Title

Novel Adaptor-Dependent Domains Promote Processive Degradation by ClpXP

Authors

Keith L. Rood, *University of Massachusetts Amherst* Follow

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Abstract

Protein degradation by ATP dependent proteases is a universally conserved process. Recognition of substrates by such proteases commonly occurs via direct interaction or with the aid of a regulatory adaptor protein. An example of this regulation is found in *Caulobacter crescentus*, where key regulatory proteins are proteolysed in a cell-cycle dependent fashion. Substrates include essential transcription factors, structural proteins, and second messenger metabolism components. In this study, we explore sequence and structural requirements for regulated adaptor mediated degradation of PdeA, an important regulator of cyclic-di-GMP levels.

Robust degradation of PdeA is dependent on the response regulator CpdR *in vivo* and *in vitro*. Here, I structurally identify a novel PAS domain in PdeA that is necessary and sufficient for CpdR mediated PdeA degradation. The PAS domain was found to contain a unique dimerization element that is associated with PdeA function. I show specifically that PdeA engages ClpXP through C-terminal recognition motifs. Finally, we present evidence that PdeA contains cryptic ClpXP recognition sites that are revealed during partial processing. Due to these uncommon degradation characteristics of PdeA, unique proteolytic insights may be gained by investigating this model system.

First Advisor

Peter Chien

Second Advisor

Peter Chien

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