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Variant: NM_001165963.4(SCN1A):c.4910T>A (p.Val1637Glu)

Version: 1.0

CA219781

68640 (ClinVar)

Gene: SCN1A (HGNC:6323)
Condition: Dravet syndrome (MONDO:0100135)
Inheritance Mode: Autosomal dominant inheritance
UUID: 4e87a3f4-bb0d-4367-ae52-6c1fa5921bb5
Approved on: 2026/2/24
Published on: 2026/7/28

HGVS expressions

NM_001165963.4(SCN1A):c.4910T>A (p.Val1637Glu)
NM_001165963.4:c.4910T>A
NC_000002.12:g.165992365A>T
CM000664.2:g.165992365A>T
NC_000002.11:g.166848875A>T
CM000664.1:g.166848875A>T
NC_000002.10:g.166557121A>T
NG_011906.1:g.86275T>A
ENST00000689288.1:c.*2946T>A
ENST00000303395.9:c.4910T>A
ENST00000635750.1:c.4877T>A
ENST00000635776.1:c.*1743T>A
ENST00000636194.1:c.*2403T>A
ENST00000637038.1:c.1772T>A
ENST00000637988.1:c.4877T>A
ENST00000640036.1:c.4877T>A
ENST00000641575.1:c.4874T>A
ENST00000641603.1:c.4628T>A
ENST00000641996.1:c.*4464T>A
ENST00000671940.1:c.*2853T>A
ENST00000673490.1:n.7383T>A
ENST00000674923.1:c.4910T>A
ENST00000303395.8:c.4910T>A
ENST00000375405.7:c.4877T>A
ENST00000409050.1:c.4826T>A
ENST00000423058.6:c.4910T>A
NM_001165963.1:c.4910T>A
NM_001165964.1:c.4826T>A
NM_001202435.1:c.4910T>A
NM_006920.4:c.4877T>A
NR_110598.1:n.176-23248A>T
NM_001165963.2:c.4910T>A
NM_001165964.2:c.4826T>A
NM_001202435.2:c.4910T>A
NM_001353948.1:c.4910T>A

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

Likely Pathogenic

Met criteria codes 4

PM1 PM6 PP3_Moderate PM2_Supporting

Not Met criteria codes 1

PM5

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>A variant in SCN1A is a missense variant predicted to cause substitution of Valine by Glutamic acid at amino acid 1637 (p.Val1637Glu). This variant has been identified as a de novo occurrence with unconfirmed parental relationships in 1 individual with Dravet Syndrome (PM6; PMID 20392657). This variant is absent from gnomAD v4.1.0 (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 0.988, which is above the threshold of 0.773, evidence that correlates with impact to SCN1A function (PP3_moderate). In summary, this variant meets the criteria to be classified as likely pathogenic for autosomal dominant

Dravet syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen Epilepsy Sodium Channel VCEP: PM1, PM6, PP3_moderate, PM2_supporting. (Version 2.0.0; approved 02/24/2026).

Met criteria codes

PM1	✔	Loated in a Pathogenic Enriched Region (PER).
PM6	✔	This variant has been identified as a de novo occurrence with unconfirmed parental relationships in one individual with Dravet Syndrome (PMID 20392657).
PP3_Moderate	✔	Revel= 0.988
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0.

Not Met criteria codes

PM5	✖	There is a Pathogenic change occurring in paralogous gene SCN2A: c.4879G>A (p.Val1627Met), however two variants are required to meet PM5_supporting. There is a novel missense change at an amino acid residue where a different missense change determined to be Likely Pathogenic, SCN1A c.4910T>C (p.Val1637Ala). However, PM5_supporting has already been applied, therefore to avoid double counting, PM5 is not applicable here.

Curation History

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