

Variant: *NM_033508.3:c.462G>T*

Version: 1.0

CA367401896 [↗](#)

2628364 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: 8d82fbaa-7809-471e-9743-1ba49a8fad29

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HGVS expressions

NM_033508.3:c.462G>T

NC_000007.14:g.44150974C>A
CM000669.2:g.44150974C>A
NC_000007.13:g.44190573C>A
CM000669.1:g.44190573C>A
NC_000007.12:g.44157098C>A
NG_008847.1:g.43450G>T
NG_008847.2:g.52197G>T
ENST00000395796.8:c.*463G>T
ENST00000616242.5:c.465G>T
ENST00000682635.1:n.951G>T
ENST00000345378.7:c.468G>T
ENST00000403799.8:c.465G>T
ENST00000671824.1:c.465G>T
ENST00000673284.1:c.465G>T
ENST00000345378.6:c.468G>T
ENST00000395796.7:c.462G>T
ENST00000403799.7:c.465G>T
ENST00000437084.1:c.414G>T
ENST00000616242.4:c.462G>T
NM_000162.3:c.465G>T
NM_033507.1:c.468G>T
NM_033508.1:c.462G>T
NM_000162.4:c.465G>T
NM_001354800.1:c.465G>T
NM_033507.2:c.468G>T
NM_033508.2:c.462G>T
NM_000162.5:c.465G>T
NM_033507.3:c.468G>T

Likely Pathogenic

Met criteria codes **5**

PP4_Moderate

PM2_Supporting

PP1

PP2

PP3

Evidence Links **0**

Expert Panel

Monogenic Diabetes VCEP [↗](#)

Criteria Specification Information

Evidence submitted by expert panel

Monogenic Diabetes VCEP

The c.465G>T variant in the glucokinase gene, GCK, causes an amino acid change of arginine to serine at codon 155 (p.(Arg155Ser)) 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 0.766, 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 segregated with diabetes, with three informative meioses in one family (PP1; internal lab contributors). 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 antibody negative) (PP4_Moderate; internal lab contributors). In summary, c.465G>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): PM2_Supporting, PP3, PP2, PP1, PP4_Moderate.

Met criteria codes

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 antibody negative) (PP4; internal lab contributors).
PM2_Supporting			This variant is absent from gnomAD v2.1.1 (PM2_Supporting).
PP1			This variant segregated with diabetes, with three informative meioses in a family with MODY (PP1; internal lab contributors).
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 0.766, which is greater than the MDEP VCEP threshold of 0.70 (PP3).

Curation History [↗](#)

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