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Variant: NM_002055.5(GFAP):c.256A>G (p.Lys86Glu)

Version: 1.0

CA347190

190338 (ClinVar)

Gene: GFAP (HGNC:2670)
Condition: Alexander disease (MONDO:0008752)
Inheritance Mode: Autosomal dominant inheritance
UUID: 0f898e32-81e6-4b7a-921b-542ea0f66852
Approved on: Mon, 19 Oct 2026 00:00:00 +0000
Published on: Mon, 19 Oct 2026 00:00:00 +0000

HGVS expressions

NM_002055.5:c.256A>G
NM_002055.5(GFAP):c.256A>G (p.Lys86Glu)
NC_000017.11:g.44915231T>C
CM000679.2:g.44915231T>C
NC_000017.10:g.42992599T>C
CM000679.1:g.42992599T>C
NC_000017.9:g.40348125T>C
NG_008401.1:g.5316A>G
ENST00000253408.11:c.256A>G
ENST00000435360.8:c.256A>G
ENST00000253408.10:c.256A>G
ENST00000435360.7:c.256A>G
ENST00000586793.6:c.256A>G
ENST00000588735.3:c.256A>G
ENST00000591327.2:n.269A>G
ENST00000592320.6:c.256A>G
ENST00000638281.1:c.256A>G
ENST00000639277.1:c.256A>G
ENST00000640552.1:n.270A>G
ENST00000253408.9:c.256A>G
ENST00000376990.8:c.256A>G
ENST00000435360.6:c.256A>G
ENST00000585728.5:c.181+75A>G
ENST00000586793.5:c.256A>G
ENST00000588037.1:c.256A>G
ENST00000588316.1:c.256A>G
ENST00000588735.1:c.82+174A>G
ENST00000588957.5:c.-272+586A>G
ENST00000591327.1:n.270A>G
ENST00000592320.5:c.256A>G
NM_001131019.2:c.256A>G
NM_001242376.1:c.256A>G
NM_002055.4:c.256A>G
NM_001363846.1:c.256A>G
NM_001131019.3:c.256A>G
NM_001242376.2:c.256A>G
NM_001242376.3:c.256A>G

NM_001363846.2:c.256A>G

Likely Pathogenic

Met criteria codes 4

PP4_Strong PS2 PM2_Supporting PM1

Not Met criteria codes 3

PS1 PP1 PVS1

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 NM_002055.5(GFAP): c.256A>G (p.Lys86Glu) variant GFAP is a missense variant predicted to cause a substitution of lysine by glutamate at amino acid 86 (p.Lys86Glu). This variant has been identified as a de novo occurrence with unconfirmed parental relationships in one individual with a definite diagnosis of Alexander Disease per ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0.0 who had elevated GFAP levels in plasma when compared to age-matched controls which is highly specific for Alexander disease (PM6 and PP4_Strong; the same proband was identified in PMIDs: 21572052, 21917775, 41513585 and MDBP Bioregistry). This variant resides within a region, amino acids 59 – 88, of GFAP that is defined as a region with significant missense constraint by the ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0.0 (PM1). This variant is absent from gnomAD v[4.1.1] (PM2_Supporting). In summary, this variant meets the criteria to be classified as likely pathogenic for Alexander Disease based on the ACMG/AMP criteria applied, as specified by the ClinGen Leukodystrophy and Leukoencephalopathy VCEP: PM6, PP4_Strong, PM1, and PM2_Supporting (ClinGen Leukodystrophy and Leukoencephalopathy VCEP Specifications Version 1.0.0).

Met criteria codes

PP4_Strong	✔	This variant has been identified as a de novo occurrence with unconfirmed parental relationships in one individual with a definite diagnosis of Alexander Disease per ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0.0 who had elevated GFAP levels in plasma when compared to age-matched controls which is highly specific for Alexander disease (PM6 and PP4_Strong; the same proband was identified in PMIDs: 21572052, 21917775, 41513585 and MDBP Bioregistry)
PS2	✔	This variant has been identified as a de novo occurrence with confirmed parental relationships in 1 individual(s) with Alexander Disease (PS2_[Strong]; PMIDs: 21572052 and 21917775, and MDBP Bioregistry).
PM2_Supporting	✔	This variant is absent from gnomAD v[4.1.1] (PM2_Supporting).
PM1	✔	This variant resides within a region, amino acids 59 – 88, of GFAP that is defined as a region with significant missense constraint by the ClinGen Leukodystrophy and Leukoencephalopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for GFAP Version 1.0.0 (PM1_Moderate).

Not Met criteria codes

PS1	✖	No variants with same amino acid change
PP1	✖	One case described, no family members
PVS1	✖	LOF is not a known disease mechanism

Curation History

Showing 1 to 1 of 1 rows

See Report	Preferred Variant Title	Classification	Condition	Published Date	Version	Criteria Specification	Gene
View	NM_002055.5(GFAP):c.256A>G (p.Lys8...	Likely Pathogenic	Alexander Disease	2026-10-19	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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