COMPUTATIONAL TARGET PROFILE

SLC22A15

An orphan SLC22 organic-ion transporter, characterised without an experimental structure

SLC22A15 (FLIPT1) is one of the darkest members of the SLC22 organic-ion transporter family — IDG Tdark, no experimental structure, no established physiological role, and only low-affinity, tentative substrates. There is almost nothing to look up. We resolve the canonical 547-residue sequence into a twelve-helix topology, a residue-level substrate-cavity hypothesis, post-translational features and a construct plan, computed with Orbion's Astra suite from the sequence alone.

UniProt Q8IZD6 · 547 aa · SLC22 Organic-Ion Transporter (Orphan) · IDG tier: Tdark · 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	Twelve predicted transmembrane helices, the SLC22 organic-ion-transporter fold; multi-pass plasma-membrane protein; non-enzyme.
Substrate Cavity	A residue-level substrate-cavity hypothesis from AstraBIND (confidence 0.852, HIGH), unclassified — a starting point for docking and cavity mutagenesis, not a validated ligand.
Structural Anchors	Predicted N-glycosylation at N58, N63, N80 and N106 (UniProt), clustered on the large extracellular loop between TM1 and TM2.
Flexible Regions	Elevated predicted disorder in the extracellular loop (56–76) and the cytosolic C-tail (501–546) — natural truncation boundaries for construct design.
Clean Signal	One aggregation-prone segment flagged (AstraUNFOLD amyloid max 0.513) — worth screening in construct design.

PREDICTION CONFIDENCE

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

1 The Gap

Most tractable membrane-transporter families have been structurally explored. SLC22A15 — also called FLIPT1 — has not, and unusually little else about it has either: an IDG Tdark orphan of the SLC22 organic-ion transporter family, with no experimental structure in the PDB, no disease association, and no settled physiological substrate. Reported activities are broad and low-affinity — a zwitterion/cation carrier shown in vitro to move carnitine and acetylcarnitine, glycine betaine, diet-derived ergothioneine and carnosine, and, more weakly, thiamine — but even the transport mechanism (sodium symport versus sodium-modulated diffusion) is unresolved. It is dark in the fullest sense.

That is exactly where prediction earns its keep — not to declare a function, but to give the first structural handles on an orphan: everything below is computed from the canonical 547-residue sequence with Orbion's Astra suite, with no experimental SLC22A15 structure used as input. For a target this dark, there is nothing

to look up.

2 Architecture And Topology

PREDICTED ARCHITECTURE

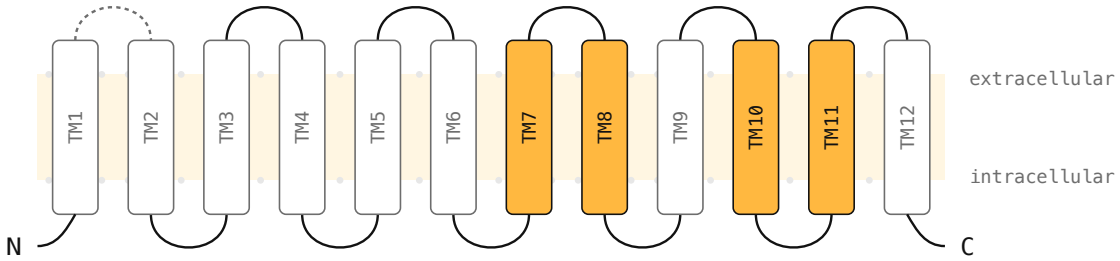

Figure 2. Predicted membrane topology from the sequence: transmembrane helices drawn in the bilayer, amber marks the pocket-lining helices, dashed loops are disordered, and the N/C termini and key modifications are placed in situ.

Element	Residues	Note
Transmembrane Helices	12 predicted	Boundaries: 22–42; 111–131; 141–161; 165–187; 201–221; 226–246; 303–323; 338–358; 368–388; 401–420; 433–453; 462–482.

PER-RESIDUE DISORDER PROFILE (ASTRAUNFOLD)

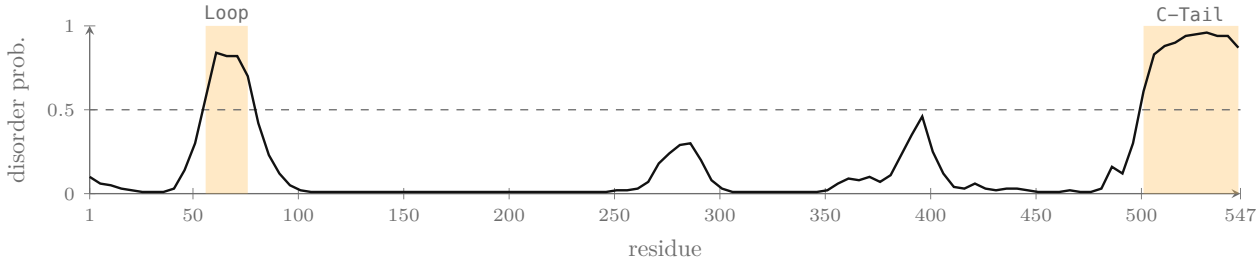

Figure 3. Predicted per-residue disorder (dashed = 0.5 call threshold); amber bands mark flexible regions — natural construct / truncation boundaries.

3 The Predicted Substrate Cavity

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

PREDICTED POCKET / FUNCTIONAL RESIDUES

TM7	315, 319, 322–323
TM8	347, 349, 351
TM10	408, 415–416, 419
TM11	439–440, 443
Loop / Surface	326

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 58, 63, 80, 106 (UniProt) — clustered on the large extracellular loop between TM1 and TM2, the glycosylated face typical of SLC22 carriers and a handle for surface-expression assays.
- **Aggregation-prone segment flagged** (AstraUNFOLD amyloid max 0.513) — a predicted amyloidogenic stretch to screen out or engineer around in construct design.

5 Recommended Experimental Follow-Up

Prediction	Experiment	Readout
Substrate-Cavity Residues (TM7, TM8, TM10, TM11)	Cavity-lining alanine scan + organic-ion uptake assay (e.g. carnitine, ergothioneine)	Loss of transport at the predicted site
Disordered Loop and C-Tail (56–76, 501–546)	Loop / terminal truncation or fusion-partner insertion	Improved expression / thermostability for structural work
Predicted SLC22 Organic-Ion Transporter Class	Uptake panel across candidate zwitterions / cations in a defined system	Confirm transport function and rank substrate selectivity

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 SLC22A15 sequence (UniProt Q8IZD6): **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 SLC22A15 structure or ligand was used as input. Predictions are computational hypotheses to prioritise experiments, not validated results.

8 References

1. UniProt Consortium. UniProtKB entry Q8IZD6 (SLC22A15, human). uniprot.org.
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