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_001354803.2:c.382G>A

Version: 1.0

CA367396913

Gene: GCK (HGNC:2645)
Condition: monogenic diabetes (MONDO:0015967)
Inheritance Mode: Semidominant inheritance
UUID: c55fbd53-753a-4f20-a5f6-37189a97b5c2
Approved on: 2026/4/17
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HGVS expressions

NM_001354803.2:c.382G>A
NC_000007.14:g.44145186C>T
CM000669.2:g.44145186C>T
NC_000007.13:g.44184785C>T
CM000669.1:g.44184785C>T
NC_000007.12:g.44151310C>T
NG_008847.1:g.49238G>A
NG_008847.2:g.57985G>A
ENST00000395796.8:c.*1346G>A
ENST00000616242.5:c.*468G>A
ENST00000683378.1:n.574G>A
ENST00000336642.9:c.382G>A
ENST00000345378.7:c.1351G>A
ENST00000403799.8:c.1348G>A
ENST00000671824.1:c.1411G>A
ENST00000672743.1:n.360G>A
ENST00000673284.1:c.1348G>A
ENST00000336642.8:c.400G>A
ENST00000345378.6:c.1351G>A
ENST00000395796.7:c.1345G>A
ENST00000403799.7:c.1348G>A
ENST00000437084.1:c.1297G>A
ENST00000459642.1:n.728G>A
ENST00000616242.4:c.1345G>A
NM_000162.3:c.1348G>A
NM_033507.1:c.1351G>A
NM_033508.1:c.1345G>A
NM_000162.4:c.1348G>A
NM_001354800.1:c.1348G>A
NM_001354801.1:c.337G>A
NM_001354802.1:c.208G>A
NM_001354803.1:c.382G>A
NM_033507.2:c.1351G>A
NM_033508.2:c.1345G>A
NM_000162.5:c.1348G>A
NM_033507.3:c.1351G>A
NM_033508.3:c.1345G>A

Likely Pathogenic

Met criteria codes 5

PM2_Supporting PP2 PP3 PS4_Moderate PM5_Supporting

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 GCK Version 3.1.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Monogenic Diabetes VCEP

The c.1348G>A variant in the glucokinase gene, GCK, causes an amino acid change of alanine to threonine at codon 450 (p.(Ala450Thr)) of NM_000162.5. GCK is defined by the ClinGen MDEP as a gene that has a low rate of benign missense variation and has pathogenic missense variants as a common mechanism of disease (PP2). 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 0.909, which is greater than the MDEP VCEP threshold of 0.70 (PP3). This variant was identified in four unrelated indivdiuals with hyperglycemia (PS4_Moderate; PMID: 19790256). Another missense variant at the same residue, c.1348G>T (p.Ala450Ser), has been classified as likely pathogenic by the ClinGen MDEP (PM5_Supporting). In summary, c.1348G>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): PP2, PP3, PM2_Supporting, PM5_Supporting, PS4_Moderate.

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
PP2	✔	GCK is defined by the ClinGen MDEP as a gene that has a low rate of benign missense variation and has pathogenic missense variants as a common mechanism of disease (PP2).
PP3	✔	This variant is predicted to be deleterious by computational evidence, with a REVEL score of 0.909, which is greater than the MDEP VCEP threshold of 0.70 (PP3).
PS4_Moderate	✔	This variant was identified in four unrelated indivdiuals with hyperglycemia (PS4_Moderate; PMID: 19790256).
PM5_Supporting	✔	Another missense variant at the same residue, c.1348G>T (p.Ala450Ser), has been classified as likely pathogenic by the ClinGen MDEP (PM5_Supporting).

Curation History

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