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Variant: NM_002055.5(GFAP):c.382G>A (p.Asp128Asn)

Version: 1.0

CA217191

66484 (ClinVar)

Gene: GFAP (HGNC:2670)
Condition: Alexander disease (MONDO:0008752)
Inheritance Mode: Autosomal dominant inheritance
UUID: 5c632544-680c-4e32-b678-f0b09756fefa
Approved on: 2026/8/18
Published on: 2026/8/18

HGVS expressions

NM_002055.5:c.382G>A
NM_002055.5(GFAP):c.382G>A (p.Asp128Asn)
NC_000017.11:g.44915105C>T
CM000679.2:g.44915105C>T
NC_000017.10:g.42992473C>T
CM000679.1:g.42992473C>T
NC_000017.9:g.40347999C>T
NG_008401.1:g.5442G>A
ENST00000253408.11:c.382G>A
ENST00000435360.8:c.382G>A
ENST00000253408.10:c.382G>A
ENST00000435360.7:c.382G>A
ENST00000586793.6:c.382G>A
ENST00000588735.3:c.382G>A
ENST00000591327.2:n.395G>A
ENST00000592320.6:c.382G>A
ENST00000638281.1:c.382G>A
ENST00000638618.1:c.37G>A
ENST00000639277.1:c.382G>A
ENST00000640552.1:n.396G>A
ENST00000253408.9:c.382G>A
ENST00000376990.8:c.382G>A
ENST00000435360.6:c.382G>A
ENST00000585728.5:c.*26G>A
ENST00000586793.5:c.382G>A
ENST00000588037.1:c.382G>A
ENST00000588316.1:c.382G>A
ENST00000588735.1:c.82+300G>A
ENST00000588957.5:c.-272+712G>A
ENST00000591327.1:n.396G>A
ENST00000592320.5:c.382G>A
NM_001131019.2:c.382G>A
NM_001242376.1:c.382G>A
NM_002055.4:c.382G>A
NM_001363846.1:c.382G>A
NM_001131019.3:c.382G>A
NM_001242376.2:c.382G>A

NM_001242376.3:c.382G>A
NM_001363846.2:c.382G>A

Pathogenic

Met criteria codes 4

PS4_Moderate PP1_Moderate PS3_Very Strong PP4_Moderate

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.382G>A, variant in GFAP is a missense variant predicited to cause a substitution of aspartic acid by asparagine at amino acid 128 (p.Asp128Asn). This variant has been reported in two probands who met 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_Moderate; PMID: 28882119, PMID: 25997626). At least one proband with this variant displayed the existence of Rosenthal fibers in addition to gliosis and loss of myelin which is highly specific for Alexander Disease (PP4_[Moderate], PMID: 25997626). The variant has been reported to segregate with Alexander Disease in four affected family members from one family (PP1_Moderate]; ClinVar SCVs: SCV005400625.1). An aggregation assay in zebrafish model showed a significantly higher number of GFAP aggregates than wild-type GFAP indicating that this variant impacts protein function (PMID: 28882119) (PS3_[Very Strong]). In summary, this variant meets the criteria to be classified as Pathogenic for Alexander Disease based on the ACMG/AMP criteria applied, as specified by the ClinGen Leukodystrophy and Leukoencephalopathy VCEP: PS4_Moderate, PS3_Very Strong, PP1_Moderate, PP4_Moderate (ClinGen Leukodystrophy and Leukoencephalopathy VCEP Specifications Version 1.0.0).

Met criteria codes

PS4_Moderate	✔	This variant has been reported in two probands who met 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_Moderate; PMID: 28882119, PMID: 25997626)
PP1_Moderate	✔	The variant has been reported to segregate with Alexander Disease in four affected family members from one family (PP1_Moderate]; ClinVar SCVs: SCV005400625.1).
PS3_Very Strong	✔	An aggregation assay in zebrafish model showed a significantly higher number of GFAP aggregates than wild-type GFAP indicating that this variant impacts protein function (PMID: 28882119) (PS3_[Very Strong]).
PP4_Moderate	✔	At least one patient with this variant displayed the existence of Rosenthal fibers in addition to gliosis and loss of myelin which is highly specific for Alexander Disease (PP4_[Moderate], PMID: 26478912).

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.382G>A (p.Asp1...	Pathogenic	Alexander Disease	2026-08-18	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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