

Variant: *NM_000162.5(GCK):c.630G>T (p.Met210Ile)*

Version: 2.0

CA213814 [↗](#)

36236 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: d17187f9-d65a-4117-af07-cfcb9e907236

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HGVS expressions

NM_000162.5:c.630G>T

NM_000162.5(GCK):c.630G>T (p.Met210Ile)

NC_000007.14:g.44149809C>A

CM000669.2:g.44149809C>A

NC_000007.13:g.44189408C>A

CM000669.1:g.44189408C>A

NC_000007.12:g.44155933C>A

NG_008847.1:g.44615G>T

NG_008847.2:g.53362G>T

ENST00000395796.8:c.*628G>T

ENST00000616242.5:c.630G>T

ENST00000682635.1:n.1116G>T

ENST00000345378.7:c.633G>T

ENST00000403799.8:c.630G>T

ENST00000671824.1:c.630G>T

ENST00000673284.1:c.630G>T

ENST00000345378.6:c.633G>T

ENST00000395796.7:c.627G>T

ENST00000403799.7:c.630G>T

ENST00000437084.1:c.579G>T

ENST00000616242.4:c.627G>T

NM_000162.3:c.630G>T

NM_033507.1:c.633G>T

NM_033508.1:c.627G>T

NM_000162.4:c.630G>T

NM_001354800.1:c.630G>T

NM_033507.2:c.633G>T

NM_033508.2:c.627G>T

NM_033507.3:c.633G>T

NM_033508.3:c.627G>T

Pathogenic

Met criteria codes 5

- PM2_Supporting
- PM5_Strong
- PS1
- PP2
- PP3

Not Met criteria codes 2

- PS4
- PP4

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 1.2.0*

[Criteria Specification Approval History](#)

[Criteria Specifications for this VCEP](#)

Evidence submitted by expert panel

Monogenic Diabetes VCEP

The c.630G>T variant in the glucokinase gene, GCK, causes an amino acid change of methionine to isoleucine at codon 210 (p.(Met210Ile)) 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 0.9399, which is greater than the MDEP VCEP threshold of 0.70 (PP3). This variant is absent in gnomAD v2.1.1 (PM2_Supporting), and was identified in an individual with diabetes; however, PP4 is unable to be evaluated due to lack of clinical information (ClinVar ID 36236). Two other missense variants, c.629T>A (p.Met210Lys) and c.629T>C (p.Met210Thr), have been classified as pathogenic by the ClinGen MDEP (PM5_Strong). The nucleotide change c.630G>A, which causes the same amino acid change, has been classified as pathogenic for monogenic diabetes by the ClinGen MDEP (PS1). Taken together, the c.630G>T meets the criteria to be classified as pathogenic for monogenic diabetes. ACMG/AMP criteria applied, as specified by the ClinGen MDEP (specification version 1.3.0, approved 8/11/2023): PM5_Strong, PS1, PP2, PP3, PM2_Supporting.

Met criteria codes

PM2_Supporting			This variant is absent in gnomAD v2.1.1 (PM2_Supporting).
PM5_Strong			Two other missense variants, c.629T>A (p.Met210Lys) and c.629T>C (p.Met210Thr), have been classified as pathogenic by the ClinGen MDEP (PM5_Strong).
PS1			The nucleotide change c.630G>A, which causes the same amino acid change, has been classified as pathogenic for monogenic diabetes by the ClinGen MDEP (PS1).
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 0.9399, which is greater than the MDEP VCEP threshold of 0.70 (PP3).

Not Met criteria codes

PS4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP4			This variant was identified in an individual with diabetes; however, PP4 is unable to be evaluated due to lack of clinical information (ClinVar ID 36236).

Curation History 

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