The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

# *Variant: NM_000545.8(HNF1A):c.626C>A (p.Ala209Glu)*

Version: 1.1

*CA386964506*

*586794 (ClinVar)*

**Gene**: HNF1A (HGNC:6927)
**Condition**: monogenic diabetes (MONDO:0015967)
**Inheritance Mode**: Autosomal dominant inheritance
**UUID:** c0152b3d-4ecf-4235-8d8a-9d4f8c160a86
**Approved on**: 2026/2/6
**Published on**: 2026/2/6

## *HGVS expressions*

**NM_000545.8(HNF1A):c.626C>A (p.Ala209Glu)**
**NM_000545.8:c.626C>A**
NC_000012.12:g.120993619C>A
CM000674.2:g.120993619C>A
NC_000012.11:g.121431422C>A
CM000674.1:g.121431422C>A
NC_000012.10:g.119915805C>A
NG_011731.2:g.19874C>A
ENST00000560968.6:c.626C>A
ENST00000257555.11:c.626C>A
ENST00000257555.10:c.626C>A
ENST00000400024.6:c.626C>A
ENST00000402929.5:n.761C>A
ENST00000535955.5:n.43-3872C>A
ENST00000538626.2:n.191-3872C>A
ENST00000538646.5:c.527-545C>A
ENST00000540108.1:c.*66C>A
ENST00000541395.5:c.626C>A
ENST00000541924.5:c.626C>A
ENST00000543427.5:c.626C>A
ENST00000544413.2:c.626C>A
ENST00000544574.5:c.73-2998C>A
ENST00000560968.5:c.769C>A
ENST00000615446.4:c.-257-2643C>A
ENST00000617366.4:c.586+40C>A
NM_000545.5:c.626C>A
NM_000545.6:c.626C>A
NM_001306179.1:c.626C>A
NM_001306179.2:c.626C>A

**Likely Pathogenic**

**Met criteria codes** 5

PM1_Supporting PP3 PP4 PS4_Moderate PM2_Supporting

**Not Met criteria codes** 1

## Expert Panel

Monogenic Diabetes VCEP

## Criteria Specification Information

PP1

Evidence Links 0

**Criteria Specification:** *ClinGen Monogenic Diabetes Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for HNF1A Version 3.1.0*

**Criteria Specification Approval History**

**Criteria Specifications for this VCEP**

Evidence submitted by expert panel

***Monogenic Diabetes VCEP***

**The c.626C>A variant in the HNF1 homeobox A gene, HNF1A, causes an amino acid change of alanine to glutamic acid at codon 209 (p.(Ala209Glu)) 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). It is also predicted to be deleterious by computational evidence, with a REVEL score of 0.822, which is greater than the MDEP VCEP threshold of 0.70 (PP3). This variant is absent in gnomAD v4.1.0 (PM2_Supporting), and was identified in six unrelated individuals with non- autoimmune and non-absolute/near-absolute insulin-deficient diabetes (PS4_Moderate; internal lab contributors). One of these individuals has a clinical history highly specific for HNF1A-MODY (MODY probability calculator result >50%, negative genetic testing for HNF4A) (PP4; internal lab contributor). In summary, c.626C>A 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): PS4_Moderate, PP3, PP4, PM1_Supporting, PM2_Supporting.**

**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). |
| **PP3** | ✔ | This variant is predicted to be deleterious by computational evidence, with a REVEL score of 0.822, which is greater than the MDEP VCEP threshold of 0.70 (PP3). |
| **PP4** | ✔ | 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 contributor). |
| **PS4_Moderate** | ✔ | This variant was identified in six unrelated individuals with non- autoimmune and non-absolute/near-absolute insulin-deficient diabetes (PS4_Moderate; internal lab contributors). |
| **PM2_Supporting** | ✔ | This variant is absent in gnomAD v4.1.0 (PM2_Supporting). |

**Not Met criteria codes**

| | | |
|---|---|---|
| **PP1** | ✖ | This variant segregated with diabetes with one meiosis in a single family; however, this does not meet the thresholds for PP1 set by the ClinGen MDEP (PMID: 27236918, [internal lab contributors]). |

## Curation History

Showing 1 to 2 of 2 rows

| See Report | Preferred Variant Title | Classification | Condition | Published Date | Version | Criteria Specification | Gene |
|---|---|---|---|---|---|---|---|
| View | NM_000545.8(HNF1A):c.626C>A (p.Ala… | Likely Pathogenic | Monogenic Diabetes | 2026-02-06 | 1.1 | ClinGen Monogenic Diabetes Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for HNF1A Version 3.1.0 | HNF1A |
| View | NM_000545.8(HNF1A):c.626C>A (p.Ala… | Likely Pathogenic | Monogenic Diabetes | 2022-07-01 | 1.0 | ClinGen Monogenic Diabetes Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 1.1 | HNF1A |

Showing 1 to 2 of 2 rows

Showing 1 to 2 of 2 rows

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.

ClinGen Terms of Use.
¤ Powered by BCM's Genboree.