

PT13 Insights into the dissociation processes of structurally diverse proteins

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polydisperse proteins, structural constraints, non-sequential CID

CID provides insights into the substructure of oligomeric proteins

1. The α -crystallins are polydisperse small heat shock proteins that are implicated in a number of protein deposition diseases. We have employed novel mass spectrometry techniques to investigate changes in quaternary structure associated with a switch from chaperone to adjuvant of aggregation. We replicated the oligomeric rearrangements observed for post-translationally modified α -crystallins, without altering the protein sequence, which resulted in a loss of dimeric substructure and augmentation of substrate affinity. We show that packaging of small heat shock proteins into dimeric units is used to control the level of chaperone function. We propose that a bias toward monomeric substructure is responsible for the aberrant chaperone behavior associated with the α -crystallins.

2. Asymmetric dissociation of multiply charged proteins assemblies has been frequently reported. Gas-phase dissociation studies of the brown snake venom, textilotoxin, reveal the existence of two distinct isoforms. Interestingly, the mechanism of dissociation of textilotoxin was unusual, as rather than one subunit being largely removed prior to sequential dissociation of a second, the process was predominantly concurrent for the two smallest subunits. Furthermore, a small proportion of the dissociated species was observed to be a noncovalently associated dimer. A comparison of dissociation pathways for two neighboring charge states demonstrates that, in agreement with previous reports, variations in quaternary structure are responsible for the distinct charge states of a protein.