

Variant: *NM_001330260.2(SCN8A):c.2533T>C (p.Ser845Pro)*

Version: 1.0

CA16042904 [↗](#)

373333 (ClinVar) [↗](#)

Gene: SCN8A ([HGNC:6334](#))

Condition: complex neurodevelopmental disorder ([MONDO:0100038](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 384cff6d-77c4-4955-84eb-ed960c74d6dc

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HGVS expressions

NM_001330260.2(SCN8A):c.2533T>C (p.Ser845Pro)

NM_001330260.2:c.2533T>C

NC_000012.12:g.51762665T>C

CM000674.2:g.51762665T>C

NC_000012.11:g.52156449T>C

CM000674.1:g.52156449T>C

NC_000012.10:g.50442716T>C

NG_021180.2:g.176430T>C

NG_021180.3:g.177708T>C

ENST00000354534.11:c.2533T>C

ENST00000548086.3:c.380T>C

ENST00000627620.5:c.2533T>C

ENST00000636945.2:c.537T>C

ENST00000662684.1:c.2533T>C

ENST00000668547.1:c.2533T>C

ENST00000354534.10:c.2533T>C

ENST00000355133.7:c.2533T>C

ENST00000545061.5:c.2533T>C

ENST00000550891.4:n.2661T>C

ENST00000599343.5:c.2566T>C

ENST00000627620.2:c.2533T>C

NM_001177984.2:c.2533T>C

NM_014191.3:c.2533T>C

NM_001330260.1:c.2533T>C

NM_001369788.1:c.2533T>C

NM_014191.4:c.2533T>C

NM_001177984.3:c.2533T>C

Likely Pathogenic

Met criteria codes 4

PM2_Supporting

PM1

PP3_Moderate

PM5_Supporting

Not Met criteria codes 17

BA1

BP4

BP3

BP2

BP5

BP7

BS2

BS1

BS3

PP1

PM4

Expert Panel

Epilepsy Sodium Channel VCEP [↗](#)

Criteria Specification Information

[↗](#) **Criteria Specification:** ClinGen Epilepsy Sodium Channel
Expert Panel Specifications to the ACMG/AMP Variant

Evidence submitted by expert panel

Epilepsy Sodium Channel VCEP

The NM_001330260.2:c.2533T>C variant in SCN8A is a missense variant predicted to cause substitution of serine by proline at amino acid 845 (p.Ser845Pro). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). The computational predictor REVEL gives a score of 0.960, which is above the threshold of 0.773, evidence that correlates with impact to SCN8A function (PP3_Moderate). Another missense variant (c.2534C>T (p.Ser845Phe), ClinVar Variation ID: 207109) in the same codon has been classified as likely pathogenic for autosomal dominant complex neurodevelopmental disorder by the ClinGen Epilepsy Sodium Channel VCEP (PM5_Supporting). This variant resides within a region, amino acids 844-852, of SCN8A that is defined as a mutational hotspot and/or critical functional domain by the ClinGen Epilepsy Sodium Channel VCEP (PM1). In summary, this variant meets the criteria to be classified as likely pathogenic for autosomal dominant complex neurodevelopmental disorder based on the ACMG/AMP criteria applied, as specified by the ClinGen Epilepsy Sodium Channel VCEP: PM1, PP3_Moderate, PM2_Supporting, PM5_Supporting. (VCEP specifications version 2.0.0; approved 8/26/25).

Met criteria codes

PM2_Supporting			This variant is absent from gnomAD v4.1.0 (PM2_Supporting).
PM1			This variant resides within a region, amino acids 844-852, of SCN8A that is defined as a mutational hotspot and/or critical functional domain by the ClinGen Epilepsy Sodium Channel VCEP (PM1).
PP3_Moderate			The computational predictor REVEL gives a score of 0.960, which is above the threshold of 0.773, evidence that correlates with impact to SCN8A function (PP3_Moderate).
PM5_Supporting			Another missense variant (c.2534C>T (p.Ser845Phe), ClinVar Variation ID: 207109) in the same codon has been classified as likely pathogenic for autosomal dominant complex neurodevelopmental disorder by the ClinGen Epilepsy Sodium Channel VCEP (PM5_Supporting).

Not Met criteria codes

BA1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP3			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP2			

No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline			
BP5			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BP7			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
BS3			To our knowledge, functional assays have not been reported for this variant.
PP1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PM6			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS2			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3			To our knowledge, functional assays have not been reported for this variant.
PS4			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PVS1			No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Showing 1 to 1 of 1 rows

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