

Variant: *NM_033508.3:c.440T>C*

Version: 1.0

CA367401964 [↗](#)

2628363 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: 23de3c7f-3540-4b18-a9b7-d11b2414fb01

Approved on: 2023/10/3

Published on: 2023/10/3

HGVS expressions

NM_033508.3:c.440T>C

NC_000007.14:g.44150996A>G
CM000669.2:g.44150996A>G
NC_000007.13:g.44190595A>G
CM000669.1:g.44190595A>G
NC_000007.12:g.44157120A>G
NG_008847.1:g.43428T>C
NG_008847.2:g.52175T>C
ENST00000395796.8:c.*441T>C
ENST00000616242.5:c.443T>C
ENST00000682635.1:n.929T>C
ENST00000345378.7:c.446T>C
ENST00000403799.8:c.443T>C
ENST00000671824.1:c.443T>C
ENST00000673284.1:c.443T>C
ENST00000345378.6:c.446T>C
ENST00000395796.7:c.440T>C
ENST00000403799.7:c.443T>C
ENST00000437084.1:c.392T>C
ENST00000616242.4:c.440T>C
NM_000162.3:c.443T>C
NM_033507.1:c.446T>C
NM_033508.1:c.440T>C
NM_000162.4:c.443T>C
NM_001354800.1:c.443T>C
NM_033507.2:c.446T>C
NM_033508.2:c.440T>C
NM_000162.5:c.443T>C
NM_033507.3:c.446T>C

Uncertain Significance

Met criteria codes **3**

PP2 PP3 PM2_Supporting

Not Met criteria codes **2**

PP4 PM5

Expert Panel

Monogenic Diabetes VCEP [↗](#)

Criteria Specification Information

Evidence submitted by expert panel

Monogenic Diabetes VCEP

The c.443T>C variant in the glucokinase gene, GCK, causes an amino acid change of phenylalanine to serine at codon 148 (p.(Phe148Ser)) of NM_000162.5. This variant is absent from gnomAD v2.1.1 (PM2_Supporting). Another missense variant, c.442T>A (p.(Phe148Ile)), has been classified as a VUS by the ClinGen MDEP; therefore, PM5 will not be applied. 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 0.991, which is greater than the MDEP VCEP threshold of 0.70 (PP3). This variant was identified in an individual with a phenotype suggestive of GCK-hyperglycemia; however, PP4 is unable to be evaluated due to insufficient clinical information (internal lab contributors). In summary, c.443T>C meets the criteria to be classified as a variant of uncertain significance for monogenic diabetes. ACMG/AMP criteria applied, as specified by the ClinGen MDEP (specification version 1.3.0, approved 8/11/2023): PM2_Supporting, PP2, PP3.

Met criteria codes

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 0.991, which is greater than the MDEP VCEP threshold of 0.70 (PP3).
PM2_Supporting			This variant is absent from gnomAD v2.1.1 (PM2_Supporting).

Not Met criteria codes

PP4			This variant was identified in an individual with a phenotype suggestive of GCK-hyperglycemia; however, PP4 is unable to be evaluated due to insufficient clinical information (internal lab contributors).
PM5			Another missense variant, c.442T>A (p.(Phe148Ile)), has been classified as a VUS by the ClinGen MDEP; therefore, PM5 will not be applied.

▾

▾

Showing 1 to 1 of 1 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.