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Supramolecular assembly and acid-resistance of *Helicobacter pylori* urease

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Abstract

Helicobacter pylori, 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 becomes associated with the surface of intact cells upon lysis of some neighboring bacteria. The role of this external enzyme has been a subject of controversy, because the enzyme is irreversibly inactivated below pH 5. We have determined the crystal structure of *H. pylori* urease which reveals a 1.1 megadalton spherical assembly of twelve catalytic units with an outer diameter of ~160 Å. Under physiologically relevant conditions, the activity of the enzyme remains unaffected even down to pH 3. Activity assays under different conditions indicated 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 a molecular assembly adapted for acid-resistance, which is likely to enable the organism to inhabit the hostile niche together with a quite low K_M value of the enzyme.