Variant: NM_002880.4(RAF1):c.1108+9_1108+21del

Version: 2.0

CA182757

178666 (ClinVar)

Gene: RAF1 (HGNC:5894)
Condition: RASopathy (MONDO:0021060)
Inheritance Mode: Autosomal dominant inheritance
UUID: e3caac03-d88a-45f8-bcde-e41975fe8745
Approved on: 2024-12-03
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HGVS expressions

NM_002880.4:c.1108+9_1108+21del
NM_002880.4(RAF1):c.1108+9_1108+21del
NC_000003.12:g.12599673_12599685del
CM000665.2:g.12599673_12599685del
NC_000003.11:g.12641172_12641184del
CM000665.1:g.12641172_12641184del
NC_000003.10:g.12616172_12616184del
NG_007467.1:g.69498_69510del
ENST00000423275.6:c.*773+9_*773+21del
ENST00000432427.3:c.428+9_428+21del
ENST00000465826.6:n.699+9_699+21del
ENST00000491290.2:n.1485+9_1485+21del
ENST00000684903.1:c.*785+9_*785+21del
ENST00000685348.1:c.*785+9_*785+21del
ENST00000685437.1:c.1009+9_1009+21del
ENST00000685653.1:c.1108+9_1108+21del
ENST00000685738.1:c.1108+9_1108+21del
ENST00000686409.1:n.2159+9_2159+21del
ENST00000686455.1:n.1471+9_1471+21del
ENST00000686479.1:n.1488_1500del
ENST00000686762.1:c.1108+9_1108+21del
ENST00000687257.1:n.1344+9_1344+21del
ENST00000687326.1:c.1108+9_1108+21del
ENST00000687486.1:c.300+9_300+21del
ENST00000687505.1:n.1226+9_1226+21del
ENST00000687923.1:c.997+21_997+33del
ENST00000687940.1:n.1485+9_1485+21del
ENST00000688269.1:n.1704+9_1704+21del
ENST00000688326.1:c.428+9_428+21del
ENST00000688444.1:n.1434+9_1434+21del
ENST00000688543.1:c.1009+9_1009+21del
ENST00000688625.1:c.*686+9_*686+21del
ENST00000688803.1:n.1339+9_1339+21del
ENST00000688914.1:n.94+9_94+21del
ENST00000689097.1:c.*785+9_*785+21del
ENST00000689389.1:c.1108+9_1108+21del
ENST00000689418.1:c.*785+9_*785+21del

ENST00000689481.1:c.*785+9_*785+21del
ENST00000689540.1:n.1258+9_1258+21del
ENST00000689876.1:c.1108+9_1108+21del
ENST00000689914.1:c.1108+9_1108+21del
ENST00000690397.1:c.997+9_997+21del
ENST00000690460.1:c.1096+9_1096+21del
ENST00000690625.1:n.1411+9_1411+21del
ENST00000691396.1:c.*901+9_*901+21del
ENST00000691724.1:c.*65+9_*65+21del
ENST00000691779.1:c.*686+9_*686+21del
ENST00000691899.1:c.1108+9_1108+21del
ENST00000692069.1:n.1674+9_1674+21del
ENST00000692093.1:c.1009+9_1009+21del
ENST00000692311.1:n.1932+9_1932+21del
ENST00000692558.1:n.1473+9_1473+21del
ENST00000692773.1:c.*845+9_*845+21del
ENST00000692830.1:c.*853+9_*853+21del
ENST00000693069.1:c.1009+9_1009+21del
ENST00000693312.1:c.883+9_883+21del
ENST00000693664.1:c.1108+9_1108+21del
ENST00000693705.1:c.*785+9_*785+21del
ENST00000251849.9:c.1108+9_1108+21del
ENST00000442415.7:c.1168+9_1168+21del
ENST00000251849.8:c.1108+9_1108+21del
ENST00000423275.5:c.*785+9_*785+21del
ENST00000432427.2:c.745+9_745+21del
ENST00000442415.6:c.1168+9_1168+21del
ENST00000460610.1:n.65+9_65+21del
ENST00000465826.5:n.352+9_352+21del
NM_002880.3:c.1108+9_1108+21del
NM_001354689.1:c.1168+9_1168+21del
NM_001354690.1:c.1108+9_1108+21del
NM_001354691.1:c.865+9_865+21del
NM_001354692.1:c.865+9_865+21del
NM_001354693.1:c.1009+9_1009+21del
NM_001354694.1:c.925+9_925+21del
NM_001354695.1:c.766+9_766+21del
NR_148940.1:n.1523+9_1523+21del
NR_148941.1:n.1523+9_1523+21del
NR_148942.1:n.1521+9_1521+21del
NM_001354689.3:c.1168+9_1168+21del
NM_001354690.2:c.1108+9_1108+21del
NM_001354691.2:c.865+9_865+21del
NM_001354692.2:c.865+9_865+21del
NM_001354693.2:c.1009+9_1009+21del
NM_001354694.2:c.925+9_925+21del
NM_001354695.2:c.766+9_766+21del
NR_148940.2:n.1439+9_1439+21del
NR_148941.2:n.1439+9_1439+21del
NR_148942.2:n.1437+9_1437+21del
NM_001354690.3:c.1108+9_1108+21del
NM_001354691.3:c.865+9_865+21del

NM_001354692.3:c.865+9_865+21del
NM_001354693.3:c.1009+9_1009+21del
NM_001354694.3:c.925+9_925+21del
NM_001354695.3:c.766+9_766+21del
NR_148940.3:n.1439+9_1439+21del
NR_148941.3:n.1439+9_1439+21del
NR_148942.3:n.1437+9_1437+21del

Benign

Met criteria codes 3

BA1 BP5 BP7

Evidence Links 0

Expert Panel

RASopathy VCEP

Criteria Specification Information

Criteria Specification: *ClinGen RASopathy Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for RAF1 Version 2.3.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

RASopathy VCEP

The c.1108+9_1108+21del variant is located in intron 10 of the RAF1 gene. This variant has a filtering allele frequency of 0.05951% in the European (non-Finnish) population in gnomAD v2, which is higher than the ClinGen RASopathy VCEP threshold (>0.0005) for BA1 and therefore meets this criterion (BA1). The variant is a synonymous (silent) variant at a nucleotide that is not highly conserved and is not predicted to impact splicing (BP7). Additionally, this variant has been identified in a patient with an alternate molecular basis for disease (BP5; GeneDx, Partners LMM internal data; GTR Lab ID's: 26957, 21766; ClinVar SCV000205113.4, SCV000209007.2). In summary, this variant meets criteria to be classified as benign for autosomal dominant RASopathies based on the ACMG/AMP criteria applied, as specified by the ClinGen RASopathy Variant Curation Expert Panel: BA1, BP5, BP7. (Specification Version 2.3, 12/3/2024)

Met criteria codes

BA1	✔	This variant has a filtering allele frequency of 0.08037% in the European (non-Finnish) population in gnomAD v4, which is higher than the ClinGen RASopathy VCEP threshold (>0.0005) for BA1
BP5	✔	The c.1108+9_1108+21del variant in the RAF1 gene has been identified in a patient with an alternate molecular basis for disease (BP5; GeneDx, Partners LMM internal data; GTR Lab ID's: 26957, 21766; ClinVar SCV000205113.4, SCV000209007.2).
BP7	✔	The variant is not predicted by SpliceAI to impact splicing

Curation History

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