

Variant: *NM_000545.8(HNF1A):c.745T>C (p.Ser249Pro)*

Version: 2.0

CA386965901 [↗](#)

1676716 (ClinVar) [↗](#)

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

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

Inheritance Mode: Autosomal dominant inheritance

UUID: 29080ea6-8328-4407-b6f6-59950e3aec2f

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HGVS expressions

NM_000545.8(HNF1A):c.745T>C (p.Ser249Pro)

NM_000545.8:c.745T>C

NC_000012.12:g.120994195T>C

CM000674.2:g.120994195T>C

NC_000012.11:g.121431998T>C

CM000674.1:g.121431998T>C

NC_000012.10:g.119916381T>C

NG_011731.2:g.20450T>C

ENST00000560968.6:c.745T>C

ENST00000257555.11:c.745T>C

ENST00000257555.10:c.745T>C

ENST00000400024.6:c.745T>C

ENST00000402929.5:n.880T>C

ENST00000535955.5:n.43-3296T>C

ENST00000538626.2:n.191-3296T>C

ENST00000538646.5:c.558T>C

ENST00000540108.1:c.*185T>C

ENST00000541395.5:c.745T>C

ENST00000541924.5:c.713+489T>C

ENST00000543427.5:c.633+569T>C

ENST00000544413.2:c.745T>C

ENST00000544574.5:c.73-2422T>C

ENST00000560968.5:c.888T>C

ENST00000615446.4:c.-257-2067T>C

ENST00000617366.4:c.586+616T>C

NM_000545.5:c.745T>C

NM_000545.6:c.745T>C

NM_001306179.1:c.745T>C

NM_001306179.2:c.745T>C

Likely Pathogenic

Met criteria codes **5**

PM1_Supporting

PS4_Moderate

PP4_Moderate

PM2_Supporting

PP3

Expert Panel

Monogenic Diabetes VCEP [↗](#)

Criteria Specification Information

Evidence submitted by expert panel

Monogenic Diabetes VCEP

The c.745T>C variant in the HNF1 homeobox A gene, HNF1A, causes an amino acid change of serine to proline at codon 249 (p. (Ser249Pro)) of NM_000545.8. This variant is located within a conserved region of 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). Additionally, this variant is absent from gnomAD v4.1.0 (PM2_Supporting). This variant is predicted to be deleterious by computational evidence, with a REVEL score of 0.924, which is greater than the MDEP VCEP threshold of 0.70 (PP3). This variant was identified in four unrelated individuals with non-autoimmune and non-absolute/near-absolute insulin-deficient diabetes (PS4_Moderate; PMID: 16249556, 23771925, internal lab contributors). Additionally, one of these individuals had a clinical history highly specific for HNF1A-monogenic diabetes (MODY probability estimated between 45.5-75.5% based on available clinical information, negative genetic testing for HNF4A, and antibody negative) (PP4_Moderate; internal lab contributor). In summary, c.745C>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): PM1_Supporting, PM2_Supporting, PP3, PP4_Moderate, PS4_Moderate.

Met criteria codes

PM1_Supporting			This variant is located within a conserved region of 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).
PS4_Moderate			This variant was identified in four unrelated individuals with non-autoimmune and non-absolute/near-absolute insulin-deficient diabetes (PS4_Moderate; PMID: 16249556, 23771925, internal lab contributors).
PP4_Moderate			This variant was identified in an individual with a clinical history highly specific for HNF1A-monogenic diabetes (MODY probability estimated between 45.5-75.5% based on available clinical information, negative genetic testing for HNF4A, and antibody negative) (PP4_Moderate; internal lab contributor).
PM2_Supporting			This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
PP3			This variant is predicted to be deleterious by computational evidence, with a REVEL score of 0.924, which is greater than the MDEP VCEP threshold of 0.70 (PP3).

Curation History [↗](#)

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