The function of the molecular co-chaperone prefoldin during mitochondrial stress

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Proteins must obtain their correct fold to fulfill their cellular functions. If proteins cannot be folded properly they tend to aggregate causing a burden for protein homeostasis. Failure to maintain a correctly folded proteome is linked with numerous diseases. Molecular chaperones are dedicated machinery that folds newly synthesized proteins, but also protect unfolded proteins from aggregation, help to rescue the function of proteins by facilitating disaggregation and guide proteins for degradation.

The co-chaperone prefoldin is a hexameric protein complex also called the Gim complex in the yeast Saccharomyces cerevisiae. It is mainly known to assist the folding of the newly synthesized cytoskeleton proteins actin and tubulin. However, recent research indicates that prefoldin might play a role during protein homeostasis maintenance. We analysed the consequences of the loss of prefoldin subunits for yeast growth under various stress conditions. We found that prefoldin is necessary to withstand a variety of exogenously added stressors. Moreover, we are investigating the role of prefoldin during the physiological processes of mitochondrial biogenesis. The function of mitochondria is linked with cellular protein homeostasis depending on the import of proteins, which are encoded by genes in the nucleus and synthesized on cytosolic ribosomes. While much is known about the import of mitochondrial proteins, little knowledge exists on the fate of mitochondrial destined proteins in the cytosol under basic and stressed cellular conditions. Our data show that the loss of some prefoldin subunits compromises mitochondrial morphology. Thus, we aim to understand mechanisms of how prefoldin is involved in the maintenance of cellular and/or mitochondrial protein homeostasis upon mitochondrial stress conditions. The prefoldin substrate landscape might also include mitochondrial precursor proteins.

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