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Variant: NM_002055.5(GFAP):c.1111G>A (p.Glu371Lys)

Version: 1.0

CA399843382

1199219 (ClinVar)

Gene: GFAP (HGNC:2670)
Condition: Alexander disease (MONDO:0008752)
Inheritance Mode: Autosomal dominant inheritance
UUID: ec7c1c6c-a706-4758-91f2-ba4468cd757c
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>A (p.Glu371Lys)
NM_002055.5:c.1111G>A
NC_000017.11:g.44911252C>T
CM000679.2:g.44911252C>T
NC_000017.10:g.42988620C>T
CM000679.1:g.42988620C>T
NC_000017.9:g.40344146C>T
NG_008401.1:g.9295G>A
ENST00000253408.11:c.1111G>A
ENST00000435360.8:c.1111G>A
ENST00000253408.10:c.1111G>A
ENST00000435360.7:c.1111G>A
ENST00000585543.6:n.264G>A
ENST00000586125.2:c.46G>A
ENST00000586127.6:n.1640G>A
ENST00000586793.6:c.976G>A
ENST00000587997.6:n.587G>A
ENST00000588735.3:c.1111G>A
ENST00000591327.2:n.2265G>A
ENST00000591880.2:c.41G>A
ENST00000592320.6:c.688G>A
ENST00000638281.1:c.1111G>A
ENST00000638304.1:c.30G>A
ENST00000638488.1:n.52G>A
ENST00000638618.1:c.766G>A
ENST00000639042.1:c.48G>A
ENST00000639277.1:c.1111G>A
ENST00000639921.1:c.68G>A
ENST00000640552.1:n.1125G>A
ENST00000253408.9:c.1111G>A
ENST00000435360.6:c.1111G>A
ENST00000585543.5:n.264G>A
ENST00000586793.5:c.1111G>A
ENST00000588640.5:n.491G>A
ENST00000588735.1:c.83-3136G>A
ENST00000592320.5:c.688G>A
NM_001131019.2:c.1111G>A

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

Pathogenic

Met criteria codes 4

PP4_Strong PM2_Supporting PS4_Supporting PS2

Not Met criteria codes 5

PM6 PM1 BS2 BP5 PS3

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>A variant in GFAP is a missense variant predicted to cause substitution of glutamic acid by lysine at amino acid 371 (p.Glu371Lys). This variant has been reported as a de novo occurrence with confirmed parental relationships in one proband with elevated GFAP in CSF meeting definite diagnostic criteria for Alexander Disease per ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0.0 (PP4_strong, PS2_Strong; PMID: 41513585). This variant has also been reported in another proband meeting definite diagnostic criteria for Alexander Disease (PS4_supporting; ClinVar Accession: SCV002956346.4). This variant is absent from gnomAD v4.1.0 (PM2_Supporting). In summary, this variant meets the criteria to be classified as a pathogenic variant 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, PS2_strong, PS4_supporting, PM2_supporting.

Met criteria codes

PP4_Strong	✔	This variant has been reported in 1 proband meeting definite diagnostic criteria for Alexander disease per ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0.0.and who has elevated GFAP level in CSF/blood compared to controls PMID: 41513585
PM2_Supporting	✔	This variant is absent from gnomAD v4.1.0 [PM2_Supporting].
PS4_Supporting	✔	This variant has been reported in 1 proband meeting definite diagnostic criteria for Alexander disease per ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0.0. [PS4_supporting]; Labcorp Genetics SCV002956346.4

PS2		✔	This variant has been identified as a de novo occurrence with confirmed parental relationships in 1 individual meeting definite diagnostic criteria of Alexander Disease per ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0.0. PMID: 41513585

Not Met criteria codes

PM6		✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
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 Leukoencephalopathy VCEP.
BS2		✖	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
PS3		✖	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_002055.5(GFAP):c.1111G>A (p.Glu...	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

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