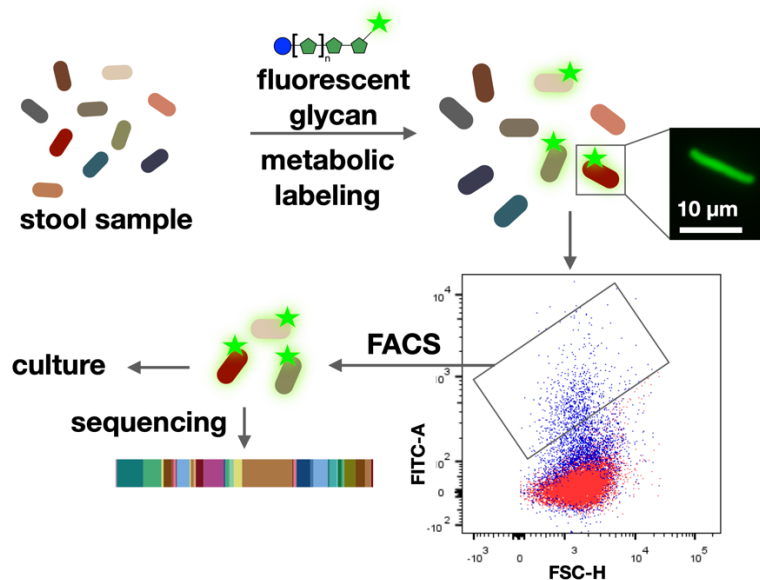


Figure 1. Metabolic labeling of human stool samples followed by fluorescence-activated cell sorting and amplicon sequencing or culturomics.

### Bibliographic references:

[1] N. M. Koropatkin, E.A. Cameron, E.C. Martens (2012), *Nature reviews Microbiology* (10), 323-335

[2] L. Dridi, F. Altamura, E. Gonzalez, O. Lui, R. Kubinski, R. Pidgeon, A. Montagut, J. Chong, J. Xia, C. F. Maurice, B. Castagner, (2023) *Nat. Commun.*, in press.

[3] O. Lui, L. Dridi, E. Gonzalez, S. Yasmine, R. Kubinski, H. Billings, J. Bohlmann, S. Withers, C. Maurice, B. Castagner, (2023) *ACS Chem. Biol.*, DOI:10.1021/acscchembio.2c00791