The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_033508.3:c.881G>T

Version: 1.0

CA367400134

2578352 (ClinVar)

Gene: GCK (HGNC:2645)
Condition: monogenic diabetes (MONDO:0015967)
Inheritance Mode: Semidominant inheritance
UUID: 34d44fed-c8c6-4919-8669-2ee9f8113079
Approved on: 2023/8/11
Published on: 2023/8/11

HGVS expressions

NM_033508.3:c.881G>T
NC_000007.14:g.44146598C>A
CM000669.2:g.44146598C>A
NC_000007.13:g.44186197C>A
CM000669.1:g.44186197C>A
NC_000007.12:g.44152722C>A
NG_008847.1:g.47826G>T
NG_008847.2:g.56573G>T
ENST00000395796.8:c.*882G>T
ENST00000616242.5:c.*4G>T
ENST00000683378.1:n.110G>T
ENST00000345378.7:c.887G>T
ENST00000403799.8:c.884G>T
ENST00000671824.1:c.947G>T
ENST00000673284.1:c.884G>T
ENST00000345378.6:c.887G>T
ENST00000395796.7:c.881G>T
ENST00000403799.7:c.884G>T
ENST00000437084.1:c.833G>T
ENST00000473353.1:n.182G>T
ENST00000616242.4:c.881G>T
NM_000162.3:c.884G>T
NM_033507.1:c.887G>T
NM_033508.1:c.881G>T
NM_000162.4:c.884G>T
NM_001354800.1:c.884G>T
NM_001354801.1:c.8+21G>T
NM_033507.2:c.887G>T
NM_033508.2:c.881G>T
NM_000162.5:c.884G>T
NM_033507.3:c.887G>T

Likely Pathogenic

Met criteria codes 6

PP2 PP3 PM1 PM5 PP4_Moderate PM2_Supporting

Expert Panel

Monogenic Diabetes VCEP

Evidence Links 0

Criteria Specification Information

Criteria Specification: *ClinGen Monogenic Diabetes Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GCK Version 1.3.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Monogenic Diabetes VCEP

The c.884G>T variant in the glucokinase gene, GCK, causes an amino acid change of glycine to valine at codon 295 (p.(Gly295Val)) of NM_000162.5. 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 3 generation family history of diabetes/hyperglycemia) (PP4_Moderate; internal lab contributors). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). Additionally, this variant is predicted to be deleterious by computational evidence, with a REVEL score of 0.0.961, which is greater than the MDEP VCEP threshold of 0.70 (PP3). 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). Additionally, another missense variant, c.883G>A p.Gly295Ser, has been classified as likely pathogenic by the ClinGen MDEP (PM5_Supporting). Lastly, this variant resides in an amino acid that directly binds ATP, which is defined as critical for the protein's function by the ClinGen MDEP (PM1). In summary, c.884G>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): PP4_Moderate, PM2_Suporting, PP2, PP3, PM1, PM5_Supporting.

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 0.961, which is greater than the MDEP VCEP threshold of 0.70 (PP3).
PM1	✔	This variant resides in an amino acid that directly binds ATP, which is defined as critical for the protein's function by the ClinGen MDEP (PM1).
PM5	✔	Another missense variant, c.883G>A p.Gly295Ser, has been classified as likely pathogenic by the ClinGen MDEP (PM5_Supporting).
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 3 generation family history of diabetes/hyperglycemia) (PP4_Moderate; internal lab contributors).
PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).

Curation History

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.

ClinGen Terms of Use.
⌑ Powered by BCM's Genboree.