

Ejemplo comparación de resultados predictores in silico

Cambio de estudio NEB c.6915+1336A>G (chr 2:151652656 A/G, NM_001164507.2: c.6915+1336A>G)

Exón 50 e intrones adyacentes:

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tattcactctgttaggtaaacttttccctaataatctattgatattcttttatatagacaga
ataatgctgaagaatatctttaattttcag
AAACTCTATAAACTTGGATGGGAAGAAGCTTTGAAGAAAGGCTATGATCTCCCACTTGAT
GCAATTTCGTACAGCTAGCTAAAGCTTCAAGAGACATTGCTAGTGAT
gtgagtactagtttgagttctataaaggctatatattttatctgaatcaggtgacttaatgt
cggtaactatttttatggatagtccttacctttcaaaatataatgcttccttcattttct
cctaccctcttcatttatacggaggttcactcttctcttctcactgttcatatgtcaaaagg
gcttcctgaatagagggtcgggcccagacgacctcgaagatccattagagtaagatgctcta
cttggagatgtttacaaaggaccgagattgcaagttttccctactttgcctgaaaatata
ataatttttactgcttttctacttgtctatttttagacaaattcaagtgccagatgataaat
caactctcaaacttgatgctgatagatttttatatgcacatattttaaaataggctgtca
gttatttcagtttagccattttgacttatataaattgtaataaattaccttgggacata
aaaaatccaagaagggtccagaaatttaggtttaagttcccaagggttacttaactcttc
tttctgaaaatccaatctaagggtcatagattcactctccaaaggtagattccagttat
gattagaaaaggtagcaaatctggtgaaaaactagggtattgtctctatttaggtattgtc
tctattggttaatttttttaacagatattttacttagatatctctgcatattgctagcatac
atattgttaatccaaaaacttaaccacaaaaattcagaaggtcttggttatagtgaataa
attaccaggattttcatagggaaagttaggadctcttaatcaaaatctttgaaagaaaacagg
gatttgggttaataggcaggttgagtagacagagtgcaggaaaggatgcctaaaaatggaa
tctgacaataaattctaagaatatagggaagattttattttaattcacttaattttctggc
actccagaaatgttggaataataatgatgatataattataccactctccagcttgca
ggtcaatcccttattaaaaataatcaatgagggtgataagcctaaagcaataatgatgtgt
aaactcattttcatttagtgctatgtgctaaagatagttaggaattgaagaataacat
caataatttcctaacaacatttgatagctacctcattttcttttgtgtgaaccatttaatt
cgaaccttttgaaatcttactccaaatgaactataagtgaacttcccactattataga
gatgtatttccctcaatttcaaatgtcttctgtatttataaaattttcagaaaaattaaaaca
attttataagtatttataatgaattagaattcatagaatttagaagcggagagataacataaag
gacattttaatctaattctccactcaggatccctaccttctctccatctccaaaattctgta
gatacttaaaaaataagaattttggaggctgggtgcagtggcccggtcccataatctca
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El cambio se encuentra en la antepenúltima línea del intrón 50 (la **a** en color granate).

Se va a obtener los resultados que produce analizar esta variable con los diferente predictores y ver cuál de ellos es más preciso.

NetGene2

Donor splice sites, direct strand

pos	5'→3'	phase	strand	confidence	5'	exon	intron	3'
199		0	+	0.91	TGCTAGTGAT	^	GTGAGTACTA	H
834		1	+	0.31	GAAAACTAG	^	GTATTGTCTC	

Donor splice sites, complement strand

pos 3'→5'	pos 5'→3'	phase	strand	confidence	5'	exon	intron	3'
1612	87	0	-	0.00	TGGAGAGAAG	^	GTAGGATGCT	
1368	331	2	-	0.35	AAGAAATGAG	^	GTAATATCAA	
728	971	1	-	0.54	GAAGAGTTAA	^	GTAAGCCCTT	
667	1032	0	-	0.37	ATGTCCCAAG	^	GTAATTTATT	
323	1376	1	-	0.39	AATGAAGAGG	^	GTAAGGAGAAA	
287	1412	1	-	0.37	ATTTTGAAAG	^	GTAAGAGCTA	

Acceptor splice sites, direct strand

pos	5'→3'	phase	strand	confidence	5'	intron	exon	3'
115		1	+	0.07	GGATGGGAAG	^	AAGCTTTGAA	
531		0	+	0.57	TCTATTTTAG	^	ACAAATTCAA	
850		0	+	0.33	CTCTATTTAG	^	GTATTGTCTC	

Acceptor splice sites, complement strand

pos 3'→5'	pos 5'→3'	phase	strand	confidence	5'	intron	exon	3'
1022	677	1	-	0.53	TCTTTCAAAG	^	ATTTTGATTA	
819	880	1	-	0.17	TTTTCAACAG	^	ATTTGCTACC	
488	1211	2	-	0.33	ATATTTTCAG	^	GCAAAGTAGG	

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Splice Site Prediction by Neural Network (NNSplice)

Donor site predictions for 10.42.0.139.574515.0 :

Start	End	Score	Exon	Intron
192	206	0.95	tagtgat	gt gagtac
240	254	0.64	gaatcag	gt gactta
254	268	0.96	aatgtcg	gt aactat
419	433	0.81	cattaga	gt aagatg
777	791	0.91	cccaaag	gt agattc
1243	1257	0.58	caatgag	gt gataag

Acceptor site predictions for 10.42.0.139.574515.0 :

Start	End	Score	Intron	Exon
35	75	0.92	ctattgatattctttatat	ag acagaataatgctgaagaat
226	266	0.51	ctatatattttatctgaatc	ag gtgacttaatgtcggttaact
511	551	0.99	ctttctacttgtctatttt	ag acaaattcaaagtgccagat
830	870	0.89	ctaggtattgtctctatttt	ag gtattgtctctattggtaa
1145	1185	0.57	acttaatttctggcactcc	ag aaatgttggaataataat
1199	1239	0.75	taccactctccagcttgc	ag gtcaatcccttattaaaata
1437	1477	0.48	tgaactttcccactatttat	ag agatgtatttccctcaattt

Donor site predictions for 10.42.1.119.574527.0 :

Start	End	Score	Exon	Intron
192	206	0.95	tagtgat	gt gagtac
240	254	0.64	gaatcag	gt gactta
254	268	0.96	aatgtcg	gt aactat
419	433	0.81	cattaga	gt aagatg
777	791	0.91	cccaaag	gt agattc
1243	1257	0.58	caatgag	gt gataag

Acceptor site predictions for 10.42.1.119.574527.0 :

Start	End	Score	Intron	Exon
35	75	0.92	ctattgatattctttatat	ag acagaataatgctgaagaat
226	266	0.51	ctatatattttatctgaatc	ag gtgacttaatgtcggttaact
511	551	0.99	ctttctacttgtctatttt	ag acaaattcaaagtgccagat
830	870	0.89	ctaggtattgtctctatttt	ag gtattgtctctattggtaa
1145	1185	0.57	acttaatttctggcactcc	ag aaatgttggaataataat
1199	1239	0.75	taccactctccagcttgc	ag gtcaatcccttattaaaata
1437	1477	0.48	tgaactttcccactatttat	ag agatgtatttccctcaattt

Spliceman

Point mutation	Wildtype (wt)	Mutation (mt)	L1 distance	Ranking (L1)
tat tt (a/g)atgaa	tttaat	tttgat	29966	74%

Human Splicing Finder

<div><div></div>Alteration of auxiliary sequences</div> <div>Significant alteration of ESE / ESS motifs ratio (3)</div>		
Algorithm/Matix	position	sequence
ESS_hnRNPA1 (ESS Site Broken)	chr2:151652657	TAATGA
RESCUE ESE (New ESE Site)	chr2:151652657	TGATGA
IIE (New ESS Site)	chr2:151652657	TGATGA
Sironi_motif2 (New ESS Site)	chr2:151652657	TGATGAA
PESS (ESS Site Broken)	chr2:151652657	TAATGAAT
PESS (ESS Site Broken)	chr2:151652659	TTTAATGA
EIE (New ESE Site)	chr2:151652660	ATTTGA
IIE (New ESS Site)	chr2:151652660	ATTTGA
PESS (ESS Site Broken)	chr2:151652661	TATTTAAT

SVM-BPfinder

seq_id	agez	ss_dist	bp_seq	bp_scr	y_cont	ppt_off	ppt_len	ppt_scr	svm_scr				
wt	15	78	ttttcagaa		-2.70211898349	0.356164383562	15	6	13				-1.3695675
wt	15	70	aaattaaaa		-3.55055560732	0.369230769231	7	6	13				-1.191164
wt	15	69	aattaaaac		-0.709023521857	0.375	6	6	13				-0.01340828
wt	15	59	attttataa		-4.94195942364	0.351851851852	54	0	0				-4.8377043
wt	15	56	ttataagta		-2.02610137058	0.352941176471	51	0	0				-3.5057613
wt	15	49	tattttaatg		-3.20745702824	0.318181818182	44	0	0				-3.5364559
wt	15	48	attttaatga		-0.706554062214	0.325581395349	43	0	0				-2.491546
wt	15	45	taatgaatt		-1.02793661227	0.325	40	0	0				-2.4276752
wt	15	41	gaattagaa		-3.43859928475	0.305555555556	36	0	0				-3.1246504
wt	15	35	gaatcatag		-1.77467332989	0.3	30	0	0				-2.095149
wt	15	26	aatttagag		-4.39996390828	0.238095238095	21	0	0				-2.5733829
mut	15	78	ttttcagaa		-2.70211898349	0.356164383562	15	6	13				-1.3695675
mut	15	70	aaattaaaa		-3.55055560732	0.369230769231	7	6	13				-1.191164
mut	15	69	aattaaaac		-0.709023521857	0.375	6	6	13				-0.01340828
mut	15	59	attttataa		-4.94195942364	0.351851851852	54	0	0				-4.8377043
mut	15	56	ttataagta		-2.02610137058	0.352941176471	51	0	0				-3.5057613
mut	15	48	attttagatga		-0.70062753547	0.325581395349	43	0	0				-2.4892255
mut	15	45	tgatgaatt		-1.37180623181	0.325	40	0	0				-2.5623165
mut	15	41	gaattagaa		-3.43859928475	0.305555555556	36	0	0				-3.1246504
mut	15	35	gaatcatag		-1.77467332989	0.3	30	0	0				-2.095149
mut	15	26	aatttagag		-4.39996390828	0.238095238095	21	0	0				-2.5733829

Desaparece uno de los BP (49) mientras que los otros cambian a raíz de la presencia de la mutación (48 y 45). Como todos tienen puntuaciones positivas, no se van a tener en cuenta.

Variant Effect Predictor tool

ENST00000604864.5:c.6915+1336A>G	2:151652656-151652656	C	intron_variant	NEB	ENSG00000183091	Transcript	ENST00000172853.14	protein_coding	-
ENST00000604864.5:c.6915+1336A>G	2:151652656-151652656	C	intron_variant	NEB	ENSG00000183091	Transcript	ENST00000397345.7	protein_coding	-
ENST00000604864.5:c.6915+1336A>G	2:151652656-151652656	C	intron_variant	NEB	ENSG00000183091	Transcript	ENST00000409198.5	protein_coding	-
ENST00000604864.5:c.6915+1336A>G	2:151652656-151652656	C	intron_variant	NEB	ENSG00000183091	Transcript	ENST00000427231.6	protein_coding	-
ENST00000604864.5:c.6915+1336A>G	2:151652656-151652656	C	intron_variant	NEB	ENSG00000183091	Transcript	ENST00000603639.5	protein_coding	-
ENST00000604864.5:c.6915+1336A>G	2:151652656-151652656	C	intron_variant	NEB	ENSG00000183091	Transcript	ENST00000604864.5	protein_coding	-
ENST00000604864.5:c.6915+1336A>G	2:151652656-151652656	C	intron_variant	NEB	ENSG00000183091	Transcript	ENST00000618972.4	protein_coding	-

ESEfinder

No se obtienen puntuaciones positivas para ninguna predicción en ninguna de las secuencias.