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Variant: NM_033508.3:c.1007A>C

Version: 2.0

CA367399714

3602116 (ClinVar)

Gene: GCK (HGNC:2645)
Condition: monogenic diabetes (MONDO:0015967)
Inheritance Mode: Semidominant inheritance
UUID: a0bc2ca7-34c3-45dd-939a-f747245041ac
Approved on: 2026/8/17
Published on: 2026/9/1

HGVS expressions

NM_033508.3:c.1007A>C
NC_000007.14:g.44146472T>G
CM000669.2:g.44146472T>G
NC_000007.13:g.44186071T>G
CM000669.1:g.44186071T>G
NC_000007.12:g.44152596T>G
NG_008847.1:g.47952A>C
NG_008847.2:g.56699A>C
ENST00000395796.8:c.*1008A>C
ENST00000616242.5:c.*130A>C
ENST00000683378.1:n.236A>C
ENST00000345378.7:c.1013A>C
ENST00000403799.8:c.1010A>C
ENST00000671824.1:c.1073A>C
ENST00000673284.1:c.1010A>C
ENST00000345378.6:c.1013A>C
ENST00000395796.7:c.1007A>C
ENST00000403799.7:c.1010A>C
ENST00000437084.1:c.959A>C
ENST00000473353.1:n.308A>C
ENST00000616242.4:c.1007A>C
NM_000162.3:c.1010A>C
NM_033507.1:c.1013A>C
NM_033508.1:c.1007A>C
NM_000162.4:c.1010A>C
NM_001354800.1:c.1010A>C
NM_001354801.1:c.8+147A>C
NM_033507.2:c.1013A>C
NM_033508.2:c.1007A>C
NM_000162.5:c.1010A>C
NM_033507.3:c.1013A>C

Pathogenic

Met criteria codes 6

PP1 PP2 PP3 PS4 PP4_Moderate PM2_Supporting

Expert Panel

Monogenic Diabetes VCEP

Not Met criteria codes 1

PM1

Evidence Links 0

Criteria Specification Information

Criteria Specification: *ClinGen Monogenic Diabetes Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GCK Version 3.1*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Monogenic Diabetes VCEP

The c.1010A>C variant in the glucokinase gene, GCK, causes an amino acid change of glutamine to proline at codon 337 (p.(Gln337Pro)) of NM_000162.5. GCK is defined by the ClinGen MDEP as a gene that has a low rate of benign missense variation and has pathogenic missense variants as a common mechanism of disease (PP2). This variant is absent from gnomAD v2.1.1 and v4.1 (PM2_Supporting). This variant is predicted to be deleterious by computational evidence, with a REVEL score of 0.914, which is greater than the MDEP VCEP threshold of 0.70 (PP3). This variant was identified in ten unrelated individuals with hyperglycemia (PS4; PMIDs: 24918535, 36257325, 19790256, and internal lab contributors). Furthermore, one of these individuals had a clinical history highly specific for GCK-hyperglycemia (fasting glucose 5.5-8 mmol/L and HbA1c 5.6 - 7.6% and negative antibodies) (PP4_Moderate; internal lab contributors). This variant segregated with diabetes with two informative meioses in two families (PP1; PMID: 36257325, internal lab contributors). In summary, c.1010A>C meets the criteria to be classified as pathogenic for monogenic diabetes. ACMG/AMP criteria applied, as specified by the ClinGen MDEP (specification version 3.1, approved 10/10/2025): PS4, PP4_Moderate, PM2_Supporting, PP1, PP2, PP3.

Met criteria codes

PP1	✔	This variant segregated with diabetes with two informative meioses in two families (PP1; PMID: 36257325, internal lab contributors).
PP2	✔	GCK is defined by the ClinGen MDEP as a gene that has a low rate of benign missense variation and has pathogenic missense variants as a common mechanism of disease (PP2).
PP3	✔	This variant is predicted to be deleterious by computational evidence, with a REVEL score of 0.914, which is greater than the MDEP VCEP threshold of 0.70 (PP3).
PS4	✔	This variant was identified in ten unrelated individuals with hyperglycemia (PS4; PMIDs: 24918535, 36257325, 19790256, and internal lab contributors).
PP4_Moderate	✔	This variant was identified in an individual with a clinical history highly specific for GCK-hyperglycemia (fasting glucose 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 and v4.1 (PM2_Supporting).

Not Met criteria codes

PM1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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