

Variant: *NM_000180.4(GUCY2D):c.1236C>T (p.Asp412=)*

Version: 1.0

CA226041 [↗](#)

98539 (ClinVar) [↗](#)

Gene: GUCY2D ([HGNC:3000](#))

Condition: GUCY2D-related recessive retinopathy ([MONDO:0100453](#))

Inheritance Mode: Autosomal recessive inheritance

UUID: 45f6975c-bff9-4f3a-a3d7-620d7df1e15e

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HGVS expressions

NM_000180.4(GUCY2D):c.1236C>T (p.Asp412=)

NM_000180.4:c.1236C>T

NC_000017.11:g.8006572C>T

CM000679.2:g.8006572C>T

NC_000017.10:g.7909890C>T

CM000679.1:g.7909890C>T

NC_000017.9:g.7850615C>T

NG_009092.1:g.8903C>T

ENST00000254854.5:c.1236C>T

ENST00000254854.4:c.1236C>T

NM_000180.3:c.1236C>T

Likely Benign

Met criteria codes **2**

BP7 BP4

Not Met criteria codes **2**

PM2 BS1

Evidence Links **0**

Expert Panel

[Leber Congenital Amaurosis/early onset Retinal Dystrophy VCEP](#) [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** *ClinGen Leber Congenital Amaurosis/early onset Retinal Dystrophy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GUCY2D Version 1.0.0*

[↗](#) **Criteria Specification Approval History**

[↗](#) **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Leber Congenital Amaurosis/early onset Retinal Dystrophy VCEP

NM_000180.4(GUCY2D):c.1236C>T (p.Asp412=) is a synonymous variant in exon 4 of 20. This variant is present in gnomAD v4.1.0 at a total allele frequency of 0.001028 with 1659 alleles / 1,613,498 total alleles, which is higher than the ClinGen LCA/eoRD VCEP PM2_Supporting threshold of <0.0004 and fails to meet this criterion. This variant has a Grpmax allele frequency of 0.001233, with 1519 alleles / 1180008 total alleles in the European (non-Finnish) population, which is lower than the ClinGen LCA/eoRD VCEP BS1 threshold of >0.0016 and fails to meet this criterion as well. The computational predictor REVEL has no data as this is a synonymous variant. The splicing impact predictor SpliceAI gives a delta score of 0, which is below the ClinGen LCA/eoRD VCEP recommended threshold of <0.1 and does not

predict an impact on splicing (BP4, BP7). In summary, this variant meets the criteria to be classified as Likely Benign for GUCY2D-related recessive retinopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen LCA/eoRD VCEP: BP4, BP7. (VCEP specifications version 1.0.0; date of approval 01/22/2025).

Met criteria codes

BP7			The splicing impact predictor SpliceAI gives a delta score of 0.00, which is below the ClinGen LCA / eoRD VCEP recommended threshold of <0.1 and does not predict an impact on splicing (BP7).
BP4			The computational predictor REVEL has no data as this is a synonymous variant. The splicing impact predictor SpliceAI gives a delta score of 0, which is below the ClinGen LCA/eoRD VCEP recommended threshold of <0.1 and does not predict an impact on splicing (BP4).

Not Met criteria codes

PM2			This variant is present in gnomAD v.4.1.0 at a total allele frequency of 0.001028 with 1659 alleles / 1,613,498 total alleles, which is higher than the ClinGen LCA/eoRD VCEP PM2_Supporting threshold of <0.0004 and fails to meet this criterion.
BS1			This variant is present in gnomAD v.4.1.0 at a Grpmax frequency of 0.001233 with 1519 alleles / 1180008 total alleles in the European (non-Finnish) population, which is lower than the ClinGen LCA/eoRD VCEP BS1 threshold of >0.0016 and fails to meet this criterion.

Curation History



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