

c.1243_1245del — WFS1 Molecular Atlas Card

Variant type: In-frame indel

Change: 1 residue(s) deleted in frame at position 415

Domain context: Transmembrane helix 4

SCHEMA CATEGORY: I1 — SINGLE-RESIDUE DELETION IN A TRANSMEMBRANE HELIX — LIKELY CATASTROPHIC KINK

A single residue removed inside Transmembrane helix 4 shifts the helical register, which typically kinks or unwinds the helix and disrupts membrane insertion — structurally similar to a severe TM missense. Gene therapy track. Predicted structure pending (ColabFold).

STRUCTURAL PREDICTION

- **Reading frame:** preserved (in-frame) — no premature stop, NMD does not apply.
- **Affected domain:** Transmembrane helix 4
- **Predicted modified structure:** _pending — AlphaFold/ColabFold prediction of the modified sequence and backbone-RMSD vs wild-type backfill here (Wave 2)._
[backfill here \(Wave 2\).](#)

CLINICAL EVIDENCE

- **Classification:** Pathogenic
- **Review status:** criteria provided, multiple submitters, no conflicts
- **Associated conditions:** WFS1-Related Spectrum Disorders; Early-onset non-syndromic cataract; Rare genetic deafness; Wolfram-like syndrome; Cataract 41; Wolfram syndrome 1; Autosomal dominant nonsyndromic hearing loss 6; Type 2 diabetes mellitus
- **cDNA change:** c.1243_1245del
- **ClinVar accession:** VCV000215406

- **Last evaluated:** 2026/01/25 00:00
 - **Submissions:** 1
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Card generated by `wolfram-atlas-batch` (in-frame indel pipeline) on 2026-06-08T02:41:02.167061Z.

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