

# c.2455\_2502del — WFS1 Molecular Atlas Card

**Variant type:** In-frame indel

**Change:** 16 residue(s) deleted in frame at position 819

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

---

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

---

16 residues removed in frame around position 819 (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:** Autosomal dominant nonsyndromic hearing loss 6; Type 2 diabetes mellitus; Wolfram syndrome 1; Cataract 41; Wolfram-like syndrome
- **cDNA change:** c.2455\_2502del
- **ClinVar accession:** VCV001958301

- **Last evaluated:** 2025/10/03 00:00
  - **Submissions:** 1
- 

Card generated by `wolfram-atlas-batch` (in-frame indel pipeline) on 2026-06-08T02:41:50.637086Z.

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