Functional proteomics in representative species of the human gut microbiome

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Aims of this project:

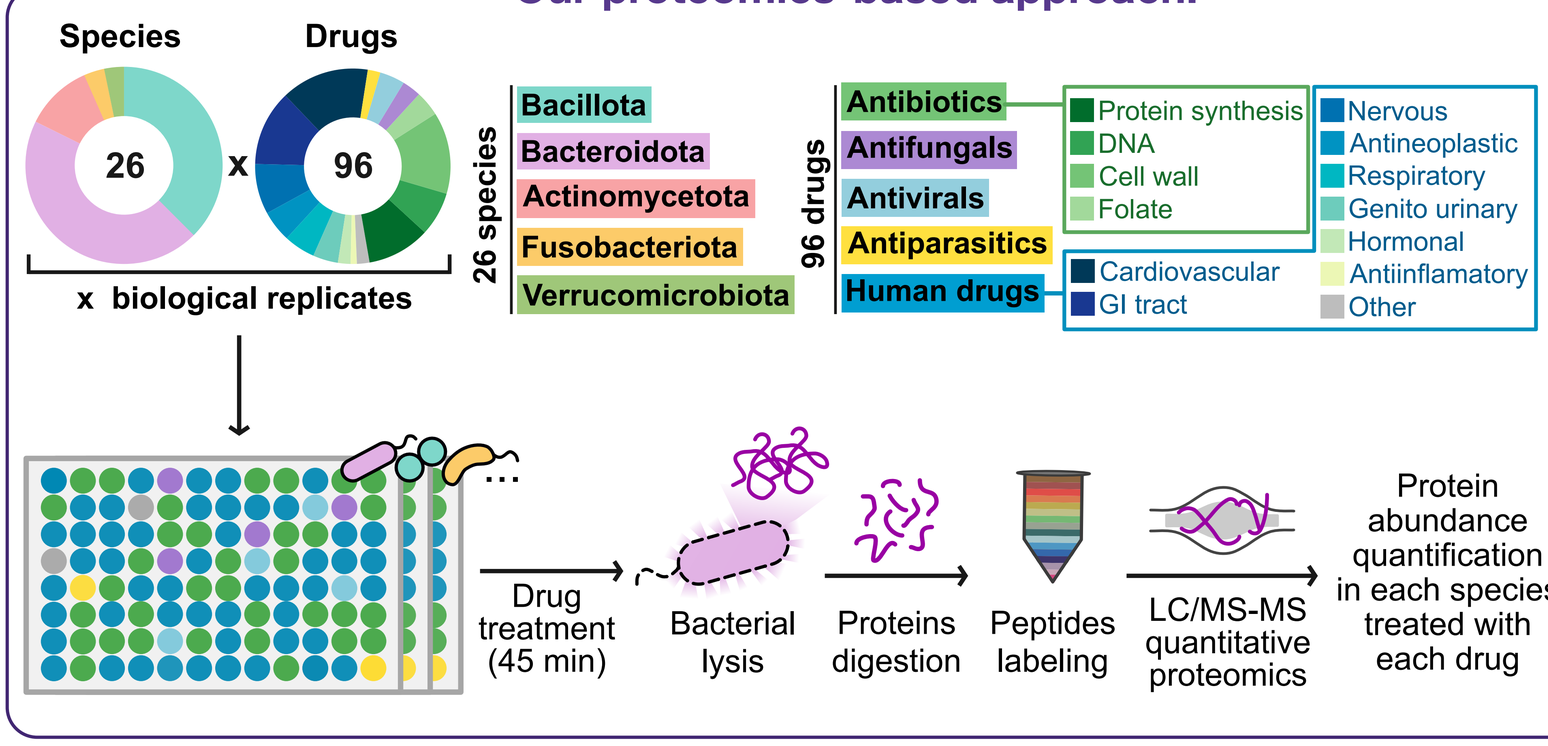
We have implemented a **proteomics approach using a panel of 96 drugs to treat 26 representative gut bacterial species**. Specifically, we aim:

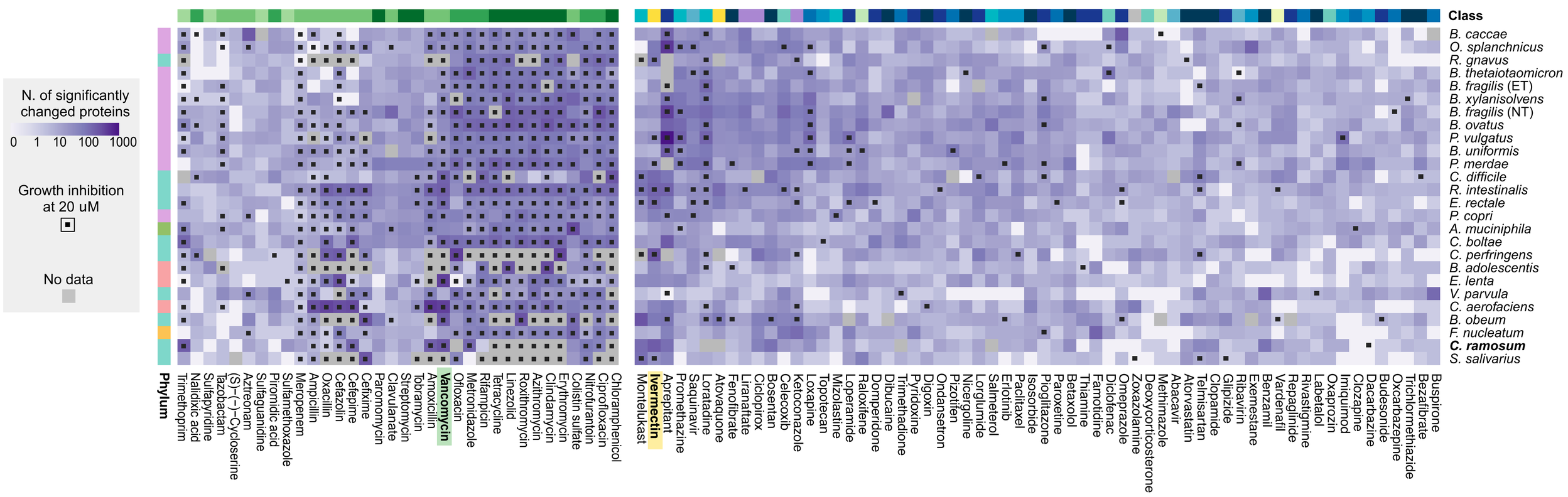
- To **quantify the changes in the proteome** (protein abundance) of gut bacterial species treated with a panel of drugs.
- To **identify the mechanism of action or resistance** of a panel of drugs in gut bacterial species.

Conclusions:

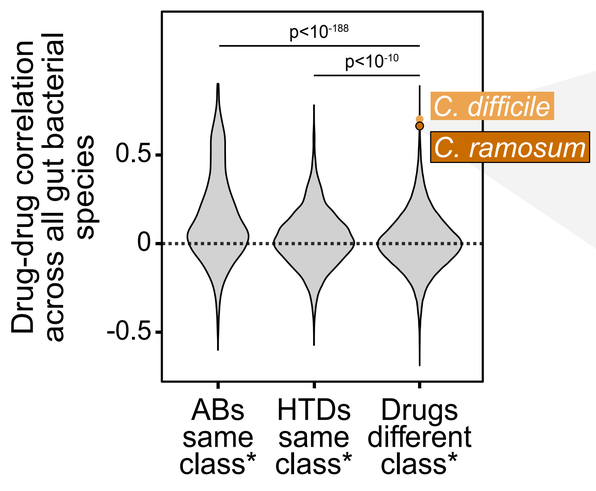
- Drugs that **inhibit the growth** of the studied gut bacterial species also lead to the **largest proteomic responses.**
- This approach help us investigating the **mode of action of drugs** previously reported to influence gut bacterial species but **with unknown or less well-defined targets**.

Our proteomics-based approach:

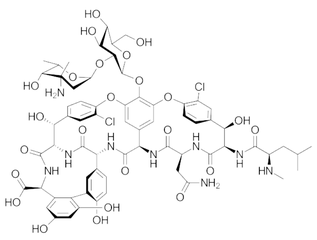




Vancomycin and ivermectin lead to similar proteomic changes

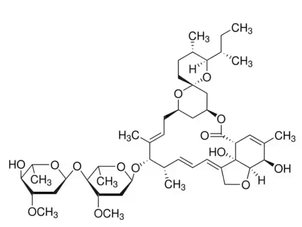


Vancomycin



Acts by binding to the D-alanyl-D-alanine end of bacterial peptidoglycan.

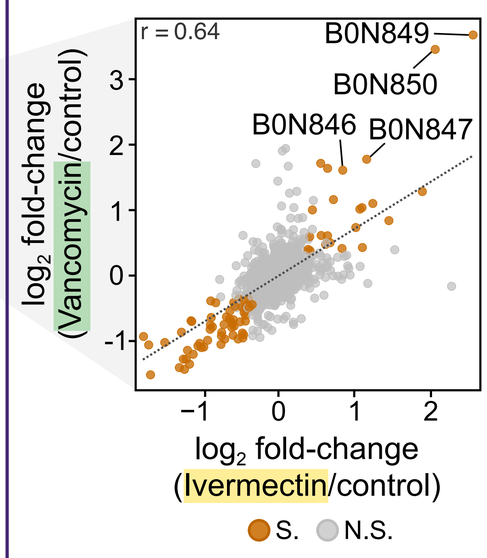
Ivermectin



Acts by binding to glutamate-gated chloride channels of nematodes and insects. **Unknown in bacteria!**

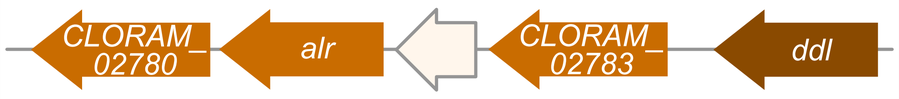
*Based on ATC (Anatomical Therapeutic Chemical) classification

Correlated protein abundance changes in *C. ramosum* reveal proteins with coordinated abundance levels



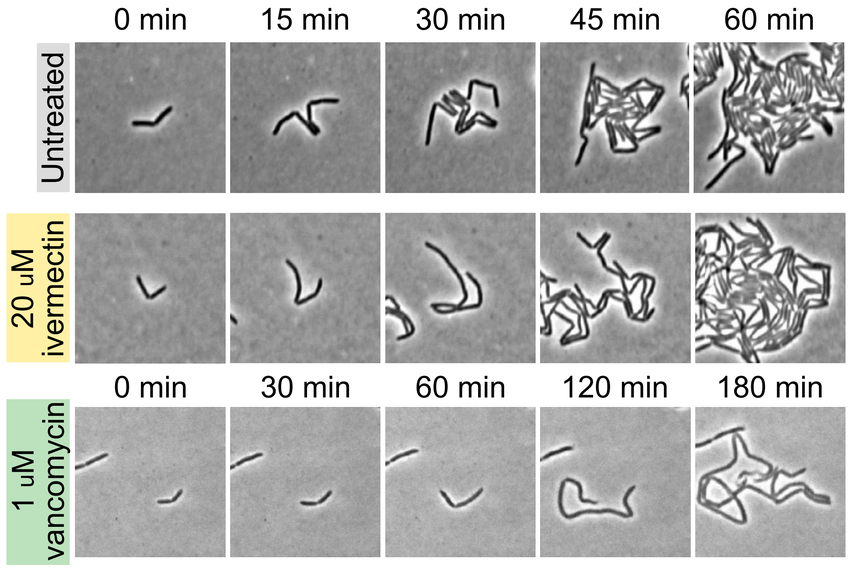
UniProt ID	Gene name
B0N846	CLORAM_02780
B0N847	alr
B0N849	CLORAM_02783
B0N850	ddl

Highly abundant proteins were predicted to be in a same operon, which is related to the **vancomycin resistance pathway.**



Serine-type D-Ala-D-Ala carboxypeptidase — Alanine racemase — Serine-type D-Ala-D-Ala carboxypeptidase — D-Alanine-D-Alanine ligase

Time lapse microscopy in *C. ramosum* shows a filamentation phenotype



Ivermectin affected the growth of *C. ramosum* less than vancomycin, but both drugs induced a **filamentation phenotype** characteristic of impaired cell division, suggesting that ivermectin could be targeting the bacterial cell wall.

Ongoing work and future perspectives:

- We are investigating the **molecular processes affected by other non-antibiotic drugs** and studying the correlation between **protein abundance changes and metabolites.**
- We are identifying novel **drug-drug interactions** in a species-specific manner.
- This information will help us to **infer protein function** based on annotated proteins.

Want to know more?
Ask me!
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Info about the lab and other projects:
www.mateuslab.com

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