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Sommario/riassunto

Members of the HSP70 family form a central hub of the molecular chaperone network, controlling protein homeostasis in prokaryotes and in the ATP-containing compartments of the eukaryotic cells. The heat-inducible form HSPA1A (HSP70), its constitutive cytosolic cognate HSPA8 (Hsc70), its endoplasmic reticulum form HSPA5 (BiP), and its mitochondrial form HSPA9 (Mortalin), as well as the more distantly related HSPHs (HSP110s), make up 1-2 % of the total mass of proteins in human cells. They use the energy of ATP-hydrolysis to prevent and forcefully revert the process of protein misfolding and aggregation during and following various stresses, presumably by working as unfoldases to lift aberrant conformers out of kinetic traps. As such, HSP70s, in cooperation with their J-domain co-chaperones and nucleotide exchange factors (NEFs) and co-disaggregases, form an efficient network of cellular defenses against the accumulation of cytotoxic misfolded protein conformers, which may cause degenerative diseases such as Parkinson's and Alzheimer's disease, diabetes, and aging in general. In addition to their function in repair of stress-induced damage, HSP70s fulfill many housekeeping functions, including assisting the de novo folding and maturation of proteins, driving the translocation of protein precursors across narrow membrane pores into organelles, and by controlling the oligomeric state of key regulator protein complexes involved in signal transduction and vesicular trafficking. For reasons not well understood, HSP70s are

also found on the surface of some animal cells, in particular cancer cells where they may serve as specific targets for cancer immunotherapy. Here, we gathered seven mini reviews, each presenting a complementary aspect of HSP70's structure and function in bacteria and eukaryotes, under physiological and stressful conditions. These articles highlight how, the various members of this conserved family of molecular chaperones, assisted by their various J-domain and NEF cochaperones and co-disaggregases, harness ATP hydrolysis to perform a great diversity of life-sustaining cellular functions using a similar molecular mechanism.