Crystal Structure of the Hexameric Traffic ATPase of the *Helicobacter pylori* Type IV Secretion System

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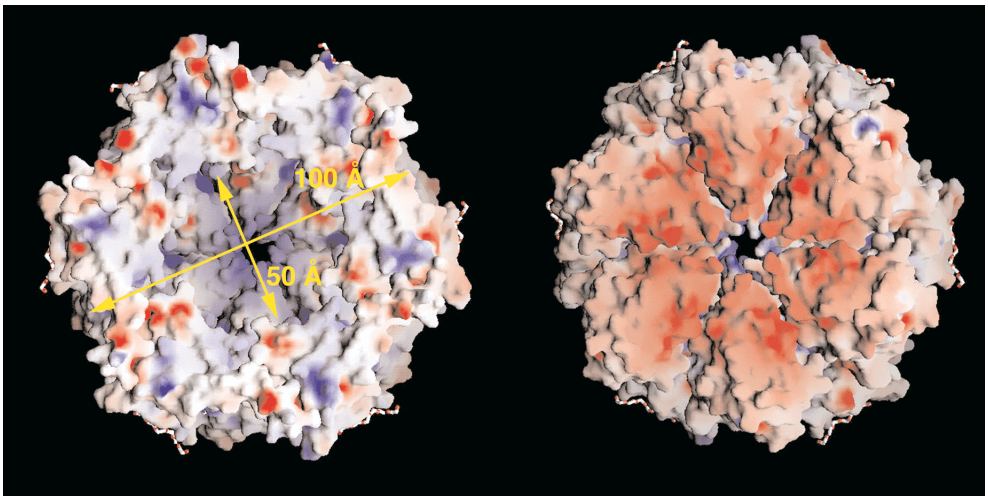

FIG. 1. At left: Surface of the HP0525-ADP complex viewed down the large hole. The inside and outside dimensions of the HP0525 chamber are indicated in yellow. At right: Surface of the HP0525-ADP complex viewed down the small hole of the chamber.

The type IV secretion system of *Helicobacter pylori* encoded by the Cag pathogenicity island (PAI) is implicated in peptic ulcer and gastric cancer. This system, which consists of about 10-15 proteins, is responsible for transport and injection of the toxic protein CagA into target epithelial cells. Secretion of CagA crucially depends on the hexameric ATPase, HP0525, encoded by the *hp0525* gene, a member of the Cag PAI. Here we present the crystal structure of a binary complex of HP0525 bound to ADP at a resolution of 2.5 Å.[1] Each monomer consists of two domains formed by the N- and C-terminal halves of the sequence. ADP is bound at the interface between the two domains. In the hexamer, the N- and C-terminal domains form two rings, which together form a chamber open on one side and closed on the other. The open side of the chamber is formed by the N-terminal domain ring and has an inner dimension of 50 Å in diameter (Fig. 1). This ring is believed to be partly embedded in the membrane. The closed side is formed by the C-terminal domains, has a conical shape shrinking to 10 Å in diameter, and is believed to be exposed to the cytoplasm (Fig. 1). Overall, the hexameric HP0525 has the shape of a closed grapple, where the claws of the grapple, formed by the C-terminal domains, are coming together to form the base of the chamber. The structure has features reminiscent of chaperones and suggests a role for HP0525 in translocating proteins through the inner membrane. A model is proposed in which HP0525 functions as a pore, the closure and opening of which is regulated by ATP binding and ADP release.

Reference

[1] H.-J. Yeo, S.N. Savvides, A.B. Herr, E. Lanka, and G. Waksman, Mol. Cell. **6**,1461-1472 (2000).