RARERESEARCH.AI · WFS1 MOLECULAR ATLAS · IN-FRAME INDEL

c.1312_1320dup — WFS1 Molecular Atlas Card

Variant type: In-frame indel

Change: 3 residue(s) deleted in frame at position 438

Domain context: Transmembrane helix 5

SCHEMA CATEGORY: I3 — MULTI-RESIDUE IN-FRAME INDEL — LIKELY MAJOR STRUCTURAL DISRUPTION

3 residues removed in frame around position 438 (Transmembrane helix 5). A change this size usually perturbs local packing and can propagate to the fold. Gene therapy is the primary path unless an AlphaFold prediction of the modified sequence shows a surprisingly intact fold. Predicted structure pending (ColabFold).

STRUCTURAL PREDICTION

- **Reading frame:** preserved (in-frame) — no premature stop, NMD does not apply.
- **Affected domain:** Transmembrane helix 5
- **Predicted modified structure:** _pending — AlphaFold/ColabFold prediction of the

modified sequence and backbone-RMSD vs wild-type backfill here (Wave 2)._

CLINICAL EVIDENCE

- **Classification:** Uncertain significance
- **Review status:** criteria provided, single submitter
- **cDNA change:** c.1312_1320dup
- **ClinVar accession:** VCV004720441
- **Last evaluated:** 2025/05/29 00:00
- **Submissions:** 1

Card generated by `wolfram-atlas-batch` (in-frame indel pipeline) on 2026-06-08T02:41:06.067714Z.

Schema: `reference/card schemaextension.md` (I1–I3). WFS1: UniProt O76024, AlphaFold v6.