MOLECULAR ATLAS · VARIANT CARD

WFS1 K287N — Wolframin

Lysine (K) → Asparagine (N) at position 287 · N-terminal cytoplasmic (intrinsically disordered)

IDENTITY

Variant	K287N (p.Lysine287Asparagine)
DNA change	c.861G>T
Gene · Protein	WFS1 · Wolframin (890 aa)
UniProt	O76024 · WFS1_HUMAN
ClinVar accession	VCV004306964
Amino acid change	Lysine (K) → Asparagine (N)

STRUCTURAL CONTEXT

AlphaFold model	AF-O76024-F1, v6
pLDDT at residue 287	**53.44** CONFIDENT
Domain	N-terminal cytoplasmic (intrinsically disordered)
Position context	N-terminal cytoplasmic (intrinsically disordered)
IDR flag	No — pLDDT well above 50 threshold

COMPUTATIONAL PREDICTIONS

ALPHAMISSENSE

0.931

am_class: **likely pathogenic** — threshold > 0.564

DYNAMUT2 ΔΔG

-0.78 kcal/mol

Destabilising · Job 178092103937

PLDDT (ALPHAFOLD)

53.44

confident

CLINICAL EVIDENCE

ClinVar classification	NOT IN CLINVAR
Review status	None
Last evaluated	1/01/01 00:00
Inheritance	—
WFS1 variant landscape	K287N is 1 of ~326 pathogenic-spectrum variants in WFS1 (out of 2,243 in ClinVar)

- (no 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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> **Category 3/4 — Most Druggable**
>
> Mildly destabilizing fold; AlphaMissense confirms functional impact. Fold intact, specific local contacts/sites disrupted. Priority for docking and pharmacological chaperone screening.
