COMPUTATIONAL TARGET PROFILE

ABHD17A

A dark α/β-hydrolase that depalmitoylates N-Ras, characterised without an experimental structure

ABHD17A is a serine hydrolase that strips palmitate from S-acylated proteins — among them N-Ras, whose membrane localisation and oncogenic signalling depend on an intact palmitoylation cycle. Yet it remains an IDG Tbio enzyme with no experimental structure in the PDB and a thin literature. We resolve the canonical 310-residue sequence into its α/β-hydrolase fold, a residue-level active-site hypothesis clustered around the catalytic triad, post-translational features and a construct / validation plan — all computed with Orbion's Astra suite from sequence alone.

UniProt Q96GS6 · 310 aa · α/β-Hydrolase; Palmitoyl-Protein Thioesterase · IDG tier: Tbio · 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	A single-domain α/β-hydrolase (soluble fold), membrane-anchored in vivo via N-terminal palmitoylation; see the domain map and disorder profile.
Active-Site Region	AstraBIND's highest-confidence call on this target (0.903) — a residue-level active-site hypothesis clustered around the catalytic triad. A concrete starting point for docking and covalent-probe design; no validated inhibitor.
Flexible Regions	Elevated predicted disorder across the N-terminus (1–55) — the natural truncation boundary for a crystallisable construct.
Clean Signal	No amyloidogenic segments predicted.

PREDICTION CONFIDENCE

Figure 1. Model-reported confidence for the headline calls (amber = load-bearing / soft prediction).

1 The Gap

Most tractable enzyme families have been structurally explored. ABHD17A has not: an IDG Tbio α/β-hydrolase with no experimental structure in the PDB and only a handful of functional studies. UniProt records that it hydrolyses fatty acids from S-acylated cysteines and depalmitoylates both NRAS and the postsynaptic scaffold PSD-95 — placing it squarely in the RAS palmitoylation cycle that many tumour cells depend on. But the fold, the catalytic machinery and the druggable surface all have to be inferred.

That combination — a credible oncology rationale with near-zero structural information — is where prediction earns its keep: everything below is computed from the canonical 310-residue sequence, with no experimental ABHD17A structure used as input.

2 Architecture And Topology

PREDICTED ARCHITECTURE

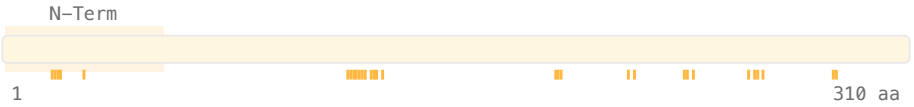

Figure 2. Predicted domain architecture along the sequence: annotated domains as boxes, disordered regions shaded, and the predicted active-site / pocket residues marked as amber ticks.

Element	Residues	Note
Chain	1–310	Single-chain; see disorder profile and pocket below.

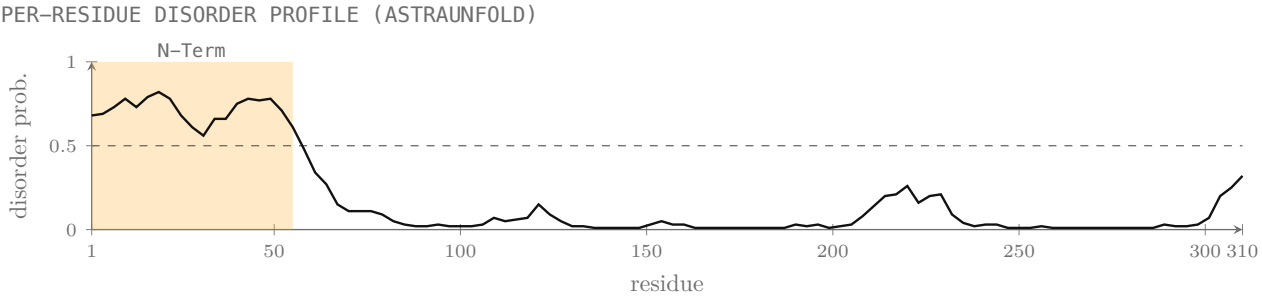

Figure 3. Predicted per-residue disorder (dashed = 0.5 call threshold); amber bands mark flexible regions — natural construct / truncation boundaries.

3 The Predicted Active-Site Region

Astra resolves a residue-level site — the input a docking run or a mutagenesis plan actually needs. Predicted location: **Predicted substrate / cofactor-facing residues**.

PREDICTED POCKET / FUNCTIONAL RESIDUES

Loop / Surface	17–20, 28, 118–124, 126–128, 130, 189–191, 214, 216, 233–234, 236, 255, 257–258, 260, 284–285

A residue-level active-site hypothesis from AstraBIND. As a positive control, the predicted residues recover the UniProt-annotated catalytic triad (190, 255, 284) — the detector lands on the known active site, not an arbitrary surface. Still a computational hypothesis for prioritising experiments, not a validated inhibitor or a proven druggable site.

4 Post-Translational And Structural Features

- **Catalytic triad (charge-relay system).** The serine-hydrolase triad at positions 190, 255 and 284 — the active site that carries out depalmitoylation, and the obvious mutagenesis handle (a Ser190→Ala mutant is the natural catalytic-dead control).
- **No amyloidogenic segments predicted.** The ordered core is a clean expression target once the disordered N-terminus is trimmed.

5 Recommended Experimental Follow-Up

Prediction	Experiment	Readout
Catalytic Triad (190 / 255 / 284)	Ser190→Ala point mutant + protein-depalmitoylation assay	Loss of thioesterase activity — confirms the predicted active site
Predicted Active-Site Pocket	Covalent-fragment / activity-based-probe screen at the predicted site	Engagement or inhibition — a starting point for chemical tools
Disordered N-Terminus (1–55)	N-terminal truncation	Improved expression / crystallisability

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	Construct boundaries, disordered regions, fusion / deletion ideas
Medicinal Chemistry	Pocket / active-site residues for docking and SAR
BD / Platform Evaluation	Evidence Orbion can prioritise dark targets quickly

7 Methods

All predictions were generated with Orbion's Astra suite from the canonical ABHD17A sequence (UniProt Q96GS6): **AstraSUIT** and **AstraROLE** (membrane / functional class), **AstraUNFOLD** (topology, disorder, aggregation), **AstraPTM** (modification sites) and **AstraBIND** (binding pocket). Reported values are model outputs; model internals are out of scope. No experimental ABHD17A structure or ligand was used as input. Predictions are computational hypotheses to prioritise experiments, not validated results.

8 References

1. UniProt Consortium. UniProtKB entry Q96GS6 (ABHD17A, human). uniprot.org.
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3. McClafferty H et al. Site-specific deacylation by ABHD17a controls BK channel splice variant activity. (2020). https://doi.org/10.1074/jbc.ra120.015349
4. Lin DT, Conibear E. ABHD17 proteins are novel protein depalmitoylases that regulate N-Ras palmitate turnover and subcellular localization. (2015). https://doi.org/10.7554/elife.11306
5. Shi X et al. The Unconventional Role of ABHD17A in Increasing the S-Palmitoylation and Antiviral Activity of IFITM1 by Downregulating ABHD16A. (2025). https://doi.org/10.3390/biom15070992