Ssq1-Jac1, a specialized chaperone system involved in biogenesis of Fe-S cluster containing proteins in yeast mitochondria.

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In yeast mitochondria specialized chaperone system consisting of Ssq1 (Hsp70), and Jac1 (J-protein) function in the biogenesis of Fe-S clusters. Unlike typical Hsp70-J-protein systems, Ssq1 and Jac1 interact very specifically with a single substrate protein- Isu, a scaffold on which Fe-S clusters are built prior to its transmission to a recipient protein. Moreover, studies using purified proteins indicated that like a typical J-protein, Jac1 specifically stimulates the ATPase of its Hsp70 partner, thus promoting formation of a stable Ssq1-Isu1 complex in the presence of ATP.

To assess whether interactions of Ssq1-Jac1 chaperones with Isu substrate are important for their in vivo function we have taken advantage of the fact that inactivation of either Ssq1 or Jac1 leads to easily detectable phenotypes. Therefore, we asked if defects in contacts amongst components of the system leads to similar phenotypic effects. We found that substitutions within Isu1 that resulted in an inability to form a stable complex with Ssq1 in vitro correlated well with profound growth phenotypes. Moreover, a substitution within the substrate binding cleft of Ssq1, which dramatically affected its affinity for Isu in vitro, strongly compromised its in vivo functions. These results underscore the importance of Ssq1-Isu1 complex formation for in vivo function. The Jac1-Ssq1 interaction for in vivo function is also required, as alteration within the J-domain results in a decreased ability to stimulate ATPase activity of Ssq1 in vitro and significant phenotypic effect in vivo.

Surprisingly, another alteration in the Ssq1 substrate binding cleft that had only a slightly less drastic effect on the Ssq1-Isu interact resulted in only mild phenotypic effects. Thus this chaperone system is very robust, tolerating a decrease in affinity for its substrate surprisingly well in vivo. in vitro increasing concentrations of Isu1 and Jac1, which form a stable complex, were able to compensate for a lowered affinity of Ssq1 for Isu . Thus, the ability of Jac1 to target Isu for Ssq1 binding could explain robustness of the system.