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Variant: NM_001165963.4(SCN1A):c.4910T>C (p.Val1637Ala)

Version: 1.0

CA349070310

1008671 (ClinVar)

Gene: SCN1A (HGNC:6323)
Condition: generalized epilepsy with febrile seizures plus (MONDO:0018214)
Inheritance Mode: Autosomal dominant inheritance
UUID: cfd01a95-6f29-41fe-b4b2-e953dc667afb
Approved on: 2026/2/24
Published on: 2026/7/28

HGVS expressions

NM_001165963.4(SCN1A):c.4910T>C (p.Val1637Ala)
NM_001165963.4:c.4910T>C
NC_000002.12:g.165992365A>G
CM000664.2:g.165992365A>G
NC_000002.11:g.166848875A>G
CM000664.1:g.166848875A>G
NC_000002.10:g.166557121A>G
NG_011906.1:g.86275T>C
ENST00000689288.1:c.*2946T>C
ENST00000303395.9:c.4910T>C
ENST00000635750.1:c.4877T>C
ENST00000635776.1:c.*1743T>C
ENST00000636194.1:c.*2403T>C
ENST00000637038.1:c.1772T>C
ENST00000637988.1:c.4877T>C
ENST00000640036.1:c.4877T>C
ENST00000641575.1:c.4874T>C
ENST00000641603.1:c.4628T>C
ENST00000641996.1:c.*4464T>C
ENST00000671940.1:c.*2853T>C
ENST00000673490.1:n.7383T>C
ENST00000674923.1:c.4910T>C
ENST00000303395.8:c.4910T>C
ENST00000375405.7:c.4877T>C
ENST00000409050.1:c.4826T>C
ENST00000423058.6:c.4910T>C
NM_001165963.1:c.4910T>C
NM_001165964.1:c.4826T>C
NM_001202435.1:c.4910T>C
NM_006920.4:c.4877T>C
NR_110598.1:n.176-23248A>G
NM_001165963.2:c.4910T>C
NM_001165964.2:c.4826T>C
NM_001202435.2:c.4910T>C
NM_001353948.1:c.4910T>C

NM_001353949.1:c.4877T>C
NM_001353950.1:c.4877T>C
NM_001353951.1:c.4877T>C
NM_001353952.1:c.4877T>C
NM_001353954.1:c.4874T>C
NM_001353955.1:c.4874T>C
NM_001353957.1:c.4826T>C
NM_001353958.1:c.4826T>C
NM_001353960.1:c.4823T>C
NM_001353961.1:c.2468T>C
NM_006920.5:c.4877T>C
NR_148667.1:n.5346T>C
NM_001165963.3:c.4910T>C
NM_001165964.3:c.4826T>C
NM_001202435.3:c.4910T>C
NM_001353948.2:c.4910T>C
NM_001353949.2:c.4877T>C
NM_001353950.2:c.4877T>C
NM_001353951.2:c.4877T>C
NM_001353952.2:c.4877T>C
NM_001353954.2:c.4874T>C
NM_001353955.2:c.4874T>C
NM_001353957.2:c.4826T>C
NM_001353958.2:c.4826T>C
NM_001353960.2:c.4823T>C
NM_001353961.2:c.2468T>C
NM_006920.6:c.4877T>C
NR_148667.2:n.5327T>C

Likely Pathogenic

Met criteria codes 4

PM2_Supporting PM1 PM5_Supporting PP3_Moderate

Not Met criteria codes 1

PS4

Evidence Links 0

Expert Panel

Epilepsy Sodium Channel VCEP

Criteria Specification Information

Criteria Specification: *ClinGen Epilepsy Sodium Channel Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for SCN1A Version 2.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Epilepsy Sodium Channel VCEP

The c.4910T>C variant in SCN1A is a missense variant predicted to cause substitution of Valine by Alanine at amino acid 1637 (p.Val1637Ala). This variant was seen in 1/1179806 alleles in the European (non-Finnish) population v4.1.0, meeting this criterion (PM2_Supporting) and resides within a region of SCN1A that is defined as a mutational hotspot and/or critical functional domain by the ClinGen Epilepsy Sodium Channel VCEP (PM1). The computational predictor REVEL gives a score of 0.954, which is above the threshold of 0.773, evidence that correlates with impact to SCN1A function (PP3_moderate). Novel missense change at an amino acid residue where a different missense change determined to be likely pathogenic, SCN1A c.4910T>A (p.Val1637Glu), has been seen before (PM5_supporting).

This variant has been identified in one individual who was referred under a cardiology-related indication (Invitae/Labcorp internal data). As we cannot rule out that the patient has an undisclosed neurological clinical phenotype, PS4 is not met. In summary, this variant meets the criteria to be classified as likely pathogenic for autosomal dominant generalized epilepsy with febrile seizures plus based on the ACMG/AMP criteria applied, as specified by the ClinGen Epilepsy Sodium Channel VCEP: PM1, PM5_supporting, PP3_moderate, PM2_supporting. (Version 2.0.0; approved 02/24/2026).

Met criteria codes

PM2_Supporting	✔	This variant was seen in 1/1179806 alleles in the European (non-Finnish) population v4.1.0, meeting this criterion (PM2_Supporting).
PM1	✔	Located in Pathogenic Enriched Region (PER)
PM5_Supporting	✔	Novel missense change at an amino acid residue where a different missense change determined to be Likely Pathogenic, SCN1A c.4910T>A (p.Val1637Glu), has been seen before.
PP3_Moderate	✔	Revel= 0.954

Not Met criteria codes

PS4	✖	This variant has been identified in one individual who was referred under a cardiology-related indication (Invitae/Labcorp internal data). Cannot rule out that the patient has an undisclosed neurological clinical phenotype, therefore PS4 not met.

Curation History

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