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Variant: NM_001306179.2:c.282dup

Version: 1.2

CA2573051039

1676696 (ClinVar)

Gene: HNF1A (HGNC:6927)
Condition: monogenic diabetes (MONDO:0015967)
Inheritance Mode: Autosomal dominant inheritance
UUID: fca6ab0d-ccd3-41ae-b000-163d2c424bdd
Approved on: 2025/6/9
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HGVS expressions

NM_001306179.2:c.282dup
NC_000012.12:g.120979050dup
CM000674.2:g.120979050dup
NC_000012.11:g.121416853dup
CM000674.1:g.121416853dup
NC_000012.10:g.119901236dup
NG_011731.2:g.5305dup
ENST00000560968.6:c.282dup
ENST00000257555.11:c.282dup
ENST00000257555.10:c.282dup
ENST00000400024.6:c.282dup
ENST00000402929.5:n.417dup
ENST00000535955.5:n.42+358dup
ENST00000538626.2:n.190+210dup
ENST00000538646.5:c.282dup
ENST00000540108.1:c.282dup
ENST00000541395.5:c.282dup
ENST00000541924.5:c.282dup
ENST00000543427.5:c.282dup
ENST00000544413.2:c.282dup
ENST00000544574.5:c.72+210dup
ENST00000560968.5:c.425dup
ENST00000615446.4:c.-258+339dup
ENST00000617366.4:c.282dup
NM_000545.5:c.282dup
NM_000545.6:c.282dup
NM_001306179.1:c.282dup
NM_000545.8:c.282dup

Likely Pathogenic

Met criteria codes 2

PVS1 PM2_Supporting

Not Met criteria codes 2

PS4 PP4

Expert Panel

Monogenic Diabetes VCEP

Criteria Specification Information

Evidence Links 0

Criteria Specification: *ClinGen Monogenic Diabetes Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for HNF1A Version 2.1.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Monogenic Diabetes VCEP

The c.282dup variant in the HNF1 homeobox A gene, HNF1A, results in a premature termination at codon 95 (p.(Glu95Ter)) of NM_000545.8. This variant, located in biologically-relevant exon 1 of 10, is predicted to lead to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1; PMID: 23348805). Additionally, this variant is absent from gnomAD v2.1.1 and v4.1.0 (PM2_Supporting). This variant was identified in two unrelated individuals with non-autoimmune and non-absolute/near-absolute insulin-deficient diabetes; however, PS4_Moderate cannot be applied because this number is below the ClinGen MDEP threshold (internal lab contributors). This variant was identified in an individual with a clinical history suggestive of HNF1A-MODY (MODY probability calculator result >50%); however, HNF4A was not tested (internal lab contributors); therefore, PP4 cannot be applied. In summary, c.282dup meets the criteria to be classified as likely pathogenic for monogenic diabetes. ACMG/AMP criteria applied, as specified by the ClinGen MDEP (specification version 2.1.0, approved 8/11/23): PVS1, PM2_Supporting.

Met criteria codes

PVS1	✔	Predicted to lead to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1; PMID: 23348805).
PM2_Supporting	✔	Absent from gnomAD v2.1.1; absent from gnomAD v4.1.0.

Not Met criteria codes

PS4	✖	This variant was identified in two unrelated individuals with non-autoimmune and non-absolute/near-absolute insulin-deficient diabetes; however, PS4_Moderate cannot be applied because this number is below the ClinGen MDEP threshold (internal lab contributors).
PP4	✖	This variant was identified in an individual with a clinical history suggestive of HNF1A-MODY (MODY probability calculator result >50%); however, HNF4A was not tested (internal lab contributors).

Curation History

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