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Crystal Structure of *Helicobacter pylori* Urease Reveals an Exquisite Molecular Design Suitable for Surviving Gastric Acid

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Helicobacter pylori (*Hp*), an important etiologic agent in a variety of gastroduodenal diseases, produces a large amount of urease, which is believed to neutralize gastric acid by producing ammonia for the survival of the bacteria. Up to 30% of the enzyme is associated with the surface of intact cells by lysis of neighboring bacteria. However, the role of the external enzyme has been a subject of controversy, because the enzyme is irreversibly inactivated below pH 5. We have determined the crystal structure of *Hp* urease which reveals a 1.15 megadalton spherical assembly of twelve catalytic units with an outer diameter of ~160 Å. Under a physiologically relevant condition, the enzyme is not affected even at pH 3.0. Activity assays at different conditions indicate that the cluster of the twelve active sites on the supramolecular assembly is critically important for the survival of the enzyme at low pH. The structure provides a novel example of molecular evolution that has acquired acid resistance and thereby enabled the organism to inhabit the hostile niche. In addition, the structure provides valuable information of the enzyme active site for developing therapeutic agents against *Hp*.