Variant: NM_002834.4(PTPN11):c.1678C>T (p.Leu560Phe)

Version: 2.0

CA134647

44599 (ClinVar)

Gene: PTPN11 (HGNC:5781)
Condition: RASopathy (MONDO:0021060)
Inheritance Mode: Autosomal dominant inheritance
UUID: 1de1c18c-c026-4034-afda-2b4516c6cdae
Approved on: 2024-09-17
Published on: 2024-10-01

HGVS expressions

NM_002834.4:c.1678C>T
NM_002834.4(PTPN11):c.1678C>T (p.Leu560Phe)
NC_000012.12:g.112502222C>T
CM000674.2:g.112502222C>T
NC_000012.11:g.112940026C>T
CM000674.1:g.112940026C>T
NC_000012.10:g.111424409C>T
NG_007459.1:g.88491C>T
ENST00000639857.2:c.1678C>T
ENST00000685487.1:c.*880C>T
ENST00000687120.1:n.1061C>T
ENST00000687906.1:c.1564C>T
ENST00000688597.1:c.1303C>T
ENST00000688701.1:n.922C>T
ENST00000690210.1:c.1678C>T
ENST00000690472.1:n.887C>T
ENST00000692624.1:c.*224C>T
ENST00000351677.7:c.1678C>T
ENST00000351677.6:c.1678C>T
ENST00000635625.1:c.1690C>T
NM_002834.3:c.1678C>T
NM_001330437.1:c.1690C>T
NM_001330437.2:c.1690C>T
NM_001374625.1:c.1675C>T
NM_002834.5:c.1678C>T

Likely Benign

Met criteria codes 2

BS3 **BP5**

Evidence Links 1

Expert Panel

RASopathy VCEP

Criteria Specification Information

- **Criteria Specification:** *ClinGen RASopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for PTPN11 Version 2.1.0*
- **Criteria Specification Approval History**

Criteria Specifications for this VCEP

Evidence submitted by expert panel

RASopathy VCEP

The c.1678C>T (p.Leu560Phe) variant in PTPN11 (NM_002834.5(PTPN11):c.1678C>T (p.Leu560Phe)) has been identified in individuals with some features of a RASopathy but none were diagnosed with a RASopathy (PS4 not met; GeneDx, Partners LMM, APHP-Robert Debré Hospital internal data; GTR ID's: 28338, 26957, 21766; SCV000061285.5; SCV000208999.2; SCV000207690.1). This variant has been identified in a patient with an alternate molecular basis for disease (BP5; GeneDx internal data: GTR ID: 26957; SCV000208999.2). In vitro functional studies provide some evidence that the p.Leu560Phe variant does not impact protein function (BS3; PMID: 15987685). In summary, this variant meets criteria to be classified as likely benign. RASopathy-specific ACMG/AMP criteria applied: BS3, BP5 (Version 2.1; 09/17/2024).

Met criteria codes

BS3		✓	In vitro functional studies provide some evidence that the p.Leu560Phe variant does not impact protein function (BS3; PMID: 15987685). In vitro functional studies provide some evidence that the p.Leu560Phe variant does not impact protein function (BS3; PMID: 15987685). **PubMed:15987685**
BP5	ℹ	✓	This variant has been identified in a patient with an alternate molecular basis for disease (BP5; GeneDx internal data: GTR ID: 26957; SCV000208999.2).

Curation History

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