GENE*ie* Report: NM_020223.4:c.957-3C>G

This report was produced for **Demo Admin** of **Demo Account** on Tuesday, 24 September 2024

This report is for research use only. It is not intended for diagnostic or clinical purposes.

Splice-Altering

90% PROBABILITY

- Annotated acceptor splice-site variant.
- Risk of cryptic mis-splicing. Competitive cryptic splice-site within 250 nt or in SpliceVault Top4.

NIF	Similar Impact	Same Sequence	SpliceVault Top4	Cryptic Risk
★★★	☆☆☆	☆☆☆	Mixed Frames	Yes

Variant	NM_020223.4:c.957-3C>G		
Gene	*FAM20C*	**Coordinates (GRCh38)**	7:248312 C>G
Location	(NM_020223.4) Intron 4 acceptor / Distance from acceptor: -3		
Variant Databases	VCV000001026 (ClinVar) - Pathogenic CS075122 (HGMD) - DM FAM20C_000037 (LOVD) - pathogenic (recessive)		

Native Intron Frequency (NIF)

Relative frequency of a given splice-site sequence among all human splice-site sequences

Window	Reference (REF)	Variant (VAR)	Frequency		% Scale		NIF Impact VAR/REF
			REF	VAR	REF	VAR	
A9 - A1	tcttgcc**ag**GA	tcttgc**g****ag**GA	108	0	0.45	0	-100%
A8 - E1	tcttgcc**ag**GA	tcttgc**g****ag**GA	105	0	0.47	0	-100%
A7 - E2	tcttgcc**ag**GA	tcttgc**g****ag**GA	73	1	0.42	0.01	-97%

NIF-ML Power (Machine Learning)	
ML Score	1.00
Pathogenic	98%
Benign	2%
n	545

Cryptic Splice-site Modification

Cryptic splice-site overlapping the annotated splice-site that is modified by this variant

Splice-site Position	Reference (REF)	Variant (VAR)	REF	VAR	SpliceVault Top-10	In Frame
			A9 - A1 | A8 - E1 | A7 - E2	A9 - A1 | A8 - E1 | A7 - E2		
Annotated	tcttgccagGA	tcttgcgagGA	0.45 | 0.47 | 0.42	0.00 | 0.00 | 0.01	N/A	N/A

Same Splice-site Variants

Variants affecting the same splice-site as the test variant

Test Variant	Distance from Acceptor	NIF Impact	Classification	Variant ID
		A9 - A1 | A8 - E1 | A7 - E2		
NM_020223.4:c.957-3C>G	-3	-100% | -100% | -97%	P; P; P	VCV000001026; CS075122; FAM20C_000037

Similar Impact Variants	Distance from Acceptor	NIF Impact	Classification	Variant ID
		A9 - A1 | A8 - E1 | A7 - E2		
No Similar Impact variants reported at this splice-site				

Different Impact Variants	Distance from Acceptor	NIF Impact	Classification	Variant ID
		A9 - A1 | A8 - E1 | A7 - E2		
NM_020223.4(FAM20C):c.957-5G>A	-5	-24% | -26% | -31%	LB	VCV002134596
NM_020223.4(FAM20C):c.957-5G>C	-5	+79% | +87% | +98%	LB	VCV000741476

Same Sequence Variants

Variants making the same sequence change at a different splice-site

Window	Reference (REF)	Variant (VAR)	NIF Impact	Pathogenic		Benign	
			VAR/REF	introns	*n*	introns	*n*
A9 - A1	tcttgccagGA	tcttgcgagGA	-100%	0	0	0	0
A8 - E1	tcttgccagGA	tcttgcgagGA	-100%	0	0	0	0
A7 - E2	tcttgccagGA	tcttgcgagGA	-97%	0	0	0	0

A9 - A1	NIF Impact	Classification	Variant ID
	A9 - A1 | A8 - E1 | A7 - E2		
No same sequence variants for this window			

A8 - E1	NIF Impact	Classification	Variant ID
	A9 - A1 | A8 - E1 | A7 - E2		
No same sequence variants for this window			

A7 - E2	NIF Impact	Classification	Variant ID
	A9 - A1 | A8 - E1 | A7 - E2		
No same sequence variants for this window			

SpliceVault Top-10

Natural splicing mistakes around this splice-site that may be enhanced by this variant

Event	Same Frame	Skipped Exons	Cryptic Position	Cryptic mean NIF	Samples (GTEx)	Samples (SRA)	Max Reads (GTEx)	Total Samples	Splice Junction
Annotated Splicing	✓				18,683	126,362	1,844	145,045	246508-248314
Exon Skipping		4-5			229	546	4	775	208977-255848
Exon Skipping		5			11	57	2	68	246508-255848
Cryptic acceptor [4]	✓		+39	0.17	3	50	1	53	246508-248353
Cryptic acceptor [4]			-62	0.09	2	32	1	34	246508-248253
Cryptic acceptor			-54	0.07	7	23	2	30	246508-248261
Cryptic acceptor			-66	0.03	4	20	2	24	246508-248249
Cryptic acceptor			-27	0.05	7	11	1	18	246508-248288
Cryptic acceptor	✓		-130	0.08	1	16	1	17	246508-248185
Cryptic acceptor			-122	0.07	2	11	1	13	246508-248193

[4] Cryptic is >= 50% strength of annotated splice-site

Understanding your report

Assertion and Probability

Splice - Altering

Clinical and genetic evidence indicate this variant has a given probability of altering pre-mRNA splicing for this gene.

Splice-Neutral

Clinical and genetic evidence indicate this variant has a given probability of maintaining the existing pattern of pre-mRNA splicing for this gene

Uncertain

Clinical and genetic evidence for pre-mRNA splicing disruption by this variant is weak and/or conflicting; and cannot be assigned a probability.

Flags

Summary

Native Intron Frequency (NIF)

NIF-ML Power (Machine Learning)

Cryptic Splice-site Modification

Same Splice-site Variants

Same Sequence Variants

SpliceVault Top-10

Report MetaData

REPORT DATE	GENEIE VERSION	API VERSION
24-Sept-2024	0.0.229.0	0.0.50
ML DONOR VERSION	**ML ACCEPTOR VERSION**	**CLINVAR RELEASE**
v1.0.6	v1.0.5	2023-07
HGMD RELEASE		
2019.1		