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.1113C>A (p.Cys371Ter)

Version: 1.0

CA367398930

617645 (ClinVar)

Gene: GCK (HGNC:2645)
Condition: monogenic diabetes (MONDO:0015967)
Inheritance Mode: Semidominant inheritance
UUID: d3ce12e9-9571-487e-9837-de8a67580d76
Approved on: 2023/8/9
Published on: 2023/8/10

HGVS expressions

NM_000162.5:c.1113C>A
NM_000162.5(GCK):c.1113C>A (p.Cys371Ter)
NC_000007.14:g.44145637G>T
CM000669.2:g.44145637G>T
NC_000007.13:g.44185236G>T
CM000669.1:g.44185236G>T
NC_000007.12:g.44151761G>T
NG_008847.1:g.48787C>A
NG_008847.2:g.57534C>A
ENST00000395796.8:c.*1111C>A
ENST00000616242.5:c.*233C>A
ENST00000683378.1:n.339C>A
ENST00000336642.9:c.147C>A
ENST00000345378.7:c.1116C>A
ENST00000403799.8:c.1113C>A
ENST00000671824.1:c.1176C>A
ENST00000672743.1:n.125C>A
ENST00000673284.1:c.1113C>A
ENST00000336642.8:c.165C>A
ENST00000345378.6:c.1116C>A
ENST00000395796.7:c.1110C>A
ENST00000403799.7:c.1113C>A
ENST00000437084.1:c.1062C>A
ENST00000459642.1:n.493C>A
ENST00000616242.4:c.1110C>A
NM_000162.3:c.1113C>A
NM_033507.1:c.1116C>A
NM_033508.1:c.1110C>A
NM_000162.4:c.1113C>A
NM_001354800.1:c.1113C>A
NM_001354801.1:c.102C>A
NM_001354802.1:c.-28C>A
NM_001354803.1:c.147C>A
NM_033507.2:c.1116C>A
NM_033508.2:c.1110C>A
NM_033507.3:c.1116C>A
NM_033508.3:c.1110C>A

NM_001354803.2:c.147C>A

Pathogenic

Met criteria codes 3

PVS1 PP4_Moderate PM2_Supporting

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 1.0.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Monogenic Diabetes VCEP

The c.1113C>A variant in the glucokinase gene, GCK, results in a premature termination at codon 371 (p.(Cys371Ter)) of NM_000162.5. This variant, located in biologically-relevant exon 9/10, is predicted to lead to nonsense-mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). 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 antibodies) (PP4_Moderate; internal lab contributors). In summary, this variant meets the criteria to be classified as pathogenic for monogenic diabetes. ACMG/AMP criteria applied, as specified by the ClinGen MDEP VCEP (specification version 1.2.0, approved 6/7/2023): PVS1, PM2_Supporting, PP4_Moderate.

Met criteria codes

PVS1	✔	This variant, located in biologically-relevant exon 9/10, is predicted to lead to nonsense-mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
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 antibodies) (PP4_Moderate; internal lab contributors).
PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).

Curation History

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