

# c.1021\_1032del — WFS1 Molecular Atlas Card

**Variant type:** In-frame indel

**Change:** 4 residue(s) deleted in frame at position 341

**Domain context:** Transmembrane helix 2

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

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4 residues removed in frame around position 341 (Transmembrane helix 2). 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).

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## STRUCTURAL PREDICTION

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

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## CLINICAL EVIDENCE

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- **Classification:** Uncertain significance
- **Review status:** criteria provided, single submitter
- **Associated conditions:** Autosomal dominant nonsyndromic hearing loss 6; Cataract 41; Wolfram syndrome 1; Wolfram-like syndrome; Type 2 diabetes mellitus
- **cDNA change:** c.1021\_1032del
- **ClinVar accession:** VCV003590678

- **Last evaluated:** 2024/02/12 00:00
  - **Submissions:** 1
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Card generated by `wolfram-atlas-batch` (in-frame indel pipeline) on 2026-06-08T02:40:54.399420Z.

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