Variant: NM_000419.5(ITGA2B):c.998+1G>C

Version: 1.0

CA399804688

812734 (ClinVar)

Gene: ITGA2B (HGNC:3674)
Condition: Glanzmann thrombasthenia (MONDO:0100326)
Inheritance Mode: Autosomal recessive inheritance
UUID: aff8f164-2aa9-4376-b011-420535e3a386
Approved on: 2021-09-15
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HGVS expressions

NM_000419.5:c.998+1G>C
NM_000419.5(ITGA2B):c.998+1G>C
NC_000017.11:g.44383893C>G
CM000679.2:g.44383893C>G
NC_000017.10:g.42461261C>G
CM000679.1:g.42461261C>G
NC_000017.9:g.39816787C>G
NG_008331.1:g.10613G>C
ENST00000262407.6:c.998+1G>C
ENST00000648408.1:c.429+1G>C
ENST00000262407.5:c.998+1G>C
ENST00000589645.5:n.450G>C
ENST00000591990.5:n.543+1G>C
ENST00000592226.5:n.238+1G>C
NM_000419.3:c.998+1G>C
NM_000419.4:c.998+1G>C

Pathogenic

Met criteria codes 3

PM3_Supporting PM2_Supporting PVS1

Not Met criteria codes 1

PP4

Evidence Links 0

Expert Panel

Platelet Disorders VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

Platelet Disorders VCEP

NM_000419.5(ITGA2B):c.998+1G>C occurs within the canonical splice donor site of intron 11. It is predicted to cause skipping of biologically-relevant-exon 11/30, resulting in the p.(Met316Glufs*3) frameshift in exon 12, 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 v2.1.1 (PM2_Supporting). One homozygous patient has been reported with Glanzmann thrombasthenia (PMID: 32581362; PM3_supporting). In summary, this variant

meets the criteria to be classified as Pathogenic for autosomal recessive Glanzmann Thrombasthenia based on the ACMG/AMP criteria applied, as specified by the ClinGen PD VCEP: PVS1, PM2_supporting, PM3_supporting. (VCEP specifications version 2; date of approval xx/xx/xxxx)

Met criteria codes

PM3_Supporting	✔	One homozygous patient has been reported with Glanzmann thrombasthenia (PMID: 32581362; PM3_supporting).
PM2_Supporting	✔	This variant is absent from gnomAD v2.1.1 (PM2_Supporting).
PVS1	✔	NM_000419.5(ITGA2B):c.998+1G>C in occurs within the canonical splice donor site of intron 11. It is predicted to cause skipping of biologically-relevant-exon 11/30, resulting in the p.(Met316Glufs*3) frameshift in exon 12, leading to nonsense mediated decay in a gene in which loss-of-function is an established disease mechanism (PVS1).

Not Met criteria codes

PP4	✖	One patient has been reported with Glanzmann thrombasthenia in PMID: 32581362, however phenotypic information was not provided.

Curation History

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