Variant: NM_001040142.2(SCN2A):c.1108T>C (p.Phe370Leu)

Version: 1.0

CA349020765

1342669 (ClinVar)

Gene: SCN2A (HGNC:6326)
Condition: complex neurodevelopmental disorder (MONDO:0100038)
Inheritance Mode: Autosomal dominant inheritance
UUID: 9a095c25-848d-4cbd-9210-00f564676318
Approved on: 2024-05-09
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HGVS expressions

NM_001040142.2:c.1108T>C
NM_001040142.2(SCN2A):c.1108T>C (p.Phe370Leu)
NC_000002.12:g.165313693T>C
CM000664.2:g.165313693T>C
NC_000002.11:g.166170203T>C
CM000664.1:g.166170203T>C
NC_000002.10:g.165878449T>C
NG_008143.1:g.79292T>C
ENST00000631182.3:c.1108T>C
ENST00000375437.7:c.1108T>C
ENST00000635945.1:n.1471T>C
ENST00000636071.2:c.1108T>C
ENST00000636135.1:c.979T>C
ENST00000636384.2:c.1108T>C
ENST00000636662.2:c.*1631T>C
ENST00000636769.1:c.1108T>C
ENST00000636985.2:c.712T>C
ENST00000637266.2:c.1108T>C
ENST00000637367.1:c.*1041T>C
ENST00000638151.1:n.1192T>C
ENST00000283256.10:c.1108T>C
ENST00000375427.4:c.1108T>C
ENST00000375437.6:c.1108T>C
ENST00000424833.5:c.1108T>C
ENST00000480032.4:n.1251T>C
ENST00000631182.2:c.1108T>C
NM_001040142.1:c.1108T>C
NM_001040143.1:c.1108T>C
NM_021007.2:c.1108T>C
NM_001040143.2:c.1108T>C
NM_001371246.1:c.1108T>C
NM_001371247.1:c.1108T>C
NM_021007.3:c.1108T>C

Uncertain Significance

Met criteria codes 3

PM6_Supporting PP3_Moderate PM2_Supporting

Not Met criteria codes 1

PM1

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 SCN2A Version 1.0.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Epilepsy Sodium Channel VCEP

The c.1108C>T variant in SCN2A is a missense variant predicted to cause substitution of phenylalanine by leucine at amino acid 370 (p.Phe370Leu). The variant has been identified as a de novo occurrence with unconfirmed parental relationships in one individual with a consistent phenotype (early infantile developmental and epileptic encephalopathy) in the published literature (PMID:35431799) (PM6_Supporting). It is absent from the population database gnomAD v2.1.1 and v4.0 (PM2_Supporting). The computational predictor REVEL gives a score of 0.977, which is above the threshold of 0.773, evidence that correlates with a maximum strength of PP3_Moderate. In summary, this variant meets the criteria to be classified as a variant of uncertain significance for autosomal dominant complex neurodevelopmental disorder based on the ACMG/AMP criteria applied, as specified by the ClinGen Epilepsy Sodium Channel VCEP: PM6_Supporting, PM2_Supporting, PP3_Moderate. (version 1.0; March 26, 2024).

Met criteria codes

PM6_Supporting	✔	This variant has been reported as de novo in 1 male patient (Zeng et a, 2022; pt 11) with EIDEE. All patients in series had either epilepsy panel or trio ES, however the testing modality used for this patient was unclear, so the conservative PM6 was used (rather than PS2).
PP3_Moderate	✔	REVEL = 0.977, per UCSC genome browser
PM2_Supporting	✔	Variant is absent from gnomAD v2.1.1 and v4.0.

Not Met criteria codes

PM1	✖	Variant does not fall within a pathogenic enriched region.

Curation History

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