A novel approach to determine how carcinogenic bacteria find their targets

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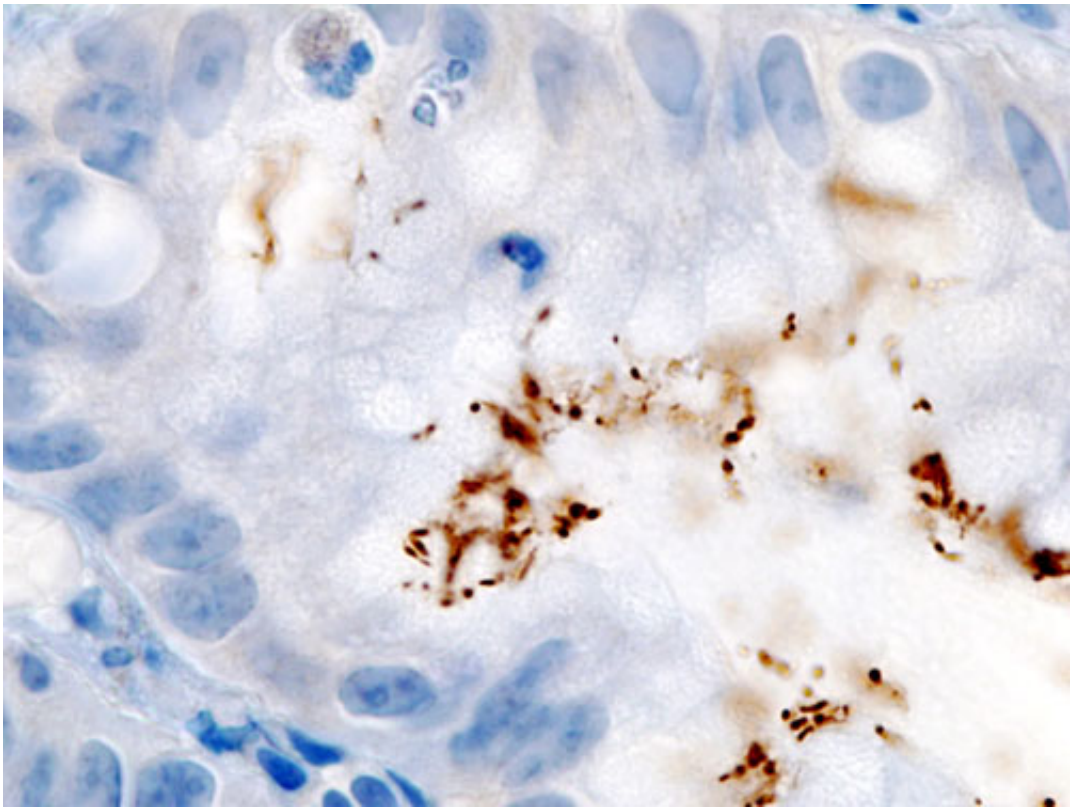

Histopathology of Helicobacter pylori infection in a gastric foveolar pit demonstrated in endoscopic gastric biopsy. Credit: Wikipedia.

The gram-negative bacteria Helicobacter pylori (H. pylori) colonize the stomachs of the majority of the world's population. Although most people may never experience major complications due to the pathogen, H. pylori infections increase the risk of certain types of gastric cancer, as

well as other illnesses such as peptic ulcers and gastritis. Currently, H. pylori infections are treatable with a cocktail of antibiotics, but the rapid emergence of antibiotic resistance in H. pylori is a significant concern. To counter these threats, Dr. Pushkar Lele, assistant professor in the Artie McFerrin Department of Chemical Engineering at Texas A&M University, investigated how H. pylori locate their ideal environment within a host's stomach.

Motile bacteria such as H. pylori swim by rotating string-like appendages called flagella. They navigate by sensing chemical signals in their environment, a process known as chemotaxis. An intracellular signaling pathway—the chemotaxis network—aids navigation by controlling the direction of rotation of the flagella. Current understanding of how the chemotaxis network operates is based on studies of Escherichia coli (E. coli), which is a model system for bacterial chemotaxis and motility. The chemotaxis network in E. coli modulates the probability of clockwise rotation in otherwise counterclockwise-rotating flagella to help the cell migrate toward favorable chemical environments. How the chemotaxis network modulates flagellar functions in H. pylori is not known.

Popular techniques that use probes to study chemotactic function in bacteria do not work well in H. pylori. This creates significant challenges in understanding flagellar functions in this species. To overcome these challenges, Lele's group pioneered a novel probe-free approach to study flagellar functions in H. pylori. Their approach exploited the fact that cells swam around in clockwise circles near glass surfaces when their flagella rotated counterclockwise, and counterclockwise circles when their flagella rotated clockwise. In a paper published in *eLife*, Lele and his research team used this approach to report the probability of the clockwise rotation in H. pylori for the first time. Jyot Antani, a doctoral student in Lele's group, performed the experiments that further showed that H. pylori's chemotaxis network modulates flagellar functions similar to that in E. coli.

Lele said the similarity in the form of flagellar control in the two bacterial species is intriguing given that they differ in many key aspects. Whereas H. coli prefer the stomach, E. coli are found in the lower gastrointestinal tract. The physical characteristics of H. pylori are such that they run forward and reverse, unlike E. coli, which run forward and then tumble. As a result, the modulation of the probabilities of clockwise flagellar rotation, which suits E. coli very well, is predicted to cause errors in chemotaxis in H. pylori. Lele predicts that future work with their new approach will reveal how H. pylori reach their targets despite the errors and how dietary interventions can be developed to inhibit chemotaxis.

More information: Jyot D Antani et al. Asymmetric random walks reveal that the chemotaxis network modulates flagellar rotational bias in Helicobacter pylori, *eLife* (2021). DOI: 10.7554/eLife.63936

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