

CHAPERONES PROTEIN FUNCTION

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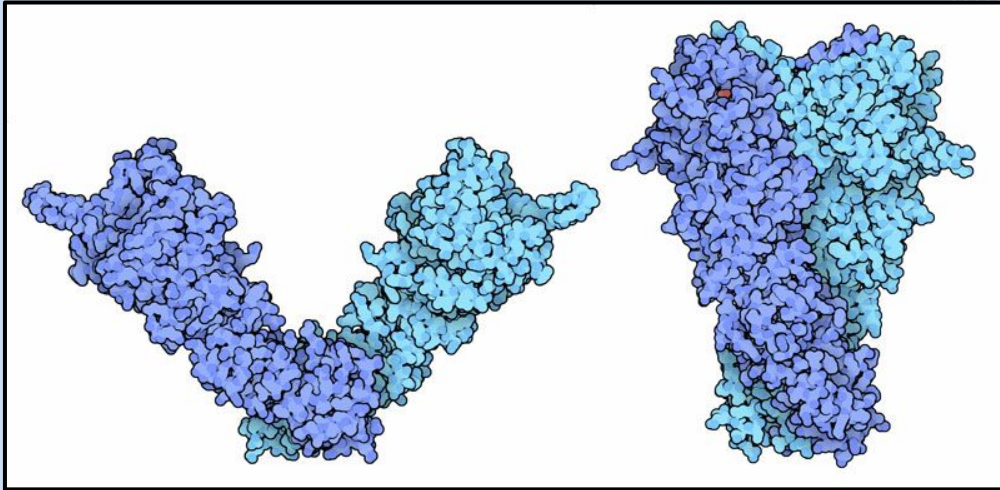
06

MUTATION ANALYSIS

CHAPERONES FUNCTION

KEY ROLES	DIVERSE ROLES	DISEASE PREVENTION	VERSATILITY
<p>Ensures correct 3D structure of proteins.</p> <p>Crucial in:</p> <ul style="list-style-type: none">Cell cycle controlSignal transductionMitochondrial import <p>Maintains stability and function of various proteins.</p>	<p>Unique co-chaperones and client proteins lead to varied cellular processes involvement.</p> <p>Influences:</p> <ul style="list-style-type: none">Protein traffickingSignal transductionImmune responseStress response	<p>Vital in avoiding diseases linked to protein misfolding .</p> <p>Function conserved across species.</p>	<p>Acts as a cellular quality control manager.</p> <p>Adapts to various needs and conditions.</p>
			MECHANISM
			<p>ATP-dependent, interacts with co-chaperones and client proteins for correct protein structure</p>

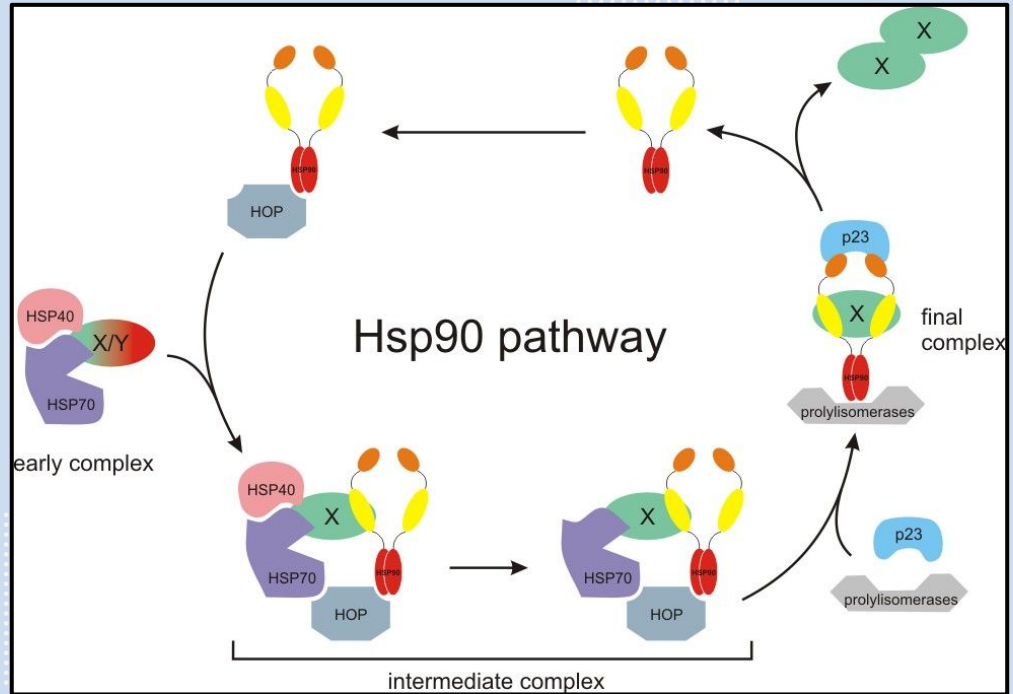
HSP90 FUNCTION



- Refolds proteins in stressed cells
- Secretory chaperon in prokaryotes
- Cytoprotection and intracellular signaling
- Controls protein homeostasis
- Has a critical ATPase activity, ATP binding and hydrolysis → modulates conformation dynamics

CHAPERONE CYCLE

- **X/Y** represents an immature incompletely folded protein such a steroid receptor.
- **Hsp40**, **Hsp70**, and **p23** are partner chaperones.
- **Hop** is a co-chaperone.
- **X-X** represents a mature properly folded protein dimer.



FOLD OF THE PROTEIN HSP90

FOLD

Hsp90 co-chaperone CDC37

multihelical, consists of 2 all-alpha subdomains connected by a long helix

FOLD

GHKL domain-like

2 layers: alpha/beta; 8-stranded mixed beta-sheet, order: 87126345, strands 1 and 7 are parallel to each other

FOLD

HSP90 C-terminal domain

alpha-beta(3)-alpha(3), 2 layers, a/b, mixed beta-sheet, order:132, crossing loops

FOLD

HSP90 middle pre-C-terminal domain

3 layers, a/b/a; mixed beta-sheet of 4 strands, first strand antiparallel to the rest, order 1324

We chose **6XG6** as a representative family.

FOLD

GHKL domain-like

2 layers: alpha/beta; 8-stranded mixed beta-sheet, order: 87126345, strands 1 and 7 are parallel to each other

Keywords [mixed beta-sheet](#)

Superfamilies [1 entry]

- [GHKL \(Gyrase, Hsp90, Histidine Kinase, MutL\) domain-like](#) SCOP ID 3000091
- Families: 5

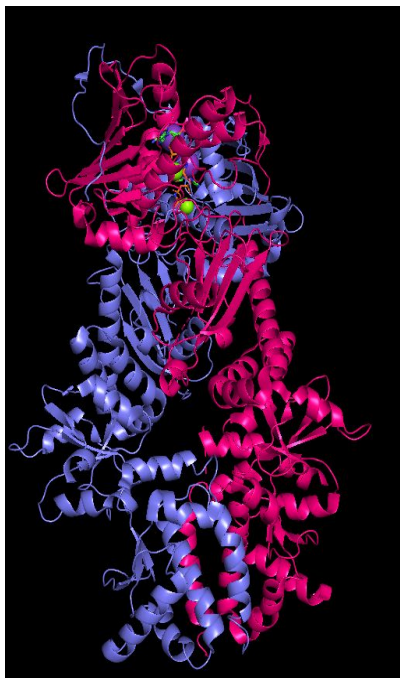
class 1000003
Alpha and beta proteins (a+b)

fold 2000066
GHKL domain-like

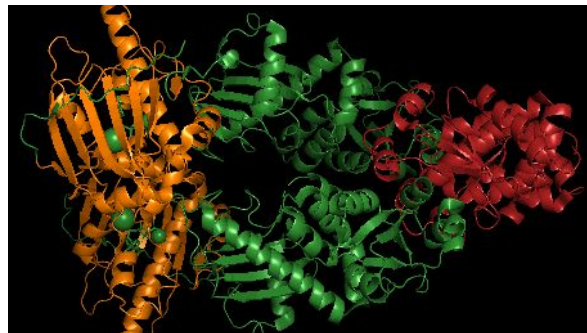
superfamily 3000091




like

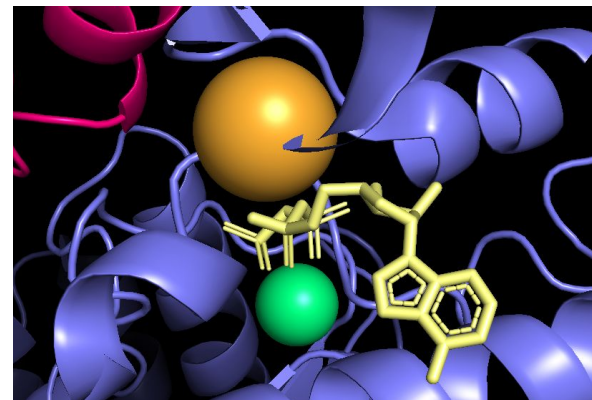
6XG6






Chains: **Alpha** / **Beta**



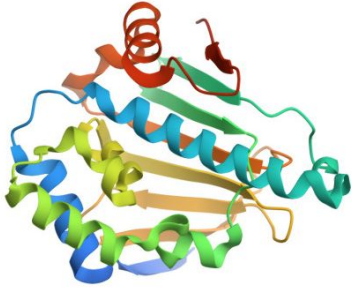
 N-terminal
 Middle Domain
 C-Terminal



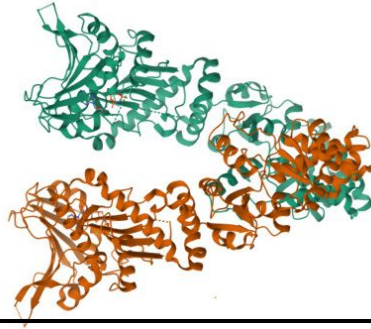
Ligands:

 ANP
 K
 MG

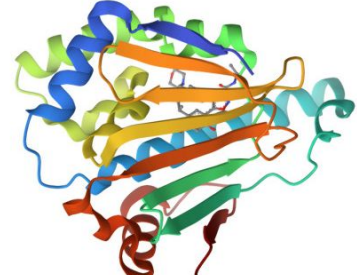
Other structures for the chaperone protein family



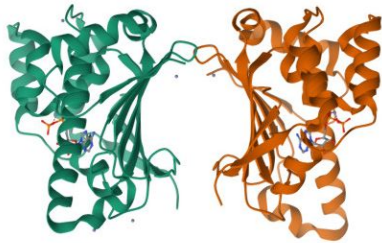
1UYL



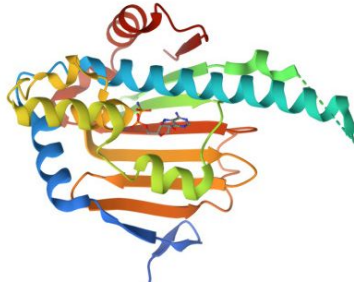
2OIU



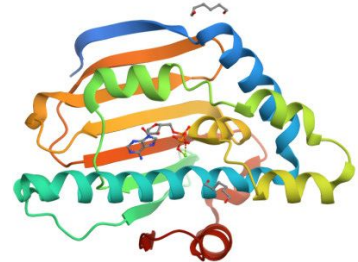
7K9S



4GQT



3IED



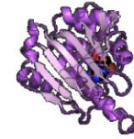
2IOR

REGION FUNCTIONALITY

1byq

HSP90 N-TERMINAL DOMAIN BOUND TO ADP-MG

PDB



A

100 200

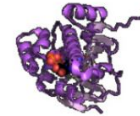


N-Terminal: domain Hsp90 from eukaryotes and its bacterial homologues, known as HtpG (High temperature protein G).

1am1

ATP BINDING SITE IN THE HSP90 MOLECULAR CHAPERONE

PDB



A

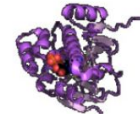
100 200



1amw

ADP BINDING SITE IN THE HSP90 MOLECULAR CHAPERONE

PDB



A

100 200



C-Terminal: this domain has an α - β (3)- α (3) fold arranged in two layers (α/β) with mixed β -sheet and crossing loops.

REGION FUNCTIONALITY: CONSERVED REGION

**Biological
Process**

Protein folding
(GO:0006457)

**Molecular
Function**

ATP binding(GO:0005524)
Unfolded protein binding
(GO:0051082)

**Cellular
Component**

None

Domains shared between family protein

InterPro: Protein Family Classification

[InterPro: Classification of protein families](#)

Chains	Accession	Name	Type
A	IPR003594	Histidine kinase/HSP90-like ATPase	Domain
A	IPR020568	Ribosomal protein uS5 domain 2-type superfamily	Homologous Superfamily
A	IPR001404	Heat shock protein Hsp90 family	Family
A	IPR020575	Heat shock protein Hsp90, N-terminal	Domain
A	IPR019805	Heat shock protein Hsp90, conserved site	Conserved Site
A	IPR036890	Histidine kinase/HSP90-like ATPase superfamily	Homologous Superfamily
A	IPR037196	HSP90, C-terminal domain	Homologous Superfamily

MUTATION ANALYSIS

R>H

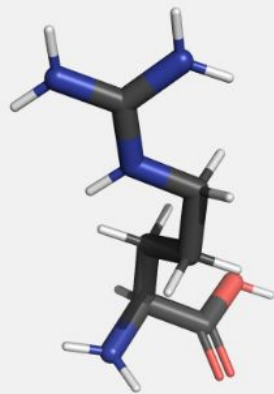
cGc/cAc (-)

Missense

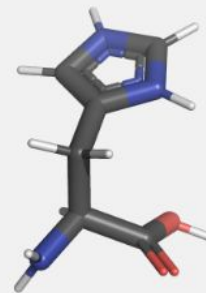
Conservation score: 0.808

Position: 469

$\Delta\Delta G_{\text{pred}}$: 3.91427



Arginine



Histidine



THE END!