

c.1060_1062del — WFS1 Molecular Atlas Card

Variant type: In-frame indel

Change: 1 residue(s) deleted in frame at position 354

Domain context: Transmembrane helix 2

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

A single residue removed inside Transmembrane helix 2 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 2
- **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:** Conflicting classifications of pathogenicity
- **Review status:** criteria provided, conflicting classifications
- **Associated conditions:** Autosomal dominant nonsyndromic hearing loss 6; Cataract 41; Wolfram-like syndrome; Type 2 diabetes mellitus; Wolfram syndrome 1; Monogenic diabetes; Rare genetic deafness
- **cDNA change:** c.1060_1062del
- **ClinVar accession:** VCV000228420

- **Last evaluated:** 2025/12/27 00:00
 - **Submissions:** 1
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Card generated by `wolfram-atlas-batch` (in-frame indel pipeline) on 2026-06-08T02:41:00.221742Z.

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