Structure Based Design of Inhibitors for Bacterial Hsp70 System

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Abstract:
The structure-based drug designing is a rapidly growing field which resulted in successful lead molecules against important targets in recent years. This approach requires target macromolecule and its structural information. The lead molecules can be designed by *in silico* docking of the small molecules against these targets and the best fit candidate molecules can be tested both *in vitro* and *in vivo*. In recent years, researchers are targeting protein-protein interaction (PPI) interfaces, which play an active role in the progression of both intra- and extracellular processes in the living system. PPIs also play essential roles in bacterial survival, and any alteration in these interactions may hamper the bacterial growth.

The disruption or stabilization of PPIs in bacteria could potentially be one of the therapeutic targets, and it opens a new area of antibiotic drug discovery. Towards this goal, we are targeting the Hsp70 system, chaperone machinery in bacteria essential under stress condition. Hsp70 called DnaK in bacteria operates via the concerted action of two other co-chaperones; DnaJ, and GrpE. By using structure-based inhibitor design, our aim is to develop small molecule inhibitors to disrupt Hsp70 chaperone interactions in bacteria, which could be a potential leads for antibacterial drug development.