Abstract

Intracellular proteolysis is an essential regulatory process that affects cellular physiology. Since proteolysis destroys proteins irreversibly, this process must be strictly controlled. The AAA+ proteins are the key factors in regulated proteolysis in bacteria. These proteins consist of two functional domains, the AAA+ chaperone domain and the protease domain. One particular group of these AAA+ protein is the Clp protein family. Functional domains of the Clp family are formed by seperate proteins. The hexameric unfoldase ClpX is a member of this protein family. This unfoldase can interact with the highly conserved ClpP protease to form a ClpXP proteolytic complex. This proteolytic complex utilizes the energy of ATP binding and hydrolysis to unfold and translocate the specifically tagged substrate into the ClpP degradation chamber. Substrate recognition is mediated by the binding of ClpX to short unstructured sequences called degradation tags. ClpX recognizes several degradation tags, but the most important one is recognition of the ssrA degradation tag, which is the output of the tmRNA ribosome rescue system. Although ClpX interacts with ClpP, it affects a variety of cellular processes such as the expression of virulence factors or the adaptation to stress factors, ClpX can work independently of ClpP. Such roles include for example the regulation of the Rot protein expression. Rot is responsible for the production of the major staphylococci virulence factor protein A. Since ClpX and ClpP are involved in the production of virulence factors, it appears that they could be an ideal alternative target for the development of new antimicrobial substances that can be targeted to restore the sensitivity of the resistant bacteria.

Key words

AAA+ proteases, ClpX, ClpP, ClpXP, function, structure, bacteria, virulence, physiology