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.392C>A

Version: 1.0

CA367396876

3024416 (ClinVar)

Gene: GCK (HGNC:2645)
Condition: monogenic diabetes (MONDO:0015967)
Inheritance Mode: Semidominant inheritance
UUID: b9e09be9-ed98-4fb5-924d-48c6fdf61bb0
Approved on: 2023/7/29
Published on: 2023/7/29

HGVS expressions

NM_001354803.2:c.392C>A
NC_000007.14:g.44145176G>T
CM000669.2:g.44145176G>T
NC_000007.13:g.44184775G>T
CM000669.1:g.44184775G>T
NC_000007.12:g.44151300G>T
NG_008847.1:g.49248C>A
NG_008847.2:g.57995C>A
ENST00000395796.8:c.*1356C>A
ENST00000616242.5:c.*478C>A
ENST00000683378.1:n.584C>A
ENST00000336642.9:c.392C>A
ENST00000345378.7:c.1361C>A
ENST00000403799.8:c.1358C>A
ENST00000671824.1:c.1421C>A
ENST00000672743.1:n.370C>A
ENST00000673284.1:c.1358C>A
ENST00000336642.8:c.410C>A
ENST00000345378.6:c.1361C>A
ENST00000395796.7:c.1355C>A
ENST00000403799.7:c.1358C>A
ENST00000437084.1:c.1307C>A
ENST00000459642.1:n.738C>A
ENST00000616242.4:c.1355C>A
NM_000162.3:c.1358C>A
NM_033507.1:c.1361C>A
NM_033508.1:c.1355C>A
NM_000162.4:c.1358C>A
NM_001354800.1:c.1358C>A
NM_001354801.1:c.347C>A
NM_001354802.1:c.218C>A
NM_001354803.1:c.392C>A
NM_033507.2:c.1361C>A
NM_033508.2:c.1355C>A
NM_000162.5:c.1358C>A
NM_033507.3:c.1361C>A
NM_033508.3:c.1355C>A

Likely Pathogenic

Met criteria codes 2

PVS1 PM2_Supporting

Not Met criteria codes 2

PS4 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.1358C>A variant in the glucokinase gene, GCK, results in a premature termination at codon 453 (p.(Ser453Ter)) 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; PMID: 19790256). Additionally, this variant is absent from gnomAD v2.1.1 (PM2_Supporting). This variant was identified in an individual with diabetes/hyperglycemia; however, PP4 could not be assessed due to lack of clinical information (PMID: 11508276, per author the variant was mistakenly published as Ser452X). In summary, the c.1358C>A variant meets the criteria to be classified as likely pathogenic for monogenic diabetes. ACMG/AMP criteria applied, as specified by the ClinGen MDEP (specification version 1.2.0, approved 6/7/2023): PVS1, PM2_Supporting.

Met criteria codes

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; PMID: 19790256).
PM2_Supporting	✔	Absent in gnomAD v2.1.1 (PM2_Supporting).

Not Met criteria codes

PS4	✖	Identified in one family (PMID: 11508276, published as Ser452X)
PP4	✖	This variant was identified in an individual with diabetes/hyperglycemia; however, PP4 could not be assessed due to lack of clinical information (PMID: 11508276).

Curation History

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