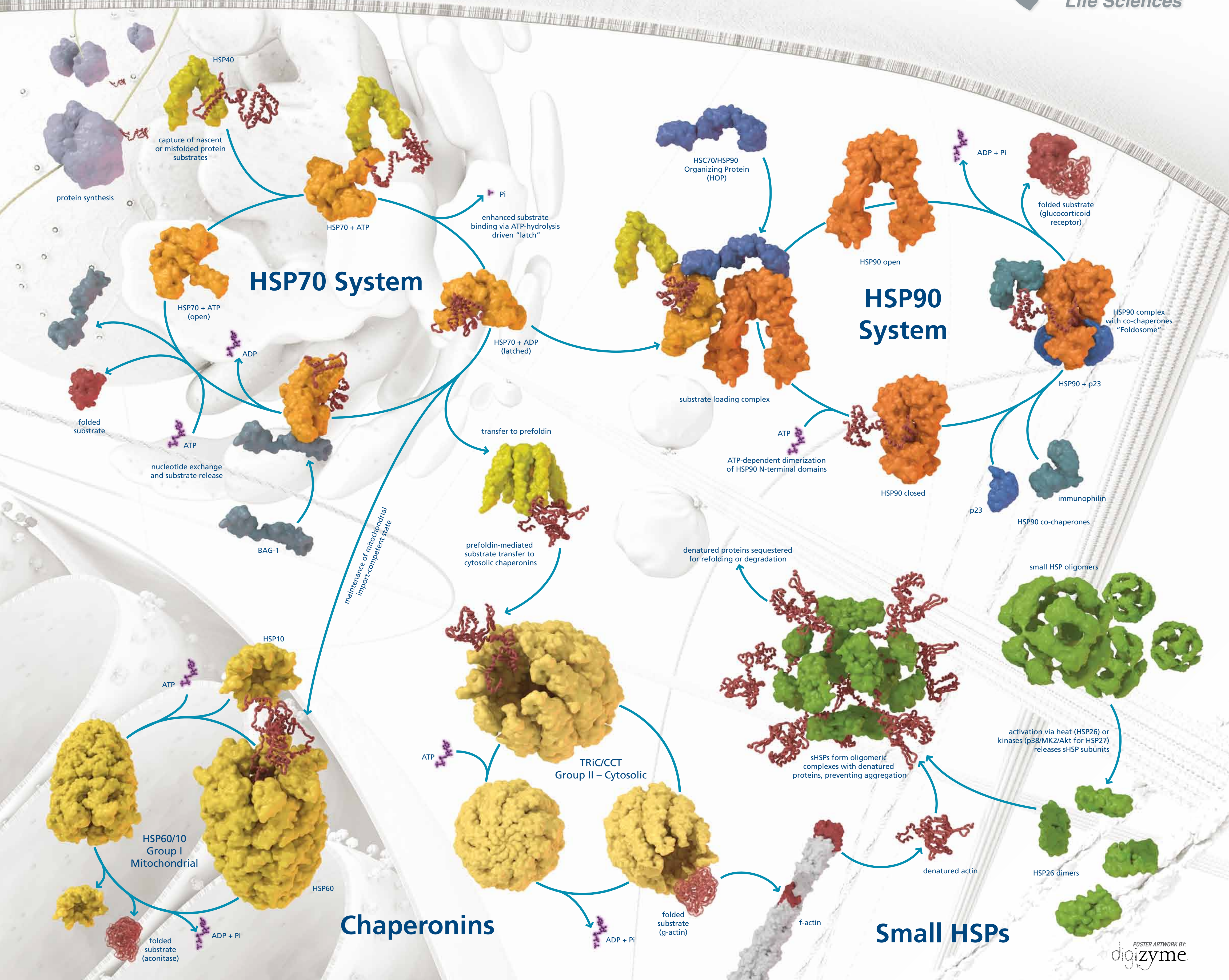


# Heat Shock Protein Chaperone Complexes



The heat shock response is a well-studied mechanism by which organisms maintain homeostasis in response to environmental stress. Heat shock protein (HSP) family members and their associated cofactors often function together in complexes, acting in concert as molecular chaperones to facilitate the proper folding and activation of many cellular proteins. Enzo Life Sciences provides the research community with a comprehensive portfolio of kits, antibodies, proteins, inhibitors and reagents for the study of heat shock proteins and the cellular response to stress.

Chaperone Family	Organism	Chaperone	Co-chaperone	Localization	Activity	Associated Disease
HSP70	Bacterial	DnaK	DnaJ, GrpE, ClpB	Cytosol	Folding, export of nascent peptides; major regulator of heat shock response; coordinates reactivation, degradation, disaggregation of stress-induced misfolding	Inhibits polyglutamine fibril formation; dysregulation of HSP70 family proteins associated with diseases typified by protein misfolding and aggregation such as Alzheimer's Disease, Multiple Sclerosis, Parkinson's Disease, Schizophrenia, Crohn's Disease, and Tuberculosis
	Mammalian	HSC70 (HSP73), HSP70 (HSP72)	HSP40, Hop, Bag1-5, Hip, HSPBP1, CHIP, SGT, HSP110 homologs, Tom70, TPR1	Cytosol	Cognate form (HSC70/HSP73) assists constitutive folding and transport of proteins to organelles such as the mitochondria, nucleus, and ER; HSP70/HSP72 is induced upon heat shock and mediates similar functions in response to stress-induced increases in protein misfolding and aggregation	
		HSP110	HSP70	Cytosol	Stress responsive, prevents protein aggregation	
		HSP70L1	MPP11	Cytosol	Mammalian homolog of yeast Ssz1; assists folding of new proteins on ribosome	
		Bip/Grp78	DnaJ-like ER proteins (e.g., Grp170, Sil1/Sls1)	ER	Binds folding and translocation intermediates to prevent aggregation; involved in calcium homeostasis, translocation, folding, transport, and retrotranslocation of polypeptides; regulator of unfolded protein response.	
		mtHSP70 (Grp75/Mortalin)		Mitochondria	Protein folding and translocation in the mitochondria	
HSP40	Bacterial	DnaJ	DnaK, GrpE	Cytosol	Modulates ATPase activity of DnaK, association of DnaK with nascent polypeptides, binds unfolded proteins	Huntington's Disease, Parkinson's Disease
	Mammalian	Hdj1/2 (HSP40), Auxilin	HSP70, Hip	Cytosol	Modulates ATPase activity and peptide loading of HSC70/HSP70; auxilin coordinates HSC70-mediated uncoating of clathrin vesicles	
HSP90	Bacterial	HtpG		Cytosol	Stress responsive protein refolding	Target of Geldanamycin-derived anti-cancer drugs (e.g., 17-AAG, 17-DMAG) which disrupt HSP90-chaperoned oncogenic signaling pathways; Immunophilin FK506 associated with Leber congenital amaurosis
	Mammalian	HSP90/83/89	Hop, Hip, HSP70, p50, p23, CHIP, Sgt1, TPR2, Immunophilins	Cytosol	Folding and conformational regulation of signaling proteins, regulation of steroid hormone receptors and kinases	
		Grp94	Grp78	ER	Folding and assembly of secretory proteins	
Chaperonin	Bacterial	GroEL	GroES	Cytosol	Involved in folding of some cytosolic proteins, especially overproduced proteins; stabilizes proteins in response to stress, assists in protein refolding	Impaired chaperonin function associated with McKusick-Kaufman and Bardet-Biedl syndromes, mitochondrial protein folding defects in lactic acidemia and hereditary spastic paraplegia
	Mammalian	mtHSP60	HSP10	Mitochondria	Folds newly imported mitochondrial proteins	
		TRiC/CCT	Prefoldin	Cytosol	Folds about 10% of cytosolic polypeptide chains; downstream of the HSP70 machinery	
Small HSP	Bacterial	IbpA, IbpB		Cytosol	Associated with inclusion bodies, prevents heat denatured protein aggregation	Williams syndrome, cataract, desmin-related myopathy, Multiple Sclerosis, Charcot-Marie Tooth disease, hereditary motor neuropathies, tauopathies
	Mammalian	$\alpha$ -Crystallin/HSP27		Cytosol	Prevent heat denatured protein aggregation via ATP-independent formation of high-molecular weight oligomers; phosphorylation of HSP27 monomers/dimers regulate microfilament polymerization	
Ribosome Associated	Bacterial	Trigger Factor (TF)		Cytosol	Generally associates with nascent polypeptide chains to assist folding; catalyzes peptidyl-prolyl isomerization <i>in vitro</i>	Altered intracellular levels of NAC subunits associated with Alzheimer's Disease, AIDS, Trisomy 21, brain tumors, ductal carcinoma <i>in situ</i> ; TF contributes to bacterial virulence
	Mammalian	NAC		Cytosol	Similar to bacterial Trigger Factor; consists of heterodimer of $\alpha$ and $\beta$ subunits, dissociates from peptide as it is released from ribosome	
HSP100	Bacterial	ClpA	ClpP, SspB	Cytosol	ATP-dependent protein unfolding and proteolysis	HSP100 family members involved in pathogenicity and virulence of <i>Listeria</i> and <i>Leishmania</i> infection
		ClpB	DnaK, DnaJ, GrpE	Cytosol	DnaK, ATP-dependent processing of aggregated proteins	
Chaperones	Bacterial	HSP33, SecB	SecA	Cytosol	Prevent aggregation of oxidatively/thermally damaged proteins (HSP33); shuttling of secretory proteins (SecA/B)	HSP47 associated with preterm premature membrane rupture and autoimmune disorders such as rheumatoid arthritis, systemic lupus erythematosus, Sjögren's syndrome, mixed connective tissue disease
		Skp, PapD, FimC	PapC, FimD	Periplasm	Maintenance of periplasm protein solubility, Pili assembly	
	Mammalian	Calnexin, Calreticulin, PDI, HSP47 (Colliglin)	ERp57 (Cnx/Crt)	ER	Folding of ER glycosylated proteins (Cnx, Crt); collagen biosynthesis (HSP47); and assist disulfide bond formation (PDI)	

IMAGE PROTEIN DATA BANK REFERENCES: HSP70: HSC70 ATP domain + substrate binding domain (1yuu), HSC70 latch (1udo); Bag-1: bag domain (1hx1), ubiquitin domain (1twxv); HSP40: (Sis-1) 2b26; HSP90 and Co-chaperones: HSP90 closed form (Sba-1 with p23-2c9g); HSP90 open form (closed form deformed to match 2c9g-C-terminal only, but open); Immunophilin FKBP42 (2if4); Chaperonins: TRiC/CCT (1a6d) open form deformed from closed, after Meyer et al. (2003) Cell 113, 369-381; Prefoldin (1fxk); HSP60/HSP10 (GroEL/GroES-2c7d); Small HSPs: HSP26 subunits (2h53); HSP26 oligomer (emd\_1221.map) Substrates: Glucocorticoid Receptor (1m2z), Actin Fibers (hol\_41\_374), tubulin (1tff), aconitase (1c96); kinesin (3kin); F1 ATP Synthase (1tq01). TABLE REFERENCES: Chang, H.C., et al. (2007) Cell 128, 212; Tang, Y.C., et al. (2007) Cell 128, 412; Macario, A. and Macario, E.C. (2005) N Eng J Med. 353, 1489-1501.