Variant: NM_000535.7(PMS2):c.1144+1G>A

Version: 2.0

CA009232

162508 (ClinVar)

Gene: PMS2 (HGNC:5395)
Condition: colorectal cancer, hereditary nonpolyposis, type 4 (MONDO:0013699)
Inheritance Mode: Autosomal dominant inheritance
UUID: 399b7542-9fcc-474f-9408-99aa3c9f8663
Approved on: 2024-09-18
Published on: 2025-08-07

HGVS expressions

NM_000535.7:c.1144+1G>A
NM_000535.7(PMS2):c.1144+1G>A
NC_000007.14:g.5989799C>T
CM000669.2:g.5989799C>T
NC_000007.13:g.6029430C>T
CM000669.1:g.6029430C>T
NC_000007.12:g.5995956C>T
NG_008466.1:g.24308G>A
ENST00000699814.2:c.*540+1G>A
ENST00000699840.2:c.1141+1G>A
ENST00000699930.2:c.1036+1G>A
ENST00000406569.8:c.1144+1G>A
ENST00000644110.2:c.*738+1G>A
ENST00000699752.1:c.988+2174G>A
ENST00000699753.1:c.*565+1G>A
ENST00000699754.1:c.946+1G>A
ENST00000699755.1:c.*543+1G>A
ENST00000699756.1:c.*731+1G>A
ENST00000699757.1:c.*401+1G>A
ENST00000699758.1:c.*401+1G>A
ENST00000699759.1:n.1998+1G>A
ENST00000699760.1:c.826+1G>A
ENST00000699761.1:c.739+1G>A
ENST00000699762.1:c.571+1G>A
ENST00000699763.1:c.*234+1G>A
ENST00000699764.1:c.1144+1G>A
ENST00000699765.1:c.*240+1G>A
ENST00000699766.1:c.1144+1G>A
ENST00000699767.1:c.1144+1G>A
ENST00000699768.1:c.1144+1G>A
ENST00000699811.1:c.739+1G>A
ENST00000699813.1:n.1257+1G>A
ENST00000699814.1:c.767+1G>A
ENST00000699815.1:c.*636+1G>A
ENST00000699816.1:c.739+1G>A
ENST00000699817.1:c.*738+1G>A
ENST00000699818.1:c.739+1G>A

ENST00000699819.1:c.*301+1G>A
ENST00000699820.1:c.1144+1G>A
ENST00000699821.1:c.739+1G>A
ENST00000699822.1:c.*596+1G>A
ENST00000699823.1:c.739+1G>A
ENST00000699824.1:c.*647+1G>A
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ENST00000699826.1:c.*543+1G>A
ENST00000699827.1:c.976+1G>A
ENST00000699828.1:c.*234+1G>A
ENST00000699829.1:c.*645+1G>A
ENST00000699830.1:c.*543+1G>A
ENST00000699833.1:n.2916+1G>A
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ENST00000699916.1:c.*401+1G>A
ENST00000699917.1:c.*593+1G>A
ENST00000699918.1:c.*645+1G>A
ENST00000699919.1:c.*731+1G>A
ENST00000699920.1:c.*780+1G>A
ENST00000699928.1:c.988+2174G>A
ENST00000699929.1:c.*445+1G>A
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ENST00000699931.1:n.2572+1G>A
ENST00000699932.1:c.*362+1G>A
ENST00000699933.1:n.1125G>A
ENST00000699951.1:c.*240+1G>A
ENST00000699952.1:c.803+7527G>A
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ENST00000699954.1:c.*445+1G>A
ENST00000265849.12:c.1144+1G>A
ENST00000642292.1:c.739+1G>A
ENST00000642456.1:c.739+1G>A
ENST00000643595.1:c.*543+1G>A
ENST00000644110.1:c.826+1G>A
ENST00000265849.11:c.1144+1G>A
ENST00000382321.5:c.804-6808G>A
ENST00000406569.7:n.1144+1G>A
ENST00000441476.6:c.826+1G>A
ENST00000469652.1:n.63-6894G>A
NM_000535.5:c.1144+1G>A
NR_003085.2:n.1226+1G>A
NM_000535.6:c.1144+1G>A
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NM_001322004.1:c.739+1G>A
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NM_001322008.1:c.826+1G>A
NM_001322009.1:c.739+1G>A

NM_001322010.1:c.583+2174G>A
NM_001322011.1:c.211+1G>A
NM_001322012.1:c.211+1G>A
NM_001322013.1:c.571+1G>A
NM_001322014.1:c.1144+1G>A
NM_001322015.1:c.835+1G>A
NR_136154.1:n.1231+1G>A
NM_001322003.2:c.739+1G>A
NM_001322004.2:c.739+1G>A
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NM_001322006.2:c.988+2174G>A
NM_001322008.2:c.826+1G>A
NM_001322009.2:c.739+1G>A
NM_001322010.2:c.583+2174G>A
NM_001322011.2:c.211+1G>A
NM_001322012.2:c.211+1G>A
NM_001322013.2:c.571+1G>A
NM_001322014.2:c.1144+1G>A
NM_001322015.2:c.835+1G>A
NM_001322007.2:c.826+1G>A

Likely Pathogenic

Met criteria codes 3

PVS1_Strong | PP4 | PM2_Supporting

Evidence Links 0

Expert Panel

InSiGHT Hereditary Colorectal Cancer/Polyposis VCEP

Criteria Specification Information

Criteria Specification: *ClinGen InSiGHT Hereditary Colorectal Cancer/Polyposis Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for PMS2 Version 1.0.0*

Criteria Specification Approval History

Criteria Specifications for this VCEP

Evidence submitted by expert panel

InSiGHT Hereditary Colorectal Cancer/Polyposis VCEP

The NM_000535.7:c.1144+1G>A p.(?) variant in PMS2 occurs within the canonical splice donor site (+1) of intron 10. It is predicted to result in an in-frame exon skipping and the altered region is critical to protein function (PVS1_Strong). The variant was detected in one CRC/Endometrial MSI-H tumour using a standard panel of 5-10 markers and/or loss of MMR protein expression consistent with the variant location (PP4). This variant is extremely rare (2 in 267958 alleles) in gnomAD using the non cancer dataset and also the gnomAD v4.1 Grpmax AF is 6.856e-7 (PM2_Supporting). In summary, this variant meets the criteria to be classified as likely pathogenic for Lynch-Syndrome based on the ACMG/AMP criteria applied, as specified by the ClinGen InSiGHT Hereditary Colorectal Cancer/ Polyposis VCEP: PVS1_STR, PM2_SUP, PP4 (VCEP specifications version 1)

Met criteria codes

PVS1_Strong ✔

The variant occurs within the canonical splice donor site (+1) of intron 10. It is predicted to result in an in-frame exon skipping and the altered region is critical to protein function (PVS1_Strong).

PP4	✔	The variant was detected in one CRC/Endometrial MSI-H tumour using a standard panel of 5-10 markers and/or loss of MMR protein expression consistent with the variant location (PP4).
PM2_Supporting	✔	This variant is extremely rare (2 in 267958 alleles) in gnomAD using the non cancer dataset (PM2_Supporting) (Update: gnomAD v4.1 Grpmax AF = 6.856e-7)

Curation History

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