

Msp1/ATAD1: The Molecular Vacuum Cleaner

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When cells experience stress, the efficiency and faithfulness of protein targeting are compromised, leading to homeostatic imbalances and damage to organelles. Yeast Msp1 (mitochondrial sorting of proteins 1) and mammalian ATAD1 (ATPase family AAA domain-containing 1) are orthologous AAA proteins that, fueled by ATP hydrolysis, recognize and extract mislocalized membrane proteins from the outer mitochondrial membrane. Msp1 and ATAD1 are implicated in multiple diseases in various animal models, including male infertility in fruit flies and neurological disorders in mammals. Through the cryo-EM structures and cell-based assays for protein mislocalization, we show that Msp1 and ATAD1 possess several features that are specifically adapted to removing membrane proteins.