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Structure of the month

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The *Legionella* HtrA homologue DegQ is a self-compartmentizing protease that forms large 12-meric assemblies

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Abstract

Proteases of the HtrA family are key factors dealing with folding stress in the periplasmatic compartment of prokaryotes. In *Escherichia coli,* the well-characterized HtrA-family members DegS and DegP counteract the accumulation of unfolded outer-membrane proteins (OMPs) under stress conditions. Whereas DegS serves as a folding-stress sensor, DegP is a chaperone-protease facilitating refolding or degradation of defective OMPs. Here we report the 2.15-Å resolution crystal structure of the second major chaperone-protease of the periplasm, DegQ from *Legionella fallonii*. DegQ

assembles into large, cage-like 12-mers which form independently of unfolded substrate proteins. We provide evidence that 12-mer formation is essential for the degradation of substrate proteins but not for the chaperone activity of DegQ. In the current model for the regulation of periplasmatic chaperone-proteases, 6-meric assemblies represent important protease-resting states. However, DegQ is unable to form such 6-mers suggesting divergent regulatory mechanisms for DegQ and DegP. To understand how the protease activity of DegQ is controlled, we probed its functional properties employing designed protein variants. Combining crystallographic, biochemical and mutagenic data, we present a mechanistic model that suggests how protease activity of DegQ 12-mers is intrinsically regulated and how deleterious proteolysis by free DegQ 3-mers is prevented. Our study sheds light on a previously uncharacterized component of the prokaryotic stress-response system with implications for other members of the HtrA family.

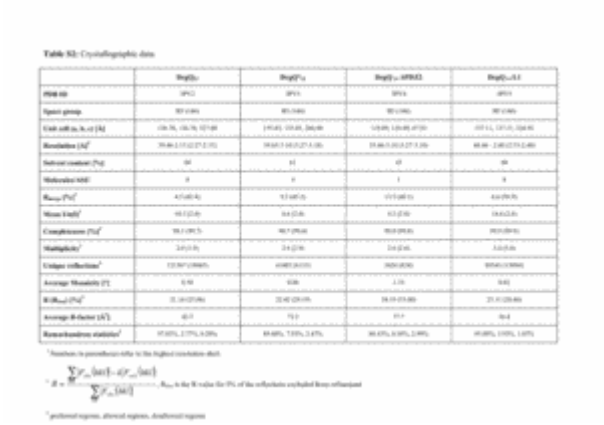

Table 1.

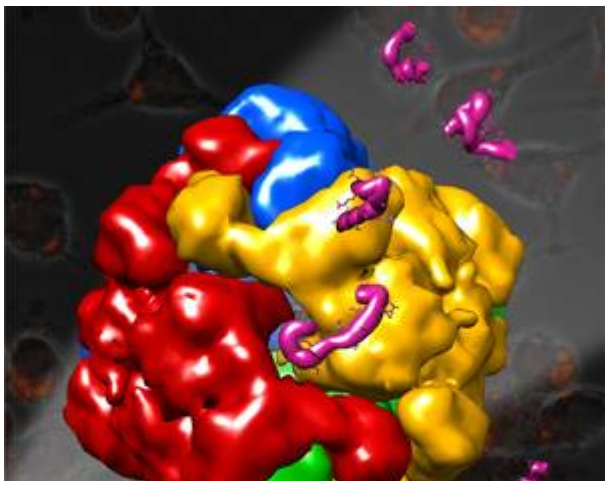

Figure 1.

DegQ from Legionella fallonii is a chaperone-protease responsible for protein quality control in the bacterial periplasm. A DegQ 12-mer composed of 4 trimers (red, blue, yellow, green) is shown in surface representation. To visualize the proteolytic activity of the 12-mer, fragments of a misfolded substrate molecule (purple) undergoing degradation have been manually added. Macrophages infected with Legionella bacteria are shown in the background.

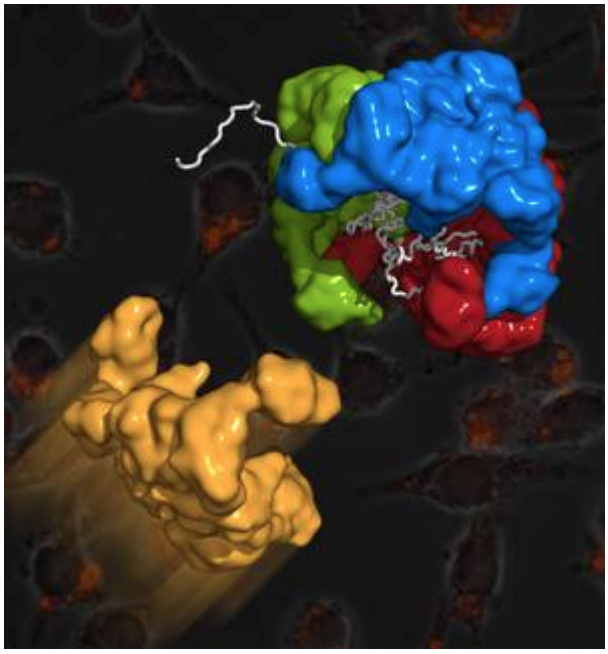

Figure 2.

Model of a DegQ molecule in the process of encapsulating a substrate molecule. DegQ trimers (red, blue, yellow, green) are shown in surface representation and a substrate molecule as ribbons (white).

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