

Variant: *NM_000162.5(GCK):c.1079C>A (p.Ser360Ter)*

Version: 1.0

CA367399113 [↗](#)

1679547 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: f78a7f33-0ea6-4e33-8a48-de91dd23b81a

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HGVS expressions

NM_000162.5:c.1079C>A

NM_000162.5(GCK):c.1079C>A (p.Ser360Ter)

NC_000007.14:g.44145671G>T

CM000669.2:g.44145671G>T

NC_000007.13:g.44185270G>T

CM000669.1:g.44185270G>T

NC_000007.12:g.44151795G>T

NG_008847.1:g.48753C>A

NG_008847.2:g.57500C>A

ENST00000395796.8:c.*1077C>A

ENST00000616242.5:c.*199C>A

ENST00000683378.1:n.305C>A

ENST00000336642.9:c.113C>A

ENST00000345378.7:c.1082C>A

ENST00000403799.8:c.1079C>A

ENST00000671824.1:c.1142C>A

ENST00000672743.1:n.91C>A

ENST00000673284.1:c.1079C>A

ENST00000336642.8:c.131C>A

ENST00000345378.6:c.1082C>A

ENST00000395796.7:c.1076C>A

ENST00000403799.7:c.1079C>A

ENST00000437084.1:c.1028C>A

ENST00000459642.1:n.459C>A

ENST00000473353.1:n.377C>A

ENST00000616242.4:c.1076C>A

NM_000162.3:c.1079C>A

NM_033507.1:c.1082C>A

NM_033508.1:c.1076C>A

NM_000162.4:c.1079C>A

NM_001354800.1:c.1079C>A

NM_001354801.1:c.68C>A

NM_001354802.1:c.-62C>A

NM_001354803.1:c.113C>A

NM_033507.2:c.1082C>A

NM_033508.2:c.1076C>A

NM_033507.3:c.1082C>A

NM_033508.3:c.1076C>A
NM_001354803.2:c.113C>A

Pathogenic

Met criteria codes 5

PM2_Supporting PP4_Moderate
PVS1 PP1_Strong PS4

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.1079C>A variant in the glucokinase gene, GCK, results in a premature termination at codon 360 (p.(Ser360Ter)) of NM_000162.5. This variant, located in biologically-relevant exon 9 of 10, is predicted to lead to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1; PMID: 19790256). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). This variant was identified in 11 unrelated individuals with hyperglycemia (PS4; PMID: 31638168, 9049484, ClinVar, internal lab contributors). Additionally, at least one of these individuals had a clinical history highly specific for GCK-hyperglycemia (fasting glucose 5.5-8 mmol/L and HbA1c 5.6 - 7.6% and antibody negative) (PP4_Moderate; internal lab contributors). This variant segregated with hyperglycemia, with 16 informative meioses in one family (PP1_Strong; PMID: 9049484/internal lab contributors). In summary, c.1079C>A meets the criteria to be classified as pathogenic for monogenic diabetes. ACMG/AMP criteria applied, as specified by the ClinGen MDEP (specification version 3.1.0, approved 10/10/2025): PVS1, PS4, PP1_Strong, PP4_moderate, PM2_supporting.

Met criteria codes

PM2_Supporting		✓	This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
PP4_Moderate		✓	This variant was identified in an individual with a clinical history highly specific for GCK-hyperglycemia (fasting glucose 5.5-8 mmol/L and HbA1c 5.6 - 7.6% and antibody negative) (PP4_Moderate; internal lab contributors).
PVS1		✓	This variant, located in biologically-relevant exon 9 of 10, is predicted to lead to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1; PMID: 19790256).
PP1_Strong		✓	This variant segregated with hyperglycemia, with 16 informative meioses in one family (PP1_Strong; PMID: 9049484/internal lab contributors).
PS4		✓	This variant was identified in 12 unrelated individuals with hyperglycemia (PS4; PMID: 9049484, 31638168, ClinVar, internal lab contributors).

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