The ClinGen Evidence Repository is an **FDA-recognized human genetic variant database** containing expert-curated assertions regarding variants' pathogenicity and supporting evidence summaries. [Disclaimer]

Variant: NM_000419.5(ITGA2B):c.1973del (p.Ala658fs)

Version: 1.0

CA915940791

627027 (ClinVar)

Gene: ITGA2B (HGNC:3674)
Condition: Glanzmann thrombasthenia (MONDO:0100326)
Inheritance Mode: Autosomal recessive inheritance
UUID: 7415a211-2eb0-4521-8a85-075386d2c25f
Approved on: 2024/5/2
Published on: 2024/5/3

HGVS expressions

NM_000419.5:c.1973del
NM_000419.5(ITGA2B):c.1973del (p.Ala658fs)
NC_000017.11:g.44378483del
CM000679.2:g.44378483del
NC_000017.10:g.42455851del
CM000679.1:g.42455851del
NC_000017.9:g.39811377del
NG_008331.1:g.16023del
ENST00000262407.6:c.1973del
ENST00000648408.1:c.1404del
ENST00000262407.5:c.1973del
ENST00000592462.5:n.768del
NM_000419.3:c.1973del
NM_000419.4:c.1973del

Likely Pathogenic

Met criteria codes 2
PM2_Supporting PVS1

Not Met criteria codes 2
PP4 PM3

Evidence Links 0

Expert Panel
Platelet Disorders VCEP

Criteria Specification Information

Criteria Specification: *ClinGen Platelet Disorders Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines Version 2.1*
PDF
Criteria Specification Approval History
Criteria Specifications for this VCEP

Evidence submitted by expert panel

Platelet Disorders VCEP

The frameshift variant NM_000419.5(ITGA2B):c.1973del (p.Ala658GlufsTer?) has been reported in one individual with a disorder of platelet function, (TGP0048 in PMID:31064749). Communication with the authors confirmed a diagnosis of Glanzmann thrombasthenia. The patient had impaired platelet aggregation and prolonged bleeding after dental extraction. This individual, TGP0048, is compound heterozygous for

this frameshift variant and a variant of uncertain significance (NM_000419.5(ITGA2B):c.188+5G>T). The c.1973del frameshift variant causes a premature stop codon in exon 20/30, which is predicted to undergo nonsense mediated decay in a disease that is loss of function (PVS1). The highest population minor allele frequency in gnomAD v4.0.0 is 0.00006335 (1/15786 alleles) in the African/African American population, which is lower than the ClinGen PD VCEP threshold (<0.0001; PM2_Supporting). In summary, this variant meets the criteria to be classified as Likely Pathogenic for autosomal recessive Glanzmann Thrombasthenia based on the ACMG/AMP criteria applied, as specified by the ClinGen PD VCEP: PVS1 and PM2_supporting (VCEP specifications version 2.1.0).

Met criteria codes

PM2_Supporting	✔	The highest population minor allele frequency in gnomAD v4.0.0 is 0.00006335 (1/15786 alleles) in the African/African American population, which is lower than the ClinGen PD VCEP threshold (<0.0001; PM2_Supporting).
PVS1	✔	The c.1973del causes a premature stop codon in exon 20/30, which is predicted to undergo nonsense mediated decay in a disease that is loss of function.

Not Met criteria codes

PP4	✖	TGP0048 of PMID: 31064749 is reported to have a disease of platelet function. Communication with the authors confirmed a diagnosis of Glanzmann thrombasthenia. The patient had Impaired platelet aggregation and prolonged bleeding after dental extraction. Insufficient information for PP4, specific aggregation information not provided.
PM3	✖	TGP0048 of of PMID: 31064749 is reported to be compound heterozygous for a disorder of platelet function with the c.1973del and a variant of uncertain significance c.188+5G>T, phasing unknown (0 points, PM3 not met).

Curation History

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