World Academy of Science, Engineering and Technology
International Journal of Biotechnology and Bioengineering
Vol:11, No:09, 2017

Folding Pathway and Thermodynamic Stability of Monomeric GroEL

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Abstract : Chaperonin GroEL is a tetradecameric Escherichia coli protein having identical subunits of 57 kDa. The elucidation of thermodynamic parameters related to stability for the native GroEL is not feasible as it undergoes irreversible unfolding because of its large size (800kDa) and multimeric nature. Nevertheless, it is important to determine the thermodynamic stability parameters for the highly stable GroEL protein as it helps in folding and holding of many substrate proteins during many cellular stresses. Properly folded monomers work as building-block for the formation of native tetradecameric GroEL. Spontaneous refolding behavior of monomeric GroEL makes it suitable for protein-denaturant interactions and thermodynamic stability based studies. The urea mediated unfolding is a three state process which means there is the formation of one intermediate state along with native and unfolded states. The heat mediated denaturation is a two-state process. The unfolding process is reversible as observed by the spontaneous refolding of denatured protein in both urea and head mediated refolding processes. Analysis of folding/unfolding data provides a measure of various thermodynamic stability parameters for the monomeric GroEL. The proposed mechanism of unfolding of monomeric GroEL is a three state process which involves formation of one stable intermediate having folded apical domain and unfolded equatorial, intermediate domains. Research in progress is to demonstrate the importance of specific residues in stability and oligomerization of GroEL protein. Several mutant versions of GroEL are under investigation to resolve the above mentioned issue.

Keywords : equilibrium unfolding, monomeric GroEl, spontaneous refolding, thermodynamic stability
Conference Title : ICBB 2017 : International Conference on Biophysics and Bioengineering
Conference Location : Zurich, Switzerland
Conference Dates : September 15-16, 2017