COMPUTATIONAL TARGET PROFILE

WDR89

An Uncharacterised WD40 β-Propeller, Characterised Without An Experimental Structure

The conserved-but-dark propeller, newly tied to genome maintenance. A predicted seven-bladed β-propeller with **no solved structure** — resolved into a fold, a protein-interaction pocket, and a validation plan for a protein whose function is only now emerging.

UniProt Q96FK6 · 387 aa · Soluble · IDG tier: T_{dark} · PDB: none · July 2026

Have your own under-characterised target? Send a UniProt ID to contact@orbion.life for a preview like this one.

At A Glance

Fold	Soluble, predominantly ordered single chain built from **six WD40 repeats** — predicted to close into a **seven-bladed β-propeller**. Non-enzyme.
Interaction Pocket	**High-confidence hypothesis (0.84).** A residue-level pocket on the propeller face / central channel — the surface a WD40 scaffold uses to bind partners, and the one thing a fold alone does not tell you.
Function Context	Non-enzyme scaffold; recently implicated as an **ATM-dependent genome-maintenance factor** required for p53 accumulation [3].
Flexible Regions	Only ~8% disordered — a compact, ordered propeller, well-suited to structural work.
Clean Signal	No membrane, and no amyloidogenic segments predicted.

PREDICTION CONFIDENCE

Figure 1. Model-reported confidence for the headline calls. The interaction pocket (amber) is the load-bearing prediction — the partner-binding surface on a propeller with no experimental structure.

1 The Gap

WDR89 is a paradox of the dark proteome: **evolutionarily conserved yet almost entirely uncharacterised**. It sits at IDG T_{dark} [2] — essentially no dedicated primary literature, no known ligand, **no experimental structure in the PDB**. Until recently there was nothing to say about what it does. That changed in early 2026, when a Dependency-Map correlation analysis pulled WDR89 out of obscurity as a **genome-maintenance factor**: it relocalises to the nucleolus on DNA damage in an ATM-dependent manner, is required for p53 accumulation after irradiation, and its depletion increases DNA damage [3].

So interest is arriving **faster than structural information exists**. That is exactly where prediction earns its keep: everything below is computed from the canonical 387-residue sequence and derived structural predictions, with no experimental WDR89 structure used as input. For a newly-interesting orphan, there is nothing to look up.

2 Sequence Architecture And Fold

WDR89 is a small (387 aa), **predominantly ordered** soluble protein (only ~8% predicted disorder, no amyloid). Its sequence is built from **six annotated WD40 repeats** — the tandem ~40-residue motifs that fold into the blades of a β-propeller. Six sequence repeats plus the N-/C-terminal "velcro" closure is the classic signature of a **seven-bladed WD40 propeller**: a disc-shaped scaffold whose job is to present protein-interaction surfaces.

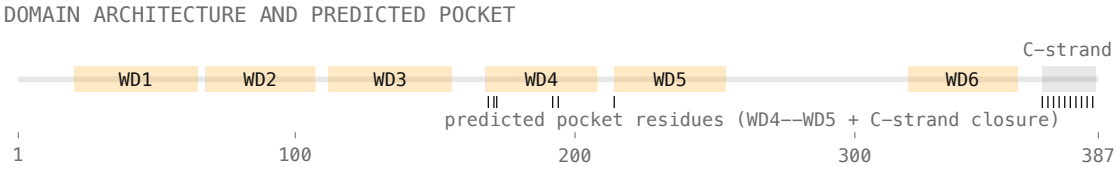

Figure 2. Sequence architecture. Six WD40 repeats (amber) tile the chain; the predicted interaction-pocket residues (ticks) cluster in the WD4–WD5 loops and the C-terminal strand that closes the propeller — i.e. they converge on one face of the disc rather than scattering along the sequence, which is what a genuine binding surface looks like.

3 The Predicted Interaction Pocket

Every WD40 protein folds into a propeller; that is not the finding. The useful question is *which face, and which residues*, form the partner-binding surface — the input a docking run or an interaction-mapping experiment needs, and the one thing you cannot read off the sequence. Astra resolves that residue set and places a **high-confidence pocket (0.84)** on the propeller. Because the contributing residues are scattered across the sequence (WD4–WD5 loops and the C-terminal closure) but converge in space, the pocket is a spatial prediction, not a sequence artefact.

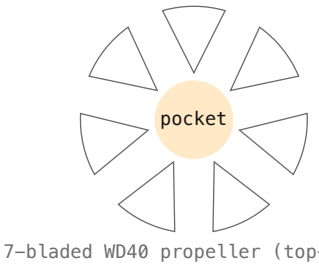

Figure 3. Schematic top-down propeller; the predicted pocket sits on the central axis / top face.

PREDICTED POCKET RESIDUES

WD4–WD5 face	169, 171–172, 192, 194, 214
C-terminal closure	367–386 (propeller "velcro" strand)
Confidence	HIGH (0.84); no known binders — a genuine orphan surface

For a scaffold protein, the pocket *is* the function: it is where WDR89 would recruit the partners implicated in its genome-maintenance role. No small-molecule binder is claimed.

AlphaFold gives a fold; Astra adds the annotation. An AlphaFold model of WDR89 exists and is a useful input — but a propeller model alone does not tell you which face is the interaction hub or which residues line it. This profile is that annotation layer. As a control, the same pocket detection recovers the known interaction/ligand surfaces on WD40 proteins whose structures *are* solved, so the WDR89 pocket is a like-for-like prediction rather than a guess. The net effect: a bare sequence becomes a **ranked, testable interaction hypothesis**.

4 Post-Translational And Structural Features

The predicted modification map is consistent with a regulated nuclear scaffold:

- **Ubiquitination-rich.** The dominant predicted modification — consistent with a protein whose abundance and DNA-damage response are regulated by the ubiquitin system.
- **Phosphorylation sites.** A smaller set of predicted phosphosites — candidate control points for the ATM-dependent, damage-induced relocalisation reported for WDR89 [3].
- **No membrane, disorder or amyloid signal.** A clean, compact, ordered propeller — the whole chain is

a viable target for structural work.

5 Recommended Experimental Follow-Up

This turns a bare sequence into a ranked, executable plan: each prediction is paired with the experiment that would test it and the readout to watch for.

Prediction	Experiment	Readout
Seven-bladed β-propeller fold	Limited proteolysis / recombinant expression of the propeller	A stable, well-behaved construct
Interaction pocket (WD4–WD5 + C-strand)	Alanine scan at the pocket + AP-MS partner mapping	Loss of specific partner binding
Genome-maintenance role [3]	Pocket-mutant rescue of the DNA-damage / p53 phenotype	Which partners the pocket controls
Ubiquitination sites	Point mutants at predicted sites	Change in WDR89 stability / turnover
Phospho sites	Phosphomimetic / phospho-null mutants	Change in damage-induced relocalisation

Its emerging role in genome maintenance and p53 signalling [3] indicates where a validated interaction map would first be worth pursuing.

6 Where This Fits In A Discovery Workflow

Team	What they get from this profile
Target biology	Testable residue-level hypotheses and a validation plan
Structural biology	A predicted fold, construct boundaries, and a surface to focus on
Medicinal chemistry	Pocket residues for docking and interaction-inhibitor design
BD / platform evaluation	Evidence Orbion can prioritise dark targets quickly

7 Methods

All predictions were generated with Orbion's Astra suite from the canonical WDR89 sequence (UniProt Q96FK6 [1]). Modules used, with method publications cited where available: **AstraSUIT2** and **AstraROLE2** [4] (membrane and functional class, oligomeric state), **AstraUNFOLD** (topology, disorder, aggregation), **AstraPTM2** [5] (modification sites) and **AstraBIND** [6] (binding pocket). Reported values are model outputs; model internals are out of scope. Confidence scores are model-estimated probabilities (0–1) that rank and gate each call — not calibrated rates of experimental success.

PREDICTION PROVENANCE

Target & input	WDR89 · UniProt Q96FK6, canonical isoform (387 aa)
Structure source	AlphaFold2 predicted model (no experimental PDB entry)
Feature inputs	ESM-2 embeddings + AlphaFold2-derived structural features [4–6]
Models	AstraSUIT2 · AstraROLE2 · AstraUNFOLD · AstraPTM2 · AstraBIND
Binding-site model	GATv2 detector trained on >250k protein–ligand complexes [6]
Confidence & calibration	Per-call model probability; per-model calibration, thresholds and benchmarks reported in [4]–[6]

Scope And Limitations

- **Prediction, not experiment.** These are computational hypotheses to prioritise experiments — not a substitute for a structure or an assay. No result here has been validated in the wet lab.
- **The pocket is predicted; no binder is named.** For a scaffold the honest output is a residue-level interaction-surface hypothesis, not a ligand or a proven complex.
- **The seven-blade count is an inference.** UniProt annotates six WD40 repeats; the seven-bladed β-propeller is the standard predicted fold for that architecture, not an explicit experimental fact. The genome-maintenance role rests on a single 2026 preprint [3] — treat it as an emerging, not settled, function.

8 References

[1] UniProt Consortium. UniProtKB entry Q96FK6 (WDR89, human). uniprot.org.

[2] Pharos / Illuminating the Druggable Genome. WDR89 target record — T_{dark}. pharos.nih.gov/targets/Q96FK6.

[3] Minaker S.W., Negri G.L., Morin G.B., Stirling P.C. Dependency Map correlation analysis reveals WDR89 as a genome maintenance factor. *bioRxiv* 2026.01.28.698016 (2026; preprint). doi:10.64898/2026.01.28.698016.

[4] Bozkurt Ç., Vasilyeva A., Goteti A. AstraROLE2 & AstraSUIT2: Multi-Task Annotation Models for Functional Profiling of Proteins. *bioRxiv* 2025.06.21.660734 (2025). doi:10.1101/2025.06.21.660734.

[5] Bozkurt Ç., Vasilyeva A., Goteti A. AstraPTM2: A Context-Aware Transformer for Broad-Spectrum PTM Prediction. *bioRxiv* 2025.10.03.680341 (2025). doi:10.1101/2025.10.03.680341.

[6] Goteti A., Vasilyeva A., Bozkurt Ç. AstraBIND: Graph Attention Network for Predicting Ligand Binding Sites. *bioRxiv* 2025.11.10.687555 (2025). doi:10.1101/2025.11.10.687555.