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Variant: NM_000251.3(MSH2):c.211G>C (p.Gly71Arg)

Version: 1.0

CA020066

142708 (ClinVar)

Gene: MSH2 (HGNC:4436)
Condition: Lynch syndrome (MONDO:0005835)
Inheritance Mode: Autosomal dominant inheritance
UUID: 37d6267b-b7c7-4b94-b086-40428da17513
Approved on: 2024/9/19
Published on: 2024/10/11

HGVS expressions

NM_000251.3(MSH2):c.211G>C (p.Gly71Arg)
NM_000251.3:c.211G>C
NC_000002.12:g.47403402G>C
CM000664.2:g.47403402G>C
NC_000002.11:g.47630541G>C
CM000664.1:g.47630541G>C
NC_000002.10:g.47484045G>C
NG_007110.2:g.5279G>C
ENST00000644900.2:c.211G>C
ENST00000233146.7:c.211G>C
ENST00000543555.6:c.13G>C
ENST00000644092.1:c.211G>C
ENST00000645339.1:c.211G>C
ENST00000645506.1:c.211G>C
ENST00000646415.1:c.211G>C
ENST00000233146.6:c.211G>C
ENST00000406134.5:c.211G>C
ENST00000454849.5:c.13G>C
ENST00000543555.5:c.13G>C
ENST00000610696.4:c.211G>C
ENST00000613514.4:c.211G>C
ENST00000617333.3:c.211G>C
ENST00000617938.4:c.211G>C
ENST00000621359.2:c.211G>C
NM_000251.2:c.211G>C
NM_001258281.1:c.13G>C

Pathogenic

Met criteria codes 3

PM2_Supporting PVS1 PP4_Strong

Not Met criteria codes 3

BA1 PP1 BS1

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 MSH2 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 MSH2 (NM_000251.3):c.211G>C variant affects the last G of exon 1. mRNA assays using RNA derived from patient constitutional biological samples indicates that the variant allele results in a splicing aberration (with evidence that the variant allele produces no full-length/reference transcript) leading to a premature stop codon (PVS1). It was identified in 4 CRC/EC tumours showing loss of MSH2/MSH6 expression in >2 families (PP4_strong). It was absent in gnomAD v2.1, v3.1 and v4.1 datasets (PM2_Supporting). In summary, this variant meets the criteria to be classified as pathogenic for Lynch Syndrome, based on the MMR gene specific ACMG/AMP criteria established by the ClinGen InSiGHT Hereditary Colorectal Cancer/ Polyposis VCEP: PVS1, PP4_Strong, and PM2_Sup (VCEP specifications version 1).

Met criteria codes

PM2_Supporting	✔	Absent in gnomAD v2.1, v3.1 and v4.1
PVS1	✔	mRNA assay using RNA derived from patient constitutional biological sample indicates that the variant allele results in a splicing aberration (with evidence that the variant allele produces no full-length/reference transcript) leading to a premature stop codon
PP4_Strong	✔	4 CRC/EC tumours with loss of MSH2/MSH6 expression

Not Met criteria codes

BA1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline
PP1	✖	Segregation LR 1,9 (PMID 28577310)
BS1	✖	No code specific comments provided, please refer to the summary above or general recommendations provided in the guideline

Curation History

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