COMPUTATIONAL TARGET PROFILE

METTL7B

An orphan thiol methyltransferase, characterised without an experimental structure

The dark thiol-methyltransferase sitting between xenobiotic metabolism and cancer biology. METTL7B has no solved structure, no named ligand, and a scattered literature — yet it is reported to methylate small-molecule thiols such as hydrogen sulfide and the drug captopril, and to be required for tumour-cell proliferation. We resolve the canonical 244-residue sequence into a membrane topology, a residue-level active-site hypothesis, and a construct / validation plan, computed with Orbion's Astra suite from sequence alone.

UniProt Q6UX53 · 244 aa · Methyltransferase (MTase) · 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 membrane-associated — UniProt classifies it as a peripheral ER-membrane protein with a hydrophobic N-terminal segment annotated as a signal peptide (1–23), consistent with its reported ER-membrane and lipid-droplet localisation.
Active-Site Region	AstraBIND unclassified hypothesis (confidence 0.704) — a residue-level, substrate/cofactor-facing starting point for docking / mutagenesis; no validated ligand.
Clean Signal	One aggregation-prone segment flagged (AstraUNFOLD amyloid max 0.533) — 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. METTL7B (also catalogued as thiol S-methyltransferase TMT1B) has not: an IDG Tbio target with no experimental structure in the PDB and only a handful of functional studies. It is reported to transfer a methyl group from S-adenosyl-L-methionine onto small-molecule thiol acceptors — metabolising substrates such as hydrogen sulfide and the drug captopril — and to sit on the endoplasmic-reticulum membrane and lipid droplets. Interest is real (oncology and lipid metabolism), yet 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 244-residue sequence with Orbion's Astra suite, with no experimental METTL7B structure used as input. For a target this dark, there is no structure to consult.

2 Architecture And Topology

PREDICTED ARCHITECTURE

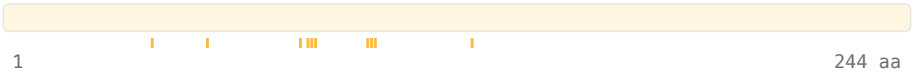

Figure 2. Predicted domain architecture along the sequence: annotated domains as boxes, disordered regions shaded, and the predicted active-site / pocket residues marked as amber ticks.

Element	Residues	Note
Signal Peptide	1–23	UniProt.

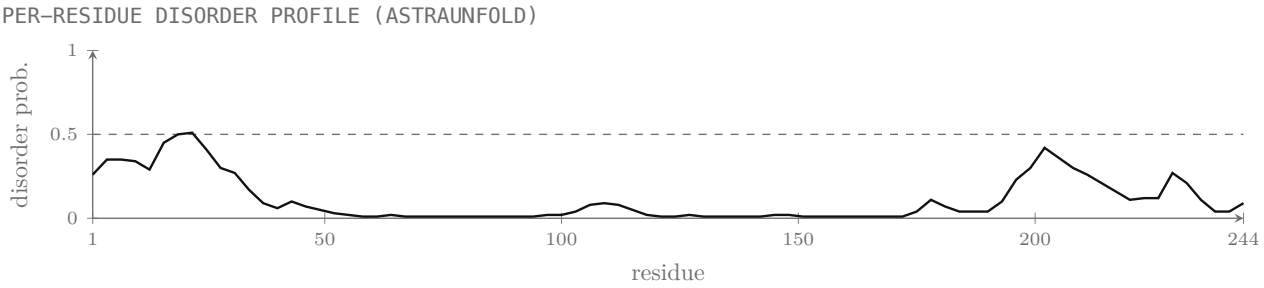

Figure 3. Predicted per-residue disorder (dashed = 0.5 call threshold); amber bands mark flexible regions — natural construct / truncation boundaries.

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 40, 55, 80, 82–84, 98–100, 126

A residue-level binding hypothesis from AstraBIND (confidence 0.704, HIGH). AstraBIND is retrieval-based: candidate binders are drawn from public panels (PDB, IUPHAR, ChEMBL, homology), not designed de novo. Treat these as a starting point for docking / mutagenesis, not a validated ligand or a proven druggable site.

4 Post-Translational And Structural Features

- **Aggregation-prone segment flagged** (AstraUNFOLD amyloid max 0.533) — a short hydrophobic stretch worth screening or engineering out when designing a soluble construct for expression.

5 Recommended Experimental Follow-Up

Prediction	Experiment	Readout
Active-Site Region Residues	Alanine scan at the predicted site + thiol S-methyltransferase assay (SAM donor, thiol acceptor such as hydrogen sulfide)	Loss of methyl-transfer activity at the predicted site
Disordered / Flexible Regions	Fusion-partner insertion or terminal truncation	Improved expression / thermostability for structural work
Predicted Peripheral Membrane Association	Protease-protection / membrane-fractionation assay	Confirm ER-membrane / lipid-droplet association

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 METTL7B sequence (UniProt Q6UX53): **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 METTL7B structure or ligand was used as input. Predictions are computational hypotheses to prioritise experiments, not validated results.

8 References

1. UniProt Consortium. UniProtKB entry Q6UX53 (METTL7B, human). uniprot.org.
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3. McKinnon CM et al. The tumor suppressor RhoBTB1 controls Golgi integrity and breast cancer cell invasion through METTL7B. (2017). https://doi.org/10.1186/s12885-017-3138-3
4. Liu D et al. METTL7B Is Required for Cancer Cell Proliferation and Tumorigenesis in Non-Small Cell Lung Cancer. (2020). https://doi.org/10.3389/fphar.2020.00178
5. Maldonato BJ et al. Human METTL7B is an alkyl thiol methyltransferase that metabolizes hydrogen sulfide and captopril. (2021). https://doi.org/10.1038/s41598-021-84218-5