COMPUTATIONAL TARGET PROFILE

CLPTM1L

A CLPTM1-like ER scramblase at the 5p15.33 cancer-risk locus, characterised without an experimental structure

A membrane protein famous for its address, not its mechanism. CLPTM1L sits beside TERT at 5p15.33 — one of the most repeatedly cancer-associated loci in the genome — yet its day job, scrambling GPI-precursor lipids across the ER membrane, has no solved structure to reason over. We resolve the canonical 538-residue sequence into a six-helix topology, a residue-level membrane-facing pocket hypothesis, post-translational features and a construct / validation plan, computed with Orbion's Astra suite from sequence alone.

UniProt Q96KA5 · 538 aa · CLPTM1-Like Multi-Pass Membrane Protein · 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	Multi-pass endoplasmic-reticulum membrane protein; six transmembrane helices predicted (boundaries in the domain map).
Binding Pocket	A residue-level membrane-facing pocket from AstraBIND (confidence 0.897) — a starting point for docking or mutagenesis, not a validated ligand.
Structural Anchors	N-linked glycosylation at N91, N101 and N229 (UniProt), on the large loop between TM1 and TM2.
Flexible Regions	A short disordered loop (146–156) is the main flexible insert — a natural boundary for construct or truncation design.
Clean Signal	Not entirely clean: one aggregation-prone segment flagged (AstraUNFOLD amyloid max 0.545) — screen it out in construct design.

PREDICTION CONFIDENCE

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

1 The Gap

Most tractable protein families have been structurally explored; CLPTM1L has not. It is an IDG Tbio multi-pass membrane protein with no experimental structure in the PDB and a functional literature only recently taking shape. UniProt describes it as a lipid scramblase that flips glucosaminyl-phosphatidylinositol (GlcN-PI) across the endoplasmic-reticulum membrane during GPI-anchor biosynthesis, and can move other phospholipids in vitro. Its prominence, though, is genetic: CLPTM1L lies at the TERT-CLPTM1L locus on chromosome 5p15.33, whose common variants have been tied to lung and many other cancer types.

That combination — a much-associated cancer-risk locus, near-zero structural information — is where prediction earns its keep: everything below is computed from the canonical 538-residue sequence with Orbion's Astra suite, with no experimental CLPTM1L structure used as input. For a genuine orphan, there is nothing to look up.

2 Architecture And Topology

PREDICTED ARCHITECTURE

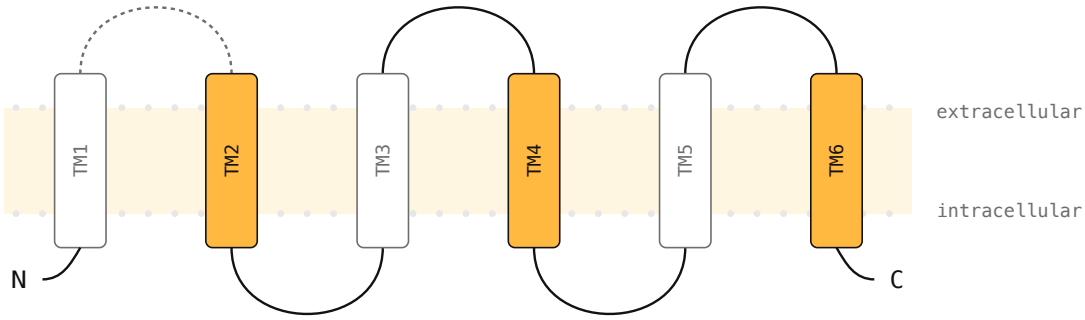

Figure 2. Predicted membrane topology from the sequence: transmembrane helices drawn in the bilayer, amber marks the pocket-lining helices, dashed loops are disordered, and the N/C termini and key modifications are placed in situ.

Element	Residues	Note
Transmembrane Helices	6 predicted	Boundaries: 11–31; 285–305; 325–342; 347–364; 403–423; 429–449.

PER-RESIDUE DISORDER PROFILE (ASTRAUNFOLD)

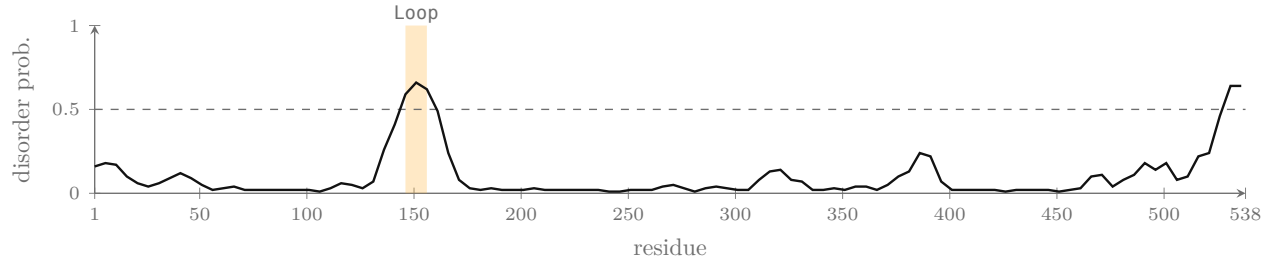

Figure 3. Predicted per-residue disorder (dashed = 0.5 call threshold); amber bands mark flexible regions — natural construct / truncation boundaries.

3 A Predicted Binding Pocket

Astra resolves a residue-level site — the input a docking run or a mutagenesis plan actually needs. Predicted location: **Predicted membrane-facing cavity**.

PREDICTED POCKET / FUNCTIONAL RESIDUES

TM2	291–297
TM4	355, 363
TM6	441, 443–445
Loop / Surface	471–480, 482, 484, 492, 495, 498–500

For this genuine orphan, AstraBIND has no ligand-bound relative to retrieve from — so these residues are a structure-based cavity prediction, not a retrieval-grounded pocket, and the score reflects cavity geometry rather than a known binding site. Treat them as an exploratory starting point for mutagenesis only; the topology, disorder and modification maps above are the higher-confidence outputs for this target. No validated ligand; not a proven druggable site.

4 Post-Translational And Structural Features

- **N-glycosylation** at position 91, 101, 229 (UniProt) — three N-linked sequons on the large loop between TM1 and TM2, a handle for validating membrane topology.
- **Aggregation-prone segment flagged** (AstraUNFOLD amyloid max 0.545) — a single hydrophobic stretch worth screening out or mutating before recombinant expression.

5 Recommended Experimental Follow-Up

Prediction	Experiment	Readout
Membrane-Facing Pocket (AstraBIND, 0.897)	Docking + alanine scan of the TM2 / TM4 / TM6 pocket residues	Binding or lipid-transport change at the predicted cavity
Predicted Scramblase / Lipid-Transport Function	Reconstituted phospholipid-scramblase assay (GlcN-PI / PI flip)	Confirms the lipid-translocation annotation
Disordered Loop (146–156)	Loop deletion or fusion-partner insertion	Improved expression / thermostability for structural work

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 CLPTM1L sequence (UniProt Q96KA5): **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 CLPTM1L structure or ligand was used as input. Predictions are computational hypotheses to prioritise experiments, not validated results.

8 References

1. UniProt Consortium. UniProtKB entry Q96KA5 (CLPTM1L, human). uniprot.org.
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