

Why Helicobacter Pylori Needs To Stay in Shape

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One of the greatest controversies and most surprising discoveries in modern medicine was that stomach ulcers are caused by the bacterium *Helicobacter pylori*. Thanks to Drs. Robin Warren and Barry Marshall, it is now well-established that *H. pylori* colonizes in the viscous epithelial mucus layer of the human stomach, which protects both the underlying epithelial cells and *H. pylori* from the stomach lumen. Indeed, *H. pylori* can survive direct exposure to stomach acid for only minutes. Yet despite the advent of antibiotics, *H. pylori* persists in approximately one half of the world's population and leads to severe complications, including stomach cancer, in 15-20% of chronically infected individuals.

To access and maintain its niche, *H. pylori* moves via flagella in response to chemotactic signals. It has been proposed that the helical shape of *H. pylori* also contributes to its motility in viscous mucus; however, this has never been directly assessed. Therefore, former graduate student Dr. Laura Sycuro, her advisor Dr. Nina Salama of the Human Biology Division, and colleagues made a series of *H. pylori* mutants with altered morphology to evaluate whether its helical shape enables it to traverse viscous solutions and thus colonize stomach mucosa.

Salama and colleagues previously generated a library of *H. pylori* mutants, using transposons to randomly disrupt *H. pylori* genes, and sequencing to locate the resulting disruptions. Sycuro *et al.* screened this library for morphology changes by light microscopy and identified two mutants that yielded predominantly straight rod shaped bacteria (disruption in *Csd5* gene), and exclusively straight rod shaped bacteria (disruption in *Csd4* gene).

Whilst both mutants were unaffected in terms of their ability to grow *in vitro* and withstand extreme osmotic stress, they did exhibit significantly reduced motility in soft agar compared to wild-type *H. pylori*. In addition, the *Csd4* mutant exhibited decreased colonization of murine stomachs (n.b., the *Csd5* mutant was not analyzed due to its heterogeneous shape phenotype). The Salama Lab has ongoing efforts to evaluate whether the soft agar results will translate with epithelial mucus and to understand how *Csd4* and *Csd5* fit into a larger network of genes that regulate cell shape. Nonetheless, the results of this study go a long way to support the hypothesis that the helical shape of *H. pylori* is indeed integral to its motility and niche acquisition.

[Sycuro LK, Wyckoff TJ, Biboy J, Born P, Pincus Z, Vollmer W, Salama NR](#). 2012. Multiple peptidoglycan modification networks modulate *Helicobacter pylori*'s cell shape, motility, and colonization potential. *PLoS Pathogens* 8:e1002603.

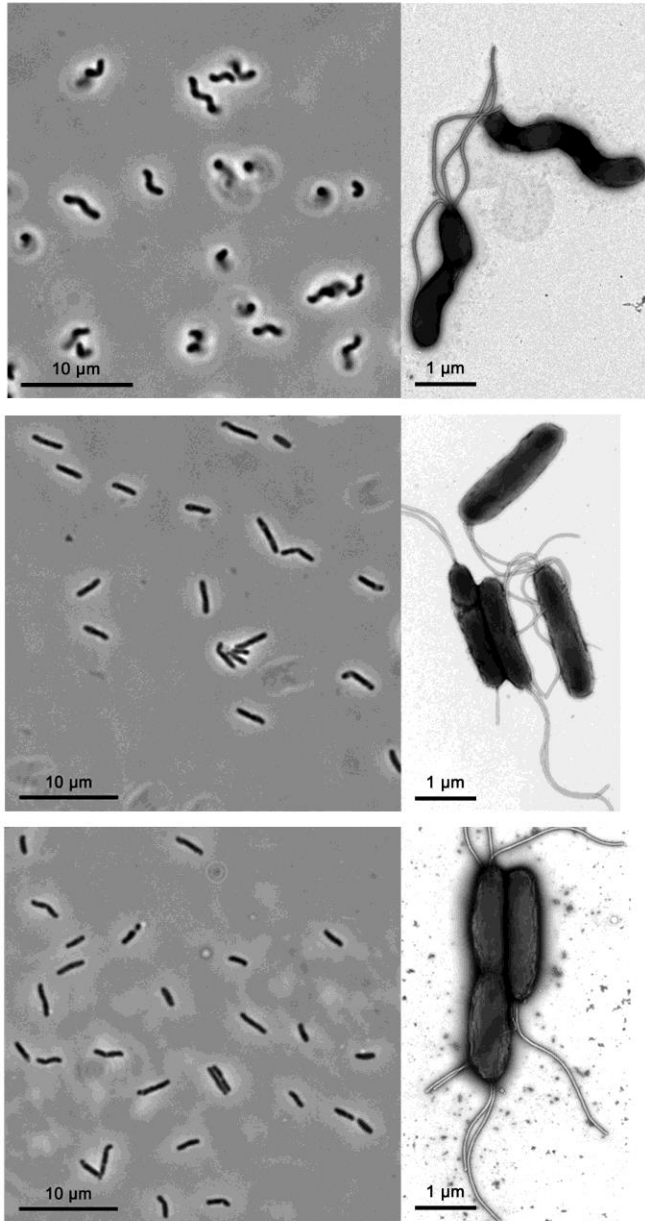


Image provided by Dr. Laura Sycuro

Disruption of the *Helicobacter pylori* genes *Csd4* and *Csd5* result in rod-shaped bacteria (center and bottom panels, respectively) that exhibit impaired motility in soft agar compared to wild-type *H. pylori* (top panel). The *Csd4* mutant also showed impaired stomach colonization, which implicates *H. pylori*'s helicity in niche acquisition (n.b., the *Csd5* mutant was not evaluated due to its heterogeneous straight rod phenotype).