

Hsp70 with a Two-fold Function to Guide Protein Folding in Living Cells

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The Hsp70 family of molecular chaperones is extensively reported to prevent aggregation from unfolded proteins or dissolve toxic protein aggregates. Recent studies suggest they may also actively assist proteins to fold or prevent the native state from misfolding. Nevertheless, there is little evidence for these latter chaperone functions. Also, the multiplicity of Hsp70 function may remain uncovered in vitro utilizing isolated chaperone components. Here, we uncovered the mechanistic action of Hsp70 chaperones on protein folding landscapes inside living cells. We show that Hsp70 chaperones catalyse folding of a set of barnase and superoxide dismutase 1 (SOD1) variants while protecting the native state from unfolding under heat stress. Our study identifies two different ways Hsp70 chaperones aid proteins to fold inside cells, essential to understand protein homeostasis in health and disease.