

Variant: *NM_000162.5(GCK):c.1285A>C (p.Arg429=)*

Version: 1.0

CA213745 [↗](#)

36192 (ClinVar) [↗](#)

Gene: GCK ([HGNC:2645](#))

Condition: monogenic diabetes ([MONDO:0015967](#))

Inheritance Mode: Semidominant inheritance

UUID: d79afd5b-fa4f-4521-a81c-e231b58460a6

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HGVS expressions

NM_000162.5:c.1285A>C

NM_000162.5(GCK):c.1285A>C (p.Arg429=)

NC_000007.14:g.44145249T>G

CM000669.2:g.44145249T>G

NC_000007.13:g.44184848T>G

CM000669.1:g.44184848T>G

NC_000007.12:g.44151373T>G

NG_008847.1:g.49175A>C

NG_008847.2:g.57922A>C

ENST00000395796.8:c.*1283A>C

ENST00000616242.5:c.*405A>C

ENST00000683378.1:n.511A>C

ENST00000336642.9:c.319A>C

ENST00000345378.7:c.1288A>C

ENST00000403799.8:c.1285A>C

ENST00000671824.1:c.1348A>C

ENST00000672743.1:n.297A>C

ENST00000673284.1:c.1285A>C

ENST00000336642.8:c.337A>C

ENST00000345378.6:c.1288A>C

ENST00000395796.7:c.1282A>C

ENST00000403799.7:c.1285A>C

ENST00000437084.1:c.1234A>C

ENST00000459642.1:n.665A>C

ENST00000616242.4:c.1282A>C

NM_000162.3:c.1285A>C

NM_033507.1:c.1288A>C

NM_033508.1:c.1282A>C

NM_000162.4:c.1285A>C

NM_001354800.1:c.1285A>C

NM_001354801.1:c.274A>C

NM_001354802.1:c.145A>C

NM_001354803.1:c.319A>C

NM_033507.2:c.1288A>C

NM_033508.2:c.1282A>C

NM_033507.3:c.1288A>C

NM_033508.3:c.1282A>C

Likely Benign

Met criteria codes 3

BP7 BP4 BP2

Not Met criteria codes 4

PS4 BA1 PM2 BS1

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 1.1.0](#)
- [Criteria Specification Approval History](#)
- [Criteria Specifications for this VCEP](#)

Evidence submitted by expert panel

Monogenic Diabetes VCEP

The c.1285A>C variant in the glucokinase gene, GCK, is a synonymous (silent) variant at codon 429 (p.(Arg429=)) of NM_000162.5. The Popmax filtering frequency of the c.1285A>C variant in gnomAD v2.1.1 is 0.000007310, which falls between ClinGen MDEP-established cutoffs for PM2_Supporting and BS1; thus, neither criterion will be applied. This variant is not predicted by SpliceAI to impact splicing (SpliceAI score less than the MDEP cutoff of 0.2) and is not highly conserved (phyloP100way score of -0.068, which is below the MDEP cutoff of 2.0) (BP4, BP7). This variant has been observed in unknown phase with the variant c.106C>T p.Arg36Trp, which is classified as likely pathogenic by the ClinGen MDEP (BP2). In summary, c.1285A>C meets the criteria to be classified as likely benign for monogenic diabetes. ACMG/AMP criteria applied, as specified by the ClinGen MDEP VCEP (specification version 1.2, approved 6/7/2023): BP2, BP4, BP7.

Met criteria codes

BP7	i	✓	No impact on splicing based on SpliceAI, Δ score below 0.2 and phyloP100 way <2.0. (-0.068).
BP4	i	✓	SpliceAI score of 0.1 for Acceptor loss, 0.03 for Acceptor gain, which is below the MDEP cutoff of 0.2.
BP2	i	✓	This variant has been observed in unknown phase with the variant c.106C>T p.Arg36Trp, which is classified as likely pathogenic by the ClinGen MDEP (BP2).

Not Met criteria codes

PS4	i	✗	No PS4 at any level if not met PM2_Supporting.
BA1	i	✗	gnomAD popmax filtering AF=0.000007310 <0.0001
PM2		✗	The Popmax frequency of the c.1285A>C variant in gnomAD v2.1.1 is 0.000007310, which falls between ClinGen MDEP-established cutoffs for PM2_Supporting and BS1; thus, neither criterion will be applied.

BS1

gnomAD popmax filtering AF=0.000007310 <0.00004

Curation History [↗](#)

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