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

c.2605_2616dup — WFS1 Molecular Atlas Card

Variant type: In-frame indel

Change: 4 residue(s) deleted in frame at position 869

Domain context: C-terminal ER-lumenal (calcium binding, calmodulin, chaperone)

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

4 residues removed in frame around position 869 (C-terminal ER-lumenal (calcium binding, calmodulin, chaperone)). 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:** C-terminal ER-lumenal (calcium binding, calmodulin, chaperone)
- **Predicted modified structure:** _pending — AlphaFold/ColabFold prediction of the

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

CLINICAL EVIDENCE

- **Classification:** Likely pathogenic
- **Review status:** criteria provided, single submitter
- **Associated conditions:** Autosomal dominant nonsyndromic hearing loss 6
- **cDNA change:** c.2605_2616dup

- **ClinVar accession:** VCV003601040
- **Last evaluated:** 2025/01/09 00:00
- **Submissions:** 1

Card generated by `wolfram-atlas-batch` *(in-frame indel pipeline) on 2026-06-08T02:42:00.424587Z.*

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