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Variant: NM_002055.5(GFAP):c.1111G>C (p.Glu371Gln)

Version: 1.0

CA217114

66436 (ClinVar)

Gene: GFAP (HGNC:2670)
Condition: Alexander disease (MONDO:0008752)
Inheritance Mode: Autosomal dominant inheritance
UUID: 9c9bfe72-2452-46ec-a391-76338f4889f6
Approved on: Fri, 23 Oct 2026 00:00:00 +0000
Published on: Fri, 23 Oct 2026 00:00:00 +0000

HGVS expressions

NM_002055.5(GFAP):c.1111G>C (p.Glu371Gln)
NM_002055.5:c.1111G>C
NC_000017.11:g.44911252C>G
CM000679.2:g.44911252C>G
NC_000017.10:g.42988620C>G
CM000679.1:g.42988620C>G
NC_000017.9:g.40344146C>G
NG_008401.1:g.9295G>C
ENST00000253408.11:c.1111G>C
ENST00000435360.8:c.1111G>C
ENST00000253408.10:c.1111G>C
ENST00000435360.7:c.1111G>C
ENST00000585543.6:n.264G>C
ENST00000586125.2:c.46G>C
ENST00000586127.6:n.1640G>C
ENST00000586793.6:c.976G>C
ENST00000587997.6:n.587G>C
ENST00000588735.3:c.1111G>C
ENST00000591327.2:n.2265G>C
ENST00000591880.2:c.41G>C
ENST00000592320.6:c.688G>C
ENST00000638281.1:c.1111G>C
ENST00000638304.1:c.30G>C
ENST00000638488.1:n.52G>C
ENST00000638618.1:c.766G>C
ENST00000639042.1:c.48G>C
ENST00000639277.1:c.1111G>C
ENST00000639921.1:c.68G>C
ENST00000640552.1:n.1125G>C
ENST00000253408.9:c.1111G>C
ENST00000435360.6:c.1111G>C
ENST00000585543.5:n.264G>C
ENST00000586793.5:c.1111G>C
ENST00000588640.5:n.491G>C
ENST00000588735.1:c.83-3136G>C
ENST00000592320.5:c.688G>C
NM_001131019.2:c.1111G>C

NM_001242376.1:c.1111G>C
NM_002055.4:c.1111G>C
NM_001363846.1:c.1111G>C
NM_001131019.3:c.1111G>C
NM_001242376.2:c.1111G>C
NM_001242376.3:c.1111G>C
NM_001363846.2:c.1111G>C

Likely Pathogenic

Met criteria codes 3

PP4_Strong PM5 PM2_Supporting

Not Met criteria codes 2

PS4 PM1

Evidence Links 0

Expert Panel

Leukodystrophy and Leukoencephalopathy VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0*
- **Criteria Specification Approval History**
- **Criteria Specifications for this VCEP**

Evidence submitted by expert panel

Leukodystrophy and Leukoencephalopathy VCEP

The c.1111G>C variant in GFAP is a missense variant predicted to cause substitution of glutamic acid by glutamine at amino acid 371 (p.Glu371Gln). This variant has been reported in 1 proband meeting consistent diagnostic criteria for Alexander disease and displayed elevated GFAP level in the blood (704ng/L), which is highly specific for Alexander disease (PMID: 26478912) (PP4_strong). One missense variant, c.1111G>A, p.Glu371Lys (ClinVar Variation ID 1199219), in the same codon has been classified as likely pathogenic/pathogenic for Alexander disease by the ClinGen Leukodystrophy and Leukoencephalopathy VCEP [PM5]. This variant is absent from gnomAD v4.1.0 [PM2_Supporting]. In summary, this variant meets the criteria to be classified as a likely pathogenic for Alexander disease based on the ACMG/AMP criteria applied, as specified by the ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0.0): (PP4_strong, PM5, PM2_supporting).

Met criteria codes

PP4_Strong	✔	At least one patient with this variant displayed elevated GFAP level in the blood (704ng/L), which is highly specific for Alexander disease (PP4_strong). The reported patient has a diagnosis consistent with Alexander disease (A3, A4) (PMID: 26478912) per VCEP criteria.
PM5	✔	1 missense variant, c.1111G>A, p.Glu371Lys (ClinVar Variation ID 1199219), in the same codon has been classified as likely pathogenic/pathogenic for Alexander disease by the ClinGen Leukodystrophy and Leukoencephalopathy VCEP [PM5].
PM2_Supporting	✔	This variant is absent from gnomAD v4.1 (PM2_Supporting).

Not Met criteria codes

PS4	✖	PS4 not met: This variant has been reported in 1 proband (PMID: 21917775) that did not meet diagnostic criteria (B8) and in 1 proband in (PMID: 26478912) meeting consistent diagnostic criteria (A3, A4). We suspect that the two probands are the same individual. Therefore, PS4_ cannot be applied because proband was counted towards PP4_Strong.
PM1	✖	This variant does not reside within a region of amino acids 59-88 that is defined as a mutational hotspot or critical functional domain by the ClinGen Leukodystrophy and Leukencephalopathy VCEP.

Curation History

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See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_002055.5(GFAP):c.1111G>C (p.Glu...	Likely Pathogenic	Alexander Disease	2026-10-23	1.0	ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0	GFAP

Showing 1 to 1 of 1 rows

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