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Variant: NM_000180.4(GUCY2D):c.2577G>T (p.Pro859=)

Version: 1.0

CA201118

194323 (ClinVar)

Gene: GUCY2D (HGNC:3000)
Condition: GUCY2D-related recessive retinopathy (MONDO:0100453)
Inheritance Mode: Autosomal recessive inheritance
UUID: cefe2555-c84b-4da1-82ed-0ec80d60c9ba
Approved on: 2025/1/30
Published on: 2025/1/30

HGVS expressions

NM_000180.4(GUCY2D):c.2577G>T (p.Pro859=)
NM_000180.4:c.2577G>T
NC_000017.11:g.8014859G>T
CM000679.2:g.8014859G>T
NC_000017.10:g.7918177G>T
CM000679.1:g.7918177G>T
NC_000017.9:g.7858902G>T
NG_009092.1:g.17190G>T
ENST00000254854.5:c.2577G>T
ENST00000254854.4:c.2577G>T
NM_000180.3:c.2577G>T

Benign

Met criteria codes 3

BS2 BP4 BA1

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

The NM_000180.4(GUCY2D):c.2577G>T (p.Pro859=) variant is located at the first base of exon 14 and does not alter the amino acid (proline) at position p.859. The splicing impact predictor SpliceAI gives a delta score of 0.03, which is below the ClinGen LCA/eoRD VCEP recommended threshold of <0.1 and does not predict an impact on splicing (BP4). This variant is present in gnomAD v.4.1.0 at a GrpMax allele frequency of 0.04139, with 3871 alleles / 91074 total alleles in the South Asian population, which is higher than the ClinGen LCA / eoRD VCEP BA1 threshold of >0.016 (BA1). This variant has been found in the homozygous state in 141 adult individuals in gnomAD which exceeds the LCA/eoRD VCEP threshold of ≥6 (gnomAD version 4.1.0; BS2). In summary, this variant meets the criteria to be classified as

Benign for GUCY2D-related recessive retinopathy based on the ACMG/AMP criteria applied, as specified by the ClinGen LCA/eoRD VCEP: BA1, BS2, BP4. (VCEP specifications version 1.0.0; date of approval 01/22/2025).

Met criteria codes

BS2	✔	This variant has been found in the homozygous state in 141 adult individuals in gnomAD which exceeds the LCA/eoRD VCEP threshold of ≥6 (gnomAD version 4.1.0; BS2)
BP4	✔	The splicing impact predictor SpliceAI gives a delta score of 0.03, which is below the ClinGen LCA / eoRD VCEP recommended threshold of <0.1 and does not predict an impact on splicing (BP4).
BA1	✔	This variant is present in gnomAD v.4.1.0 at a GrpMax allele frequency of 0.04139, with 3871 alleles / 91074 total alleles in the South Asian population, which is higher than the ClinGen LCA / eoRD VCEP BA1 threshold of >0.016 (BA1).

Curation History

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