COMPUTATIONAL TARGET PROFILE

SCYL1

An orphan SCY1-like pseudokinase, characterised without an experimental structure

A catalytically dead kinase look-alike whose loss causes an inherited neurodegeneration syndrome. SCYL1 is a pseudokinase — a kinase-shaped scaffold that has lost its catalytic activity — that helps run COPI-mediated retrograde traffic at the Golgi; recessive loss-of-function causes CALFAN — a childhood syndrome of low-γ-GT cholestasis, acute liver failure and spinocerebellar neurodegeneration. No solved structure, no named ligand. We resolve the canonical 808-residue sequence into a domain map, a residue-level allosteric-pocket hypothesis, disorder boundaries and a validation plan, computed with Orbion's Astra suite from sequence alone — and because it is a pseudokinase, we frame the pocket as an allosteric / regulatory site, not a catalytic one.

UniProt Q96KG9 · 808 aa · SCY1-Like Pseudokinase · 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	Predicted soluble, multi-domain protein — an N-terminal kinase-like (pseudokinase) domain (14–314) followed by an extended, partly disordered C-terminal region.
Allosteric Pocket	AstraBIND allosteric-candidate hypothesis (confidence 0.65) — a residue-level starting point for docking / mutagenesis; no validated ligand, and no catalytic activity expected.
Flexible Regions	Elevated predicted disorder across a C-terminal loop (553–585) — a natural construct / truncation boundary.
Clean Signal	One aggregation-prone segment flagged (AstraUNFOLD amyloid max 0.512) — 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 enzyme families have been structurally explored. SCYL1 has not: an IDG Tbio target with no experimental structure in the PDB and only a handful of functional studies. It is a SCY1-like pseudokinase — its N-terminal domain adopts a kinase fold but is predicted to be catalytically inactive — that works in COPI-mediated retrograde trafficking between the Golgi and the ER. Its clinical importance is not in doubt: recessive loss-of-function mutations cause CALFAN — an inherited syndrome of low-γ-GT cholestasis, acute liver failure and spinocerebellar neurodegeneration. Yet for the protein itself there is almost nothing structural to look up.

That combination — a clear disease link, near-zero structural information — is where prediction earns its keep: everything below is computed from the canonical 808-residue sequence with Orbion's Astra suite, with no experimental SCYL1 structure used as input. Because SCYL1 is a pseudokinase, we treat the model's kinase-fold signal as a scaffold, and its predicted pocket as an allosteric / regulatory site rather than a catalytic active site.

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
Protein Kinase	14–314	UniProt-annotated domain.

PER-RESIDUE DISORDER PROFILE (ASTRAUNFOLD)

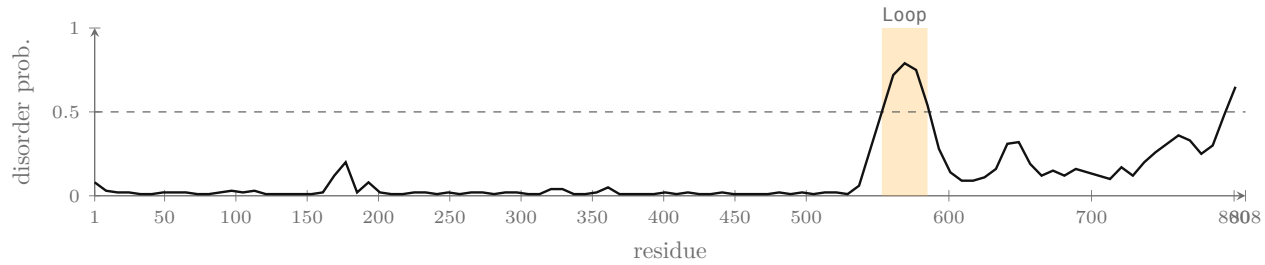

Figure 3. Predicted per-residue disorder (dashed = 0.5 call threshold); amber bands mark flexible regions — natural construct / truncation boundaries.

3 A Predicted Allosteric Pocket

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

Protein Kinase 93–96

A residue-level allosteric-candidate hypothesis from AstraBIND. SCYL1 is a pseudokinase with no catalytic activity, and AstraBIND has no ligand-bound relative to retrieve from — so this is a low-confidence, structure-based surface. The residues sit within the pseudokinase domain and are offered as a regulatory / interaction-surface hypothesis, not a druggable pocket or an enzyme-inhibition site.

4 Post-Translational And Structural Features

- **Protein kinase** domain (14–314) — the UniProt-annotated N-terminal kinase-like fold; in SCYL1 this is a pseudokinase, predicted to act as a scaffolding / interaction module rather than a catalytically active enzyme.
- **Aggregation-prone segment flagged** (AstraUNFOLD amyloid max 0.512) — a short hydrophobic stretch worth screening or engineering out when designing a soluble construct.

5 Recommended Experimental Follow-Up

Prediction	Experiment	Readout
Allosteric Pocket Residues (93–96)	Alanine scan at the predicted pocket + binding / co-immunoprecipitation with COPI partners	Change in partner binding or Golgi-trafficking function (binding, not catalysis)
Disordered / Flexible Regions	Fusion-partner insertion or terminal truncation	Improved expression / thermostability for structural work
Predicted Soluble, Cytoplasmic Localisation	Fractionation / imaging for Golgi–ER association	Confirm soluble, COPI-linked trafficking role

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 SCYL1 sequence (UniProt Q96KG9): **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 SCYL1 structure or ligand was used as input. Predictions are computational hypotheses to prioritise experiments, not validated results.

8 References

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