

Variant: NM_001354803.2:c.379G>T

CA367396925 [↗](#)

3233991 (ClinVar) [↗](#)

Gene: GCK ([HGNC:2645](#))

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

Inheritance Mode: Semidominant inheritance

UUID: 9ee0fda7-fd3d-421f-8118-fe441f1d98dc

Approved on: 2024/4/27

Published on: 2024/4/27

Version: 1.0

HGVS expressions

NM_001354803.2:c.379G>T
NC_000007.14:g.44145189C>A
CM000669.2:g.44145189C>A
NC_000007.13:g.44184788C>A
CM000669.1:g.44184788C>A
NC_000007.12:g.44151313C>A
NG_008847.1:g.49235G>T
NG_008847.2:g.57982G>T
ENST00000395796.8:c.*1343G>T
ENST00000616242.5:c.*465G>T
ENST00000683378.1:n.571G>T
ENST00000336642.9:c.379G>T
ENST00000345378.7:c.1348G>T
ENST00000403799.8:c.1345G>T
ENST00000671824.1:c.1408G>T
ENST00000672743.1:n.357G>T
ENST00000673284.1:c.1345G>T
ENST00000336642.8:c.397G>T
ENST00000345378.6:c.1348G>T
ENST00000395796.7:c.1342G>T
ENST00000403799.7:c.1345G>T
ENST00000437084.1:c.1294G>T
ENST00000459642.1:n.725G>T
ENST00000616242.4:c.1342G>T
NM_000162.3:c.1345G>T
NM_033507.1:c.1348G>T
NM_033508.1:c.1342G>T
NM_000162.4:c.1345G>T
NM_001354800.1:c.1345G>T
NM_001354801.1:c.334G>T
NM_001354802.1:c.205G>T
NM_001354803.1:c.379G>T
NM_033507.2:c.1348G>T
NM_033508.2:c.1342G>T
NM_000162.5:c.1345G>T
NM_033507.3:c.1348G>T
NM_033508.3:c.1342G>T

Likely Pathogenic

Met criteria codes 5

PM2_Supporting

PP4_Moderate

PP2

PP3

PM5

Not Met criteria codes 1

PM1

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 1.3.0

[Criteria Specification Approval History](#)

[Criteria Specifications for this VCEP](#)

Evidence submitted by expert panel

Monogenic Diabetes VCEP

The c.1345G>T variant in the glucokinase gene, GCK, causes an amino acid change of alanine to serine at codon 449 (p.(Ala449Ser)) 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 predicted to be deleterious by computational evidence, with a REVEL score of 0.878, which is greater than the MDEP VCEP threshold of 0.70 (PP3). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). This variant was identified in an individual with a clinical history highly specific for GCK-hyperglycemia (FBG 5.5-8 mmol/L and HbA1c 5.6 - 7.6% and negative antibodies and 3-generation family history of diabetes) (PP4_Moderate; PMID: 19410318). Another missense variant, c.1345G>A p.Ala449Thr, has been interpreted as pathogenic by the ClinGen MDEP, and p.Ala449Ser has a greater Grantham distance (PM5). In summary, c.1345G>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 1.3.0, approved 8/11/2023): PP4_Moderate, PM5, PP2, PP3, PM2_Supporting.

Met criteria codes

PM2_Supporting			This variant is absent from gnomAD v2.1.1 (PM2_Supporting). Absent from gnomAD v4.0.
PP4_Moderate			This variant was identified in an individual with a clinical history highly specific for GCK-hyperglycemia (FBG 5.5-8 mmol/L and HbA1c 5.6 - 7.6% and negative antibodies and 3-generation family history of diabetes) (PP4_Moderate; PMID: 19410318).
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 0.878, which is greater than the MDEP VCEP threshold of 0.70 (PP3).
PM5			Another missense variant, c.1345G>A p.Ala449Thr, has been interpreted as pathogenic by the ClinGen MDEP, and p.Ala449Ser has a greater Grantham distance (PM5).

Not Met criteria codes

PM1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
-----	---	---	--

Curation History 

▼

▼

Showing 1 to 1 of 1 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.