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Variant: NM_014191.4(SCN8A):c.615-1G>A

Version: 1.0

CA385223503

489373 (ClinVar)

Gene: SCN8A (HGNC:6334)
Condition: complex neurodevelopmental disorder (MONDO:0100038)
Inheritance Mode: Autosomal dominant inheritance
UUID: 62028ca3-878c-47e8-895c-7795e720ed04
Approved on: 2025/8/26
Published on: 2025/12/17

HGVS expressions

NM_014191.4:c.615-1G>A
NM_014191.4(SCN8A):c.615-1G>A
NC_000012.12:g.51688757G>A
CM000674.2:g.51688757G>A
NC_000012.11:g.52082541G>A
CM000674.1:g.52082541G>A
NC_000012.10:g.50368808G>A
NG_021180.2:g.102522G>A
NG_021180.3:g.103800G>A
ENST00000703687.1:n.2381G>A
ENST00000354534.11:c.615-1G>A
ENST00000627620.5:c.615-248G>A
ENST00000637709.2:c.615-1G>A
ENST00000638820.1:c.615-248G>A
ENST00000662684.1:c.615-248G>A
ENST00000667214.1:c.615-1G>A
ENST00000668547.1:c.615-248G>A
ENST00000354534.10:c.615-1G>A
ENST00000355133.7:c.615-1G>A
ENST00000545061.5:c.615-1G>A
ENST00000550891.4:n.743-248G>A
ENST00000551216.2:c.165-248G>A
ENST00000599343.5:c.615-1G>A
ENST00000627620.2:c.615-248G>A
NM_001177984.2:c.615-1G>A
NM_014191.3:c.615-1G>A
NM_001330260.1:c.615-248G>A
NM_001330260.2:c.615-248G>A
NM_001369788.1:c.615-248G>A
NM_001177984.3:c.615-1G>A

Pathogenic

Met criteria codes 3

PVS1 PM2_Supporting PS4_Supporting

Not Met criteria codes 7

PS2 PS3 PM6 PM1 BA1 BS1 BS3

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 2.0.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Epilepsy Sodium Channel VCEP

The c.615-1 G>A variant in SCN8A, also referred to as c.615-248 G>A using NM_001330260.2, occurs within the canonical acceptor site of intron 5. It is predicted to cause skipping of biologically-relevant-exon 6, resulting in a frameshift leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1). This variant is absent from gnomAD v[20210610] (PM2_Supporting). The variant has been reported in two individual with clinical features consistent with complex neurodevelopmental disorder (PS4_supporting; Invitae and GeneDx internal data). In summary, this variant meets the criteria to be classified as pathogenic for autosomal dominant complex neurodevelopmental disorder based on the ACMG/AMP criteria applied, as specified by the ClinGen Sodium Channel Epilepsy VCEP: PVS1, PM2_Supporting, PS4_Supporting (v2.0; AUgust 26, 2025).

Met criteria codes

PVS1	✔	The c.615-1 G>A variant in SCN8A occurs within the canonical acceptor site of intron 5. It is predicted to cause skipping of biologically-relevant-exon 6, resulting in a frameshift leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).
PM2_Supporting	✔	This variant is absent from gnomAD v[20210610] (PM2_Supporting).
PS4_Supporting	✔	The variant has been reported in two individual with clinical features consistent with complex neurodevelopmental disorder (PS4_supporting; Invitae and GeneDx internal data).

Not Met criteria codes

PS2	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PS3	✖	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
PM1	✖	

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

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

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_014191.4(SCN8A):c.615-1G>A	Pathogenic	Complex Neurodevelopmental Disorder	2025-12-17	1.0	ClinGen Epilepsy Sodium Channel Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for SCN2A Version 2.0.0	SCN8A

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