Enzo® Life Sciences

Heat Shock Proteins & the Cellular Stress Response

HSP90 & Co-Chaperones

HSP70/HSP40 Chaperones

HSP60/HSP10 (The Chaperonins)

Small HSP & Crystallin Proteins

Other Chaperones & Stress Proteins

ALEXIS® assay designs® BIOMOL® INTERNATIONAL Stressgen®

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Enabling Discovery in Life Science®

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02/2010

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Content

Table Abbreviations

Sample Type:
CL: Cell Lysate
CS: Cell Culture Supernatant
P: Plasma
S: Serum
T: Tissue

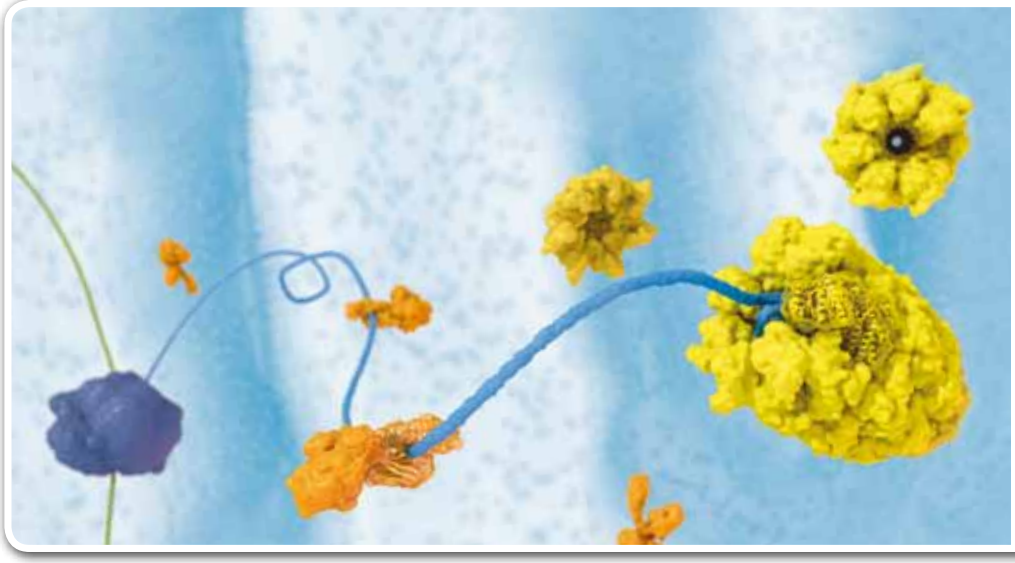
Specificity:
A: Avian
B: Bovine
BA: Bacteria
BE: Beluga
C: Canine
CE: *C. elegans*
CH: Chicken
D: *Drosophila*
F: Fish
FE: Feline
FN: Fungus
G: Goat
GP: Guinea Pig
H: Human
HA: Hamster
HO: Horse
I: Insect
M: Mouse
MO: Monkey
MU: Mussel
P: Pig
PL: Plant
R: Rat
RB: Rabbit
S: Sheep
SC: Scallop
WM: Water Mold
X: *Xenopus*
Y: Yeast

Application:
AA: ATPase Assay
EIA: Enzyme Immunoassay
EM: Electron Microscopy
FC: Flow Cytometry
IA: Inhibition Assay
ICC: Immunocytochemistry
IF: Immunofluorescence
IHC: Immunohistochemistry
IP: Immunoprecipitation
KA: Kinase Assay
WB: Western Blot

Product:
pAb: Polyclonal Antibody
mAb: Monoclonal Antibody

Conjugate:
AP: Alkaline phosphatase
FITC: Fluorescein isothiocyanate
HRP: Horseradish peroxidase
R-PE: R-Phycoerythrin

DyLight 488: DyLight™ 488 is a trademark of Thermo Fisher Scientific, Inc. and its subsidiaries.



COVER IMAGE
Conceptual image depicting HSPs as protein-folding chaperones in the mitochondria. As nascent mitochondrial peptides (light blue) emerge from the ribosome (dark blue), they are bound by the mitochondrial HSP70 (orange) via its peptide binding domain (revealed schematic ribbon structure) to prevent misfolding and aggregation. Some proteins require further folding assistance by the HSP60/HSP10 (yellow) chaperonin complexes. A single HSP60 subunit of the chaperonin complex is shown as a ribbon structure.

Introduction

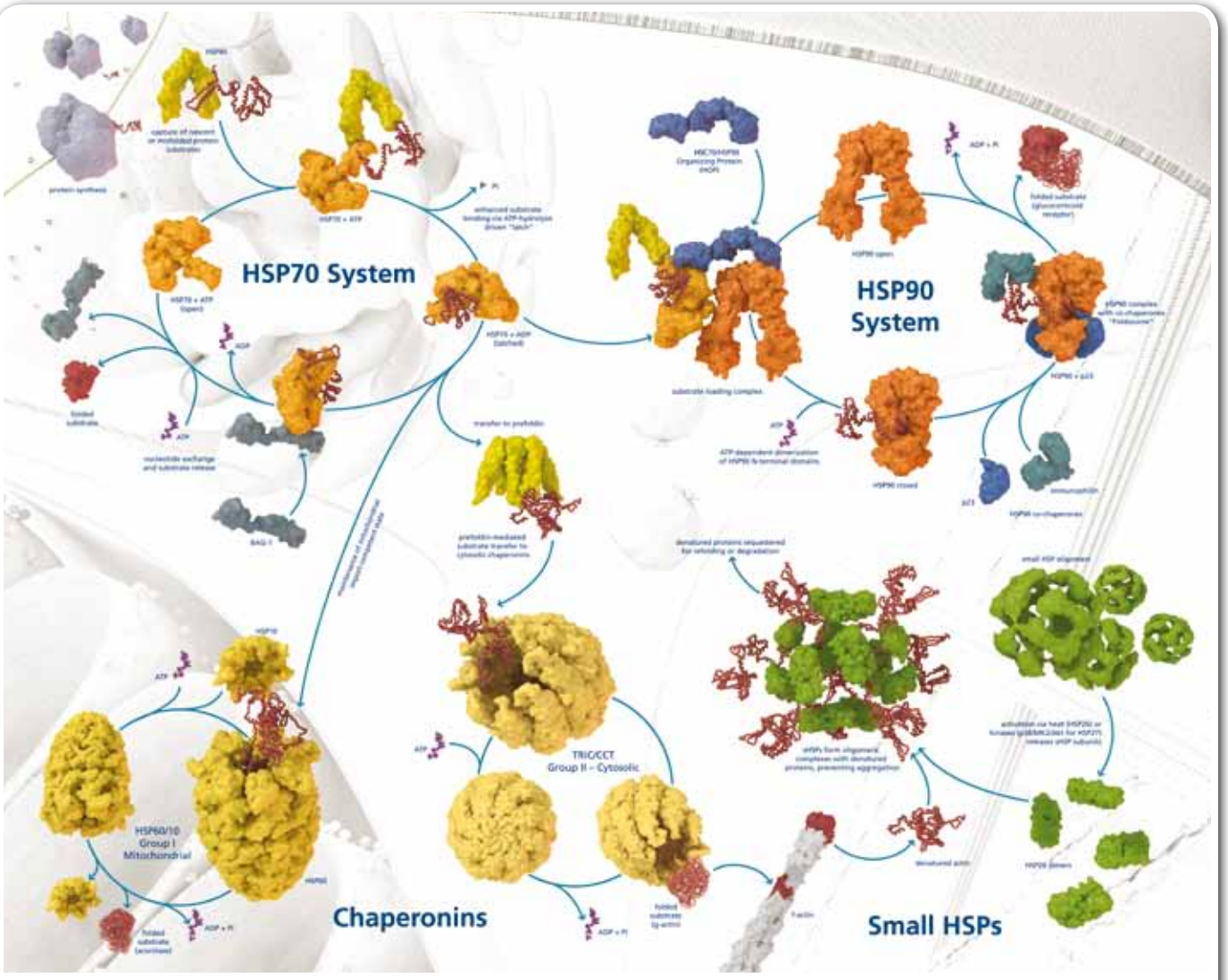


FIGURE 1: HSP chaperone complexes. HSPs and their associated cofactors often function together in complexes, acting in concert as molecular chaperones to facilitate the proper folding and activation of many cellular proteins.

Heat shock proteins (HSPs) are an evolutionary conserved family of proteins whose expression increases in response to a variety of different metabolic insults. Despite their designation, most of the HSPs are constitutively expressed and perform essential functions. Most notable is their role as molecular chaperones, facilitating the synthesis and folding of proteins throughout the cell. In addition, HSPs have been shown to participate in protein assembly, secretion, trafficking, protein degradation, and the regulation of transcription factors and protein kinases. Increased levels of HSPs after several types of stress (see Table 1) plays a central role in cellular homeostasis. As a leading life sciences and biotechnology company incorporating the experience and products of Alexis® Biochemicals, Assay Designs®, BIOMOL® International, and Stressgen®, Enzo Life Sciences is committed to providing scientists with reliable tools for scientific discovery in the area of cellular stress. Our product offering includes an extensive collection of HSP and chaperone related products including ELISA kits, antibodies, recombinant proteins, inhibitors, and peptides. We have created this "Heat Shock Proteins and the Cellular Stress Response" catalog, featuring these innovative products and an overview of the family of HSPs written by Dr. William J. Welch. For more HSP reference and product information, visit www.enzolifesciences.com/HSP.

All organisms exhibit homeostatic-like responses when subjected to rapid changes in their environment. The ability of the organism to successfully adapt or acclimate to its new environment is critical to its survival, and likely represents an integral driving force in evolution. One well studied response to sudden adverse environmental changes is the so-called heat shock or stress response. When confronted with physiologically relevant increases in temperature, cells from all organisms respond similarly by rapidly increasing the synthesis of a select group of proteins, the HSPs. Changes in the expression of the HSPs are controlled by a set of transcription factors referred to as heat shock factors (HSFs) 1-4. The resultant increase and accumulation of the HSPs now gives the stressed cell added protection, thereby allowing for continued cell survival. In addition to increased temperatures, other insults also result in increased HSP

expression. These include exposure of cells to various metals, amino acid analogues, hypoxia, and a large number of agents/treatments which result in reduced ATP levels. Because so many adverse conditions lead to increased HSP expression, the heat shock response now is commonly referred to as the "stress response."

Despite their designation as HSPs or stress proteins we now know that almost all of these proteins are in fact synthesized in cells grown under normal conditions (i.e. constitutive) and that their expression increases (i.e. induced) after metabolic stress. The realization that many of the HSPs function as "molecular chaperones" helps explain why these proteins are so critical for normal growth, as well as the ability of the cell to survive different metabolic insults. Specifically, in their role as molecular chaperones, the different HSPs facilitate the early stages of folding and assembly of other cellular proteins. Although they do not convey any information for the folding or assembly process, molecular chaperones act by stabilizing maturing polypeptides and thereby reduce the probability of incorrect folding or aggregation. Thus, under normal growth conditions where they are expressed at modest levels, members of the HSP family participate in the early stages of protein synthesis, protein folding, and the transport of newly synthesized proteins from the cytoplasm into different intracellular compartments (see Figure 1). Under conditions of stress, where protein folding/assembly events may be compromised, the increased expression and accumulation of the stress proteins facilitates the ability of cells to both repair and synthesize new proteins to replace those that were damaged after the particular metabolic insult.

In addition to their critical role in cellular homeostasis, the stress response proteins are implicated in human disease (see Table 2). Various medical conditions, including fever, ischemia, hemodynamic overload or neurological injuries are well known activators of the stress response *in vivo.* The ability of the affected tissue or organ to mount a robust stress response is thought to be important for its survival and recovery. In infectious diseases, stress proteins present within different pathogens are known to be major targets of our immune system. Most notable is the bacterial GroEL protein, the so called "common antigen," which elicits both a strong humoral and cellular immune response whenever animals are infected with different microbes. Similarly, parasitic forms of HSP70 (and in some cases HSP90) also represent immunodominant antigens prompting the idea that the immune system preferentially targets stress proteins during pathogenic infections. Perhaps not too surprising is the observation that certain members of the stress protein family, such as HSP27 along with certain members of the HSP70 family, may serve important roles in how cells decide whether to undergo apoptosis. Finally HSP90, one of the most intriguing stress proteins, now is recognized as a central player in a wide variety of cellular signaling pathways. First observed to interact with and possibly regulate tyrosine-specific protein kinases, HSP90 (along with a large number of co-factors) is now known to interact many client proteins including: steroid hormone receptors, numerous transcription factors, many protein kinases and phosphatases, and cell cycle regulatory components to name just a few. As we learn more about their structure and function, HSPs surely will continue to represent important players in our approach to diagnosing and treating human diseases.

Table 1: Cell Stressors that Induce Heat Shock Proteins

Stressor or Stressor Type	Name or Description
Physical	Heat (including fever), cold, several types of irradiation, including ultraviolet light and magnetic fields
Oxygen	Oxygen-derived free radicals (reactive oxygen species), hydrogen peroxide, a shift from anaerobiosis to aerobiosis (e.g. reperfusion), hypoxia-anoxia (ischemia)
pH	Alkalosis, acidosis, pH shift
Biologic	Infection, inflammation, fever
Psychological	Emotions, emotional conflicts, hormonal imbalance (hypothalamic-pituitary-adrenal axis and autonomic nervous system)
Osmotic	Changes in the concentrations of salt, sugars, and other osmolytes (hyperosmotic or hypo-osmotic shock)
Nutritional	Starvation involving multiple nutritional components (carbon, glucose, nitrogen, phosphate, and nitrate) or any one of these
Antibiotics	Puromycin, tetracycline, nalidixic acid, doxorubicion
Alcohols	Ethanol, methanol, butanol, propanol, octanol
Metals	Cadmium, copper, chromium, zinc, tin, aluminum, mercury, lead, nickel
Mechanical	Compression, shearing, stretching
Other	Desiccation, benzene and derivatives, phenol and derivatives, teratogens, carcinogens, mutagens, arsenite, arsenate, amino acid analogues, nicotine, anesthetics, insecticides, pesticides

Table from Macario, *et al.,* New England J. Med. **353,** 1489 (2005).

Table 2: HSP and Chaperone Associated Diseases

Family	Associated Disease	Organism	Chaperone	Co-Chaperone	Localization	Activity
Chaperonin	Impaired chaperonin function associated with McKusick-Kaufman and Bardet-Biedl syndromes, mitochondrial protein folding defects in lactic acidemia and hereditary spastic paraplegia	Bacterial	GroEL	GroES	Cytosol	Involved in folding of some cytosolic proteins, especially overproduced proteins; stabilizes proteins in response to stress, assists in protein refolding
		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
Chaperones	HSP47 associated with preterm premature membrane rupture and autoimmune disorders such as rheumatoid arthritis, systemic lupus erythemoatosus, Sjögren's syndrome, mixed connective tissue disease	Bacterial	HSP33, SecB	SecA	Cytosol	Prevent aggregation of oxidatively/thermally damaged proteins (HSP33); shuttling of secretory proteins (SecA/B)
			Skp, PapD, FimC	PapC, FimD	Periplasm	Maintenance of periplasm protein solubility, Pili assembly
		Mammalian	Calnexin, Calreticulin, PDI, HSP47 (Colligin)	ERp57 (Cnx/Crt)	ER	Folding of endoplasmic reticulum (ER) glycosylated proteins (Cnx, Crt); collagen biosynthesis (HSP47); and assist disulfide bond formation
HSP40	Huntington's Disease, Parkinson's Disease	Bacterial	DnaJ	DnaK, GrpE	Cytosol	Modulates ATPase activity of DnaK, association of DnaK with nascent polypeptides, binds unfolded proteins
		Mammalian	Hdj1/2 (HSP40), Auxilin	HSP70, Hip	Cytosol	Modulates ATPase activity and peptide loading of HSC70/HSP70; auxilin coordinates HSC70-mediated uncoating of clathrin vessicles
HSP70	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, Cancer and Tuberculosis	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
		Mammalian	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.
			HSC70 (HSP73), HSP70 (HSP72)	HSP40, Hop, Bag1-5, Hip, HSPBP1, CHIP, SGT, HSP110 homologues, 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 homologue of yeast Ssz1; assists folding of new proteins on ribosome
			mtHSP70 (Grp75/Mortalin)		Mitochondria	Protein folding and translocation in the mitochondria

Family	Associated Disease	Organism	Chaperone	Co-Chaperone	Localization	Activity
HSP90	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	Bacterial	HtpG		Cytosol	Stress responsive protein refolding
		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
HSP100	HSP100 family members involved in pathogenicity and virulence of *Listeria* and *Leishmania* infection	Bacterial	ClpA	ClpP, SspB	Cytosol	ATP-dependent protein unfolding and proteolysis
			ClpB	DnaK, DnaJ, GrpE	Cytosol	DnaK, ATP-dependent processing of aggregated proteins
Ribosome Associated	Altered intracellular levels of NAC subunits associated with Alzheimer's Disease, AIDS, Trisomy 21, brain tumors, ductal carcinoma *in situ*; TF contributes to bacterial virulence	Bacterial	Trigger Factor (TF)		Cytosol	Generally associates with nascent polypeptide chains to assist folding; catalyzes peptidyl-prolyl isomerization *in vitro*
		Mammalian	NAC		Cytosol	Consists of heterodimer of a and b subunits, dissociates from peptide as it is released from ribosome
Small HSP	Williams syndrome, cataract, desmin-related myopathy, Multiple Sclerosis, Charcot-Marie Tooth disease, hereditary motor neuropathies, tauopathies, Cancer	Bacterial	IbpA, IbpB		Cytosol	Associated with inclusion bodies, prevents heat denatured protein aggregation
		Mammalian	α-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

Additional Heat Shock Protein Resources

Text in this reference guide modified from text provided by Dr. William J. Welch. Dr. Welch previously served in the Surgical Research Laboratory at San Francisco General Hospital and the departments of Surgery, Medicine, and Physiology at the University of California, San Francisco. HSP Web resources: www.enzolifesciences.com/HSP

HSP suggested review articles:

1. Molecular chaperones and protein quality control: B. Bukau, *et al.*; Cell **125**, 443 (2006)
2. Molecular chaperones in the cytosol: From nascent chain to folded protein: F.U. Hartl, *et al.*; Science **295**, 1852 (2002)
3. Some like it hot: the structure and function of small heat-shock proteins: M. Haslbeck, *et al.*; Nat. Struct. Mol. Biol. **12**, 842 (2005)
4. Protein folding and quality control in the endoplasmic reticulum: B. Kleizen & I. Braakman; Curr. Opin. Cell Biol. **16**, 343 (2004)
5. Structure and mechanism of the Hsp90 molecular chaperone machinery: L.H. Pearl & C. Prodromou; Annu. Rev. Biochem. **75**, 271 (2006)
6. The J-protein family: modulating protein assembly, disassembly and translocation: P. Walsh, *et al.*; EMBO Rep. **5**, 567 (2004)

HSP90 and Co-Chaperones

HSP90, the most abundant of the HSPs, continues to fascinate scientists working in different areas of cell biology (see Table 3). Representing almost 1% of total cellular protein in unstressed cells the precise biological role of HSP90 is still unclear. Although the bacterial homologues, the HtpG family, are typically nonessential proteins, a functional HSP90 is required for viability under all conditions in eukaryotic cells. Unlike some of the other well characterized HSPs whose chaperone role involves their interaction with many cellular proteins, HSP90 exhibits some selectivity for a distinct set of "client" proteins. Most notably, HSP90 interacts with a variety of protein kinases and transcription factors important for growth and development. Examples of such clients are numerous and include: the Src family of kinases, the Raf family of kinases, certain MAP kinases, members of the steroid receptor family (all transcription factors), telomerase, the tumor suppressor p53, and even the heat shock transcription factor which functions to control the expression of the heat shock genes. Working with its very large number of co-chaperones, HSP90 appears to maintain its client proteins in a conformation that allows for their subsequent activation in response to appropriate growth signals. Not surprisingly, HSP90 and its co-chaperones are at the forefront of research for those studying signal transduction events and cancer (see Figures 2 and 4).

HSP90, like many of the HSPs, utilizes ATP binding and hydrolysis as part of its reaction cycle. Biochemical and structural analysis has revealed a complex mechanism by which ATPase-coupled conformational changes in HSP90 dictates interactions with its myriad of co-chaperones. These co-chaperone interactions in turn influence how and when HSP90 interacts with and activates/inactivates its client protein (see Figure 3). For example, HSP90 along with one set of its co-chaperones (and the HSP70/HSP40 chaperone machinery) binds to and stabilizes steroid hormone receptors in their inactive state within the cytosol. Upon subsequent binding to the appropriate steroid hormone ligand, the receptor undergoes a conformational change resulting in its acquisition of DNA binding and transcriptional activity. In a similar scenario, HSP90 along with another set of co-chaperones binds to and stabilizes the newly synthesized forms of various protein kinases, maintaining them in a folding-competent conformation. Thus, via its utilization of numerous co-chaperones and ATP, the very abundant HSP90 chaperone functions in unstressed cells to regulate client proteins important for growth and development. Altering the levels of HSP90 (via genetic means or manipulations with HSP90 inhibitory drugs) leads to rapid alterations in cell signaling pathways and the adaptation of new cellular phenotypes.

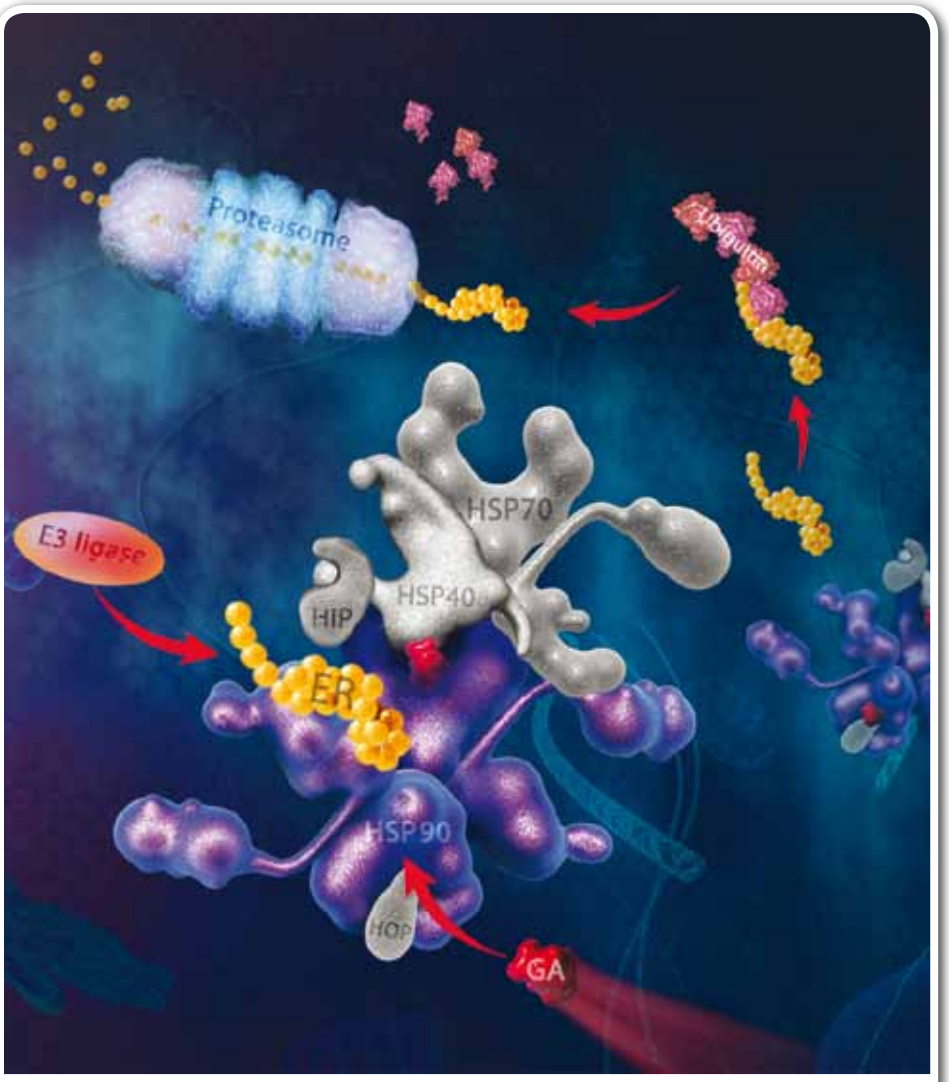


FIGURE 2: HSP90 a 'drugable' target. Inhibition of HSP90 by geldanamycin (GA) favors the ubiquintination and degradation of client proteins, such as the estrogen receptor (ER).

Less well characterized members of the HSP90 family have been described in the mammalian endoplasmic reticulum (ER) and in plants. In the case of Grp94 (glucose regulated protein in mammalian ER), there is some evidence for its involvement in facilitating the folding and transport of newly synthesized proteins destined for secretion or membrane insertion. In addition, immunologists have long been intrigued by Grp94 and its potential role in antigen presentation. Enzo Life Sciences offers a comprehensive portfolio of HSP90 products including: purified proteins, discriminating antibodies, kits, inhibitors and a host of reagents specific for the HSP90 co-chaperones.

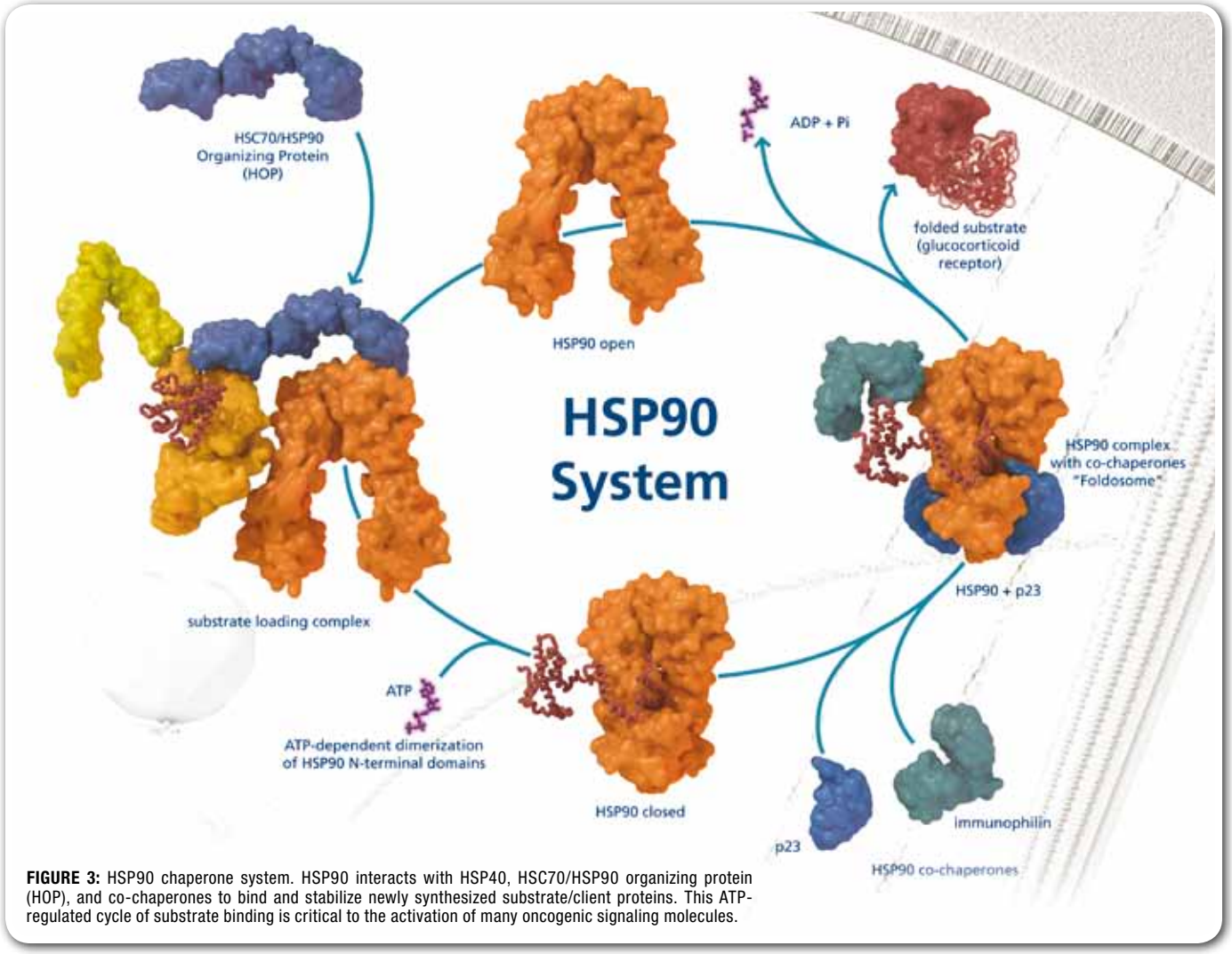


FIGURE 3: HSP90 chaperone system. HSP90 interacts with HSP40, HSC70/HSP90 organizing protein (HOP), and co-chaperones to bind and stabilize newly synthesized substrate/client proteins. This ATP-regulated cycle of substrate binding is critical to the activation of many oncogenic signaling molecules.

Table 3: HSP90 and Co-Chaperones

Name	Synonyms	Function/Structure
Aha1	Activator of HSP90 ATPase homologue 1	Stimulates the inherent ATPase activity of HSP90
Grp94	HSP90B1, Gp96	ER form; glucose regulated and induced by glucose starvation; participates in protein folding and assembly, protein secretion, protecting cells from apoptosis, and mediating immunogenicity; C-terminal sequence KDEL mediates retention in the ER; two splice variants
Hop	STIP1, STI1	Golgi; HSP70/HSP90-organizing protein; Stress-induced Phosphoprotein 1; binds EEVD motifs at the C-termini of HSP70 and HSP90; also binds Cdc37; normally found in the cytoplasm, but also seen in the nucleus depending on cell cycle/CDK activity
HSP90α	HSP90AA1, HSP86, HSP89	Cytosolic form, induced by elevated temperature; ATPase activity; three splice variants
HSP90α	HSP90AA2	Cytosolic form, induced by elevated temperature
HSP90β	HSP90AB1	Cytosolic form, constitutively expressed; ATPase activity; three splice variants
p23	TEBP, PGE Synthase 3	Binds to telomerase and progesterone receptor; also functions as a cytosolic prostaglandin E2 synthase; phosphorylated at Ser113, 118, 148 and 151 and acetylated at Lys33
p50/Cdc37		A chaperone that binds HSP90 and is required for the activity of numerous protein kinases
TRAP1	HSP75	Mitochondrial form; has ATPase activity that is inhibited by both geldanamycin and radicicol; highly conserved through evolution; phosphorylation by PINK1 prevents oxidative-stress-induced apoptosis; four splice variants

HSP90 and Co-Chaperones

Antibodies

Product	Specificity	Application	Prod. No.
Grp94, mAb (9G10)	H, M, R, B, C, CH, HA, GP, MO, P, RB, S, X	FC, IHC, WB	ADI-SPA-850
Grp94, mAb (9G10) (DyLight™ 488 conjugate)	H, M, R, B, C, CH, HA, GP, MO, P, RB, S, X	FC	ADI-SPA-850-488
Grp94, mAb (9G10) (R-PE conjugate)	H, M, R, B, C, CH, HA, GP, MO, RB, P,S, X	FC	ADI-SPA-850PE
Grp94, pAb	H, M, R, B	IP, WB	ADI-SPA-851
HSP84, pAb	H, M, R	ICC, IP, WB	ALX-210-138
HSP86, pAb	H, M, R, S	ICC, IHC, IP, WB	ALX-210-139
HSP90 co-chaperone, mAb (JJ3)	M, H	ICC, IP, WB	ALX-804-023
HSP90, mAb (16F1)	H, M, R, B, BE, C, CH, D, F, GP, HA, MO, MU, P, PL, RB, S, SC, X	WB	ADI-SPA-835
HSP90, mAb (16F1) (biotin conjugate)	H, M, R	WB	ADI-SPA-835B
HSP90, mAb (2D12)	H, M, R, BE, B, C, CH, F, GP, HA, MO, RB, S	WB	ADI-SPA-845
HSP90, mAb (3B6)	H, M, R, B	WB	ALX-804-078
HSP90, mAb (3G3)	H, M, R, CH, F	IP	ALX-804-079
HSP90, mAb (AC88)	H, M, R, BA, BE, C, CH, CE, F, GP, HA, MO, MU, P, RB, S, SC, WM	WB	ADI-SPA-830
HSP90, mAb (AC88) (DyLight™ 488 conjugate)	H, M, R, BE, C, CE, CH, F	FC	ADI-SPA-830-488
HSP90, mAb (AC88) (R-PE conjugate)	H, M, R, B, C, CH, F	FC	ADI-SPA-830PE
HSP90, pAb	H, M, R, RB	WB	ADI-SPA-836
HSP90, pAb	H, M, R, B	WB	ADI-SPA-846
HSP90α, mAb (9D2)	H, CH	FC, IHC, WB	ADI-SPA-840
HSP90α, mAb (9D2) (HRP conjugate)	H, CH	WB	ADI-SPA-840HRP
HSP90α, pAb	H, M, R, B, BE, C, F, GP, HA, MO, P, RB, S, X	WB	ADI-SPS-771
HSP90α/β, mAb (H90-10)	H, M, RB	ICC, IP, WB	ALX-804-808
HSP90β, mAb (K3701)	H, M, R, B, C, GP, HA, P, RB, S	FC, WB	ADI-SPA-843
HSP90β, mAb (K3705)	H, M, R, B, C, CH, HA, GP, P, S	IHC, WB	ADI-SPA-842
TRAP1 (human), mAb (TRAP1-6)	H	ICC, IP, WB	ALX-804-368
UNC45, mAb (AbS1)	H, M, R	WB	ADI-SRA-1800

Inhibitors

Product	Description	Prod. No.
17-AAG	Less toxic, more potent synthetic derivative of geldanamycin	BML-EI308
17-DMAG	A water soluble, less metabolized analog of 17-AAG	BML-EI337
17-GMB-APA-GA	A maleimido-containing geldanamycin analog suitable for conjugation	BML-EI338
Geldanamycin	A benzoquinoid ansamycin inhibitor of HSP90, which inhibits ATP binding	BML-EI280
Geldanamycin, (biotin conjugate)	Useful for affinity purification of HSP90 client proteins	BML-EI341
Geldanamycin, (FITC conjugate)	Fluorescent HSP90 probe suitable for fluorescent polarization assays	BML-EI361
Herbimycin A	A benzoquinoid ansamycin inhibitor of HSP90, which inhibits ATP binding	BML-EI227
Novobiocin	Binds HSP90 C-terminus rather than the ATP-binding site	BML-A256
Radicicol	Macrocyclic lactone inhibitor of HSP90 with nM affinity	BML-EI285

Kits, ImmunoSets and Sample Packs

Product	Size	Sample Type	Specificity	Prod. No.
ImmunoSet™ Grp94 ELISA development set	5 x 96 wells	CL, T	H, M, R, C	ADI-960-077
HSP90α (human), EIA kit	1 x 96 wells	CL, S, T	H	ADI-EKS-895
HSP90, Ab sample pack	8 x 25 µg	Not applicable	Multiple species	ADI-PAK-010
HSP90, Ab sample pack with protein standards	10 x 25 µg	Not applicable	Multiple species	ADI-PAK-011

HSP90 Reagents

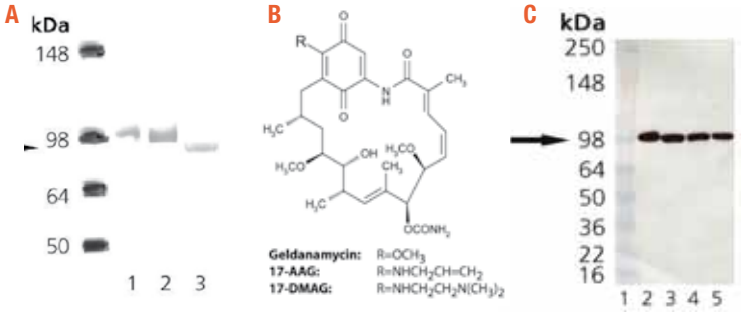


FIGURE A: Western blot analysis of HSP90 (human), (native) (ADI-SPP-770) in lane 1; HSP90α (human), (rec.) (ADI-SPP-776) in lane 2; and HeLa (heat shocked), (cell lysate) (ADI-LYC-HL101) in lane 3 probed with HSP90α, mAb (9D2) (ADI-SPA-840).

FIGURE B: Image of Geldanamycin and derivatives.

FIGURE C: Western blot analysis of Grp94 (canine), (rec.) (ADI-SPP-766) in lane 2; HeLa, (cell lysate) (ADI-LYC-HL100) in lane 3; liver (mouse), (mircosome extract) (ADI-LYT-MM100) in lane 4; and vero, (cell lysate) in lane 5 probed with Grp94, mAb (9G10) (ADI-SPA-850). (Lane 1 = molecular weight marker).

Proteins

Product	Application	Prod. No.
Activator of HSP90 ATPase 1 (human), (rec.)	Not available	ALX-201-275
Grp94 (canine), (rec.)	WB control	ADI-SPP-766
HOP (human), (rec.)	WB	ALX-201-218
HOP (human), (rec.)	WB control	ADI-SRP-1510
HSP90 (human), (native)	WB	ADI-SPP-770
HSP90 (yeast), (rec.) (His-tag)	WB	ALX-201-138
HSP90α (human), (rec.)	WB control	ADI-SPP-776
HSP90β (human), (rec.)	WB control	ADI-SPP-777
HSP90β (human), (rec.)	WB	ALX-201-147

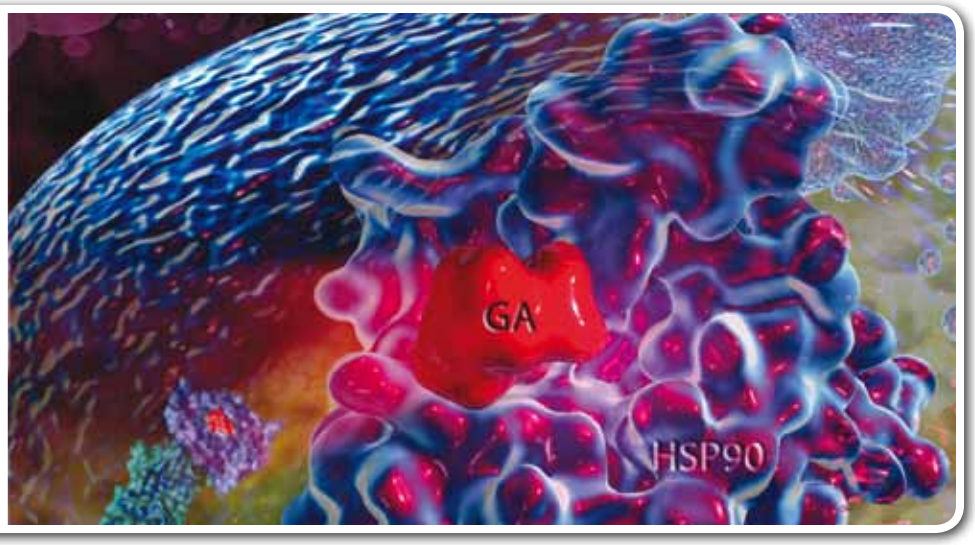


FIGURE 4: HSP90, a regulator of cell survival. Inhibition of HSP90 activity by drugs like geldanamycin (GA) destabilizes client proteins which ultimately lead to the onset of apoptosis.

HSP70/HSP40 Chaperones

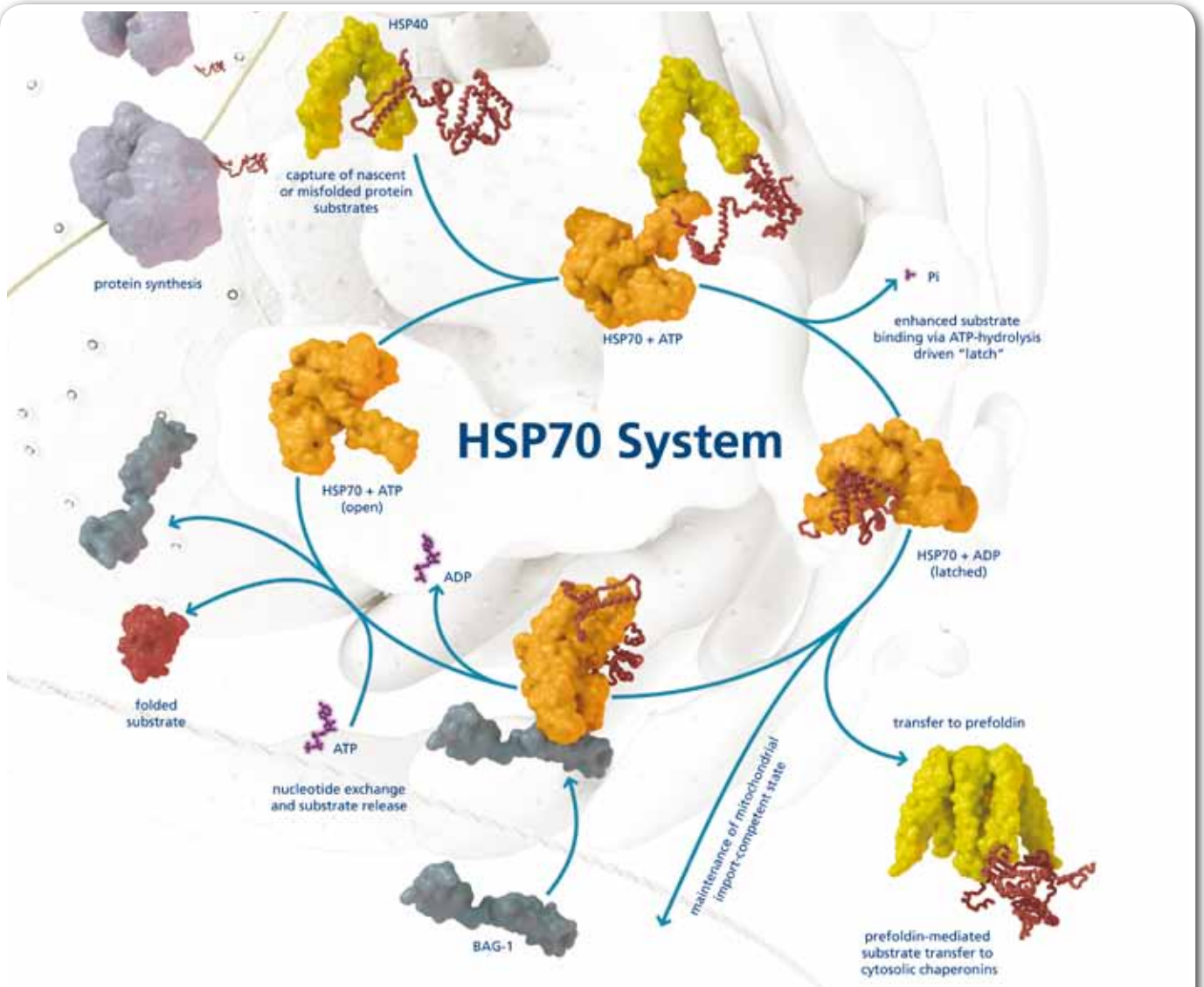


FIGURE 5: HSP70/HSP40 chaperone system. HSP70 works with HSP40 to capture and transfer misfolded client proteins to prefoldin and other chaperonins for refolding.

The HSP70 family represents one of the largest stress protein families with related members distributed throughout the cell (see Table 4). Insights into the function of the different family members originated from early work analyzing the bacterial counterpart, DnaK. Genetic studies designed to detect host-bacteriophage interactions revealed a number of bacterial genes whose expression was required for proper phage growth. One such set of genes was shown to be important for both phage and host DNA replication and therefore were referred to as DnaK, DnaJ, and GrpE. Subsequent biochemical studies revealed that the three proteins worked together in facilitating the disassembly of a large protein complex necessary for the commencement of DNA replication. These early studies indicated that the DnaK protein, later shown to be a relative of the eukaryotic HSP70 family, might function as a type of "molecular crowbar or detergent" to facilitate the disassembly of large protein complexes needed to initiate the early stages of DNA replication.

In contrast to the single DnaK protein species in bacteria, eukaryotes express a multitude of DnaK homologues referred to as the HSP70 family. The various family members are distributed throughout different intracellular compartments but nevertheless share many structural and biochemical properties. All appear to bind and hydrolyze ATP and to interact with other proteins undergoing maturation and folding. For example, HSP70 family members bind to and stabilize nascent polypeptides as they emerge from the ribosome and as they are translocated across membranes into the endoplasmic reticulum or mitochondria. The interaction of the HSP70 chaperone with its unfolded protein target is mediated by ATP and a number of co-chaperones (see Figure 5).

The reaction cycle of DnaK/DnaJ/GrpE (or mammalian equivalent HSP70/HSP70/Bag-1, respectively) machinery has been well characterized. DnaK or HSP70, in its "open" or ATP bound state, recognizes and binds to hydrophobic or unstructured sequences of amino acids within the substrate

protein. Binding to the target stimulates the hydrolysis of ATP to ADP and a conformational change in the DnaK chaperone to its closed state resulting in tight substrate binding. Subsequent exchange of bound ADP for ATP returns DnaK to its open state releasing the substrate polypeptide. This cycling of DnaK chaperone between the open and closed states is regulated by the co-chaperones DnaJ (or HSP40) and GrpE (or Bag-1). The family of DnaJ co-chaperones appears to facilitate substrate binding as well as stimulate DnaK ATP hydrolysis. The GrpE protein facilitates the nucleotide exchange reaction needed to allow for a new reaction cycle. Thus, through repeated cycles of binding and release to its target, the DnaK chaperone machinery helps prevent premature folding or aggregation, thereby facilitating high fidelity protein maturation throughout the cell.

Considering its intimate role in protein biogenesis it is not surprising that cells express multiple and related forms of HSP70, with the different family members distributed throughout various intracellular compartments. These include: the cytosolic/nuclear HSP70 proteins HSC70 and HSP70 (also known as HSP73 and HSP72 respectively), Grp78 or Bip present within the lumen of the endoplasmic reticulum, and Grp75 (also called mortalin) localized within mitochondria. Additional, but less well characterized HSP70 family members have also been described. Similar to the situation with the bacterial DnaK protein, all of the mammalian HSP70 family members require one or more co-chaperones for their reaction cycle. For example, there exists a large family of DnaJ related proteins distributed throughout the cell and which work with the different HSP70 chaperones. Examples include HSP40, the cytosolic DnaJ homologue that functions together with HSC/HSP70, a number of DnaJ homologues in the endoplasmic reticulum that work with Bip, and one or more DnaJ-like proteins in the mitochondria that function alongside of Grp75. Recently HSP110, a distant relative to HSP70, has been suggested to function as a nucleotide exchange factor for the cytosolic HSC/HSP70 proteins. Finally, a host of other proteins (Hip, Hop, CHIP, etc) are thought to influence the HSP70 chaperone machinery.

In times of stress, usually whenever the cell finds itself under conditions that are unfavorable for protein folding, members of the HSP70 family are expressed at higher levels. Increased expression of the chaperones help in the repair of proteins damaged by the particular stress event as well as guide the synthesis of new polypeptides needed to replace those irreparably damaged. In mammals, one particular HSP70 family member (e.g. HSP72) is expressed only in times of stress and therefore its appearance oftentimes serves as a critical indicator that a cell, tissue, or organ has undergone a stress response. Since their initial identification and characterization many clinicians have focused their interest on the HSP70 family. Elevated levels of HSP70 proteins have been linked with inhibition of apoptosis (see Figure 6) as well as the resistance of cells to various chemotherapeutic agents. In addition, numerous studies continue to demonstrate that changes in the levels of the different HSP70 family members may prove clinically useful for the diagnosis of many important human diseases.

Enzo Life Sciences provides the scientific and clinical community with a comprehensive panel of DnaK/HSP70 products. Included in our catalog is a diverse panel of immunological reagents specific for the different HSP70 chaperones and their co-factors such as HSP40 and HSP110. In addition, some of our HSP70 antibodies have been modified (e.g. biotinylated, conjugated with fluorophores etc.) to allow for different biochemical applications. Purified HSP70 proteins are available for biochemical and immunological studies. Finally, Enzo Life Sciences continues to provide highly specific and sensitive ELISA kits to facilitate large scale analysis of HSP70 levels in cell lysates, serum, plasma and tissue extracts.

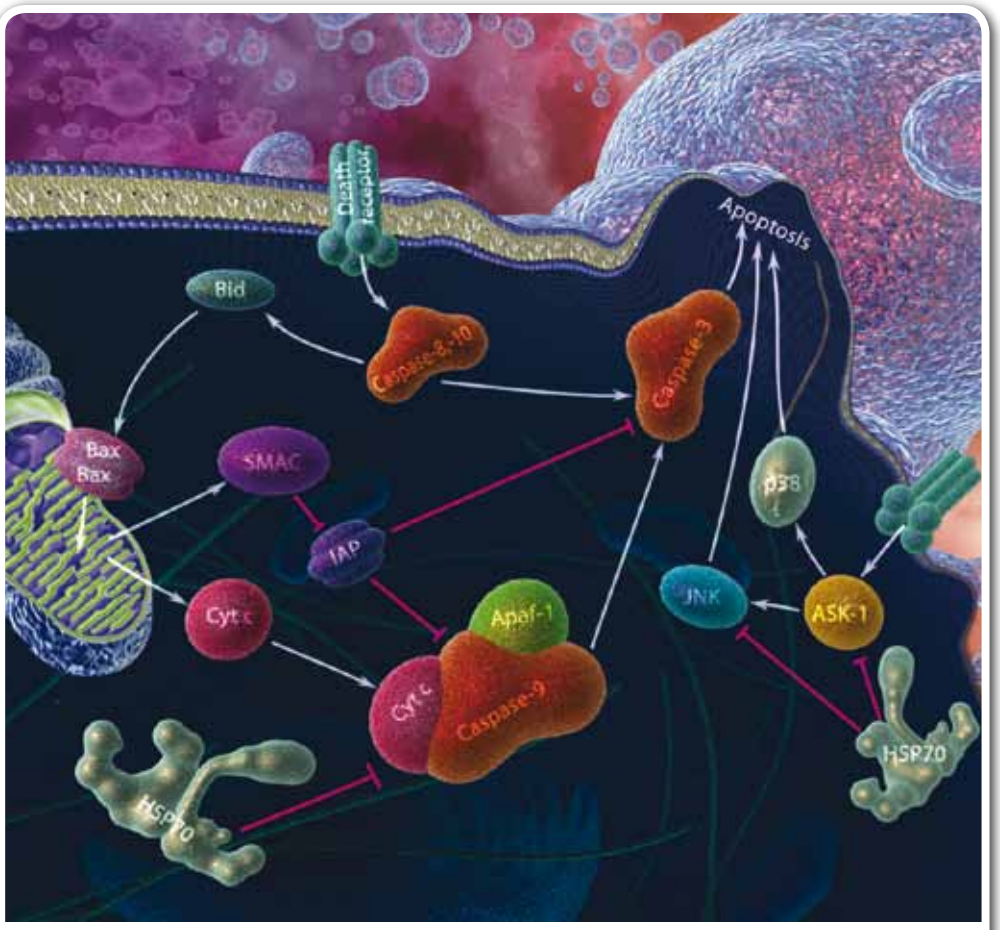


FIGURE 6: HSP70 a cell survival protein. HSP70 suppresses apoptosis by inhibiting the formation of the apoptosome and by blocking the activation of stress induced kinases including ASK1, p38 and JNK.

HSP70/HSP40 Chaperones

Table 4: HSP70/HSP40 Family Proteins

Name	Synonyms	Function/Structure
APG-1	HSPA4L, Osp94	HSP110-subfamily
APG-2	HSPA4, Irp94, HSP70RY	HSP110-subfamily; phosphorylated upon DNA damage, probably by ATM or ATR
Bag-1	HAP	Bag proteins compete with Hip for binding to the HSC70/HSP70 ATPase domain and promote substrate release; two splice variants
Bag-2	NA	Associates with CHIP and inhibits/regulates its activity by inhibiting the interaction between CHIP and its cognate ubiquitin-conjugating enzyme, UbcH5a; phosphorylated at Ser^{20} by MAPKAPK-2
Bag-3	BIS	Binds ATPase domain of HSP70/HSC70, inhibits chaperone activity
Bag-4	SODD	Inhibits HSP70/HSC70; prevents constitutive TNFRSF1A signaling; cytosolic
Bag-5	NA	Negative regulator of HSP70; two alternative splice forms
BAP	SIL1	ER localized protein that is associated with BiP/Grp94 and serves as a nucleotide exchange factor for it; mutations associated with Marinesco-Sjogren syndrome; two splice variants that encode the same protein
CHIP	STUB1, UBOX1, HSPABP2	Carboxyl terminus of HSP70 Interacting Protein; an HSP70-associated E3 ubiquitin ligase that targets chaperone substrates to the proteasome; inhibited by Hip and Bag-2; interacts with HSF1 upon heat shock; substrates include AR, Tau, Smad1/4, nNOS and Cu/Zn-SOD
CSP	Cysteine String Protein, DnaJC5	Secretory vesicle protein involved in regulated exocytosis; plays a role in CFTR biogenesis and trafficking; interacts with the inactive GDP-bound form of Ga(s) and promotes GDP/GTP exchange; guanine nucleotide exchange activity regulated by HSC70 and SGT
CSP-b	DnaJC5B	Testis specific expression; palmitoylated
CSP-g	DnaJC5G	Testis specific expression; palmitoylated
DnaJA4	NA	HSP40 homologue
DnaJA5	NA	HSP40 homologue; three splice variants; expressed in brain, placenta, kidney, and pancreas
DnaJB12	NA	Possibly membrane-associated
DnaJB13	TSARG6	Expressed specifically in adult testis, implicated in apoptosis in spermatogenic cells
DnaJB14	NA	Possibly membrane-associated; two splice variants
DnaJB8	NA	HSP40 homologue
DnaJC11	FLJ10737	Candidate tumor suppressor gene of neuroblastoma; found in mitochondria
DnaJC16	NA	Possibly type IV single-pass membrane protein; two splice variant
DnaJC17	NA	HSP40 homologue; contains RNA recognition motif
DnaJC18	NA	Possibly single-pass membrane protein
DnaJC19	TIM14	Mitochondrial protein, similar in sequence to yeast Tim14 which is involved in mitochondrial protein import; mutated in DCMA syndrome (dilated cardiomyopathy with ataxia)
DnaJC4	HSPF2, MCG18	Possibly single-pass membrane protein
DnaJC6	DJC6	Involved in uncoating of clathrin coated vesicles; interacts with HSC70; three splice variants
DnaJC7	TPR2, TTC2	Interacts with GAP domain of NF1
DnaJC8	SPF31	Splicing protein spf31
DRIP78	HDJ3, DnaJC14	May regulate trafficking of GPCR's including Angiotensin II and Dopamine Receptor; may play a role as a chaperone in the assembly of G-b/g subunits
ERdj3	DnaJB11, ERj3, HEDJ, ABBP-2	ER localized, expression induced by ER stress; stimulates BiP ATPase activity
ERdj5	JPDI, DnaJC10	ER localized, expression induced by ER stress (UPR); also a member of the Protein Disulfide Isomerase (PDI) family
Grp75/ Mortalin	MtHSP70, HSPA9, HSP70-9, MOT, Mot-2	Mitochondrial form of HSP70; constitutively expressed; cooperates with HSP60 to fold preproteins following transit across mitochondrial membrane
Grp78/BiP	HSPA5, HSP70-5	Constitutively expressed ER form of HSP70, also referred to as 'immunoglobulin heavy chain binding protein'

Name	Synonyms	Function/Structure
Hdj2	DnaJA1, DJ2, DJA1, HSDJ, HSJ2	Farnesylated; interacts with HSC70; two splice forms, one nuclear, one expressed throughout the cell
HdjC9	JDD1, DnaJC9	HSP40 homologue
Hip	HSPBP1	Nucleotide exchange factor for HSP70; inhibits the ubiquitin ligase activity of CHIP; an anti-apoptotic protein and substrate of Granzyme B
Hlj1	DnaJB4, DjB4, DnaJW	Identified in human liver
Hop	STIP1, STI1	HSP70/HSP90-organizing protein; Stress-induced Phosphoprotein 1; binds EEVD motifs at the C-termini of HSP70 and HSP90; also binds Cdc37; normally found in the cytoplasm, but also seen in the nucleus depending on cell cycle/CDK activity
HSC3	DnaJB7	ER localized, expression induced by ER stress (UPR); also a member of the Protein Disulfide Isomerase family
HSC40	DnaJB5	Constitutive HSP40 isoform
HSC70	HSPA8, HSP70-8, HSP73, HSC71	Constitutively expressed in most tissues; essential housekeeping gene; two isoforms due to alternative splicing
HSCB	DnaJC20, Jac1, HSC20	Homologue of *E. coli* HSCB, which along with the *E. coli* HSP70 homologue HSCA forms part of a specialized system for synthesizing iron-sulfur proteins; candidate gene in hereditary ataxia syndromes
Hsj1	DnaJB2, HSPF3	Neuronal tissue-specific; two isoforms (Hsj1a and Hsj1b)
HSP110	HSP105, HSPH1	HSP110-subfamily; acts as nucleotide exchange factor for HSP70
HSP40/Hdj1	DnaJB1, HSPF1	Enhances ATPase activity of HSP70 family members
HSP70-4	HSP70L1, HSPA14	HSP70-like protein 1; cloned from human dendritic cells
HSP70B	HSPA7	Tightly linked to HSP70B' locus
HSP70B'	HSPA6, HSP70-6	Strictly stress-inducible; in unstressed conditions it is expressed only in certain blood cells (dendritic cells, monocytes and NK cells)
HSP70-Hom	HSPA1L, Hum70t, HSP70-1t	Constitutive, testis-specific expression; locus adjacent to HSP72 and HSP70-2
HSPA1A	HSP70-1a, HSP72, HSP70-1	Stress-inducible; highly expressed in various cancers; correlated with increased proliferation, metastasis and poor outcome in breast cancer
HSPA1B	HSP70-1b, HSP72, HSP70-1	Stress-inducible; identical in protein sequence to HSPA1A above, but transcribed from an adjacent locus
HSPA2	HSP70-2	Constitutively expressed at high levels in brain and testis; role in spermatogenesis; upregulated in a subset of breast cancers and has growth and survival promoting effects in cancer cells
Htj1/ERdj1	DNAJC1, DNAJL1, MTJ1	Enriched in microsomes and nucleus; stimulates BiP ATPase activity; involved in transport of BiP to the cell surface
HYOU1	Hypoxia Upregulated 1, Grp170, ORP 150	Induced by hypoxia, found in the ER, upregulated in tumors; protein with alternative translation start site found in the cytoplasm
JDP1	DnaJC12	An estrogen target gene, highly expressed in ER positive breast cancer; two isoforms; conserved down to *Drosophila*
MCJ	HSD18, DNAJD1, DNAJC15	Methylation controlled J protein (MCJ) is a type II transmembrane co-chaperone localized in the Golgi network and present only in vertebrates
Mdg1/ERdj4	DnaJB9	ER localized, expression induced by UPR; expression associated with low metastatic potential; stimulates BiP ATPase activity
MPP11	MIDA1, DnaJC2, Zrf1, Zrf2	Localized to nucleus; ubiquitously expressed
Mrj	DnaJB6, Hsj2, Msj1	Enriched in the CNS; two isoforms as a result of alternative splicing; one nuclear, one expressed throughout the cell; binds and regulates NFAT
P58(IPK)	DnaJC3, PRKRI	Binds and inactivates PKR; induced by ER stress, binds and inactivates PERK
Rdj2	DnaJA2, DJA2	HSC70 co-chaperone; possibly membrane-associated and farnesylated
RME-8	DnaJC13	Functions in endosomal trafficking; human homologue of Receptor-mediated endocytosis 8 (RME8) in *C. elegans*; widely expressed, binds HSC70
Tid1	hTid-1, DnaJA3	Mitochondrial; modulates apoptotic signal transduction, cytochrome c release, and caspase 3 activation; two splice variants

HSP70/HSP40 Chaperones

Antibodies

Product	Specificity	Application	Prod. No.
Bag-1 (mouse) (CT), pAb (Bur 1702)	M	IHC, IP, WB	ALX-210-009
Bag-1 (NT), pAb (Bur 1735)	M, R	ICC, IHC, WB	ALX-210-010
Bag-1, mAb (4A2)	H, M, R	WB	ADI-AAM-400
Bag-1, pAb	H, M, R	WB	ADI-905-735
Bag-1, pAb (Bur 1680)	M, R	ICC, IHC, WB	ALX-210-011
Bag-3, mAb (AC-1)	H, M, R	ELISA, IHC, ICC, IP, WB	ALX-803-323
Bag-3, pAb (TOS-2)	H, M, R	ICC, IHC, IP, WB	ALX-210-538
BiP, pAb	M, R	WB	ALX-210-137/1
CHIP (human), pAb	H	WB	ALX-210-883
CSP, pAb	M, R, B, X	IP, WB	ADI-VAP-SV003
Cysteine string proteins, pAb	H, R	IHC, WB	BML-CL3710
DnaJ (*E. coli*), pAb	BA	IP, WB	ADI-SPA-410
DnaK (*E. coli*), mAb (8E2/2)	BA	WB	ADI-SPA-880
Grp78/BiP, pAb	M, R, B, FN, HA, MO, RB, X	WB	ADI-SPA-826
GrpE (*E. coli*), pAb	BA	WB	ADI-SPA-240
Hip, mAb (2G6)	H, CH, RB	IP, WB	ALX-804-024
Hip, pAb	H, M, R, B	WB	ADI-SPA-766
HOP, mAb (DS14F5)	H, M, R, B, C, CH, GP, HA, Mink, MO, P, RB, S, X	WB	ADI-SRA-1500
HSP40/Hdj1, mAb (2E1)	H, M	IP, WB	ADI-SPA-450
HSP40/Hdj1, pAb	H, M, R, B, BE, C, CH, F, GP, HA, MO, MU, P, RB, S, SC, X	WB	ADI-SPA-400
HSP40/Hdj1, pAb (DyLight™ 488 conjugate)	H, M, R, B, C, CH, F	FC	ADI-SPA-400-488
HSP40/Hdj1, pAb (R-PE conjugate)	H, M, R, B, C, CH, F	FC	ADI-SPA-400PE
HSP47, mAb (M16.10A1)	H, M, R, B, C, CH, GP, HA, MO, P, RB, S	IHC, WB	ADI-SPA-470
HSP47 (human), pAb	H	WB	ALX-215-005
HSC70 (plant), mAb (1D9)	PL	WB	ADI-SPA-818
HSC70 (plant), mAb (5B7)	PL	IP, WB	ADI-SPA-817
HSC70, mAb (13D3)	H, M, FE, MO	IHC, IP, WB	ALX-804-067
HSC70/HSP70 (fish), pAb	F	WB	ADI-SPA-758
HSC70/HSP70, mAb (BB70)	H, M, R, RB	WB	ADI-SPA-822
HSC70/HSP70, mAb (N27F3-4)	H, M, R, B, BE, C, CH, F, GP, HA, MO, P, PL, RB, S, X	FC, WB	ADI-SPA-820
HSC70/HSP70, mAb (N27F3-4) (DyLight™ 488 conjugate)	H, M, BE, B, C, CH, F	FC	ADI-SPA-820-488
HSC70/HSP70, mAb (N27F3-4) (R-PE conjugate)	H, M, R, B, C, CH, F	FC	ADI-SPA-820PE
HSC70/HSP70, mAb (N27F3-4) (AP conjugate)	H, M, R, B, C, CH, F	WB	ADI-SPA-820AP
HSC70/HSP70, pAb	H, M, R, B, C, CH, D, F, GP, HA, MO, P, PL, RB, S, Y	WB	ADI-SPA-757

Product	Specificity	Application	Prod. No.
HSC70/HSP73, mAb (1B5) (DyLight™ 488 conjugate)	H, M, R, B, C, CH, GP, HA, MO, RB, P, S	FC	ADI-SPA-815-488
HSC70/HSP73, mAb (1B5) (R-PE conjugate)	H, M, R, B, C, CH, GP, HA, MO, RB, P, S	FC	ADI-SPA-815PE
HSC70/HSP73, mAb (1B5)	H, M, R, B, C, CH, GP, HA, MO, P, RB, S	WB	ADI-SPA-815
HSC70/HSP73, mAb (1B5) (biotin conjugate)	H, M, R, B, C, CH, GP, HA, MO, P, RB, S	EIA, EM, ICC, IHC, IP, WB	ADI-SPA-815B
HSC70/HSP73, pAb	H, M, R	WB	ADI-SPA-819
HSC70/HSP73, pAb	H, M, R, B, C, GP, HA, MO, P, RB, S	WB	ADI-SPA-816
HSP70 (fish), pAb	H, M, R, B, C, CH, D, F	WB	ADI-SPA-763
HSP70 (human), mAb (4G4)	H	IP, WB	ALX-804-076
HSP70 (universal), mAb (5A5)	H, M, A, D, F, frog, Y	ICC, IHC, IP, WB	ALX-804-074
HSP70, mAb (2A4)	H, M, A, D, F, frog, Y	ICC, IHC, WB	ALX-804-075
HSP70, mAb (3A3)	H, M, A, arthropod, amphibian, D, F, P, PL, Y	ICC, IHC, IP, WB	ALX-804-047
HSP70/HSP72, mAb (C92F3A-5)	H, M, R, BE, CE, C, CH, D, F, GP, HA, MO, P, RB, S	EIA, IHC, WB	ADI-SPA-810
HSP70/HSP72, mAb (C92F3A-5) (AP conjugate)	H, M, R, B, C, CH, F	WB	ADI-SPA-810AP
HSP70/HSP72, mAb (C92F3A-5) (biotin conjugate)	H, M, R, HA, MO, RB, GP, B, C, S, CH, F, A, P, BE	WB	ADI-SPA-810B
HSP70/HSP72, mAb (C92F3A-5) (DyLight™ 488 conjugate)	H, M, R, B, CE, C, CH, D, F	FC	ADI-SPA-810-488
HSP70/HSP72, mAb (C92F3A-5) (FITC conjugate)	H, M, R, B, C, CH, D, F, GP, HA, MO, P, RB, S	FC	ADI-SPA-810FI
HSP70/HSP72, mAb (C92F3A-5) (R-PE conjugate)	H, M, R, B, C, CH, D, F	FC	ADI-SPA-810PE
HSP70/HSP72, mAb (C96F3-3)	H, M, R, B, F	WB	ADI-SPA-8132
HSP70/HSP72, mAb (N15F2-5)	H, BA	WB	ADI-SPA-8133
HSP70/HSP72, mAb (N21F3-2)	H	WB	ADI-SPA-8134
HSP70/HSP72, mAb (N31F2-4)	H, BA	WB	ADI-SPA-8131
HSP70/HSP72, mAb (N33F3-4)	H	WB	ADI-SPA-8135
HSP70/HSP72, mAb (N6F3-6-140)	H, BA	WB	ADI-SPA-8136
HSP70/HSP72, pAb	H, M, R, B, BE, C, HA, MO, P, S	IP, WB	ADI-SPA-811
HSP70/HSP72, pAb	H, M, R, B, C, F, GP, BE	IP, WB	ADI-SPA-812
HSP70B', mAb (165f)	H	WB	ADI-SPA-754
HSP70B', pAb	H	IP, WB	ADI-SPA-756
HSP71 (*E. coli*), mAb (5A8)	BA	WB	ADI-SPA-885
Grp75/Mortalin, mAb (30A5)	H, M, R, B, C, CH, D, GP, HA, MO, P, RB, S, X	IHC, WB	ADI-SPS-825
Grp75/Mortalin, pAb	H, M, R, B, C, GP, HA, MO, RB	WB	ADI-SPS-826
Grp75/Mortalin, pAb	H, M, R, B, C, D, GP, HA, MU, RB, X	WB	ADI-SPS-827
Grp75/Mortalin, mAb (JG1)	H, M, C, MO	ICC, IP, WB	ALX-804-077
SODD (human), pAb (AL169)	H	WB	ALX-210-919

HSP70/HSP40 Chaperones

Kits, ImmunoSets and Sample Packs

Product	Size	Sample Type	Specificity	Prod. No.
ImmunoSet™ HSP40 (human), ELISA development set	5 x 96 wells	CL	H	ADI-960-073
Anti-HSP70 IgG/A/M (human), ELISA kit	1 x 96 wells	S	H	ADI-EKS-750
HSP70 EIA kit	1 x 96 wells	CL, T	H, M, R	ADI-EKS-700B
HSP70 high sensitivity EIA kit	1 x 96 wells	S, P	H, M, R	ADI-EKS-715
HSP70B' EIA kit	1 x 96 wells	CL, S, T	H	ADI-EKS-725
ImmunoSet™ Grp75 ELISA development set	5 x 96 wells	CL	H, M, R	ADI-960-143
HSP70, Ab sample pack	8 x 25 µg	Not applicable	Multiple species	ADI-PAK-020
HSP70, Ab sample pack with protein standards	10 x 25 µg	Not applicable	Multiple species	ADI-PAK-021
HSP70 (human), mAb sample pack	8 x 25 µg	Not applicable	Multiple species	ADI-PAK-040
HSP70 (human), mAb sample pack with protein standards	10 x 25 µg	Not applicable	Multiple species	ADI-PAK-041

Proteins

Product	Application	Prod. No.
BiP (mouse), (rec.)	WB	ALX-201-219
CHIP (human), (rec.)	Not available	ALX-201-215
DnaJ (*E. coli*), (rec.)	Protein refolding assay, WB control	ADI-SPP-640
DnaJ (*E. coli*), (rec.)	Not available	ALX-201-144
DnaK (1-638) (*E. coli*), (rec.)	Not available	ALX-201-217
DnaK (ATPase domain) (1-384), (rec.)	Not available	ALX-201-187
DnaK (*E. coli*), (rec.)	AA, WB control	ADI-SPP-630
DnaK (*E. coli*), (rec.)	WB	ALX-201-143
DnaK (substrate binding domain) (385-546), (rec.)	Not available	ALX-201-186
DnaK (substrate binding domain) (385-638), (rec.)	Not available	ALX-201-188
DnaK (substrate covering lid) (508-638), (rec.)	Not available	ALX-201-189
Grp78/BiP (hamster), (rec.)	WB control	ADI-SPP-765
GrpE (*E. coli*), (rec.)	WB	ALX-201-145
GrpE (*E. coli*), (rec.)	AA, WB control	ADI-SPP-650
HDJ2 (human), (rec.)	Not available	ALX-201-212
Hip (human), (rec.)	Not available	ALX-201-216
Hip (rat), (rec.)	WB control	ADI-SPP-767
HOP (human), (rec.)	WB	ALX-201-218
HOP (human), (rec.)	WB control	ADI-SRP-1510
HSP40 (human), (rec.) (His-tag)	Not available	ALX-201-274
HSP40/Hdj1 (human), (rec.)	WB control	ADI-SPP-400
HSP40/Hdj2 (human), (rec.)	WB control	ADI-SPP-405
HSP47 (human), (rec.)	WB control	ADI-SPP-535
HSC70 (human), (rec.)	Not available	ALX-201-298

Product	Application	Prod. No.
HSC70/HSP73 (ATPase fragment) (bovine), (rec.)	AA	ADI-SPP-752
HSC70/HSP73 (bovine), (rec.)	AA, WB control	ADI-SPP-751
HSC70/HSP73 (bovine), (rec.) (biotin conjugate)	WB control	ADI-SPP-761
HSP70 (human), (rec.)	Not available	ALX-201-214
HSP70 (low endotoxin) (human), (rec.)	AA, WB control	ADI-ESP-555
HSP70 (*Medicago sativa*)	Not available	ALX-201-248
HSP70/HSP72 (Chinook salmon), (rec.)	AA, WB control	ADI-SPP-763
HSP70/HSP72 (human), (rec.)	AA, WB control	ADI-NSP-555
HSP70/HSP72 (rat), (rec.)	AA, WB control	ADI-SPP-758
HSP70-A1 (low endotoxin) (mouse), (rec.)	AA, WB control	ADI-ESP-502
HSP70-A1 (mouse), (rec.)	ATPase activity assay, WB control	ADI-SPP-502
HSP70B' (human), (rec.)	WB control	ADI-SPP-762
HSP71 (*M. tuberculosis*), (rec.)	WB control	ADI-SPP-885
Grp75/Mortalin (human), (rec.)	WB control	ADI-SPP-828
Sti1 (yeast), (rec.)	WB	ALX-201-151

The HSP70/HSP40 Reagents

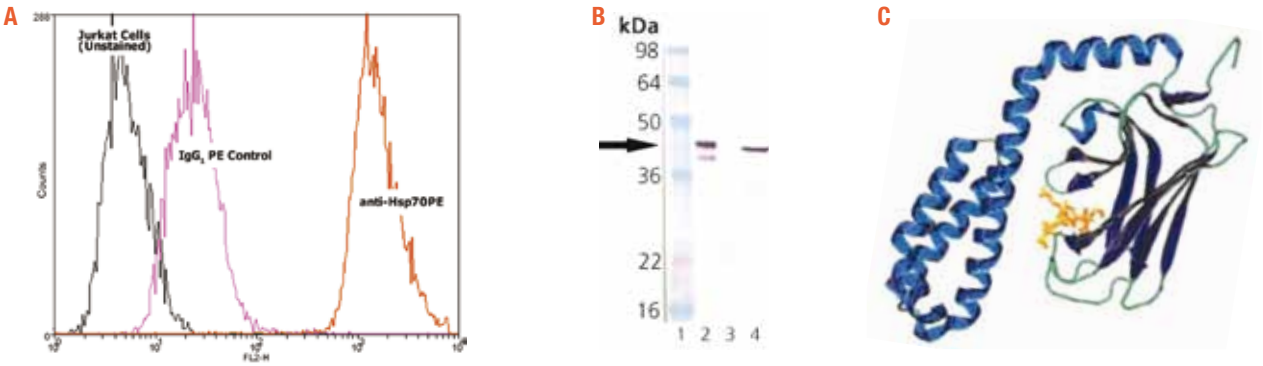


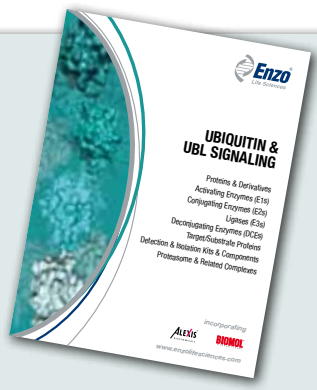
FIGURE A: Flow cytometry analysis of 10^6 Jurkat cells using HSP70, mAb (C92F3A-5) (R-PE conjugate) (ADI-SPA-810PE) and IgG_1 isotype control, mAb (MOPC-21) (R-PE conjugate) (ADI-SAB-600PE).

FIGURE B: Western blot analysis of HSP40/Hdj1 (human), (rec.) (ADI-SPP-400) in lane 2; DnaJ (*E. coli*), (rec.) (ADI-SPP-640) in lane 3; and HeLa (heat shocked), (cell lysate) (ADI-LYC-HL101) in lane 4 probed with HSP40/Hdj1, pAb (ADI-SPA-400). (Lane 1 = molecular weight marker.)

FIGURE C: A schematic of the HSP70 substrate binding domain in complex with a substrate peptide (yellow).

Ubiquitin & UBL Signaling Catalog

Enzo Life Sciences offers a comprehensive range of more than 250 products for ubiquitin and ubiquitin-like protein research including ubiquitin and ubiquitin-like proteins; E1, E2, E3 and deconjugating enzymes; substrates and inhibitors; ubiquitin-binding proteins and ubiquitin and ubiquitin-like protein-reactive antibodies. Visit www.enzolifesciences.com for a complete listing or ask for a free copy of our new Ubiquitin & UBL Signaling Catalog.



HSP60/HSP10 Family (The Chaperonins)

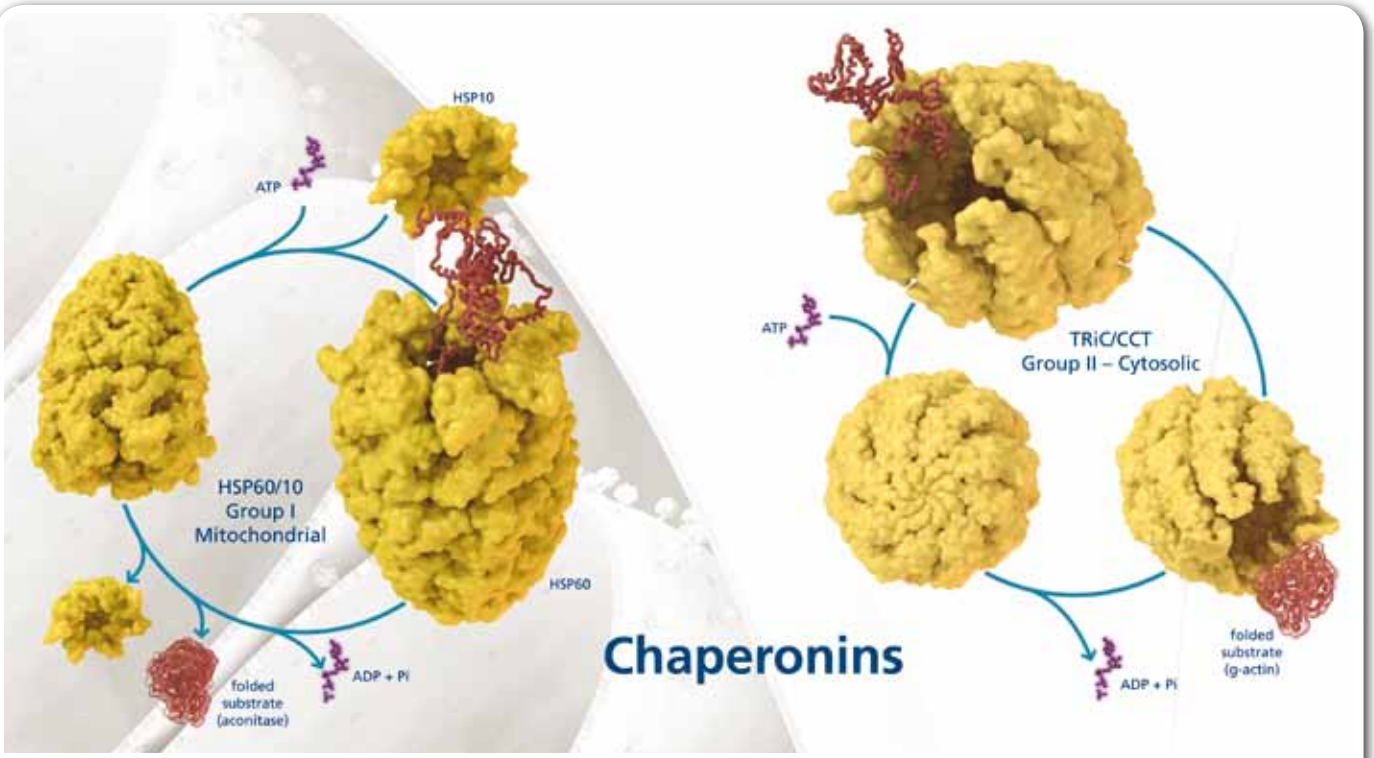


FIGURE 7: HSP60/HSP10 and TRiC/CCT chaperonins. The group I (mitochondrial) and group II (cytosolic) chaperones are large oligomeric complexes, HSP60/HSP10 and TriC/CCT, involved in ATP-dependent folding of client proteins such as aconitase and actin, respectively.

Members of the HSP60 (eukaryotes) and GroEL (bacterial) family of HSPs, like the HSP70 chaperones, also participate in protein maturation events and have been given the specialized name, chaperonins (see Table 5). All members of this chaperonin family exhibit molecular masses of around 60 kDa, but are usually part of large oligomeric structures. For example, bacterial GroEL, initially named because of its essential role in bacteriophage growth, exists as a large homo-oligomeric complex (~800 kDa). This large complex can discriminate between folded and unfolded proteins, binding selectively to the latter. In combination with its particular co-factor (HSP10 in eukaryotes or GroES in bacteria) the HSP60/GroEL proteins bind newly synthesized polypeptides and facilitate their folding to the native state in an ATP-dependent cycle. Chaperonins perform their chaperone role somewhat different from that of their HSP70 counterparts. Specifically, binding and sequestration of the substrate polypeptide occurs within the large central cavity of the chaperonin complex. It is thought that protection of the substrate protein within the central cavity of the chaperonin provides a sequestered protein folding environment, thereby reducing the probability of misfolding and aggregation of the target protein with other polypeptides. Thus, the HSP70 chaperones along with the more specialized chaperonins, together coordinate the efficient folding and assembly of many proteins throughout the cell.

The mammalian equivalent of bacterial GroEL, referred to as HSP60, is localized within mitochondria and with its co-chaperone, HSP10, participates in the folding and assembly of newly synthesized proteins as they are transported into the mitochondria from the cytosol (see Figure 8). In plants, the related Cpn60/Cpn10 similarly functions within the chloroplast to orchestrate the folding and assembly of Rubisco (and therefore is also referred to in the literature as the Rubisco-binding protein) and other chloroplast proteins. Finally, within the eukaryotic cytosol a number of proteins distantly related to HSP60 have been described but remain less well characterized. These proteins, TRiC (TCP-1 ring complex, also called CCT for chaperonin-containing TCP-1) consist of at least 8 family members. These proteins again are arranged in a large complex similar to that formed by the GroEL or HSP60 proteins (see Figure 7). So far only a few protein substrates, notably the cytoskeletal proteins actin and tubulin, appear to require the TRiC complex for their efficient folding and assembly. Curiously, no GroES/HSP10 like co-factor has been identified for this seemingly more specialized cytosolic chaperonin.

In addition to their prominent role as molecular chaperones, members of the GroEL and HSP60 families have long been recognized as highly immunogenic proteins and consequently have attracted much attention from immunologists. As mentioned earlier, the related GroEL proteins from different pathogens elicit strong humoral and cellular immune responses. Finally, chaperonins are now proving useful as it pertains to the *in vitro* folding of recombinant proteins important for clinical medicine and therapeutic purposes. Enzo Life Sciences offers a comprehensive panel of purified chaperonin proteins isolated from different sources, along with antibodies capable of discerning the various chaperonin family members isolated from different species and HSP60 ELISA kits.

Table 5: Chaperonin Family Proteins

Name	Synonyms	Function/Structure
CCT2	Chaperonin containing TCP1 subunit 2 (β), TCP1β, CCTB, CCTβ	Component of hetero-oligomeric TRiC complex
CCT3	Chaperonin containing TCP1 subunit 3 (γ), CCTG, CCTγ, TRIC5, TCP1γ	Component of hetero-oligomeric TRiC complex; three alternative splice forms
CCT4	Chaperonin containing TCP1 subunit 4 (δ), SRB, CCTδ	Component of hetero-oligomeric TRiC complex
CCT5	Chaperonin containing TCP1 subunit 5 (ε), CCTE, CCTε, TCP1ε	Component of hetero-oligomeric TRiC complex; mutation associated with autosomal recessive mutilating sensory neuropathy with spastic paraplegia; expression up-regulated in p53-mutated tumors
CCT6A	Chaperonin containing TCP1 subunit 6A (ζ1), CCT6, CCTζ, HTR3, TCPZ, TCP20, MoDP-2, TTCP20, CCTζ, CCTζ1, TCP1ζ	Component of hetero-oligomeric TRiC complex; ionizing radiation results in enhanced expression in radioresistant cancer cells compared to radiosensitive cells; two alternative splice forms
CCT6B	Chaperonin containing TCP1 subunit 6B (ζ2), CCTζ2, TCP1ζ 2	Component of hetero-oligomeric TRiC complex; testis-specific expression
CCT7	Chaperonin containing TCP1 subunit 7 (η), HIV-1 Nef interacting protein (Nip7-1), TCP1η, Ccth, CCTη	Component of hetero-oligomeric TRiC complex; two alternative splice forms
HSP10	CPN10, GroES, HSPE1	Closely linked to the HSP60 gene (HSPD1); forms chaperonin 'cap' structure
HSP60	HSPD1, CPN60, GroEL, HSP65, SPG13, HuCHA60	Mitochondrial protein essential for folding and assembly of newly imported proteins; also a signaling molecule in the innate immune system; mutations associated with autosomal recessive spastic paraplegia
TCP1	CCT1, CCTα, TCP1α	Member of the chaperonin containing TCP1 complex (CCT), also known as the TCP1 ring complex (TRiC), consisting of two identical stacked rings, each containing eight different proteins; the complex folds various proteins, including actin and tubulin, in an ATP-dependent manner; two alternative splice forms; unlike HSP60, no known associated HSP10/GroES cofactor

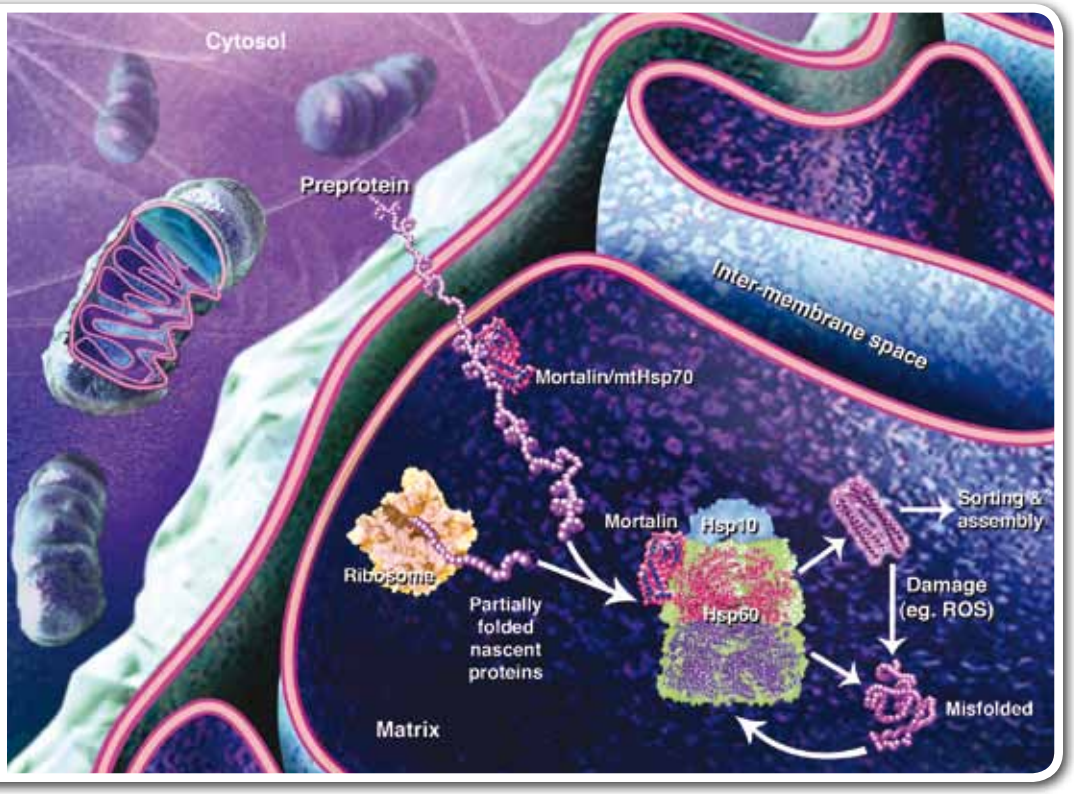


FIGURE 8: HSP60/HSP10 chaperone machinery. HSP60/HSP10 complexes cooperate with mitochondrial HSP70 (mtHSP70/mortalin) in the folding of newly imported and partially folded nascent mitochondrial proteins.

HSP60/HSP10 Family (The Chaperonins)

Antibodies

Product	Specificity	Application	Prod. No.
GroEL (*E. coli*), mAb (9A1/2)	BA	IP, WB	ADI-SPS-870
GroEL (*E. coli*), pAb	BA	WB	ADI-SPS-875
GroES (*E. coli*), pAb	BA	IP, WB	ADI-SPA-210
Cpn10 (*Chlamydia*), mAb (M1.2)	BA	EIA, ICC, IP, WB	ADI-SPA-780
Cpn10 (*Chlamydia*), mAb (M1.4)	BA	EIA, IP, WB	ADI-SPA-781
Cpn10, pAb	H, M, R, B, C, GP, P, RB, S, X	WB	ADI-SPA-110
HSP56, pAb	H, M, RB	WB	ALX-210-125
HSP60 (bacterial), mAb (A57-B9)	BA	ICC, IP, WB	ALX-804-072
HSP60 (bacterial), mAb (A57-E4)	BA	WB	ALX-804-071
HSP60 (human), mAb (2E1/53)	H	ELISA, IP, WB	ALX-804-070
HSP60 (human), mAb (4B9/89)	H	ELISA, ICC, WB	ALX-804-069
HSP60 (insect), pAb	H, M, R, BA, BE, B, CH, D, F, GP, HA, I, MO, MU, P, RB, S, SC	WB	ADI-SPA-805
HSP60, mAb (LK-1)	H, M, R, B, C, CH, D, GP, HA, MO, P, RB, S, X	EIA, FC, IP, WB	ADI-SPA-806
HSP60, mAb (LK-2)	H, M, R, B, BA	FC, IHC, WB	ADI-SPA-807
HSP60, mAb (LK-2) (DyLight™ 488 conjugate)	H, M, R, B, BA	FC	ADI-SPA-807-488
HSP60, mAb (LK-2) (R-PE conjugate)	H, M, R, B, BA	FC	ADI-SPA-807PE
HSP60, mAb (Mab11-13)	H, M, R, B, C, D, F, GP, HA, MO, P, RB, Snake	FC, WB	ADI-SPA-829
HSP60, pAb	H, M, R, BE, B, C, CH, D, BA, F, GP, HA, MO, P, RB, S, X	IP, WB	ADI-SPA-828
HSP65 (mycobacterial), mAb (3F7)	H, M, R, B, D, BA	WB	ADI-SPA-881
HSP65 (mycobacterial), mAb (4H11)	BA	WB	ADI-SPA-882
TCP-1α, mAb (23c)	H, M, R, C, HA, RB, S	IHC, IP, WB	ADI-CTA-123
TCP-1α, mAb (91a)	H, M, R, B, C, CE, D, GP, HA, MO, P, PL, RB, Y	FC, IP, WB	ADI-CTA-191
TCP-1β, mAb (PK/8/4/4i/2f)	H, M, R, B, C, CH, HA, MO, P, RB, S	WB	ADI-CTA-202

Kits and Immunosets

Product	Size	Sample Type	Specificity	Prod. No.
Anti-HSP60 IgG/A/M (human), ELISA kit	1 x 96 wells	S	H	ADI-EKS-650
HSP60 (human), EIA kit	1 x 96 wells	CL, S, T	H	ADI-EKS-600

Recombinant Proteins

Product	Application	Prod. No.
GroEL (*E. coli*), (rec.)	AA, WB control	ADI-SPP-610
GroEL (*E. coli*), (rec.)	Not available	ALX-201-141
GroES (*E. coli*), (rec.)	AA, folding assay, renaturation assay, WB control	ADI-SPP-620
GroES (*E. coli*), (rec.)	Not available	ALX-201-142
Cpn10 (human), (rec.)	WB control	ADI-SPP-110
Cpn10 (low endotoxin) (human), (rec.)	WB control	ADI-ESP-110
HSP60 (human), (rec.)	AA, WB control	ADI-NSP-540
HSP60 (low endotoxin) (human), (rec.)	AA, WB control	ADI-ESP-540
HSP60 (low endotoxin) (mouse), (rec.)	AA	ADI-ESP-741
HSP60 (mouse), (rec.)	AA, WB control	ADI-SPP-741
HSP60 (rat), (rec.)	AA, WB control	ADI-SPP-742
HSP65 (low endotoxin) (*M. bovis*), (rec.)	AA, WB control	ADI-ESP-581
HSP65 (*M. bovis*), (rec.)	WB control	ADI-NSP-581

HSP60 Reagents

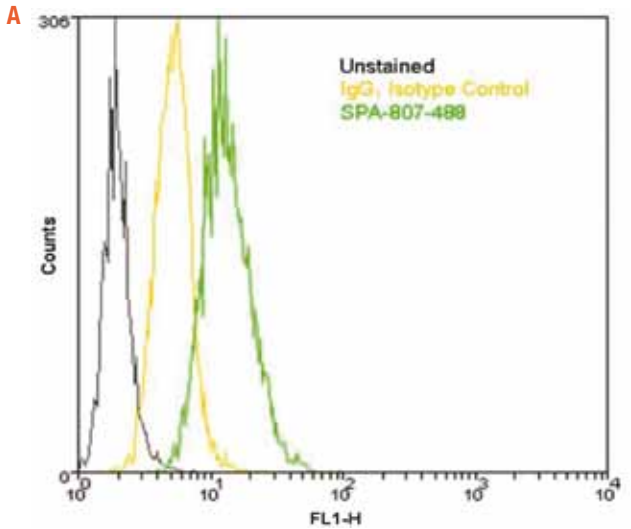


FIGURE A: Flow cytometry analysis of 10^6 Jurkat cells using HSP60, mAb (LK-2) (DyLight™ 488 conjugate) (ADI-SPA-807-488) and IgG, isotype control, mAb (MOPC-21) (DyLight™ 488 conjugate) (ADI-SAB-600-488).

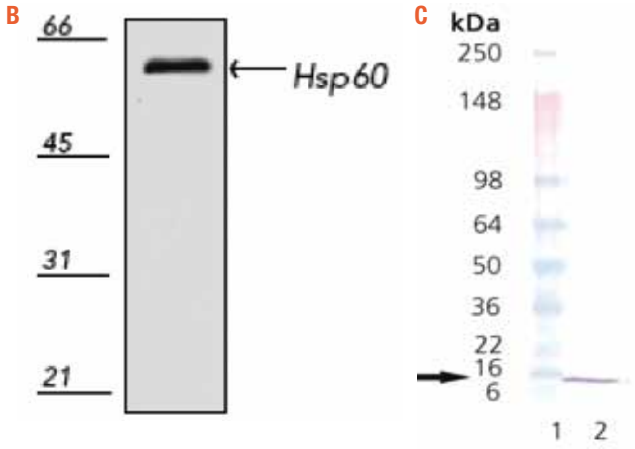


FIGURE B: Western blot analysis of vero (monkey), (cell lysate) probed with HSP60, mAb (LK-1) (ADI-SPA-806).

FIGURE C: Western blot analysis of GroES (*E. coli*), (rec.) (ADI-SPP-620) in lane 2 probed with GroES (*E. coli*), pAb (ADI-SPA-210). (Lane 1 = molecular weight marker). Bacterial GroES is equivalent to mammalian HSP10.

Small HSP and Crystallin Proteins

The small HSPs are perhaps the most widespread but least conserved members of the HSP family (see Table 6). While bacteria and single-cell eukaryotes express only one or two members, *Drosophila melanogaster* expresses 16, humans 10, and plants as many as 19. Although diverse in sequence most members of the family share a number of properties including: a low molecular mass of between 14-45 kDa with most in the 20 kDa range; sequence homology with the α-crystallin proteins; and the formation of large and dynamic oligomeric complexes (see Figure 9). In the case of the human low molecular weight HSP, collectively termed the HSP27 family, the proteins are found in complexes of 400 to 500 kDa. Phosphorylation of HSP27, in response to different stimuli, may play a role in the oligomeric dynamics of the protein (see Figure 10 and 11).

The best characterized member of the family, α-crystallin, is abundant in the lens where the overall protein concentration is quite high. In such a crowded environment, the α-crystallins (subunits A and B) are thought to help prevent protein aggregation resulting from light damage and/or other metabolic insults. Similarly, other members of the low molecular weight HSPs are now thought to function as ATP-independent molecular chaperones. Via their large surface and potential to recognize and bind exposed hydrophobic patches, HSP27 and its counterparts may act promiscuously to bind unfolded proteins and then present their substrates to the other ATP-dependent molecular chaperone machineries (e.g. HSP60, HSP70 or HSP90) for subsequent re-folding (see Figure 12). Enzo Life Sciences provides a comprehensive panel of small HSP and crystallin antibodies, kits and purified proteins for experimentation.

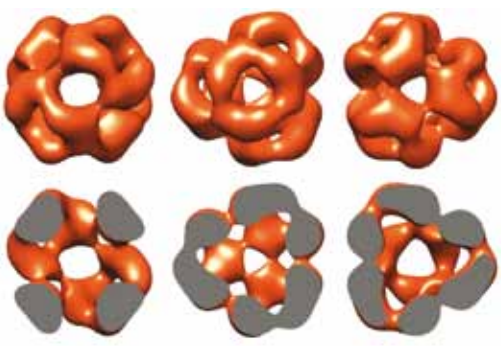


FIGURE 9: 3D Reconstruction (top, surface representations; lower, cross-section representations) of human recombinant αB-crystallin. Figure modified from PNAS **106**, 13272 (2009) with permission of author, Dr. J. Buchner, TU München, Germany.

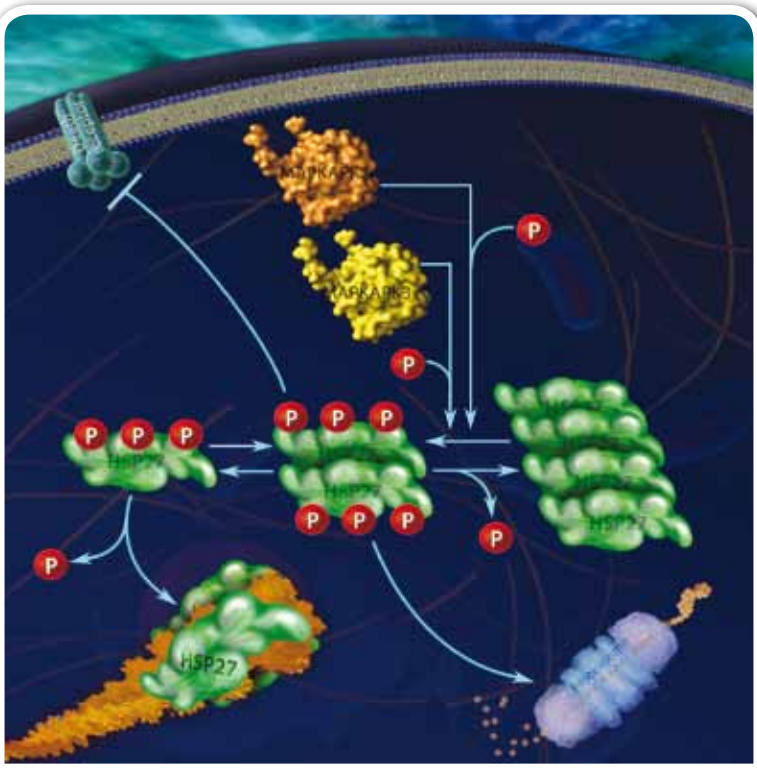


FIGURE 10: HSP27 phosphorylation linked to function. HSP27 is phosphorylated on key serine residues by MAPKAPK2 as well as MAPKAPK3 amongst other kinases. Phosphorylation is associated with the dimerization of HSP27 and its function.

FIGURE 11: HSP27 a regulator of cellular invasion. HSP27 localizes to focal adhesions, influences membrane dynamics and enhances the invasive phenotype of malignant cells.

Table 6: Small HSP and Crystallin Family Proteins

Name	Synonyms	Function/Structure
αA-Crystallin	CRYAA, CRYA1, HSPB4	Expression restricted to the lens
αB-Crystallin	CRYAB, CRYA2, HSPB5	Broad tissue expression; elevated expression in many neurological diseases; a missense mutation associated with a desmin-related myopathy
βA1-Crystallin	CRYBA1	Mutation causes the autosomal dominant disease 'zonular cataract with sutural opacities'; member of the acidic group of β crystallins; β crystallins form aggregates of different sizes and are able to self-associate to form dimers or to form heterodimers with other β crystallins
βA2-Crystallin	CRYBA2	Member of the acidic group of β crystallins
βA4-Crystallin	CRYBA4	Member of the acidic group of β crystallins; part of a gene cluster with β B1, β B2, and β B3; mutations linked to cataractogenesis and microphthalmia
βB1-Crystallin	CRYBB1	Member of the basic group of β crystallins
βB2-Crystallin	CRYBB2	Member of the basic group of β crystallins; mutation found to cause type 2 cerulean cataracts
βB3-Crystallin	CRYBB3	Member of the basic group of β crystallins
γA-Crystallin	CRYGA, CRYG1, CRYG5	Part of a gene cluster with γ B, C and D, and the pseudogenes γ E, F and G; γ crystallins are monomeric proteins and have been implicated in cataract formation
γB-Crystallin	CRYGB, CRYG2	Part of a gene cluster with γ A, C and D, and the pseudogenes γ E, F and G; γ crystallins are monomeric proteins and have been implicated in cataract formation
γC-Crystallin	CRYGC, CRYG3, CCL	Part of a gene cluster with γ A, B, and D, and the pseudogenes γ E, F and G; γ crystallins are monomeric proteins and have been implicated in cataract formation
γD-Crystallin	CRYGD, CRYG4, CCP, PCC, CACA, CCA3	Part of a gene cluster with γ A, B, and C, and the pseudogenes γ E, F and G; γ crystallins are monomeric proteins and have been implicated in cataract formation
γN-Crystallin	CRYGN	β γ hybrid crystallin; expressed in retina and lens nuclear fibers in rodents
γS-Crystallin	CRYGS, CRYG8	The most significant γ crystallin in adult eye lens tissue
Heat shock 22 kDa protein 8	H11, E2IG1, HSP22, HSPB8	Charcot-Marie-Tooth disease type 2L; Hereditary motor neuropathy type II
Heat shock 27 kDa protein 1	HSP27, HSP25, HSPB1	Charcot-Marie-Tooth disease, axonal, type 2F; distal hereditary motor neuropathy
Heat shock 27 kDa protein 2	HSPB2, MKBP	Associates with myotonic dystrophy protein kinase (DMPK)
Heat shock 27 kDa protein 3	HSPB3, HSPL27	Inhibitor of actin polymerization
Heat shock 27 kDa protein family, member 7 (cardiovascular)	cvHSP, HSPB7	Bovine βH crystallin
Heat shock protein, α-crystallin related, B6	HSPB6, HSP20	Structural component of eye lens
Heat shock protein, α-crystallin related, B9	HSPB9, CT51	Testis specific
Outer dense fiber of sperm tails 1	HSPB10, ODFP, SODF, ODF1	Component of outer dense fibers of spermatozoa; testis-specific expression

Small HSP and Crystallin Proteins

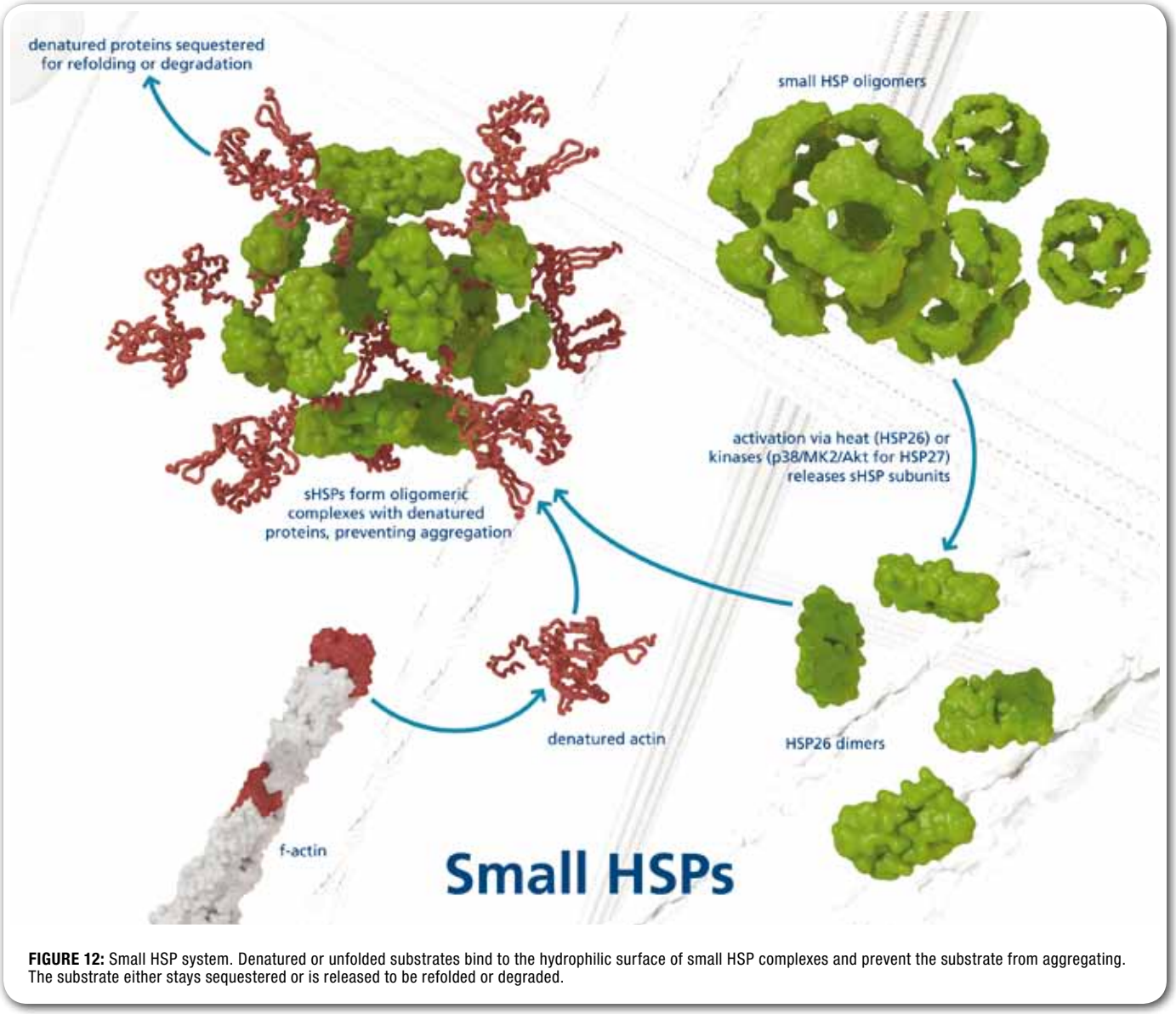


FIGURE 12: Small HSP system. Denatured or unfolded substrates bind to the hydrophilic surface of small HSP complexes and prevent the substrate from aggregating. The substrate either stays sequestered or is released to be refolded or degraded.

Antibodies

Product	Specificity	Application	Prod. No.
[pSer^{19}]αB-Crystallin, pAb	H, M, B	IP, WB	ADI-SPA-225
[pSer^{45}]αB-Crystallin, pAb	H, M, R, B, CH, C, GP, HA, MO, P, RB, SC, X	WB	ADI-SPA-226
[pSer^{59}]αB-Crystallin, pAb	H, R, B	ICC, IHC, WB	ALX-210-411
[pSer^{59}]αB-Crystallin, pAb	M, R, B, C, P, S	IP, WB	ADI-SPA-227
αA/αB-Crystallin, pAb	H, M, B	WB	ADI-SPA-224
αA-Crystallin, mAb (c9F2)	H, R	ELISA, WB	ALX-804-582
αA-Crystallin, pAb	B	IP, WB	ADI-SPA-221
αB-Crystallin (human), pAb	H	IHC, WB	BML-CA9360
αB-Crystallin, mAb (1B6.1-3G4)	H, M, R, B, CH	WB	ADI-SPA-222

Product	Specificity	Application	Prod. No.
αB-Crystallin, pAb	H, M, R, B, P	WB	ADI-SPA-223
β-Crystallin, mAb (3.H9.2)	B, RB	WB	ADI-SPA-230
ERp72, pAb	H, M, R, B, C, GP, HA, MO, RB	WB	ADI-SPS-720
HSP20, pAb	H, M, R, B, C, F	WB	ADI-SPA-796
HSP25, pAb	M, R, B, C, GP, HA	IP, WB	ADI-SPA-801
HSP25, pAb (DyLight™ 488 conjugate)	M, R, B, C, GP, HA	FC	ADI-SPA-801-488
HSP25, pAb (R-PE conjugate)	M, R, B, C, GP, HA	FC	ADI-SPA-801PE
HSP25/HSP27, mAb (8A7)	H, M, R, C	ICC, IHC, IP, WB	BML-SA662
[pSer^{15}]HSP27, pAb	H, M, R, B, C, GP, MO	IF, IHC, WB	ADI-SPA-525
[pSer^{78}]HSP27, pAb	H, B, GP, MO	WB	ADI-SPA-523
[pSer^{82}]HSP27, mAb (5B9)	H, M, R, C	IHC, WB	ALX-804-588
[pSer^{82}]HSP27, pAb	H, R, B, C, GP, HA, MO, P, S	IP, WB	ADI-SPA-524PU
[pSer^{82}]HSP27, pAb	H, M, R, B, C, CH, GP, S	IF, IP, WB	ADI-SPA-524
[pSer^{86}]HSP25, pAb	H, M	WB	ALX-210-891
HSP27, mAb (G3.1)	H, MO	WB	ADI-SPA-800
HSP27, mAb (G3.1) (biotin conjugate)	H, MO	WB	ADI-SPA-800B
HSP27, mAb (G3.1) (DyLight™ 488 conjugate)	H, MO	FC	ADI-SPA-800-488
HSP27, mAb (G3.1) (FITC conjugate)	H, MO	FC	ADI-SPA-800FI
HSP27, mAb (G3.1) (R-PE conjugate)	H, MO	FC	ADI-SPA-800PE
HSP27, pAb	H, MO	EIA, WB	ADI-SPA-803
HSP30 (fish), mAb (RT30.1)	F	WB	ADI-SPA-300

Kits and ImmunoSets

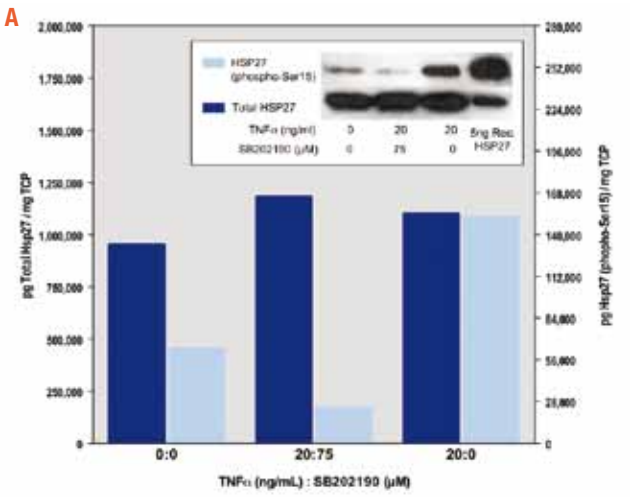
Product	Size	Sample Type	Specificity	Prod. No.
ImmunoSet™ αB-Crystallin ELISA development set	5 x 96 wells	CL	H, M, R, B	ADI-960-074
ImmunoSet™ HSP25 (rodent), ELISA development set	5 x 96 wells	CL	M, R	ADI-960-075
[pSer^{15}]HSP27 (human), EIA kit	1 x 96 wells	CL, P, S	H	ADI-900-170
[pSer^{78}]HSP27 (human), EIA kit	1 x 96 wells	CL, P, S	H	ADI-900-165
HSP27 (human), EIA kit	1 x 96 wells	CL, P, S, T	H	ADI-EKS-500
ImmunoSet™ HSP27 high sensitivity (human), ELISA development set	5 x 96 wells	CL, P, S	H	ADI-960-076

Small HSP and Crystallin Proteins

Proteins

Product	Application	Prod. No.
Blocking peptide for αB-crystallin pAb (Prod. No. BML-CA9360)	Complementary control peptide	BML-PP9360
αA-Crystallin (bovine), (native)	WB control	ADI-SPP-226
αA-Crystallin (human), (rec.)	Not available	ALX-201-191
αB-Crystallin (bovine), (native)	WB control	ADI-SPP-227
αB-Crystallin (human), (rec.)	Not available	ALX-201-192
α-Crystallin (bovine), (native)	WB control	ADI-SPP-225
β-Crystallin (bovine), (native)	WB control	ADI-SPP-235
βL-Crystallin (bovine), (native)	WB control	ADI-SPP-236
γ-Crystallin (bovine), (native)	WB control	ADI-SPP-240
HSP25 (low endotoxin) (mouse), (rec.)	WB control	ADI-ESP-510
HSP25 (mouse), (rec.)	WB control	ADI-SPP-510
HSP25 (mouse), (rec.)	KA, WB control	ADI-NSP-510
HSP26 (yeast), (rec.)	WB	ALX-201-139
HSP27 (human), (rec.)	WB control	ADI-SPP-715
HSP27 (low endotoxin) (human), (rec.)	WB control	ADI-ESP-715
HSP27 (phospho) (human), (rec.)	EIA, WB control	ADI-SPP-716

Small HSP Reagents



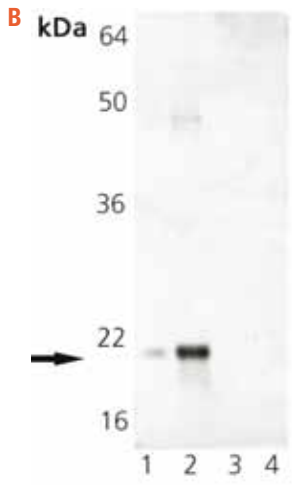


FIGURE A: HeLa cells were treated with SB-202190 (BML-EI294), a cell permeable inhibitor of p38 MAPK, followed by treatment with TNF-α, an inducer of HSP27 phosphorylation. Cell lysates were measured using [pSer[15]]HSP27 (human), EIA kit (ADI-900-170) and HSP27 (human), EIA kit (ADI-EKS-500), and evaluated by Western blot analysis probed with HSP27, pAb (ADI-SPA-803) and [pSer[15]]HSP27, pAb (ADI-SPA-525).

FIGURE B: Western blot analysis of α-Crystallin (bovine), (native) (ADI-SPP-225) in lane 1; αA-Crystallin (bovine), (native) (ADI-SPP-226) in lane 2; αB-Crystallin (bovine), (native) (ADI-SPP-227) in lane 3; and β-Crystallin (bovine), (native) (ADI-SPP-235) in lane 4 probed with αA-Crystallin, pAb (ADI-SPA-221).

Other Chaperones and Stress Proteins

Many molecular chaperones function indiscriminately as it pertains to their substrate targets, but mammalian cells in particular express molecular chaperones that exhibit substrate-specificity (see Table 7). Several of these more specialized chaperones are localized within the lumen of the endoplasmic reticulum (ER) and play an integral role in readying other proteins for their eventual secretion out of the cell or localization to different intracellular membranes (e.g. plasma membrane, lysosome). For example, HSP47 is a resident protein of the ER and appears dedicated to facilitating the early stages of collagen folding. Specifically, HSP47 binds to procollagen in the ER and is thought to mediate its maturation into fibrils. Interestingly, HSP47 is overexpressed in many fibrotic diseases (e.g. pulmonary fibrosis, liver cirrhosis, glomerulosclerosis) and therefore serves as both a biomarker and therapeutic target of a number of diseases and conditions associated with collagen.

Heme oxygenase is an ER resident and plays an essential role in the catabolism of heme. Three distinct isoforms of the protein have been identified: the stress-inducible HO-1 (also referred to as HSP32) and two constitutively expressed forms, HO-2 and HO-3. The reaction products generated by the degradation of heme, carbon monoxide and biliverdin, increase vasodilation and serve as antioxidants respectively. Hence, changes in heme oxygenase expression may play a critical role in a variety of oxidative related diseases including atherosclerosis, hypertension, and ischemia-reperfusion related injuries.

Also located exclusively within the ER is a related family of proteins that function to guide correct disulfide bond formation. These proteins, collectively referred to as the protein disulfide isomerases (PDI) are numerous, with the different family members likely acting on both common and distinct protein targets. Finally, because many secreted or membrane localized proteins are modified by glycosylation, the ER contains a number of lectin-like chaperones including calnexin and calreticulin. These latter chaperones recognize carbohydrate moieties and therefore insure that proteins being readied for secretion are properly glycosylated and folded prior to their transport out of the ER. It is believed that all of the ER localized chaperones together provide for a type of cellular "quality control." Proteins properly modified and folded are allowed to then move further along the secretory pathway. In contrast, those which appear "misfolded" are retained by the ER quality control machinery and eventually translocated back into the cytosol for their subsequent degradation, usually by the ubiquitin-dependent proteasome pathway.

Enzo Life Sciences offers a comprehensive collection of reagents for the aforementioned "specialized chaperones" including related products. As new molecular chaperones are identified and as new reagents become available, we will continue to provide the community with reliable tools for their research efforts.

Table 7: Other Chaperones and Stress Related Proteins

Name	Synonyms	Function/Structure
Calnexin	CNX, P90	Calcium-binding ER protein that interacts transiently with newly synthesized N-linked glycoproteins, facilitating protein folding and assembly; it may also play a central role in the quality control of protein folding by retaining incorrectly folded protein subunits within the ER for degradation. Transmembrane.
Calreticulin	CRTC, ERp60, grp60	Calcium-binding ER protein; also found in the nucleus; can bind and inhibit nuclear hormone receptors. Non-transmembrane.
CHIP	STUB1, UBOX1, HSPABP2	E3 ubiquitin ligase; co-chaperone that associates with HSP70 and HSP90
ERdj5	JPDI, DnaJC10	Expression induced by ER stress; also a member of the DnaJ family
ERp18	TXNDC12, AGR1, ERp19	Member of the thioredoxin superfamily; expressed in ER lumen
ERp27	NA	Interacts with PDIA3; does not contain a CXXC active site motif indicating that it is a catalytically redox-inactive member of the protein disulfide isomerase family
ERp29	ERp28, ERp31, PDI-DB	Similar in sequence to the PDI family, but lacks a thioredoxin motif, suggesting it does not function as a disulfide isomerase; the protein dimerizes and is thought to play a role in the processing of secretory proteins within the ER; two alternative splice forms
ERp44	TXNDC4	Induced by ER stress
ERp46	TXNDC5	Highly expressed in endothelial cells, where it is induced by and protects against hypoxia; contains 3 thioredoxin domains; two isoforms
ERp57	Grp58, PDIA3	ER protein with protein disulfide isomerase activity that interacts with the lectin chaperones calreticulin and calnexin to modulate the folding of newly synthesized glycoproteins
ERp72	PDIA4, ERp70	Catalyzes rearrangement of disulfide bonds
HO-1	Heme oxygenase (decyclizing) 1, HMOX1, HSP32	Highly inducible by heavy metals, endotoxin, oxidizing agents, UVA; cleaves heme ring at the α methene bridge to form biliverdin
HO-2	Heme oxygenase (decyclizing) 2, HMOX2	Non-inducible; cleaves heme ring at the α methene bridge to form biliverdin

Other Chaperones and Stress Proteins

Name	Synonyms	Function/Structure
HSF-1	HSTF1	Regulates the program of heat shock gene expression. Expression repressed by HSP90; positively and negatively regulated by phosphorylation; modified by SUMO-1 and SUMO-2 in a stress-inducible manner
HSF-2	HSTF2	Regulates the program of heat shock gene expression
HSP47	SerpinH1, Colligin, Gp46	ER-localized member of the serpin family of serine protease inhibitors; expression induced by heat shock; binds collagen and thought to be a chaperone involved in the maturation of collagen; auto-antibodies found in patients with rheumatoid arthritis
KDELR1	ERD2	Family of seven-transmembrane receptors that mediate the retention of proteins with the sequence lys-asp-glu-leu (KDEL), such as Grp78 and Grp94, in the lumen of the ER
KDELR2	ERD2.2	Two alternative splice forms
KDELR3	ERD2L3	Two alternative splice forms
P5	PDIA6, ERP5, TXNDC7	Can also function on the cell surface
PDI	PDIA1, P4HB	Catalyzes S-S bond formation, breakage, and rearrangement in nascent (ER lumen) and cell surface proteins
PDILT		Testis-specific expression
PDIP	PDIA2	Catalyzes S-S bond rearrangement; expressed in ER lumen; high expression in pancreas
PDIR	PDIA5	Contains 3 thioredoxin domains
TMX	TXNDC1	Contains one thioredoxin domain and a putative transmembrane domain
TMX2	TXNDC14	Contains one thioredoxin domain and a putative transmembrane domain
TMX3	TXNDC10	Contains one thioredoxin domain and a putative transmembrane domain
TMX4	TXNDC13	Contains one thioredoxin domain and a putative transmembrane domain
UGGT	UDP-glucose:glycoprotein glucosyltransferase, HUGT1, UGCGL1, GT, UGT1, UGTR	Recognizes glycoproteins with minor folding defects; reglucosylates single N-glycans near the misfolded part of the protein, thus providing quality control for protein folding in the endoplasmic reticulum; reglucosylated proteins are recognized by calreticulin for recycling to the endoplasmic reticulum and refolding or degradation

Antibodies

Product	Specificity	Application	Prod. No.
Calnexin, mAb (AF18)	H, M	ICC, IP, WB	ALX-804-014
Calnexin, pAb	H, M, R, B, C, CH, D, GP, HA, MO, P, RB, S, X	WB	ADI-SPA-860
Calnexin, pAb	H, M, R, B, C, CH, GP, HA, MO, P, RB, S, X	WB	ADI-SPA-865
Calreticulin (CT), pAb	H, M, R, C, HA, RB	WB	ALX-210-171
Calreticulin (NT), pAb	H, M, R, C, HA	ICC, WB	ALX-210-170/1
Calreticulin, mAb (FMC 75)	H, MO	IP, WB	ADI-SPA-601
Calreticulin, mAb (FMC 75) (DyLight™ 488 conjugate)	H, MO	FC	ADI-SPA-601-488
Calreticulin, mAb (FMC 75) (R-PE conjugate)	H, MO	FC	ADI-SPA-601PE
Calreticulin, pAb	H, M, R, C, MO, RB	FC, IHC, ICC, IP, WB	ALX-210-126
Calreticulin, pAb	H, M, R	WB	ADI-SPA-602
Calreticulin, pAb	H	WB	ADI-SPA-603
Calreticulin, pAb	H, M, R	WB	ADI-SPA-600
ERp29, pAb	H, M, R, B, C, GP, HA	ICC, IP, WB	ALX-210-404
ERp57 (human), pAb	H	WB	ALX-210-405

Product	Specificity	Application	Prod. No.
ERp57, mAb (MaP.Erp57)	H, C, HA, MO, P	WB	ADI-SPA-725
ERp57, pAb	H, M, R, B, C, GP, HA, MO, P, RB	WB	ADI-SPA-585
ERp72 (human), pAb	H	WB	ALX-210-406
FKBP59, mAb (KN382/EC1)	H, GP, HA, MO, Mink, RB	IP, WB	ADI-SRA-1400
HO-1, pAb	H	IHC, WB	BML-HC3001
HO-2, pAb	H, R	IHC, WB	BML-HC3002
HO-1, pAb	H, M, R, B, MO	ICC, IHC, WB	ALX-210-116
HO-1, mAb (HO-1-1)	H, M, R, B, C	FC, WB	ADI-OSA-110
HO-1, mAb (HO-1-2)	H, R, C, GP, GR, HA, MO, P, RB	FC, IHC, WB	ADI-OSA-111
HO-1, mAb (HO-1-2) (biotin conjugate)	R	WB	ADI-OSA-111B
HO-1, mAb (HO-1-2) (DyLight™ 488 conjugate)	H, M, R, C, GP, HA, MO	FC	ADI-OSA-111-488
HO-1, mAb (HO-1-2) (FITC conjugate)	H, M, R, C, GP, HA, MO	FC	ADI-OSA-111FI
HO-1, mAb (HO-1-2) (R-PE conjugate)	H, M, R, C, GP, HA, MO	FC	ADI-OSA-111PE
HO-1, pAb	H, M, R	WB	ADI-OSA-150
HO-1, pAb	H, M, R, C, GP, HA, MO, RB, S	WB	ADI-SPA-894
HO-1, pAb	M, R, H, C	IHC, WB	ADI-SPA-895
HO-1, pAb	H, M, R, C, HA, MO, RB	IP, WB	ADI-SPA-896
HO-2, pAb	H, M, R, B, C, GP, HA, MO, P, RB, S	IHC, WB	ADI-OSA-200
HO-2, pAb	H, M, R, C, HA, MO, P	EIA, IF, IHC, IP, WB	ADI-SPA-897
[pSer^{326}]HSF1, pAb	H	WB	ADI-SPA-902
HSF1, mAb (10H8)	H, M, R, MO, RB	WB	ADI-SPA-950
HSF1, pAb	H, M, R, MO, RB	WB	ADI-SPA-901
HSF2, mAb (3E2)	H, M, R, B, C, GP, HA, MO, P, RB, S	WB	ADI-SPA-960
HSP104 (yeast), pAb	Y	WB	ADI-SPA-1040
HSP104, pAb	H, M, HA, Y	ICC, IP, WB	ALX-210-140/1
HSP110, pAb	H, M, R, B, C, F	WB	ADI-SPA-1103
HSP110, pAb	H, M, R, B, HA, MO, S, Y	IP, WB	ADI-SPA-1101

Heme Oxygenase-1 (HSP32) Antibody

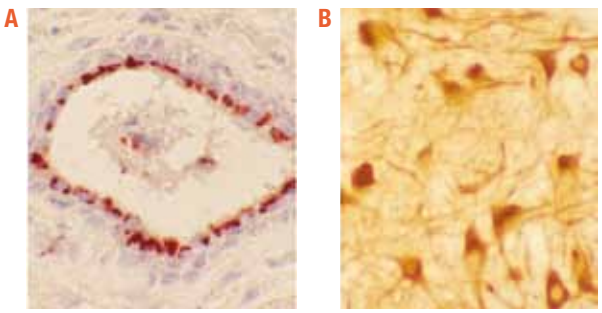


FIGURE A & B: Immunohistochemical analysis of frozen human prostate section (stressed) (A) and mouse spinal cord section after ischemic injury (B) stained using HO-1, mAb (HO-1-2) (ADI-OSA-111), an HSP32 chaperone.

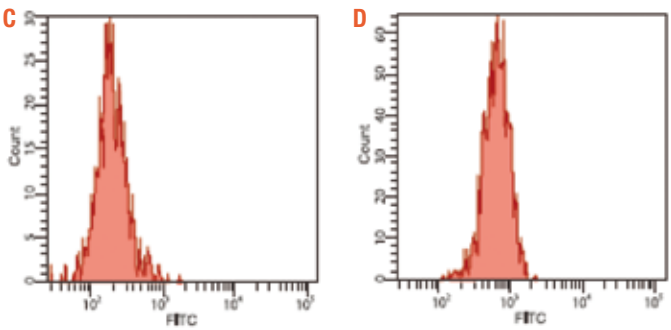


FIGURE C & D: Flow cytometry analysis of human lung cancer A2 cells using isotype control (C) and HO-1, mAb (HO-1-2) (ADI-OSA-111).

Other Chaperones and Stress Proteins

Product	Specificity	Application	Prod. No.
KDEL, mAb (10C3)	Recognizes proteins containing the KDEL	WB	ADI-SPA-827
KDEL, mAb (10C3) (DyLight™ 488 conjugate)	Recognizes proteins containing the KDEL	FC	ADI-SPA-827-488
KDEL, mAb (10C3) (R-PE conjugate)	Recognizes proteins containing the KDEL	FC	ADI-SPA-827PE
KDEL/GRP78, pAb	M, R, HA	ICC, IP, WB	ALX-210-141
KDEL Receptor, mAb (KR-10)	H, M, R	WB	ADI-VAA-PT048
PDI, mAb (1D3)	H, M, R, B, C, CH, GP, HA, MO, P, RB, S, X	IHC, WB	ADI-SPA-891
PDI, mAb (1D3) (DyLight™ 488 conjugate)	H, M, R, B, C, CH, GP, HA, MO, P, RB, S, X	FC	ADI-SPA-891-488
PDI, mAb (1D3) (R-PE conjugate)	H, M, R, B, C, CH, GP, HA, MO, P, RB, S, X	FC	ADI-SPA-891PE
PDI, mAb (RL77)	H, M, R	IHC, IP, WB	ALX-804-013
PDI, mAb (RL90)	H, M, R, HA, P	FC, IHC, ICC, IP, WB	ALX-804-012
PDI, pAb	H, M, R, B, C, GP, HA, MO, P, S, X	WB	ADI-SPA-890
PIST, pAb	H, M, R	IHC, WB	ADI-905-724
XBP-1, pAb	H	ICC, WB	ADI-905-739

Kits, ImmunoSets and Sample Packs

Product	Size	Sample Type	Specificity	Prod. No.
HO-1 (human), EIA kit	1 x 96 wells	CL, T	H	ADI-EKS-800
HO-1 (rat), EIA kit	1 x 96 wells	CL, P, S, T	R	ADI-EKS-810A
ImmunoSet™ HO-1 (human), ELISA development set	5 x 96 wells	CL, T	H	ADI-960-800
ImmunoSet™ HO-1 (mouse), ELISA development set	5 x 96 wells	CL, P, S, T	M	ADI-960-071
ImmunoSet™ HO-1 (rat), ELISA development set	5 x 96 wells	CL, P, S, T	R	ADI-960-810
ImmunoSet™ PDI ELISA development set	5 x 96 wells	CL, CS, P, T	H, M, R	ADI-960-072
Heme Oxygenase, Ab sample pack	8 x 25 µg	Not available	Multiple species	ADI-PAK-030
Heme Oxygenase, Ab sample pack with protein standards	10 x 25 µg	Not available	Multiple species	ADI-PAK-031

Proteins

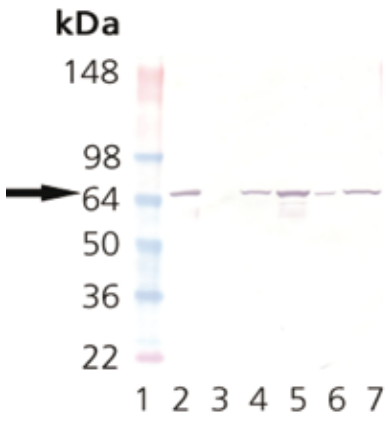
Product	Application	Prod. No.
Calnexin (dog), (rec.)	WB	ALX-201-220
Calnexin (lumenal domain) (human), (rec.)	WB control	ADI-SPP-865
Blocking peptide for antiserum to calreticulin (CT) (Prod. No. ALX-210-171)	WB	ALX-153-016
Blocking peptide for antiserum to calreticulin (NT) (Prod. No. ALX-210-170)	Not available	ALX-153-017
Calreticulin (human) (rec.), (His-tag)	Not available	ALX-201-441
Calreticulin (human), (rec.)	WB control	ADI-SPP-600
Calreticulin (rabbit), (rec.)	Not available	ALX-201-269

Product	Application	Prod. No.
HO-1 (12-25)	Not available	BML-HP9301
HO-2 (246-264)	Not available	BML-HP9302
HO-1 (human), (rec.)	WB control	ADI-SPP-732
HO-1 (rat), (rec.)	WB control	ADI-SPP-730
HSF1 (human), (rec.)	WB control	ADI-SPP-900
HSF1 (phospho) (human), (rec.)	WB control	ADI-SPP-902
HSP12 (yeast), (rec.)	Not available	ALX-201-140
HSP104 (yeast), (rec.)	Not available	ALX-201-154
PDI (human), (rec.)	Enzymatic activity, WB control	ADI-SPP-891

Treated Cell Lysates

Product	Application	Prod. No.
3T3 (heat shocked), (cell lysate)	WB control	ADI-LYC-3T101
HeLa (heat shocked) (no recovery time), (cell lysate)	WB control	ADI-LYC-HL102
HeLa (heat shocked), (cell lysate)	WB control	ADI-LYC-HL101
Jurkat (heat shocked), (cell lysate)	WB control	ADI-LYC-JK101
PC-12 (heat shocked), (cell lysate)	WB control	ADI-LYC-PC101

Antibody Sample Packs



Enzo Life Sciences antibody sample packs include a set of related antibodies and positive control(s) for molecular chaperone, heat shock, and oxidative stress research areas. They are designed to be cost effective and help you choose which of our many antibodies might work best for your particular sample type or application.

FIGURE: Western blot analysis of several components in the HSP70, Ab sample pack with protein standards (ADI-PAK-021). HSP70/HSP72 (human), (rec.) (ADI-NSP-555) in lane 2; HSC70/HSP73 (bovine), (rec.) (ADI-SPP-751) as a negative control in lane 3; PC -12 (heat shocked), (cell lysates) (ADI-LYC-PC101) in lane 4; HeLa (heat shocked), (cell lysate) (ADI-LYC-HL101) in lane 5; 3T3 (heat shocked), (cell lysate) (ADI-LYC-3T101) in lane 6; and CHO-K1 (heat shocked), (cell lysate) in lane 7 probed with HSP70/HSP72, mAb (C92F3A-5) (ADI-SPA-810). (Lane 1: molecular weight marker.)

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