

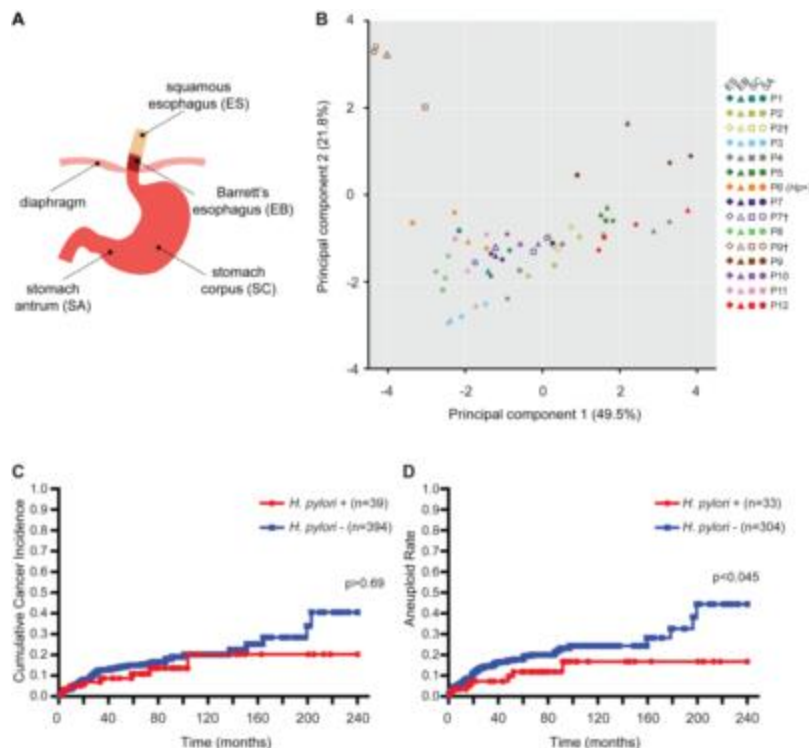
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SCIENCE SPOTLIGHT

The human microbiome in Barrett's esophagus is hard to stomach

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A Neves



(A) Diagram of the human upper gastrointestinal tract indicating regions sampled in the study. (B) Principal component analysis of phylogenetic similarity among samples collected from each participant at the four upper GI tract sites. Kaplan-Meier curves for participants within the cohort for (C) cancer incidence (n = 433, 39 infected) and (D) aneuploidy as measured by dna content flow cytometry (n = 337, 33 infected).

Image provided by Ms. Gall

It is now well known that in our bodies, microbial cells outnumber human cells 10 to 1. Furthermore, it has become increasingly clear that these microbial communities (collectively known as the human microbiome) have key roles in health and disease. For example, the bacterium *Helicobacter pylori* is well-known to cause gastric ulcers and stomach cancer in a subset of infected individuals. However, for unknown reasons, *H. pylori* infection is markedly lower in patients with esophageal adenocarcinoma (EAC). Important questions remain on the diversity of microbes present in the esophagus and stomach and how this diversity may be linked to *H. pylori*'s protective role in EAC. Such questions have remained unanswered in part, due to challenges associated with sampling the upper gastrointestinal (GI) tract. A recent Fred Hutch study from Dr. Nina Salama's Laboratory (Human Biology and Public Health Sciences Divisions) in collaboration with Dr. Brian Reid's Laboratory (Human Biology Division), led by graduate student Tina Gall and published in *PLoS*

ONE, sought to characterize the human microbiome in the upper GI tract of a subset of individuals from the Seattle Barrett's Esophagus Research Program (SBERP).

"Our study was made possible by the great collaborative environment here at the Hutch. We relied on the expertise of Dr. Brian Reid, a leader in the Barrett's Esophagus field, and utilized endoscopy samples that his group collected as part of the SBERP. Dr. Erick Matsen and his group in Computational Biology were instrumental in helping us analyze our complex genomic data. This allowed us to ask some fundamental questions like what is the best way to sample bacteria in the stomach and esophagus and do these distinct anatomical sites host the same or different bacteria?" said Ms. Gall.

The study began by collecting four distinct samples from 12 SBERP participants. These were Barrett's esophagus, normal esophagus, stomach antrum and stomach corpus (see figure). The authors found that mucosal brush sampling was the best method to enrich for bacterial diversity. To chart the microbial diversity in the sample, the authors amplified and sequenced 16S rRNA, a bacteria-specific nucleic acid. Principal component analysis of the sequencing data revealed that bacteria from the same study participant were more similar to each other than to samples from the same anatomical site in a different individual. In addition, the investigators found that bacteria belonging to the *Streptococcus* and *Prevotella* genera dominated the microbiome, both within study participants and across anatomical sites. Intriguingly, the ratio of *Streptococcus* to *Prevotella* varied among individuals and this ratio could be linked to Barrett's esophagus risk factors, such as waist-to-hip ratio. Finally, the authors examined *H. pylori* status in a larger SBERP cohort (n=433) and found that *H. pylori* infected individuals had decreased genomic instability, an important predictor of progression from Barrett's esophagus to EAC. Said Ms. Gall " We hope to focus future studies on analyzing the microbial composition in the upper GI tract of *H. pylori* positive and negative individuals to determine whether the presence of *H. pylori* in the stomach and the esophagus influences colonization of these sites by specific bacteria that may be carcinogenic and promote the observed DNA damage". In conclusion, this study developed a new method for sampling the upper GI tract, which enabled the characterization of the microbial community in both the stomach and esophagus as well as provided an intriguing link between *H. pylori* status and genomic instability.

[Gall A, Fero J, McCoy C, Claywell BC, Sanchez CA, Blount PL, Li X, Vaughan TL, Matsen FA, Reid BJ, Salama NR. 2015. Bacterial composition of the human upper gastrointestinal tract microbiome is dynamic and associated with genomic instability in a Barrett's Esophagus cohort. PLoS One, 10\(6\), e0129055.](#)