

## Ejemplo comparación de resultados predictores in silico

Cambio de estudio ABCA8 c.2765-1855T>G (chr17:68896868 T/G, COSV52194951 o NM\_001288985.2: c.2765-1855T>G)

Exón 22 e intrones adyacentes:

```
tttcatccatctgctcagaataccatgcgattttaaacttatacaatgtttatttctgga
atttttcattttgtatttttagagatgcagtggaactaaaagtaactaaaactgcagaaagt
tgttcatgttttttatccacaaatttatcgccctttccatcttaactaagcacttatcat
gcactatgggtatataactttctacagtttgaggtgcaacagcaagactagcatgagtttctt
ttttcttcttcacaattttacagaagagatttgctctcagagtagatcttaacaacctcag
catacaattttttttattggtttcttatttaagtcaataaactttcacctttccacttaagg
aagcaatatatggcttctctttgacatatccaaattgcccagcatctctctcttggtgctt
tggggcactatataagtaaaatcagggtaactgaacacaaagcactgtgatgtcttgaca
gtcgatctgataaacggaggtggcgactaagtaactaatgagtaggtagcatatgcagtg
ggacacagaagacaaagggctgattcacatctgcacaggacagagtggaagatacgaga
tttcatccatctgctcagaataccatgcgattttaaacttatacaatgtttatttctgga
atttttcattttgtatttttagagatgcagtggaactaaaagtaactaaaactgcagaaagt
gaaaccatggataaaggagcactactataaatatggtcttggtttctaggaaaagtctttg
aagcaggttattgaggtgtgtctctctccacagaagggtctctcttaaactctctgttttgc
tgctctctctagtaaaccttttagctgggtatggttcaaccaagggaattgcaatctct
gtcaattgcttaccacaacaaactcttgatgggtttttggtgcactcttaggctgaacttc
ccaaactctgttccaaactaaagtcagtttatttagggagagtttcagcacatactgttct
tatggcttgccgctgttctctgaacaagaatctcaccattgcttcagagctggaagcatg
gatcggtgctgattctcttggtgtggaaacctgatttgtagcaggttacttggcagg
gtgggggctctgtctctcagcttgctctctctgtcggtggaactctgacctacaagt
gagatgggacaaggatgattgtgtcccggtgttttgggcctcttattcctagggtagagc
ttcacaacttaggattaggggaatgggtggaggaagagaactccagatctcttagccactct
tgctgtgattgatcttctgcaacgcagatgtggggaaatgagaaaagtccgatgggaagc
ccctcccgtagaatactatagccctgaactgggcttggtgggaatagggaatccctgttctt
gcccacaacctttcagagtgaagctctctattacacagatctgggaagggaagtggggagta
gacggatcaggctgtggctcaaatgccacaatttctcagtggtcttactgagatttaata
cattttattaaataaatgtgtcatcattttctgtatgctcttataaacaatttcaaacat
tttaatttgggtgttttttaggaatttttataggttatgattgttttctggggagaagg
tctataggcttctcactgctagctctacatgttgtcttccagtatcaagaaattttg
aaataattaatatctagcagtagtaaaatgacttagcaatttgggtggttaataat
ggaagtatcagtatcatataagctttattgggtatggacattcattgcaagatttctaaa
atctattttgaaagacacttggaactaaaaaatcttttaacattataataatcataagc
aaataaaaaatcatgaagggaattccatgagaaataatagatgtatgtatgttatgtag
aaaatatctgacagtcataattactgcttccacataatgacatttaactgtaatttgacta
cacaacttgacattaatgttttttagttttgtgatacctaataatctttaactacaccttag
GGCAGCATTGATGACTTTATACAGTCTGTGGAGCACAGAACATAGCTTTGAAGTGG
ATGCATTTGGAACAGAAATGCACAGATGACCATCTTATAATGGAGCCATCACAGTGT
GTTGTAATCAAAAG
gtatgcaggtcttaataaacttttctgaaaaatgtgaaaagctaacaataatcaatat
ctcaggcttccaacttaagaaataaaaatgaaaagcaatactgttttcatttattactt
```

El cambio se encuentra en la tercera línea del intrón 21 (la **t** 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'
796	1	+	0.41	AGTTATTGAG	^GTGTGTCCTC		
1128	1	+	0.50	TGTGAGCAGG	^GTACTTGCCA		
1199	1	+	0.41	TGCCCTACAC	^GTGAGATGGG		
2235	0	+	0.93	TAATGAAAAG	^GTATGCAGGT	H	

### Donor splice sites, complement strand

pos 3'→5'	pos 5'→3'	phase	strand	confidence	5'	exon	intron	3'
1548	807	1	-	0.34	TTAAATCTCA	^GTAAGAACAC		
1056	1299	1	-	0.37	TGAAGCAATG	^GTGAGATTCT		
913	1442	1	-	0.70	GATTTTGTTG	^GTAAGCAATT		

### Acceptor splice sites, direct strand

pos 5'→3'	phase	strand	confidence	5'	intron	exon	3'
81	2	+	0.00	TGTATTTTAG	^AGATGCAGTG		
359	1	+	0.26	CCACTTAAAG	^GAAGCAATAT		
579	1	+	0.16	TCCTGCACAG	^GACAGAGTGG		
681	0	+	0.43	TGTATTTTAG	^AGATGCAGTG		
1348	1	+	0.26	TGCAACGCAG	^ATGTGGGGAA		
1641	1	+	0.17	GGTTTTTTAG	^GAATTTTAT		
2065	2	+	0.07	ATGTTTTTAG	^TTTTGTGATA		
2100	1	+	0.43	TACACCTTAG	^GGGCAAGCAT		
2126	0	+	0.17	CTTTATACAG	^TCTGTGGAGC		
2135	0	+	0.07	GTCTGTGGAG	^CACCAGAACA		

### Acceptor splice sites, complement strand

pos 3'→5'	pos 5'→3'	phase	strand	confidence	5'	intron	exon	3'
1480	875	1	-	0.53	TCCTTCCCAG	^ATCTGTGTAA		
1338	1017	1	-	0.41	TGCGTTGCAG	^AAGATCAATA		
1193	1162	1	-	0.33	TCACGTGTAG	^GGCAGAGTTT		
1039	1316	2	-	0.30	CTTGTTTCAG	^GAACAGCGGC		
572	1783	0	-	0.33	TCCTGTGCAG	^GATGTGAATC		

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1199	1	+	0.41	TGCCCTACAC	^GTGAGATGGG		
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572	1783	0	-	0.33	TCCTGTGCAG	^GATGTGAATC		

Splice Site Prediction by Neural Network (NNSplice)

Donor site predictions for 10.42.0.139.574272.0 :

Start	End	Score	Exon	Intron
93	107	0.85	actaaaa	<b>g</b> t <sup>aa</sup> actaa
503	517	0.44	cgactaa	<b>g</b> t <sup>aa</sup> actaa
693	707	0.85	actaaaa	<b>g</b> t <sup>aa</sup> actaa
789	803	0.99	tattgag	<b>g</b> t <sup>gt</sup> gtcc
975	989	0.45	aactaaa	<b>g</b> t <sup>c</sup> agttt
1192	1206	0.72	cctacac	<b>g</b> t <sup>g</sup> agatg
2228	2242	0.99	tgaaaag	<b>g</b> t <sup>at</sup> gcag

Donor site predictions for 10.42.1.119.574284.0 :

Start	End	Score	Exon	Intron
93	107	0.85	actaaaa	<b>g</b> t <sup>aa</sup> actaa
503	517	0.44	cgactaa	<b>g</b> t <sup>aa</sup> actaa
693	707	0.85	actaaaa	<b>g</b> t <sup>aa</sup> actaa
789	803	0.99	tattgag	<b>g</b> t <sup>gt</sup> gtcc
975	989	0.45	aactaaa	<b>g</b> t <sup>c</sup> agttt
1192	1206	0.72	cctacac	<b>g</b> t <sup>g</sup> agatg
2228	2242	0.99	tgaaaag	<b>g</b> t <sup>at</sup> gcag

Acceptor site predictions for 10.42.0.139.574272.0 :

Start	End	Score	Intron	Exon
61	101	0.98	atttttcat	ttt <sup>gt</sup> gtat
242	282	0.77	tttcttcttcaca	attt <sup>ac</sup> agatg
559	599	0.76	gctgattcacat	cct <sup>gc</sup> acag
661	701	0.98	atttttcat	ttt <sup>gt</sup> gtat
748	788	0.88	taaatatggt	ctt <sup>gt</sup> gtat
792	832	0.86	tgagggtgtgt	cct <sup>cc</sup> acag
832	872	0.90	ctgttttgctg	ctc <sup>t</sup> ctat
928	968	0.79	tggtttttgg	tgact <sup>ctt</sup> at
1047	1087	0.46	agaatctcacc	att <sup>g</sup> cttc
1143	1183	0.84	ggtaggctctg	gtct <sup>ctc</sup> at
1232	1272	0.70	ttttgggcct	ctt <sup>att</sup> cct
1251	1291	0.56	aggtagagct	ttcc <sup>ac</sup> ctt
1436	1476	0.82	ttcttgcacac	cct <sup>ttc</sup> at
1457	1497	0.72	agtgaagctt	catt <sup>ac</sup> ac
1621	1661	0.86	tttaattgttg	gttt <sup>ttt</sup> at
1704	1744	0.69	agtctacatgt	gtct <sup>ccc</sup> aaa
2045	2085	0.43	acttgacatta	atgt <sup>ttt</sup> tat
2080	2120	0.50	atatctttaac	tac <sup>ctt</sup> at


Acceptor site predictions for 10.42.1.119.574284.0 :

Start	End	Score	Intron	Exon
61	101	0.98	atttttcat	ttt <sup>gt</sup> gtat
242	282	0.77	tttcttcttcaca	attt <sup>ac</sup> agatg
559	599	0.76	gctgattcacat	cct <sup>gc</sup> acag
661	701	0.98	atttttcat	ttt <sup>gt</sup> gtat
748	788	0.88	taaatatggt	ctt <sup>gt</sup> gtat
792	832	0.86	tgagggtgtgt	cct <sup>cc</sup> acag
832	872	0.90	ctgttttgctg	ctc <sup>t</sup> ctat
928	968	0.79	tggtttttgg	tgact <sup>ctt</sup> at
1047	1087	0.46	agaatctcacc	att <sup>g</sup> cttc
1143	1183	0.84	ggtaggctctg	gtct <sup>ctc</sup> at
1232	1272	0.70	ttttgggcct	ctt <sup>att</sup> cct
1251	1291	0.56	aggtagagct	ttcc <sup>ac</sup> ctt
1436	1476	0.82	ttcttgcacac	cct <sup>ttc</sup> at
1457	1497	0.72	agtgaagctt	catt <sup>ac</sup> ac
1621	1661	0.86	tttaattgttg	gttt <sup>ttt</sup> at
1704	1744	0.69	agtctacatgt	gtct <sup>ccc</sup> aaa
2045	2085	0.43	acttgacatta	atgt <sup>ttt</sup> tat
2080	2120	0.50	atatctttaac	tac <sup>ctt</sup> at

Spliceman

Point mutation	Wildtype (wt)	Mutation (mt)	L1 distance	Ranking (L1)
aaatt(t/g)atcgc	atttat	attgat	30599	78%

Human Splicing Finder

 Alteration of auxiliary sequences	Significant alteration of ESE / ESS motifs ratio (5)	
Algorithm/Matix	position	sequence
IIE (ESS Site Broken)	chr17:68896869	CTTCTT
IIE (ESS Site Broken)	chr17:68896870	TCTTCT
ESE_SRp55 (New ESE Site)	chr17:68896871	TTCGTC
IIE (ESS Site Broken)	chr17:68896871	TTCTTC
PESS (ESS Site Broken)	chr17:68896874	TTTTTCTT
PESS (New ESS Site)	chr17:68896874	TTTTTCGT
PESS (ESS Site Broken)	chr17:68896875	TTTTTTCT

SVM-BPfinder

seq_id	agez	ss_dist	bp_seq	bp_scr	y_cont	ppt_off	ppt_len	ppt_scr	svm_scr	
wt	17	85	aagtaacta		0.654614090409	0.6	17	21	34	0.09253991
wt	17	81	aactaaaac		0.699226539057	0.605263157895	13	21	34	0.36490093
wt	17	62	tgttcatgt		0.416845143828	0.666666666667	1	14	24	0.9405882
wt	17	53	tttttatcc		-3.40424372064	0.645833333333	9	20	39	-0.92892615
wt	17	41	aatttatcg		-2.95966778119	0.666666666667	1	16	32	-0.3069494
wt	17	24	atcttaact		-1.40605429078	0.526315789474	19	0	0	-1.1814423
wt	17	23	tcttaacta		0.318588757934	0.555555555556	18	0	0	-0.43342118
wt	17	19	aactaagca		0.46921544824	0.571428571429	14	0	0	-0.11612391
mut	17	85	aagtaacta		0.654614090409	0.5875	17	21	34	0.088502761
mut	17	81	aactaaaac		0.699226539057	0.592105263158	13	21	34	0.36065131
mut	17	62	tgttcatgt		0.416845143828	0.649122807018	1	14	24	0.93492205
mut	17	53	tttttatcc		-3.40424372064	0.625	13	16	32	-1.2540589
mut	17	41	aattgatcg		0.391362830925	0.666666666667	1	16	32	1.0051374
mut	17	24	atcttaact		-1.40605429078	0.526315789474	19	0	0	-1.1814423
mut	17	23	tcttaacta		0.318588757934	0.555555555556	18	0	0	-0.43342118
mut	17	19	aactaagca		0.46921544824	0.571428571429	14	0	0	-0.11612391

La diferencia entre las secuencias es que el BP que en la WT tiene puntuación negativa, en la secuencia mutante tiene puntuación positiva, lo que podría significar que se está activando un BP.

## Variant Effect Predictor tool

ENST00000586539.5:c.2765-1855T>G	<a href="#">17:68896868-68896868</a>	C	intron_variant	ABCA8	<a href="#">ENSG00000141338</a>	Transcript	<a href="#">ENST00000269080.6</a>	protein_coding	<a href="#">COSV52194951</a>
ENST00000586539.5:c.2765-1855T>G	<a href="#">17:68896868-68896868</a>	C	intron_variant	ABCA8	<a href="#">ENSG00000141338</a>	Transcript	<a href="#">ENST00000430352.6</a>	protein_coding	<a href="#">COSV52194951</a>
ENST00000586539.5:c.2765-1855T>G	<a href="#">17:68896868-68896868</a>	C	intron_variant, non_coding_transcript_variant	ABCA8	<a href="#">ENSG00000141338</a>	Transcript	<a href="#">ENST00000541225.5</a>	retained_intron	<a href="#">COSV52194951</a>
ENST00000586539.5:c.2765-1855T>G	<a href="#">17:68896868-68896868</a>	C	intron_variant	ABCA8	<a href="#">ENSG00000141338</a>	Transcript	<a href="#">ENST00000586539.6</a>	protein_coding	<a href="#">COSV52194951</a>
ENST00000586539.5:c.2765-1855T>G	<a href="#">17:68896868-68896868</a>	C	intron_variant	ABCA8	<a href="#">ENSG00000141338</a>	Transcript	<a href="#">ENST00000589533.5</a>	non_stop_decay	<a href="#">COSV52194951</a>
ENST00000586539.5:c.2765-1855T>G	<a href="#">17:68896868-68896868</a>	C	intron_variant, non_coding_transcript_variant	ABCA8	<a href="#">ENSG00000141338</a>	Transcript	<a href="#">ENST00000590359.1</a>	retained_intron	<a href="#">COSV52194951</a>
ENST00000586539.5:c.2765-1855T>G	<a href="#">17:68896868-68896868</a>	C	intron_variant	ABCA8	<a href="#">ENSG00000141338</a>	Transcript	<a href="#">ENST00000615593.4</a>	protein_coding	<a href="#">COSV52194951</a>

## ESEfinder

No hay resultados positivos para ninguna de las secuencias.