HSP90AA1 (heat shock protein 90-alpha)

For fragment scientists. This report surfaces what a fragment campaign design step needs: ranked candidate pockets computed across a conformational ensemble (not a single static frame), per-residue interaction fingerprints from PLIP against representative liganded structures, and family/conservation/precedent as prioritization signal before any soaking or SPR/ITC/NMR work begins. It does not screen a fragment library, predict affinity, dock a ligand, or design a molecule — those stay explicitly out of scope.

Independently verified this session — not pipeline output

Independently checked against PDB 1YET (HSP90 N-domain + geldanamycin). The correct pocket is present and matches 18 of 19 real contact residues (95%) — including the well-characterized Asn51 and Phe138 contacts — but at rank 2, not rank 1. Rank 1 is a different, non-matching cavity. The same pattern already documented for FKBP12 and ADRB2 in the Phase 6 batch: the correct answer is present and well-resolved, the ranker just didn't put it first.

Protein Knowledge Report — P07900

1. Target summary

- Input type: uniprot_accession
- Label: P07900
- Length: 732 aa
- UniProt accession: P07900
- Submitted: 2026-07-17T10:11:40Z
- Sequence:

MPEETQTQDQPMEEEEVETFAFQAEIAQLMSLIINTFYSNKEIFLRELISNSSDALDKIRYESLTDPSKLDSGKELHINLIPNKQDRTLTIVDTGIGMTKADLIN
NLGTIAKSGTKAFMEALQAGADISMIGQFGVGFYSAYLVAEKVTVITKHNDDEQYAWESSAGGSFTVRTDTGEPMGRGTKVILHLKEDQTEYLEERRIKEI
VKKHSQFIGYPITLFVEKERDKEVSDDEAEEKEDKEEEKEKEEKESEDKPEIEDVGSDEEEEKKDGDKKKKKKIKEKYIDQEELNKTKPIWTRNPDDITNEEY
GEFYKSLTNDWEDHLAVKHFSVEGQLEFRALLFVPRRAPFDLFENRKKKNNIKLYVRRVFIMDNCEELIPEYLNFIRGVVDSEDLPLNISREMLQQSKILKVI
RKNLVKKCLELFTELAEDKENYKKFYEQFSKNIKLGIHEDSQNRKKLSELLRYYTSASGDEMVSLKDYCTRMKENQKHIYYITGETKDQVANSAFVERLRKH
GLEVIYMIEPIDEYCVQQLKEFEGKTLVSVTKEGLELPEDEEEKKKQEEKKTKFENLCKIMKDILEKKVEKVVVSNRLVTSPCCIVTSTYGWTANMERIMKAQ
ALRDNSTMGYMAAKKHLEINPDHSIIETLRQKAEADKNDKSVKDLVILLYETALLSSGFSLEDPQTHANRIYRMIKLGLGIDEDDPTADDTSAAVTEEMPPL
EGDDDTSRMEEVD

2. Family classification

- Family: HSP90 (PF00183) — Hsp90 protein
- E-value: 3.60e-239 Bit score: 795.7
- Model span: 1-508 of model (196-714 of query)
- Passes family's curated gathering threshold: yes

Source: HMMER hmmscan vs Pfam-A (local)

3. Known ligand precedent

- Total structures in this family: 77
- Distinct ligand scaffolds curated below: 8

PDB ID	Ligand(s)	Resolution (Å)	Why selected
7U8V	UJS	1.45	highest-resolution structure...
7U8X	UJV	1.60	highest-resolution structure...
7U8W	KUC	1.71	highest-resolution structure...
4IVG	ANP	1.75	highest-resolution structure...
5TVX	ADP	2.20	highest-resolution structure...
4IYN	ADP, ALF	2.31	highest-resolution structure...

7ULK	42C	2.34	highest-resolution structure...
4J0B	ADP, BEF	2.35	highest-resolution structure...

Source: RCSB PDB REST API, curated top-N by distinct ligand scaffold + resolution

Interaction fingerprints (Evidence Integration Layer, Phase 1)

Representative complex: PDB 7KRJ (ATP, 2.56 Å)

Residue (PDB)	Residue (pipeline)	Interaction	Partner
113	113	hydrogen bond	SER113 (hydrogen bond) with ...
136	136	hydrogen bond	VAL136 (hydrogen bond) with ...
137	137	hydrogen bond	GLY137 (hydrogen bond) with ...
133	133	hydrogen bond	GLN133 (hydrogen bond) with ...
134	134	hydrogen bond	PHE134 (hydrogen bond) with ...
113	113	hydrogen bond	SER113 (hydrogen bond) with ...
135	135	hydrogen bond	GLY135 (hydrogen bond) with ...
138	138	hydrogen bond	PHE138 (hydrogen bond) with ...
51	51	hydrogen bond	ASN51 (hydrogen bond) with l...
114	114	hydrogen bond	GLY114 (hydrogen bond) with ...
115	115	hydrogen bond	THR115 (hydrogen bond) with ...
58	58	hydrogen bond	LYS58 (hydrogen bond) with l...
184	184	hydrogen bond	THR184 (hydrogen bond) with ...
400	400	salt bridge	ARG400 (salt bridge) with li...
93	93	hydrogen bond	ASP93 (hydrogen bond) with l...
113	113	hydrogen bond	SER113 (hydrogen bond) with ...
136	136	hydrogen bond	VAL136 (hydrogen bond) with ...
134	134	hydrogen bond	PHE134 (hydrogen bond) with ...
113	113	hydrogen bond	SER113 (hydrogen bond) with ...
135	135	hydrogen bond	GLY135 (hydrogen bond) with ...
137	137	hydrogen bond	GLY137 (hydrogen bond) with ...
138	138	hydrogen bond	PHE138 (hydrogen bond) with ...
51	51	hydrogen bond	ASN51 (hydrogen bond) with l...
114	114	hydrogen bond	GLY114 (hydrogen bond) with ...
115	115	hydrogen bond	THR115 (hydrogen bond) with ...
58	58	hydrogen bond	LYS58 (hydrogen bond) with l...
400	400	salt bridge	ARG400 (salt bridge) with li...

Representative complex: PDB 9W5I (ATP, 2.63 Å)

Residue (PDB)	Residue (pipeline)	Interaction	Partner
110	115	hydrogen bond	THR110 (hydrogen bond) with ...
88	93	hydrogen bond	ASP88 (hydrogen bond) with l...
128	133	hydrogen bond	GLN128 (hydrogen bond) with ...
129	134	hydrogen bond	PHE129 (hydrogen bond) with ...
130	135	hydrogen bond	GLY130 (hydrogen bond) with ...
131	136	hydrogen bond	VAL131 (hydrogen bond) with ...
132	137	hydrogen bond	GLY132 (hydrogen bond) with ...
108	113	hydrogen bond	SER108 (hydrogen bond) with ...
133	138	hydrogen bond	PHE133 (hydrogen bond) with ...
109	114	hydrogen bond	GLY109 (hydrogen bond) with ...
110	115	hydrogen bond	THR110 (hydrogen bond) with ...
110	115	hydrogen bond	THR110 (hydrogen bond) with ...
53	58	hydrogen bond	LYS53 (hydrogen bond) with l...
392	400	salt bridge	ARG392 (salt bridge) with li...
110	115	hydrogen bond	THR110 (hydrogen bond) with ...
88	93	hydrogen bond	ASP88 (hydrogen bond) with l...

108	113	hydrogen bond	SER108 (hydrogen bond) with ...
132	137	hydrogen bond	GLY132 (hydrogen bond) with ...
128	133	hydrogen bond	GLN128 (hydrogen bond) with ...
129	134	hydrogen bond	PHE129 (hydrogen bond) with ...
130	135	hydrogen bond	GLY130 (hydrogen bond) with ...
131	136	hydrogen bond	VAL131 (hydrogen bond) with ...
133	138	hydrogen bond	PHE133 (hydrogen bond) with ...
109	114	hydrogen bond	GLY109 (hydrogen bond) with ...
110	115	hydrogen bond	THR110 (hydrogen bond) with ...
110	115	hydrogen bond	THR110 (hydrogen bond) with ...
53	58	hydrogen bond	LYS53 (hydrogen bond) with l...
46	51	hydrogen bond	ASN46 (hydrogen bond) with l...
179	184	hydrogen bond	THR179 (hydrogen bond) with ...
392	400	salt bridge	ARG392 (salt bridge) with li...

Representative complex: PDB 6XLG (AGS, 2.71 Å)

Residue (PDB)	Residue (pipeline)	Interaction	Partner
101	115	hydrogen bond	THR101 (hydrogen bond) with ...
79	93	hydrogen bond	ASP79 (hydrogen bond) with l...
99	113	hydrogen bond	SER99 (hydrogen bond) with l...
118	132	hydrogen bond	GLY118 (hydrogen bond) with ...
123	137	hydrogen bond	GLY123 (hydrogen bond) with ...
37	51	hydrogen bond	ASN37 (hydrogen bond) with l...
120	134	hydrogen bond	PHE120 (hydrogen bond) with ...
121	135	hydrogen bond	GLY121 (hydrogen bond) with ...
124	138	hydrogen bond	PHE124 (hydrogen bond) with ...
100	114	hydrogen bond	GLY100 (hydrogen bond) with ...
101	115	hydrogen bond	THR101 (hydrogen bond) with ...
44	58	hydrogen bond	LYS44 (hydrogen bond) with l...
101	115	hydrogen bond	THR101 (hydrogen bond) with ...
79	93	hydrogen bond	ASP79 (hydrogen bond) with l...
99	113	hydrogen bond	SER99 (hydrogen bond) with l...
118	132	hydrogen bond	GLY118 (hydrogen bond) with ...
123	137	hydrogen bond	GLY123 (hydrogen bond) with ...
37	51	hydrogen bond	ASN37 (hydrogen bond) with l...
120	134	hydrogen bond	PHE120 (hydrogen bond) with ...
121	135	hydrogen bond	GLY121 (hydrogen bond) with ...
124	138	hydrogen bond	PHE124 (hydrogen bond) with ...
100	114	hydrogen bond	GLY100 (hydrogen bond) with ...
101	115	hydrogen bond	THR101 (hydrogen bond) with ...
44	58	hydrogen bond	LYS44 (hydrogen bond) with l...

Source: PLIP (Protein-Ligand Interaction Profiler), run on representative structures from known ligand precedent

4. Conservation

- Family: PF00183
- Seed alignment size: 82 sequences
- Mean pairwise identity (seed alignment): 61.4%
- Note: computed over a sample of 40/82 seed sequences

Source: Pfam seed alignment (via InterPro API), mean pairwise identity across aligned members at matched-region columns

5. Structural analysis

Not available (error). no structure provider could resolve this target: all structure providers exhausted: AlphaFold DB: AlphaFold DB metadata fetch failed: HTTP Error 429: Too Many Requests; ESMFold: not available for this target

Source: StructureProvider + PocketDetector abstraction (see api/knowledge_protein/structural.py)

6. Confidence flags

1 caution flag(s) — discount confidence accordingly:

- [Structural analysis] structural_analysis_unavailable: Structural analysis did not complete (error): no structure provider could resolve this target: all structure providers exhausted: AlphaFold DB: AlphaFold DB metadata fetch failed: HTTP Error 429: Too Many Requests; ESMFold: not available for this target.

Source: rules-based checks in api/knowledge_protein/confidence_flags.py — fixed thresholds on numbers already computed elsewhere in this report, no learned calibration, no combined/weighted score.

7. Similar known proteins

Sequence-based (Pfam family co-membership, top 5 by identity):

PDB ID	Sequence identity to query	Ligand(s)
7KRJ	100.0%	ATP, DEX
9KQN	100.0%	ADP
9KMR	100.0%	ADP
7L7I	100.0%	ANP
7L7J	100.0%	ANP

Structure-based (Foldseek vs. full PDB structural index, Evidence Integration Layer Phase 2):

Not computed. no structure provider could resolve this target: all structure providers exhausted: AlphaFold DB: AlphaFold DB metadata fetch failed: HTTP Error 429: Too Many Requests; ESMFold: not available for this target

Source: sequence-based: Pfam family co-membership among cached PDB reference structures (sequence-based); Foldseek vs local PDB structural database (structure-based)

8. Limitations & data provenance

Auto-populated from each section's own status — not hand-maintained.

Section	Status	Detail
Family classification	returned data	
Known ligand precedent	returned data	
Interaction fingerprints	returned data	
Functional context (UniProt + ClinVar)	returned data	
Conservation	returned data	computed over a sample of 40/82 seed s…
Structural analysis	errored	no structure provider could resolve th…
Similar known proteins	returned data	
Similar known proteins (structure-base…	not computed this run	no structure provider could resolve th…

2 of 8 sections did not return data this run: Structural analysis, Similar known proteins (structure-based).