MOLECULAR ATLAS · VARIANT CARD

WFS1 R587Q — Wolframin

Arg→Gln p587 loop AM=0.08 ddg=-0.05 pLDDT=77. ClinVar Conflicting evidence. Atlas mechanism: see structural analysis.

IDENTITY

Variant	R587Q (p.Arginine587Glutamine)
DNA change	c.1760G>A
Gene · Protein	WFS1 · Wolframin (890 aa)
UniProt	O76024 · WFS1_HUMAN
ClinVar accession	VCV000215361
Amino acid change	charge loss, amide preserved

STRUCTURAL CONTEXT

AlphaFold model	AF-O76024-F1, v6
pLDDT at residue 587	**77.38** HIGH CONFIDENCE
Domain	Connecting loop
Position context	Connecting loop
IDR flag	No — pLDDT well above 50 threshold

> Position analysis: TRP588 (2.4 Å), ALA586 (2.5 Å — same loop as R587W), THR590 (3.5 Å). Same position as R587W. The Atlas's neighbor extraction surfaces this variant's contacts and connects them to the broader multi-variant target landscape.

COMPUTATIONAL PREDICTIONS

ALPHAMISSENSE

0.081

am_class: **LBen** — threshold > 0.564

DYNAMUT2 ΔΔG

-0.05 kcal/mol

Destabilising · Job 177992521474

PLDDT (ALPHAFOLD)

77.38

high confidence

CLINICAL EVIDENCE

ClinVar classification	**CONFLICTING CLASSIFICATIONS OF PATHOGENICITY**
Review status	criteria provided, conflicting classifications
Last evaluated	2025/12/30 00:00
Inheritance	Conflicting ClinVar classifications.
WFS1 variant landscape	R587Q 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 3/4 — 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.

R587W + R587Q sister variants.
