

c.2638_2643del — WFS1 Molecular Atlas Card

Variant type: In-frame indel

Change: 2 residue(s) deleted in frame at position 880

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

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

2 residues removed in frame around position 880 (C-terminal ER-luminal (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-luminal (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:** Conflicting classifications of pathogenicity
- **Review status:** criteria provided, conflicting classifications
- **Associated conditions:** Wolfram syndrome 1
- **cDNA change:** c.2638_2643del
- **ClinVar accession:** VCV000807720
- **Last evaluated:** 2023/06/10 00:00

- **Submissions:** 1
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Card generated by `wolfram-atlas-batch` (in-frame indel pipeline) on 2026-06-08T02:42:04.315254Z.

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