

Variant: *NM_033508.3:c.446_448del*

Version: 1.0

CA2580612107 [↗](#)

3024424 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: 9414f879-23b1-4385-b942-ad1d27bcf56b

Approved on: 2024/2/23

Published on: 2024/2/23

HGVS expressions

NM_033508.3:c.446_448del

NC_000007.14:g.44150990_44150992del
CM000669.2:g.44150990_44150992del
NC_000007.13:g.44190589_44190591del
CM000669.1:g.44190589_44190591del
NC_000007.12:g.44157114_44157116del
NG_008847.1:g.43434_43436del
NG_008847.2:g.52181_52183del
ENST00000395796.8:c.*447_*449del
ENST00000616242.5:c.449_451del
ENST00000682635.1:n.935_937del
ENST00000345378.7:c.452_454del
ENST00000403799.8:c.449_451del
ENST00000671824.1:c.449_451del
ENST00000673284.1:c.449_451del
ENST00000345378.6:c.452_454del
ENST00000395796.7:c.446_448del
ENST00000403799.7:c.449_451del
ENST00000437084.1:c.398_400del
ENST00000616242.4:c.446_448del
NM_000162.3:c.449_451del
NM_033507.1:c.452_454del
NM_033508.1:c.446_448del
NM_000162.4:c.449_451del
NM_001354800.1:c.449_451del
NM_033507.2:c.452_454del
NM_033508.2:c.446_448del
NM_000162.5:c.449_451del
NM_033507.3:c.452_454del

Pathogenic

Met criteria codes **5**

PP1_Moderate PS4 PM4_Supporting
PM2_Supporting PP4_Moderate

Evidence Links **0**

Expert Panel

Monogenic Diabetes VCEP [↗](#)

Criteria Specification Information

Evidence submitted by expert panel

Monogenic Diabetes VCEP

The c.449_451del variant in the glucokinase gene, GCK, is a one-base pair deletion resulting in the in-frame deletion of phenylalanine codon 150 (p.Phe150del) within exon 4 of NM_000162.5. The c.449_451del variant is predicted to change the length of the protein due to an in-frame deletion of a single amino acid in a non-repeat region (PM4_Supporting). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). This variant was identified in 10 unrelated individuals with hyperglycemia (PS4; PMID: 19564454, 31576961, 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 negative antibody) (PP4_Moderate; internal lab contributors). This variant segregated with hyperglycemia, with 3 informative meioses in two families (PP1_Moderate, internal lab contributors). In summary, c.449_451del 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): PM2_Supporting, PM4_Supporting, PP4_Moderate, PP1_Moderate, PS4.

Met criteria codes

PP1_Moderate			This variant segregated with hyperglycemia, with 3 informative meioses in two families (PP1_Moderate, internal lab contributors).
PS4			This variant was identified in 10 unrelated individuals with hyperglycemia (PS4; PMID: 19564454, 31576961, internal lab contributors).
PM4_Supporting			The c.449_451del variant is predicted to change the length of the protein due to an in-frame deletion of a single amino acid in a non-repeat region (PM4_Supporting).
PM2_Supporting			This variant is absent from gnomAD v2.1.1 (PM2_Supporting). Absent from gnomAD 4.0.
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 negative antibody) (PP4_Moderate; internal lab contributors).

Curation History [↗](#)

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