

Variant: NM_000162.5(GCK):c.158C>T (p.Ala53Val)

Version: 1.0

CA367403352 [↗](#)

1338576 (ClinVar) [↗](#)

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

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

Inheritance Mode: Semidominant inheritance

UUID: 6feb4022-d3d1-4e37-97db-d205be11d1dc

Approved on: 2026/7/30

Published on: 2026/7/30

HGVS expressions

NM_000162.5:c.158C>T

NM_000162.5(GCK):c.158C>T (p.Ala53Val)

NC_000007.14:g.44153351G>A

CM000669.2:g.44153351G>A

NC_000007.13:g.44192950G>A

CM000669.1:g.44192950G>A

NC_000007.12:g.44159475G>A

NG_008847.1:g.41073C>T

NG_008847.2:g.49820C>T

ENST00000395796.8:c.*156C>T

ENST00000616242.5:c.158C>T

ENST00000682635.1:n.644C>T

ENST00000345378.7:c.161C>T

ENST00000403799.8:c.158C>T

ENST00000671824.1:c.158C>T

ENST00000673284.1:c.158C>T

ENST00000345378.6:c.161C>T

ENST00000395796.7:c.155C>T

ENST00000403799.7:c.158C>T

ENST00000437084.1:c.158C>T

ENST00000616242.4:c.155C>T

NM_000162.3:c.158C>T

NM_033507.1:c.161C>T

NM_033508.1:c.155C>T

NM_000162.4:c.158C>T

NM_001354800.1:c.158C>T

NM_033507.2:c.161C>T

NM_033508.2:c.155C>T

NM_033507.3:c.161C>T

NM_033508.3:c.155C>T

Pathogenic

Met criteria codes 6

PM2_SupportingPP2PP3PP4_ModeratePS4PP1_Strong

Not Met criteria codes 1

PM1

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 3.1

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Monogenic Diabetes VCEP		
<p>The c.158C>T variant in the glucokinase gene, GCK, causes an amino acid change of alanine to valine at codon 53 (p.(Ala53Val)) 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). The computational splicing predictor SpliceAI gives a score of 0.95 for donor gain, predicting that the variant variant disrupts the donor site of intron 2 of GCK (PP3). This variant has an incomputable gnomAD v4.1.0 Grpmax filtering allele frequency due to one copy in the European non-Finnish subpopulation and no copy in any other subpopulation, thereby meeting the ClinGen MDEP threshold criteria for PM2_Supporting (Grpmax FAF <= 0.000003) (PM2_Supporting). This variant was identified in 11 unrelated individuals with hyperglycemia (PS4; ClinVar: 1338576, PMIDs: 36257325, 19790256, internal lab contributors). This variant segregated with hyperglycemia, with at least four informative meioses in three families with MODY (PP1_Strong; internal lab contributors). 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 pediatric patient (prepubertal or <10 years)) (PP4_Moderate; internal lab contributors). In summary, c.158C>T meets the criteria to be classified as pathogenic for monogenic diabetes. ACMG/AMP criteria applied, as specified by the ClinGen MDEP (specification version 3.1.0, approved 10/10/2025): PS4, PP4_Moderate, PP1_Strong, PM2_Supporting, PP2, PP3.</p>		
Met criteria codes		
PM2_Supporting	<div><div></div><div></div></div>	This variant has an incomputable gnomAD v4.1.0 Grpmax filtering allele frequency due to one copy in the European non-Finnish subpopulation and no copy in any other subpopulation, thereby meeting the ClinGen MDEP threshold criteria for PM2_Supporting (Grpmax FAF <= 0.000003) (PM2_Supporting).
PP2	<div><div></div><div></div></div>	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	<div><div></div><div></div></div>	The computational splicing predictor SpliceAI gives a score of 0.95 for donor gain, predicting that the variant variant disrupts the donor site of intron 2 of GCK (PP3).
PP4_Moderate	<div><div></div><div></div></div>	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 pediatric patient (prepubertal or <10 years)) (PP4_Moderate; internal lab contributors]).
PS4	<div><div></div><div></div></div>	This variant was identified in 11 unrelated individuals with hyperglycemia (PS4; ClinVar: 1338576, PMIDs: 36257325, 19790256, internal lab contributors).
PP1_Strong	<div><div></div><div></div></div>	



This variant segregated with hyperglycemia, with at least four informative meioses in three families with MODY (PP1_Strong; internal lab contributors).

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

▼

▼

Showing 1 to 1 of 1 rows

--

The information on this website is not intended for direct diagnostic use or medical decision-making without review by a genetics professional. Individuals should not change their health behavior solely on the basis of information contained on this website. If you have questions about the information contained on this website, please see a health care professional.