



A simplified system for a complex task

Imaging the metabolite landscape of a novel infection model

Helicobacter pylori is a gram-negative bacterium that infects the stomachs of 50% of the world's population. In 1% of infected individuals *H. pylori* causes gastric cancer.

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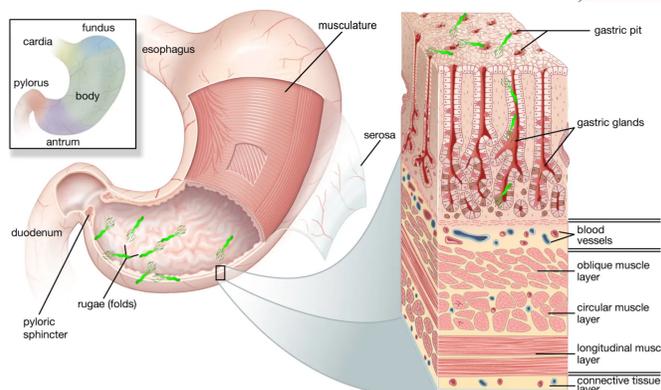
Metabolites are small molecules below 1500 Da that serve as immediate effectors that enable the nutritional exchange, communication and defense between bacteria and their hosts.

My research focuses on the site-specific chemistry *H. pylori* induces in proliferating cells deep in the gastric glands. Along the chemical changes, I want to reveal what happens at the cellular interface where both partners meet.

Questions

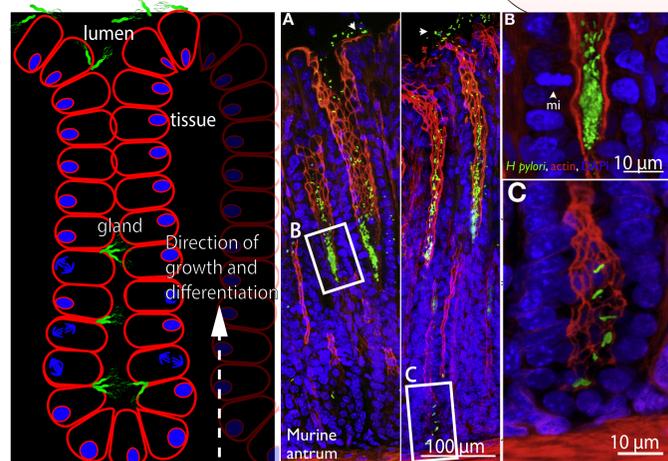
- Does *H. pylori* alter the site specific chemistry of the gastric glands?
- Does *H. pylori* have a metabolic *in situ* fingerprint?
- What is the metabolic interaction between precursor cells and *H. pylori*?

H. pylori colonizes the epithelia of the stomach's antrum



Modified after Encyclopaedia Britannica, Inc.

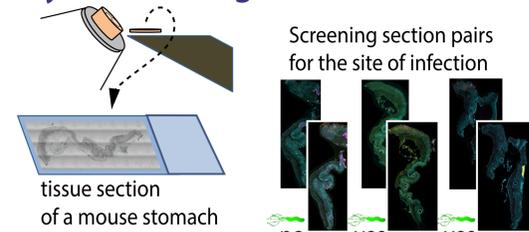
Deep in the gastric glands, *H. pylori* forms epithelial microcolonies that promote proliferation of the precursor and stem cells. *H. pylori* induces proliferation by injecting the virulence factor cytotoxin-associated gene A (CagA). Although accelerated tissue growth coincides with increased cancer risk, the molecular interactions that allow *H. pylori* to perturb the gastric gland microniche and induce cancerogenesis remain unknown.



Modified after Sigal et al., Gastroenterology, 2015

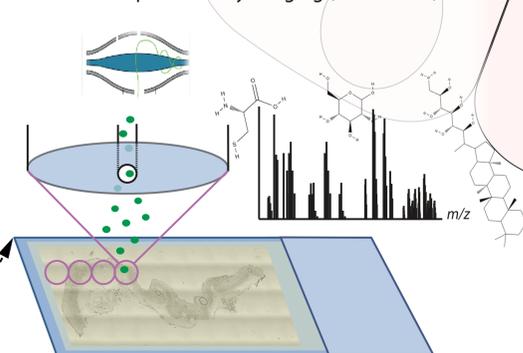
Spatial metabolomics is a label-free technique that allows imaging the tissue chemistry at micrometer scales. To measure the *in situ* metabolome of *H. pylori* at tissue sites of infection I developed a correlative chemical imaging workflow combining mass spectrometry imaging and fluorescence microscopy.

Cryo-sectioning

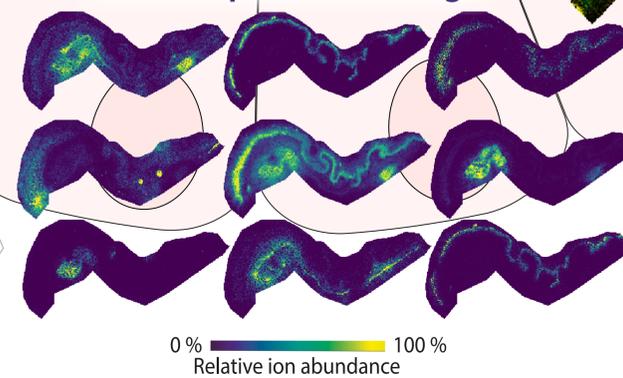


Metabolite imaging

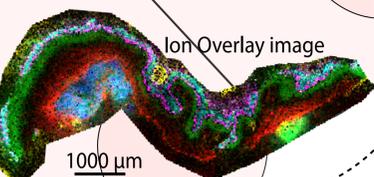
Matrix-assisted laser desorption ionization mass spectrometry imaging (MALDI-MSI)



"Each MS peak is an image!"



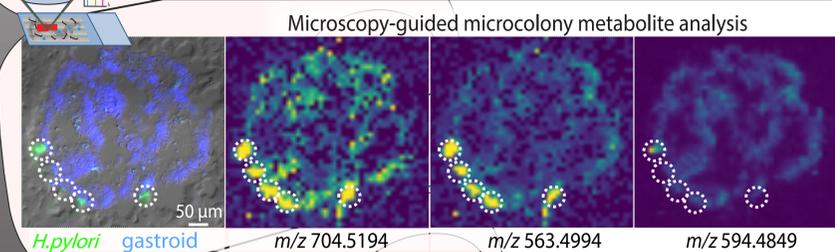
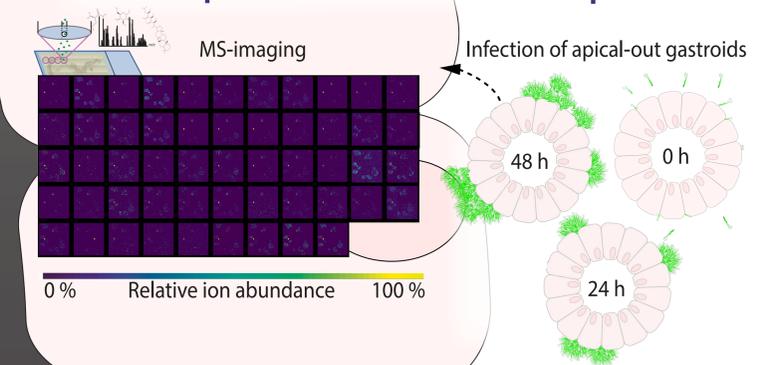
- metabolite 1
- metabolite 2
- metabolite 3
- metabolite 4
- metabolite 5
- metabolite 6



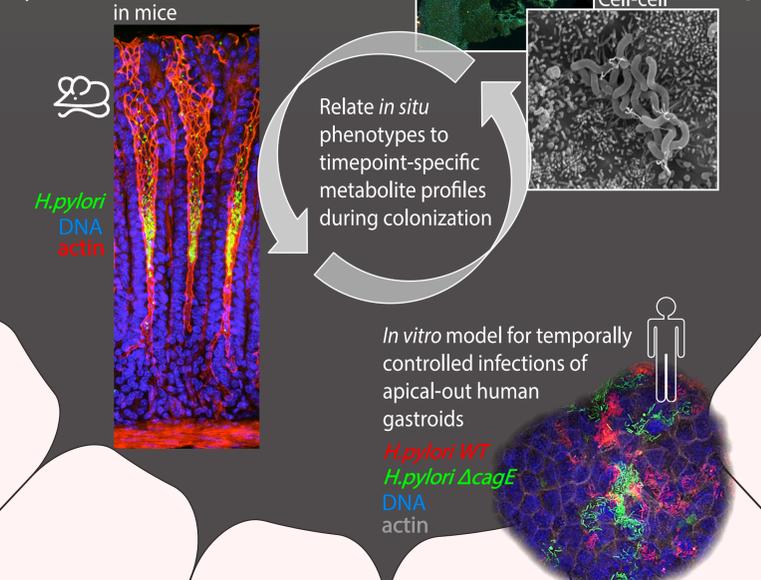
Where are the bacteria?



MS imaging of *H. pylori* microcolonies on human epithelia reveals ~50 site-specific ions

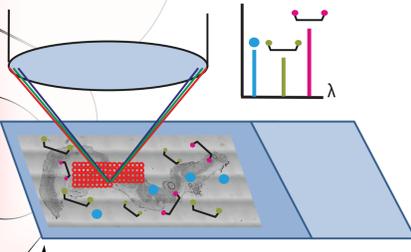


Spatial metabolomics of *H. pylori* in the gastric glands



Fluorescence Microscopy

Fluorescence *in situ* hybridization (FISH) or Immunohistochemistry



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