Variant: NM_000545.8(HNF1A):c.872del (p.Pro291fs)

Version: 1.1

CA6831848

805637 (ClinVar)

Gene: HNF1A (HGNC:6927)
Condition: monogenic diabetes (MONDO:0015967)
Inheritance Mode: Autosomal dominant inheritance
UUID: cda51153-0f7d-4a50-9f45-7ed65c1996fa
Approved on: 2021-12-31
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HGVS expressions

NM_000545.8:c.872del
NM_000545.8(HNF1A):c.872del (p.Pro291fs)
NC_000012.12:g.120994322del
CM000674.2:g.120994322del
NC_000012.11:g.121432125del
CM000674.1:g.121432125del
NC_000012.10:g.119916508del
NG_011731.2:g.20577del
ENST00000560968.6:c.750+122del
ENST00000257555.11:c.872del
ENST00000257555.10:c.872del
ENST00000400024.6:c.872del
ENST00000402929.5:n.1007del
ENST00000535955.5:n.43-3169del
ENST00000538626.2:n.191-3169del
ENST00000538646.5:c.685del
ENST00000540108.1:c.*312del
ENST00000541395.5:c.872del
ENST00000541924.5:c.713+616del
ENST00000543427.5:c.633+696del
ENST00000544413.2:c.872del
ENST00000544574.5:c.73-2295del
ENST00000560968.5:c.893+122del
ENST00000615446.4:c.-257-1940del
ENST00000617366.4:c.586+743del
NM_000545.5:c.872del
NM_000545.6:c.872del
NM_001306179.1:c.872del
NM_001306179.2:c.872del

Pathogenic

Met criteria codes 3

PVS1 PP4 PP1_Moderate

Not Met criteria codes 2

PM2 PS4

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 Version 1*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Monogenic Diabetes VCEP

The c.872del variant in the HNF1 homeobox A gene, HNF1A, causes a frameshift in the protein at codon 291 (NM_000545.8), adding 51 novel amino acids before encountering a stop codon (p.(Pro291GlnfsTer51). This variant, located in biologically-relevant exon 4 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 segregated with diabetes, with at least 30 informative meioses in multiple families with MODY (PP1_Strong; internal lab contributors). Additionally, this variant was identified in an individual with a clinical history highly specific for HNF1A-MODY (MODY probability calculator result >50%, negative genetic testing for HNF4A) (PP4; internal lab contributors). In summary, c.872del meets the criteria to be classified as pathogenic for monogenic diabetes. ACMG/AMP criteria applied, as specified by the ClinGen MDEP (specification version 1.1, approved 6/4/2021): PVS1, PP1_Strong, PP4

Met criteria codes

PVS1	✔	This variant is predicted to cause loss of function by resulting in nonsense mediated decay of a biologically relevant transcript.
PP4	✔	This variant was identified in one individual with a clinical history suggestive of HNF1A-MODY (MODY probability calculator result >50% and negative genetic testing for HNF4A) (internal laboratory contributor).
PP1_Moderate	✔	This variant segregated with disease with at least 30 informative meioses observed in multiple families with MODY (internal laboratory contributors).

Not Met criteria codes

PM2	✖	Failed gnomAD QC; all carriers have lower than 60 quality.
PS4	✖	PS4 cannot be used if PM2_supporting does not apply.

Curation History

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