

Oral Presentation

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## Protein quality control systems: Mechanisms and applications

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A protein quality control system, consisting of molecular chaperones and proteases, controls the folding status of proteins and prevents the aggregation of misfolded proteins by either refolding or degrading aggregation-prone species. During severe stress conditions or upon protein overproduction this protection system can be overwhelmed by high substrate load, resulting in the formation of protein aggregates. In such emergency situations, ClpB/Hsp104, a ring-forming AAA<sup>+</sup> chaperone, can become a key player for cell survival, as it has the extraordinary capacity to rescue proteins from an aggregated state in cooperation with an Hsp70 chaperone system.

We could recently demonstrate that ClpB/Hsp104 extracts unfolded polypeptides from an aggregate by threading them through its central pore. This translocation activity is necessary but not sufficient for aggregate solubilization. In addition, the middle (M) domain of ClpB and the Hsp70 system have essential roles, potentially by providing an additional unfolding force, which facilitates the extraction of misfolded proteins from aggregates. Here we report on both, novel mechanistic aspects of the disaggregation machinery and its application to increase the solubility of model substrates.