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_000162.5(GCK):c.1054del (p.Ile351_Leu352insTer)

Version: 1.0

CA891843077

585907 (ClinVar)

Gene: GCK (HGNC:2645)
Condition: monogenic diabetes (MONDO:0015967)
Inheritance Mode: Semidominant inheritance
UUID: 2e22ba56-4fc2-4df8-bc5c-d2d20c564281
Approved on: 2024/3/31
Published on: 2024/3/31

HGVS expressions

NM_000162.5:c.1054del
NM_000162.5(GCK):c.1054del (p.Ile351_Leu352insTer)
NC_000007.14:g.44145697del
CM000669.2:g.44145697del
NC_000007.13:g.44185296del
CM000669.1:g.44185296del
NC_000007.12:g.44151821del
NG_008847.1:g.48728del
NG_008847.2:g.57475del
ENST00000395796.8:c.*1052del
ENST00000616242.5:c.*174del
ENST00000683378.1:n.280del
ENST00000336642.9:c.88del
ENST00000345378.7:c.1057del
ENST00000403799.8:c.1054del
ENST00000671824.1:c.1117del
ENST00000672743.1:n.66del
ENST00000673284.1:c.1054del
ENST00000336642.8:c.106del
ENST00000345378.6:c.1057del
ENST00000395796.7:c.1051del
ENST00000403799.7:c.1054del
ENST00000437084.1:c.1003del
ENST00000459642.1:n.434del
ENST00000473353.1:n.352del
ENST00000616242.4:c.1051del
NM_000162.3:c.1054del
NM_033507.1:c.1057del
NM_033508.1:c.1051del
NM_000162.4:c.1054del
NM_001354800.1:c.1054del
NM_001354801.1:c.43del
NM_001354802.1:c.-87del
NM_001354803.1:c.88del
NM_033507.2:c.1057del

NM_033508.2:c.1051del
NM_033507.3:c.1057del
NM_033508.3:c.1051del
NM_001354803.2:c.88del

Likely Pathogenic

Met criteria codes 2

PVS1 PM2_Supporting

Not Met criteria codes 1

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.1054del variant in the glucokinase gene, GCK, results in a premature termination at codon 352 (p.Leu352Ter) of NM_000162.5. This variant, located in biologically-relevant exon 9 of 10, is predicted to lead to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1; PMID: 19790256). This variant is absent in gnomAD v2.1.1 (PM2_Supporting). 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.1054del 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): PVS1, PM2_supporting.

Met criteria codes

PVS1	✔	This variant, located in biologically-relevant exon 9 of 10, is predicted to lead to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1; PMID: 19790256).
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).

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.