

Variant: NM_001306179.2:c.619G>T

Version: 1.1

CA386964418 [↗](#)

1699995 (ClinVar) [↗](#)

Gene: HNF1A ([HGNC:6927](#))

Condition: monogenic diabetes ([MONDO:0015967](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: fb5299e2-08d5-4a29-9af4-2317f39b21ab

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HGVS expressions

NM_001306179.2:c.619G>T

NC_000012.12:g.120993612G>T

CM000674.2:g.120993612G>T

NC_000012.11:g.121431415G>T

CM000674.1:g.121431415G>T

NC_000012.10:g.119915798G>T

NG_011731.2:g.19867G>T

ENST00000560968.6:c.619G>T

ENST00000257555.11:c.619G>T

ENST00000257555.10:c.619G>T

ENST00000400024.6:c.619G>T

ENST00000402929.5:n.754G>T

ENST00000535955.5:n.43-3879G>T

ENST00000538626.2:n.191-3879G>T

ENST00000538646.5:c.527-552G>T

ENST00000540108.1:c.*59G>T

ENST00000541395.5:c.619G>T

ENST00000541924.5:c.619G>T

ENST00000543427.5:c.619G>T

ENST00000544413.2:c.619G>T

ENST00000544574.5:c.73-3005G>T

ENST00000560968.5:c.762G>T

ENST00000615446.4:c.-257-2650G>T

ENST00000617366.4:c.586+33G>T

NM_000545.5:c.619G>T

NM_000545.6:c.619G>T

NM_001306179.1:c.619G>T

NM_000545.8:c.619G>T

Likely Pathogenic

Met criteria codes 5

PM2_Supporting

PP4_Moderate

PM1_Supporting

PP3

PM5

Not Met criteria codes 1

PS4

Expert Panel

Monogenic Diabetes VCEP [↗](#)

Criteria Specification Information

Evidence submitted by expert panel

Monogenic Diabetes VCEP

The c.619G>T variant in the HNF1 homeobox A gene, HNF1A, causes an amino acid change of glycine to cysteine at codon 207 (p.(Gly207Cys)) of NM_000545.8. This variant is predicted to be deleterious by computational evidence, with a REVEL score of 0.923, which is greater than the MDEP threshold of 0.70 (PP3). 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, and negative antibodies) (PP4_Moderate; internal lab contributor). Additionally, this variant is located within the DNA binding domain (codons 107-174 and 201-280) of HNF1A, which is defined as critical for the protein’s function by the ClinGen MDEP (PM1_Supporting). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). Another missense variant at the same residue, c.620G>A p.(Gly207Asp), has been interpreted as pathogenic by the ClinGen MDEP and p.Gly207Cys has an equal or greater Grantham distance (PM5). This variant was identified in three 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. In summary, c.619G>T meets the criteria to be classified as likely pathogenic for monogenic diabetes. ACMG/AMP criteria applied, as specified by the ClinGen MDEP (specification version 3.1.0, approved 10/10/2025): PP3, PP4_Moderate, PM1_Supporting, PM2_Supporting, PM5.

Met criteria codes

PM2_Supporting			This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
PP4_Moderate			This variant was identified in 1 individual with a clinical history suggestive of HNF1A-MODY (MODY probability calculator result >50%, negative genetic testing for HNF4A and negative antibodies).
PM1_Supporting			This variant is located within the DNA-binding domain of HNF1A, which is defined as critical for the protein’s function by the ClinGen MDEP (PM1_Supporting)
PP3			This variant is predicted to be deleterious by computational evidence, with a REVEL score of 0.923, which is greater than the MDEP VCEP threshold of 0.70 (PP3).
PM5			The [p.Gly207Asp] variant has been interpreted as pathogenic by the MDEP and [p.Gly207Cys] has a greater Grantham distance (PM5).

Not Met criteria codes

PS4			This variant was identified in three 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).
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Curation History

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