Title
Helicobacter pylori’s Achilles’ Heel

Journal
Immuno-Gastroenterology, 2(1)

ISSN
2306-8760

Authors
Luecke, H
Sachs, G

Publication Date
2013

Immuno-Gastroenterology 2:1, 76; January/February/March 2013; © 2013 STM Publishing

Helicobacter pylori's Achilles' Heel

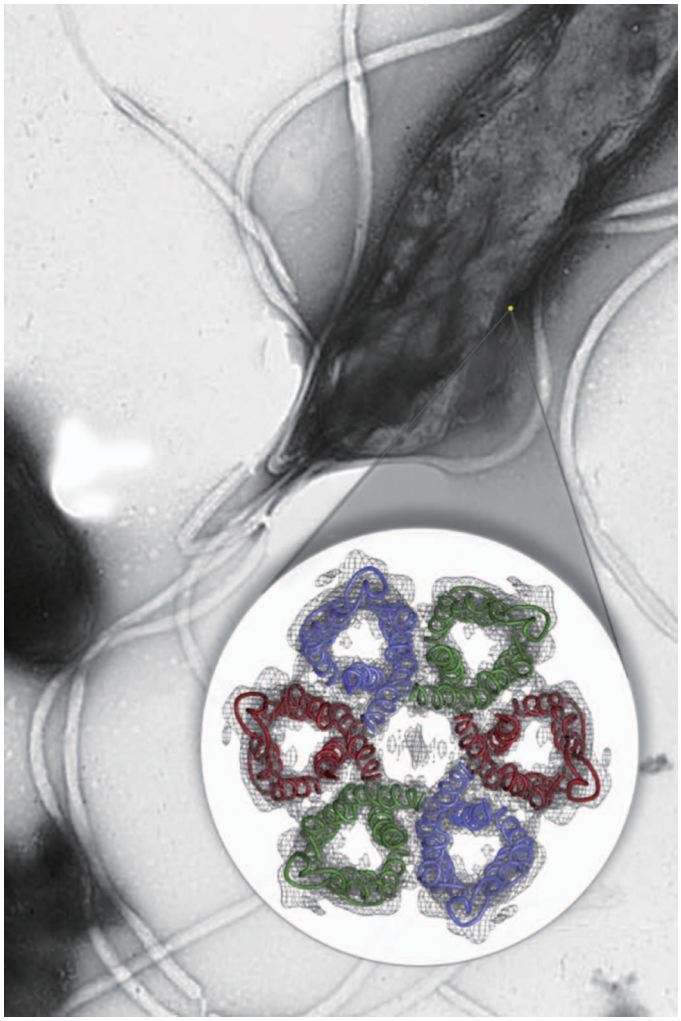
Hartmut Luecke[1], George Sachs[2]

[1]Center for Biomembrane Systems, University of California, California, USA; [2]David Geffen School of Medicine, University of California Los Angeles and Greater West Los Angeles Health Care System, California, USA

Experiments at UC Irvine (Luecke Lab), UCLA (Sachs Lab) and the U.S. Department of Energy's (DOE) SLAC National Accelerator Laboratory have revealed a potential new way to attack *Helicobacter pylori* (*H. pylori*) bacteria, via disrupting their own mechanism for protecting themselves against gastric acid. The breakthrough was achieved using powerful X-rays from SLAC's Stanford Synchrotron Radiation Lightsource (SSRL), by which the three-dimensional molecular structure of this promising drug target has been deciphered.

On the Cover of this issue of *Immuno-Gastroenterology*, we present a diagram showing the first-ever glimpse of the six-molecule ring of acid-gated urea channels embedded in the membrane of *H. pylori* bacterium. Solving the structure of the protein to find the specific area to target was rather demanding. The channels are formed by the protein embedded in the bacterium's cell membrane, and membrane proteins are notoriously difficult to crystallize, which is a prerequisite for using protein crystallography, the main technique for determining protein structures. This technique bounces X-rays off the electrons in the crystallized protein to generate the experimental data used to build a 3-D map showing how the protein's atoms are arranged.

The six-molecule ring of urea channels is embedded in the plasma membrane of *H. pylori*. When the periplasmic pH is below 6, urea passes from the gastric juice through the center of each of the six channel molecules to the cytoplasm, where cytoplasmic urease hydrolyzes it into ammonia and carbon dioxide, which in turn buffer the periplasm. The center of the ring is filled with a lipid bilayer plug. Blocking this channel with a drug would disable this protective system, leading to a new and specific treatment for people with the infection, without the side effects of broadband antibiotics, and possibly with lower failure rates due to resistance, approaching 30% for the current triple-therapy regimen.



Correspondence to: Hartmut Luecke, Center for Biomembrane Systems, University of California, California, USA; Email: hudel@uci.edu
DOI: 10.7178/ig.28