COMPUTATIONAL TARGET PROFILE

TMEM38B

An orphan endoplasmic-reticulum cation channel (TRIC-B), characterised without an experimental structure

The dark bone-disease orphan, resolved from sequence alone. TRIC-B is an endoplasmic-reticulum potassium counter-ion channel whose loss disrupts intracellular calcium release and, through it, collagen synthesis — the reported cause of a recessive form of osteogenesis imperfecta. No experimental structure and only a thin functional literature — resolved here into a seven-helix topology, a residue-level allosteric-pocket hypothesis, post-translational features and a construct / validation plan, all computed with Orbion's Astra suite from the canonical 291-residue sequence.

UniProt Q9NVV0 · 291 aa · Trimeric Intracellular Cation (TRIC-B) Channel · 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	Seven predicted transmembrane helices; a multi-pass ER-membrane channel that assembles as a trimer (TRIC family).
Allosteric Pocket	AstraBIND allosteric-candidate hypothesis (confidence 0.85) at the helix interface — a residue-level starting point for mutagenesis; no validated ligand.
Flexible Regions	Elevated predicted disorder in the cytoplasmic C-tail (232–289) — the natural truncation boundary for construct design.
Clean Signal	Aggregation-prone segment flagged (max 0.57) — 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 protein families have been structurally explored. Trimeric intracellular cation channel type B has not: an IDG Tbio target with no experimental structure in the PDB and only a handful of functional studies. UniProt summarises it as: "Intracellular monovalent cation channel required for maintenance of rapid intracellular calcium release. Acts as a potassium counter-ion channel that functions in synchronization with calcium release…" Interest is real (Osteogenesis Imperfecta), but there is almost nothing to look up.

That combination — genuine interest, near-zero structural information — is where prediction earns its keep: everything below is computed from the canonical 291-residue sequence, with no experimental TMEM38B structure used as input.

2 Architecture And Topology

PREDICTED ARCHITECTURE

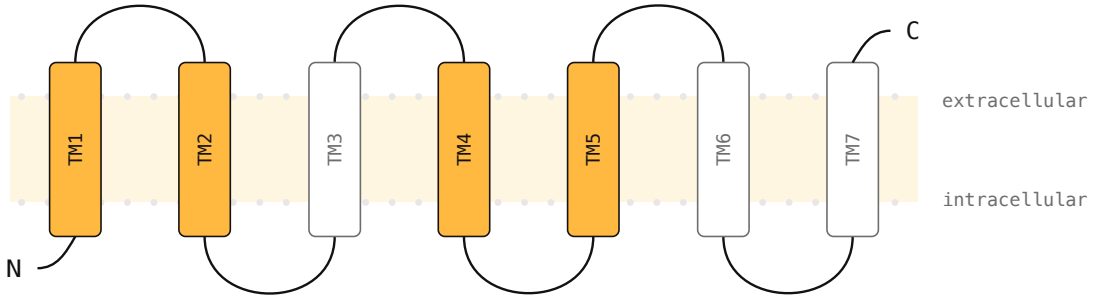

Figure 2. Predicted membrane topology from the sequence: transmembrane helices drawn in the bilayer, amber marks the pocket-lining helices, dashed loops are disordered, and the N/C termini and key modifications are placed in situ.

Element	Residues	Note
Transmembrane Helices	7 predicted	Boundaries: 20–33; 51–70; 83–99; 105–121; 140–156; 180–195; 208–227.

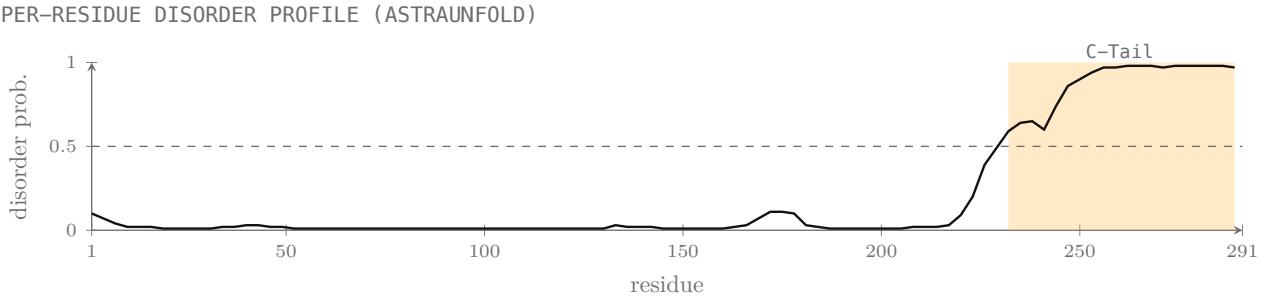

Figure 3. Predicted per-residue disorder (dashed = 0.5 call threshold); amber bands mark flexible regions — natural construct / truncation boundaries.

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 pore / gating interface**.

PREDICTED POCKET / FUNCTIONAL RESIDUES

TM1	25
TM2	52–65
TM4	122
TM5	150–158
Loop / Surface	36, 76, 125, 159–160

A residue-level hypothesis from AstraBIND. TMEM38B has no ligand-bound relative to retrieve from, so this is a low-confidence, structure-based prediction; the residues neighbour one of the two UniProt-annotated PIP -binding positions (122) but miss the other (118). Treat it as an exploratory pore / interface surface, not a validated pocket or a druggable site.

4 Post-Translational And Structural Features

- **PIP -binding residues (118, 122).** UniProt-annotated phosphatidylinositol-4,5-bisphosphate (PIP) binding sites — a lipid-regulation input to the channel and a direct mutagenesis handle.
- **Aggregation-prone segment flagged** (AstraUNFOLD amyloid max 0.57) — worth screening in construct

design.

5 Recommended Experimental Follow-Up

Prediction	Experiment	Readout
Predicted Allosteric Pocket + PIP -Binding Residues (118 / 122)	Alanine scan + ER Ca^{2+}-release / K^+-flux readout	Altered counter-ion flux or lipid regulation — tests the predicted site
Disordered C-Tail (232–289)	C-terminal truncation	Improved expression / thermostability for cryo-EM
Predicted Trimeric Assembly (TRIC Family)	Cross-linking / native mass-spec on the expressed protein	Confirm the oligomeric state

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 TMEM38B sequence (UniProt Q9NVV0): **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 TMEM38B structure or ligand was used as input. Predictions are computational hypotheses to prioritise experiments, not validated results.

8 References

1. UniProt Consortium. UniProtKB entry Q9NVV0 (TMEM38B, human). uniprot.org.
2. Pharos (Illuminating the Druggable Genome). TMEM38B target record — Tbio. pharos.nih.gov.
3. Shaheen R et al. Study of autosomal recessive osteogenesis imperfecta in Arabia reveals a novel locus defined by TMEM38B mutation. (2012). https://doi.org/10.1136/jmedgenet-2012-101142
4. Volodarsky M et al. A deletion mutation in TMEM38B associated with autosomal recessive osteogenesis imperfecta. (2013). https://doi.org/10.1002/humu.22274
5. Cabral WA et al. Absence of the ER Cation Channel TMEM38B/TRIC-B Disrupts Intracellular Calcium Homeostasis and Dysregulates Collagen Synthesis in Recessive Osteogenesis Imperfecta. (2016). https://doi.org/10.1371/journal.pgen.1006156