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_001354803.2:c.295G>T

Version: 1.0

CA367397285

2571656 (ClinVar)

Gene: GCK (HGNC:2645)
Condition: maturity-onset diabetes of the young type 2 (MONDO:0007453)
Inheritance Mode: Semidominant inheritance
UUID: f537eef7-9704-4f2f-be53-fc6f5e648353
Approved on: 2023/6/25
Published on: 2023/6/25

HGVS expressions

NM_001354803.2:c.295G>T
NC_000007.14:g.44145273C>A
CM000669.2:g.44145273C>A
NC_000007.13:g.44184872C>A
CM000669.1:g.44184872C>A
NC_000007.12:g.44151397C>A
NG_008847.1:g.49151G>T
NG_008847.2:g.57898G>T
ENST00000395796.8:c.*1259G>T
ENST00000616242.5:c.*381G>T
ENST00000683378.1:n.487G>T
ENST00000336642.9:c.295G>T
ENST00000345378.7:c.1264G>T
ENST00000403799.8:c.1261G>T
ENST00000671824.1:c.1324G>T
ENST00000672743.1:n.273G>T
ENST00000673284.1:c.1261G>T
ENST00000336642.8:c.313G>T
ENST00000345378.6:c.1264G>T
ENST00000395796.7:c.1258G>T
ENST00000403799.7:c.1261G>T
ENST00000437084.1:c.1210G>T
ENST00000459642.1:n.641G>T
ENST00000616242.4:c.1258G>T
NM_000162.3:c.1261G>T
NM_033507.1:c.1264G>T
NM_033508.1:c.1258G>T
NM_000162.4:c.1261G>T
NM_001354800.1:c.1261G>T
NM_001354801.1:c.250G>T
NM_001354802.1:c.121G>T
NM_001354803.1:c.295G>T
NM_033507.2:c.1264G>T
NM_033508.2:c.1258G>T
NM_000162.5:c.1261G>T
NM_033507.3:c.1264G>T
NM_033508.3:c.1258G>T

Pathogenic

Met criteria codes 3

PP4 PM2_Supporting PVS1

Not Met criteria codes 2

PP1 PS4

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.1261G>T variant in the glucokinase gene, GCK, results in a premature termination at codon 421 (p.(Glu421Ter)) of NM_000162.5. While this variant, located in exon 10 of 10, is predicted to cause a premature stop codon and to escape nonsense mediated decay, it is in a functionally important region of a gene where loss-of-function is an established disease mechanism (PVS1). This variant is absent in gnomAD v2.1.1 (PM2_Supporting). This variant was identified in an individual with a clinical history highly specific for GCK-MODY (FBG 5.5-8 mmol/L and HbA1c 5.6 - 7.6% and fasting glucose between 5.5-8 mmol/L) (PP4; internal lab contributors). In summary, c.1261G>T meets the criteria to be classified as pathogenic for monogenic diabetes. ACMG/AMP criteria applied, as specified by the ClinGen MDEP (specification version 1.2.0, approved 6/7/2023): PVS1, PM2_supporting, PP4.

Met criteria codes

PP4	✔	This variant was identified in an individual with a clinical history highly specific for GCK-MODY (FBG 5.5-8 mmol/L and HbA1c 5.6 - 7.6% and fasting glucose between 5.5-8 mmol/L) (PP4; internal lab contributors).
PM2_Supporting	✔	This variant is absent in gnomAD v2.1.1 (PM2_Supporting).
PVS1	✔	While this variant, located in exon 10 of 10, is predicted to cause a premature stop codon and to escape nonsense mediated decay, it is in a functionally important region of a gene where loss-of-function is an established disease mechanism (PVS1).

Not Met criteria codes

PP1	✖	1 meiosis in 1 family
PS4	✖	1 case from Exeter database

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.