MOLECULAR ATLAS · VARIANT CARD

WFS1 A787T — Wolframin

Ala→Thr p787 lumenal AM=0.06 ddg=+0.05 pLDDT=45. ClinVar Conflicting evidence. Atlas mechanism: see structural analysis.

IDENTITY

Variant	A787T (p.Alanine787Threonine)
DNA change	c.2359G>A
Gene · Protein	WFS1 · Wolframin (890 aa)
UniProt	O76024 · WFS1_HUMAN
ClinVar accession	VCV000444631
Amino acid change	polarity introduced

STRUCTURAL CONTEXT

AlphaFold model	AF-O76024-F1, v6
pLDDT at residue 787	**44.69** BELOW IDR THRESHOLD
Domain	C-terminal lumenal domain (653-869)
Position context	C-terminal lumenal IDR boundary
IDR flag	YES — pLDDT 44.69 is below 50 threshold (route to Cat 5)

> Position analysis: ASP788 (2.5 Å — partner of G789S!), GLY786 (2.6 Å), SER785 (4.4 Å). pLDDT 45 IDR boundary. Same region as S790L/W cluster. The Atlas's neighbor extraction surfaces this variant's contacts and connects them to the broader multi-variant target landscape.

COMPUTATIONAL PREDICTIONS

ALPHAMISSENSE

0.063

am_class: **LBen** — threshold > 0.564

DYNAMUT2 ΔΔG

0.05 kcal/mol

Stabilising · Job 177992529749

PLDDT (ALPHAFOLD)

44.69

BELOW IDR THRESHOLD

CLINICAL EVIDENCE

ClinVar classification	**CONFLICTING CLASSIFICATIONS OF PATHOGENICITY**
Review status	criteria provided, conflicting classifications
Last evaluated	2026/01/09 00:00
Inheritance	Conflicting ClinVar classifications.
WFS1 variant landscape	A787T is 1 of ~326 pathogenic-spectrum variants in WFS1 (out of 2,243 in ClinVar)

- (no specific conditions catalogued)

RESEARCH PATH DECISION TREE

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ΔΔG < 2 + binding site affected → CATEGORY 3 — docking experiments ΔΔG 2–4 → CATEGORY 2 — pharmacological chaperones ΔΔG > 4 → CATEGORY 1 — gene therapy pLDDT < 50 → CATEGORY 5 — IDR, experimental only Stable fold + functional site hit → CATEGORY 4 — site-specific docking
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Cat 5 IDR boundary — see structural prose. AlphaMissense below threshold (AM under-call class) but mechanism is structurally identified. Therapeutic strategy: site-directed at contacts identified above, or wet-lab validation if pLDDT borderline/below 50.

IDR boundary near S790 cluster.
