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Variant: NM_002880.3(RAF1):c.1113T>C (p.Asp371=)

Version: 1.1

CA235339

180718 (ClinVar)

Gene: RAF1 (HGNC:5894)
Condition: RASopathy (MONDO:0021060)
Inheritance Mode: Autosomal dominant inheritance
UUID: ca1f922a-c651-4ca4-8afe-a28dde261256
Approved on: 2020-03-09
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HGVS expressions

NM_002880.3:c.1113T>C
NM_002880.3(RAF1):c.1113T>C (p.Asp371=)
NC_000003.12:g.12591788A>G
CM000665.2:g.12591788A>G
NC_000003.11:g.12633287A>G
CM000665.1:g.12633287A>G
NC_000003.10:g.12608287A>G
NG_007467.1:g.77392T>C
ENST00000423275.6:c.*778T>C
ENST00000432427.3:c.430T>C
ENST00000465826.6:n.704T>C
ENST00000475353.2:n.1035T>C
ENST00000491290.2:n.1486-13T>C
ENST00000494557.2:n.924T>C
ENST00000684903.1:c.*790T>C
ENST00000685348.1:c.*790T>C
ENST00000685437.1:c.1014T>C
ENST00000685653.1:c.1113T>C
ENST00000685738.1:c.*77T>C
ENST00000686409.1:n.2164T>C
ENST00000686455.1:n.1476T>C
ENST00000686762.1:c.1113T>C
ENST00000687257.1:n.1349T>C
ENST00000687326.1:c.*47T>C
ENST00000687486.1:c.305T>C
ENST00000687505.1:n.1231T>C
ENST00000687923.1:c.1002T>C
ENST00000687940.1:n.1490T>C
ENST00000688269.1:n.1709T>C
ENST00000688326.1:c.546T>C
ENST00000688444.1:n.1439T>C
ENST00000688543.1:c.1014T>C
ENST00000688625.1:c.*691T>C
ENST00000688803.1:n.1344T>C
ENST00000688914.1:n.99T>C
ENST00000689097.1:c.*790T>C
ENST00000689389.1:c.1113T>C

ENST00000689418.1:c.*790T>C
ENST00000689481.1:c.*790T>C
ENST00000689540.1:n.1263T>C
ENST00000689876.1:c.1113T>C
ENST00000689914.1:c.*47T>C
ENST00000690397.1:c.1002T>C
ENST00000690460.1:c.1101T>C
ENST00000690585.1:c.5T>C
ENST00000690625.1:n.1416T>C
ENST00000691396.1:c.*965T>C
ENST00000691724.1:c.*70T>C
ENST00000691779.1:c.*691T>C
ENST00000691888.1:c.5T>C
ENST00000691899.1:c.1113T>C
ENST00000692069.1:n.1679T>C
ENST00000692093.1:c.1014T>C
ENST00000692311.1:n.1937T>C
ENST00000692558.1:n.1478T>C
ENST00000692773.1:c.*850T>C
ENST00000692830.1:c.*858T>C
ENST00000693069.1:c.*47T>C
ENST00000693312.1:c.888T>C
ENST00000693664.1:c.1113T>C
ENST00000693705.1:c.*790T>C
ENST00000251849.9:c.1113T>C
ENST00000442415.7:c.1173T>C
ENST00000251849.8:c.1113T>C
ENST00000423275.5:c.*790T>C
ENST00000432427.2:c.750T>C
ENST00000442415.6:c.1173T>C
ENST00000460610.1:n.70T>C
ENST00000465826.5:n.470T>C
ENST00000475353.1:n.281T>C
ENST00000494557.1:n.129T>C
NM_001354689.1:c.1173T>C
NM_001354690.1:c.1113T>C
NM_001354691.1:c.870T>C
NM_001354692.1:c.870T>C
NM_001354693.1:c.1014T>C
NM_001354694.1:c.930T>C
NM_001354695.1:c.771T>C
NR_148940.1:n.1641T>C
NR_148941.1:n.1587T>C
NR_148942.1:n.1526T>C
NM_001354689.3:c.1173T>C
NM_001354690.2:c.1113T>C
NM_001354691.2:c.870T>C
NM_001354692.2:c.870T>C
NM_001354693.2:c.1014T>C
NM_001354694.2:c.930T>C
NM_001354695.2:c.771T>C
NR_148940.2:n.1557T>C

NR_148941.2:n.1503T>C
NR_148942.2:n.1442T>C
NM_001354690.3:c.1113T>C
NM_001354691.3:c.870T>C
NM_001354692.3:c.870T>C
NM_001354693.3:c.1014T>C
NM_001354694.3:c.930T>C
NM_001354695.3:c.771T>C
NM_002880.4:c.1113T>C
NR_148940.3:n.1557T>C
NR_148941.3:n.1503T>C
NR_148942.3:n.1442T>C

Likely Benign

Met criteria codes 2

BP4 BP7

Not Met criteria codes 1

BS2

Evidence Links 0

Expert Panel

RASopathy VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

RASopathy VCEP

The c.1113T>C (p.Asp371=) is present in 7/1113684 European alleles (MAF 2.88e-05, 95% CI) gnomAD v2.1.1. Sixteen apparently unaffected parental samples involved in whole exome testing were observed with this variant supporting that this variant is likely benign; however, this evidence does not meet current scoring criteria for BS2 at this time (BS2 not met; SCV000515669.4). This variant is a synonymous (silent) variant at a nucleotide that is not highly conserved and is not predicted to impact splicing (BP7). Computational prediction tools and conservation analysis suggest that the p.Asp371= variant does not impact the protein (BP4). In summary, the clinical significance of the p.Asp371= variant is likely benign. RASopathy-specific ACMG/AMP criteria applied (PMID:29493581): BP7, BP4.

Met criteria codes

BP4	✔	No predicted splicing impact
BP7	✔	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Not Met criteria codes

BS2	✖	Not met, 3 well-phenotyped individuals needed to apply BS2. Identified by whole exome in 16 unaffected parents from 16 different trios (SCV000515669.4) observed a female in her 20's with a history of autism, type 2 diabetes, and dilated LV heart failure (SCV001010386.1).

Curation History

Showing 1 to 2 of 2 rows