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Structural diversity and similarity among Clp chaperones from plants and mycobacteria

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Unfolded or damaged proteins in a cell usually get targeted for degradation before they start accumulating and reach toxic levels. In bacteria as well as plants, chaperones and proteases perform a major role in this important protective and restorative function. Caseinolytic protease-associated chaperone C1 (ClpC1) is one such protein that performs the function of cellular protein quality control, primarily through its association with ClpP1P2 protease core in mycobacteria, wherein the chaperone aids in ATP-dependent unfolding of protein substrates to be degraded by the protease machinery. In case of plants, they have the Clp chaperones ClpC1 and ClpC2 which associate with a similar protease core - ClpPR, all within the chloroplast stroma. In addition, plants have an additional stromal chaperone called ClpD which also associates with Clp protease. ClpC and ClpD proteins belong to the family of AAA+ HSP100 proteins. Both are functional as hexamers and have a 3-domain organization wherein the N-terminal domain is mostly involved in substrate recognition and the middle and C-terminal domains are with ATPase activity, aiding substrate unfolding. Crystal structures reveal the N-terminal domain of ClpC1 from *M. tuberculosis* and *A. thaliana* to be very similar in organization; however, the plant specific AtClpD has a structural organization quite different from any known Clp chaperones that have been characterized so far. Herein, we discuss the findings from our structural studies on Clp chaperone proteins from *Mycobacterium* and Arabidopsis.

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