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Variant: NM_000162.5(GCK):c.371A>T (p.Asp124Val)

Version: 1.0

CA367402205

522504 (ClinVar)

Gene: GCK (HGNC:2645)
Condition: monogenic diabetes (MONDO:0015967)
Inheritance Mode: Semidominant inheritance
UUID: 180e8e42-c11a-4d3a-938c-f9470b35a42b
Approved on: 2024/3/14
Published on: 2024/3/14

HGVS expressions

NM_000162.5:c.371A>T
NM_000162.5(GCK):c.371A>T (p.Asp124Val)
NC_000007.14:g.44151068T>A
CM000669.2:g.44151068T>A
NC_000007.13:g.44190667T>A
CM000669.1:g.44190667T>A
NC_000007.12:g.44157192T>A
NG_008847.1:g.43356A>T
NG_008847.2:g.52103A>T
ENST00000395796.8:c.*369A>T
ENST00000616242.5:c.371A>T
ENST00000682635.1:n.857A>T
ENST00000345378.7:c.374A>T
ENST00000403799.8:c.371A>T
ENST00000671824.1:c.371A>T
ENST00000673284.1:c.371A>T
ENST00000345378.6:c.374A>T
ENST00000395796.7:c.368A>T
ENST00000403799.7:c.371A>T
ENST00000437084.1:c.364-44A>T
ENST00000616242.4:c.368A>T
NM_000162.3:c.371A>T
NM_033507.1:c.374A>T
NM_033508.1:c.368A>T
NM_000162.4:c.371A>T
NM_001354800.1:c.371A>T
NM_033507.2:c.374A>T
NM_033508.2:c.368A>T
NM_033507.3:c.374A>T
NM_033508.3:c.368A>T

Uncertain Significance

Met criteria codes 4

PM2_Supporting PP2 PP3 PM5

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 1.3.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Monogenic Diabetes VCEP

The c.371A>T variant in the glucokinase gene, GCK, causes an amino acid change of aspartate to valine at codon 124 (p.(Asp124Val)) 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 predicted to be deleterious by computational evidence, with a REVEL score of 0.986, which is greater than the MDEP VCEP threshold of 0.70 (PP3). This variant is absent from gnomAD v2.1.1 (PM2_Supporting). Another missense variant, c.370G>A, p.(Asp124Asn) has been interpreted as pathogenic by the ClinGen MDEP, and p.(Asp124Val) has a greater Grantham distance (PM5). In summary, c.449T>C meets the criteria to be classified as uncertain significance for monogenic diabetes. ACMG/AMP criteria applied, as specified by the ClinGen MDEP (specification version 1.3.0 approved 8/11/2023): PM5, PP2, PP3, PM2_Supporting.

Met criteria codes

PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting). absent from gnomAD v4.0.0
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 0.986, which is greater than the MDEP VCEP threshold of 0.70 (PP3).
PM5	✔	Another missense variant, c.370G>A, p.(Asp124Asn) has been interpreted as pathogenic by the ClinGen MDEP, and p.(Asp124Val) has a greater Grantham distance (PM5).

Curation History

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