

Variant: NM_001354803.2:c.122A>G

Version: 2.0

CA367399062 [↗](#)

3383915 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: 25d4e611-dd25-493a-9da0-eef2a541dd19

Approved on: 2025/9/19

Published on: 2025/9/19

HGVS expressions

NM_001354803.2:c.122A>G

NC_000007.14:g.44145662T>C

CM000669.2:g.44145662T>C

NC_000007.13:g.44185261T>C

CM000669.1:g.44185261T>C

NC_000007.12:g.44151786T>C

NG_008847.1:g.48762A>G

NG_008847.2:g.57509A>G

ENST00000395796.8:c.*1086A>G

ENST00000616242.5:c.*208A>G

ENST00000683378.1:n.314A>G

ENST00000336642.9:c.122A>G

ENST00000345378.7:c.1091A>G

ENST00000403799.8:c.1088A>G

ENST00000671824.1:c.1151A>G

ENST00000672743.1:n.100A>G

ENST00000673284.1:c.1088A>G

ENST00000336642.8:c.140A>G

ENST00000345378.6:c.1091A>G

ENST00000395796.7:c.1085A>G

ENST00000403799.7:c.1088A>G

ENST00000437084.1:c.1037A>G

ENST00000459642.1:n.468A>G

ENST00000473353.1:n.386A>G

ENST00000616242.4:c.1085A>G

NM_000162.3:c.1088A>G

NM_033507.1:c.1091A>G

NM_033508.1:c.1085A>G

NM_000162.4:c.1088A>G

NM_001354800.1:c.1088A>G

NM_001354801.1:c.77A>G

NM_001354802.1:c.-53A>G

NM_001354803.1:c.122A>G

NM_033507.2:c.1091A>G

NM_033508.2:c.1085A>G

NM_000162.5:c.1088A>G

NM_033507.3:c.1091A>G

Pathogenic**Met criteria codes** 6

PP4_Moderate

PP2

PP3

PP1_Strong

PS4_Moderate

PM2_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 3.0.0*
- [↗](#) **Criteria Specification Approval History**
- [↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Monogenic Diabetes VCEP

The c.1088A>G variant in the glucokinase gene, GCK, causes an amino acid change of aspartic acid to glycine at codon 363 (p.(Asp363Gly)) of NM_000162.5. This variant is predicted to be deleterious by computational evidence, with a REVEL score of 0.937, which is greater than the MDEP VCEP threshold of 0.70 (PP3). 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 was identified in an individual with a clinical history highly specific for GCK-MODY (fasting glucose 5.5-8 mmol/L and HbA1c 5.6 - 7.6% and three-generation, dominant family history of diabetes (in a family not used for PP1)) (PP4_Moderate; internal lab contributors). This variant segregated with hyperglycemia, with 4 informative meioses in 2 families (PP1_Strong; internal lab contributors). This variant was identified in four unrelated individuals with hyperglycemia (PS4_Moderate; PMID: 37045781, internal lab contributors). In summary, c.1088A>G meets the criteria to be classified as pathogenic for monogenic diabetes. ACMG/AMP criteria applied, as specified by the ClinGen MDEP (specification version 3.0.0, approved 7/23/2025): PS4_Moderate, PP4_Moderate, PP1_Strong, PM2_Supporting, PP2, PP3.

Met criteria codes

PP4_Moderate		✓	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% and three-generation, dominant family history of diabetes (in a family not used for PP1)) (PP4_Moderate; internal lab contributor).
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.
PP3		✓	This variant is predicted to be deleterious by computational evidence, with a REVEL score of 0.937, which is greater than the MDEP VCEP threshold of 0.70.
PP1_Strong		✓	This variant segregated with hyperglycemia, with 4 informative meioses in 2 families (PP1_Strong; PMID: 37045781, internal lab contributors).
PS4_Moderate		✓	This variant was identified in four unrelated individuals with hyperglycemia (PS4_Moderate; PMID: 37045781, internal lab contributors).

PM2_Supporting ⓘ



This variant is absent from gnomAD v4.1.0 (PM2_Supporting).

Curation History ↗

▼

▼

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.