

*Variant: NM\_001354803.2:c.402del*

Version: 1.0

CA2017997779 [↗](#)

2571663 (ClinVar) [↗](#)

**Gene:** GCK (HGNC:2645)

**Condition:** monogenic diabetes (MONDO:0015967)

**Inheritance Mode:** Semidominant inheritance

**UUID:** 8c1172cd-9ba7-4c5e-8711-2c33aa4ac895

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### *HGVS expressions*

**NM\_001354803.2:c.402del**  
NC\_000007.14:g.44145167del  
CM000669.2:g.44145167del  
NC\_000007.13:g.44184766del  
CM000669.1:g.44184766del  
NC\_000007.12:g.44151291del  
NG\_008847.1:g.49258del  
NG\_008847.2:g.58005del  
ENST00000395796.8:c.\*1366del  
ENST00000616242.5:c.\*488del  
ENST00000683378.1:n.594del  
ENST00000336642.9:c.402del  
ENST00000345378.7:c.1371del  
ENST00000403799.8:c.1368del  
ENST00000671824.1:c.1431del  
ENST00000672743.1:n.380del  
ENST00000673284.1:c.1368del  
ENST00000336642.8:c.420del  
ENST00000345378.6:c.1371del  
ENST00000395796.7:c.1365del  
ENST00000403799.7:c.1368del  
ENST00000437084.1:c.1317del  
ENST00000459642.1:n.748del  
ENST00000616242.4:c.1365del  
NM\_000162.3:c.1368del  
NM\_033507.1:c.1371del  
NM\_033508.1:c.1365del  
NM\_000162.4:c.1368del  
NM\_001354800.1:c.1368del  
NM\_001354801.1:c.357del  
NM\_001354802.1:c.228del  
NM\_001354803.1:c.402del  
NM\_033507.2:c.1371del  
NM\_033508.2:c.1365del  
NM\_000162.5:c.1368del  
NM\_033507.3:c.1371del  
NM\_033508.3:c.1365del

Likely Pathogenic

Met criteria codes **2**

PM2\_Supporting PVS1

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.1368del variant in the glucokinase gene, GCK, causes a frameshift in the protein at codon 457 (NM\_000545.6), adding 157 novel amino acids before encountering a stop codon (p.(Cys457Valfs157)). This variant, located in exon 10 of 10, is predicted to cause loss of a stop codon and result in an elongated protein. The additional residues are expected to cause improper folding, resulting in loss of function in a gene in which loss-of-function is an established disease mechanism (PVS1; PMID 19790256). This variant is absent from gnomAD 2.1.1 (PM2\_Supporting). In summary, c.1368del 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

PM2_Supporting	<a href="#">i</a>	✓	Absent in gnomAD
PVS1	<a href="#">i</a>	✓	This variant, located in exon 10 of 10, is predicted to cause loss of a stop codon and result in an elongated protein. The additional residues are expected to cause improper folding, resulting in loss of function in a gene in which loss-of-function is an established disease mechanism (PVS1; PMID 19790256).

#### Not Met criteria codes

PS4	<a href="#">i</a>	✗	One case by internal lab contributor, no clinical information provided
PP4	<a href="#">i</a>	✗	No case-level information provided

Curation History [↗](#)

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