Abstract Submitted
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Computational modeling of protein folding assistance by the eukaryotic chaperonin CCT[1] MANORI JAYASINGHE, GEORGE STAN, University of Cincinnati — Chaperonins are biological nanomachines that promote protein folding using energy derived from ATP hydrolysis. Structurally, chaperonins are large oligomeric complexes that form double-ring construct, enclosing a central cavity that serves as folding chamber. Our focus is on the substrate binding mechanisms of the Eukaryotic chaperonin CCT and Archaeal chaperonin Thermosome. We contrast our results with the annealing action of the bacterial chaperonin GroEL of *E. coli.*, currently the best studied for chaperonin machinery. CCT was suggested to be more selective towards the substrate recognition where as GroEL is more promiscuous due to the hydrophobic interactions. We study the interaction of CCT with Tubulin, one of its stringent substrates. Using molecular docking and molecular dynamics simulations, we probe binding of a βtubulin peptide (205-274) to the CCTγ apical domain. We identify a versatile binding mechanism, involving mostly hydrophobic interactions with the helical region and electrostatic interactions with the helical protrusion region. This specific substrate-protein recognition mechanism is likely to be optimized for specific substrate protein-CCT subunit pairs.

[1]American Heart Association

Manori Jayasinghe
University of Cincinnati

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