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_000162.5(GCK):c.171G>T (p.Met57Ile)

Version: 1.0

CA16603236

377026 (ClinVar)

Gene: GCK (HGNC:2645)
Condition: monogenic diabetes (MONDO:0015967)
Inheritance Mode: Semidominant inheritance
UUID: 6ef90ebe-8dcc-4008-ba71-a117dcb69619
Approved on: 2024/10/31
Published on: 2025/2/28

HGVS expressions

NM_000162.5:c.171G>T
NM_000162.5(GCK):c.171G>T (p.Met57Ile)
NC_000007.14:g.44153338C>A
CM000669.2:g.44153338C>A
NC_000007.13:g.44192937C>A
CM000669.1:g.44192937C>A
NC_000007.12:g.44159462C>A
NG_008847.1:g.41086G>T
NG_008847.2:g.49833G>T
ENST00000395796.8:c.*169G>T
ENST00000616242.5:c.171G>T
ENST00000682635.1:n.657G>T
ENST00000345378.7:c.174G>T
ENST00000403799.8:c.171G>T
ENST00000671824.1:c.171G>T
ENST00000673284.1:c.171G>T
ENST00000345378.6:c.174G>T
ENST00000395796.7:c.168G>T
ENST00000403799.7:c.171G>T
ENST00000437084.1:c.171G>T
ENST00000616242.4:c.168G>T
NM_000162.3:c.171G>T
NM_033507.1:c.174G>T
NM_033508.1:c.168G>T
NM_000162.4:c.171G>T
NM_001354800.1:c.171G>T
NM_033507.2:c.174G>T
NM_033508.2:c.168G>T
NM_033507.3:c.174G>T
NM_033508.3:c.168G>T

Likely Pathogenic

Met criteria codes 6

PP2 PP3 PP4 PS1 PM2_Supporting PM5_Supporting

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.171G>T variant in the glucokinase gene, GCK, causes an amino acid change of methionine to isoleucine at codon 57 (p.(Met57Ile)) of NM_000162.5. This variant is absent from gnomAD v2.1.1 and v4.1 (PM2_Supporting). 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 0.987, which is greater than the MDEP VCEP threshold of 0.70 (PP3). This variant was identified in an individual with a clinical history highly specific for GCK-MODY (FBG 5.5-8 mmol/L and HbA1c 5.6 - 7.6%) (PP4; PMID: 34440516). The nucleotide change c.171G>A, which results in the same amino acid change, has been classified as pathogenic for GCK-hyperglycemia by the ClinGen MDEP (PS1). Another missense variant at the same codon, c.170T>G (p.Met57Arg), has been classified as likely pathogenic by the ClinGen MDEP (PM5_Supporting). In summary, c.171G>T p.(Met57Ile) 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): PM2_Supporting, PM5_Supporting, PP2, PP3, PP4, PS1).

Met criteria codes

PP2	✔	GCK, in which the variant was identified, is definted by the ClinGen Monogenic Diabetes Expert Panel as a gene that has a low rate of benign missense variation and where pathogenic missense variants are a common mechanism of disease (PP2).
PP3	✔	This variant is predicted to be deleterious by computational evidence with a REVEL score of 0.987, which is greater than the MDEP VCEP threshold of 0.70 (PP3).
PP4	✔	This variant was reported in an individual with a clinical history highly specific for GCK-MODY (FBG 5.5-8 mmol/L and HbA1c 5.6 - 7.6%) (PP4, PMID: 34440516).
PS1	✔	The nucleotide change c.171G>A, which causes the same amino acid change, has been classified as pathogenic for GCK-hyperglycemia by the ClinGen MDEP (PS1).
PM2_Supporting	✔	This variant is absent from gnomAD v2.1 and v4.1 (PM2_Supporting).
PM5_Supporting	✔	Another missense variant at the same codon, c.170T>G (p.Met57Arg), has been classified as likely pathogenic by the ClinGen MDEP (PM5_Supporting).

Not Met criteria codes

PM1		✖	Variant does occur in the glucose- or ATP-binding sites.

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.

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