Variant: NM_000545.8(HNF1A):c.1747C>G (p.Arg583Gly)

Version: 1.0

CA214665

14932 (ClinVar)

Gene: HNF1A (HGNC:6927)
Condition: monogenic diabetes (MONDO:0015967)
Inheritance Mode: Autosomal dominant inheritance
UUID: a7f860d6-4991-47b0-9900-8db18ab64f14
Approved on: 2024-08-01
Published on: 2024-08-01

HGVS expressions

NM_000545.8:c.1747C>G
NM_000545.8(HNF1A):c.1747C>G (p.Arg583Gly)
NC_000012.12:g.120999606C>G
CM000674.2:g.120999606C>G
NC_000012.11:g.121437409C>G
CM000674.1:g.121437409C>G
NC_000012.10:g.119921792C>G
NG_011731.2:g.25861C>G
ENST00000560968.6:c.*494C>G
ENST00000257555.11:c.1747C>G
ENST00000257555.10:c.1747C>G
ENST00000540108.1:c.*1187C>G
ENST00000541395.5:c.1840C>G
ENST00000543427.5:c.1210C>G
ENST00000544413.2:c.1768C>G
ENST00000560968.5:c.1564C>G
ENST00000615446.4:c.535C>G
ENST00000617366.4:c.*156C>G
NM_000545.5:c.1747C>G
NM_000545.6:c.1747C>G
NM_001306179.1:c.1768C>G
NM_001306179.2:c.1768C>G

Uncertain Significance

Met criteria codes 1

PM2_Supporting

Not Met criteria codes 2

PP1 **PP4**

Evidence Links 0

Expert Panel

Monogenic Diabetes VCEP

Criteria Specification Information

- **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.1747C>G variant in the e.g. HNF1 homeobox A gene, HNF1A, causes an amino acid change of arginine to glycine at codon 583 (p.(Arg583Gly)) of NM_000545.8. This variant has an incomputable gnomAD v2.1.1 Grpmax filtering allele frequency due to 0 copies in the European non-Finnish subpopulation and 1 copy in the East Asian subpopulation, thereby meeting the ClinGen MDEP threshold criteria for PM2_Supporting (ENF Grpmax FAF <= 0.000003 and <= 2 copies in ENF and <=1 copy in any other subpopulation) (PM2_Supporting). This variant was identified in an individual(s) with diabetes; however, the calculated MODY probability is <50% and HNF4A was not tested (PMID: 9313763). This variant segregated with diabetes with 1 informative meiosis in a single family; however, this does not meet the thresholds for PP1 set by the ClinGen MDEP (PMID: 27236918, 9313763). In summary, c.1747C>G meets the criteria to be classified as a variant of uncertain significance for monogenic diabetes. ACMG/AMP criteria applied, as specified by the ClinGen MDEP (specification version 2.1.0 approved 8/11/2023): PM2_Supporting.

Met criteria codes

PM2_Supporting	✓	This variant has an incomputable gnomAD v2.1.1 Grpmax filtering allele frequency due to 0 copies in the European non-Finnish subpopulation and 1 copy in the East Asian subpopulation, thereby meeting the ClinGen MDEP threshold criteria for PM2_Supporting (ENF Grpmax FAF <= 0.000003 and <= 2 copies in ENF and <=1 copy in any other subpopulation) (PM2_Supporting).

Not Met criteria codes

PP1	✗	This variant segregated with diabetes with 1 informative meiosis in a single family; however, this does not meet the thresholds for PP1 set by the ClinGen MDEP (PMID: 27236918, 9313763).
PP4	✗	This variant was identified in an individual(s) with diabetes; however, the calculated MODY probability is <50% and HNF4A was not tested (PMID: 9313763).

Curation History

Showing 1 to 1 of 1 rows
