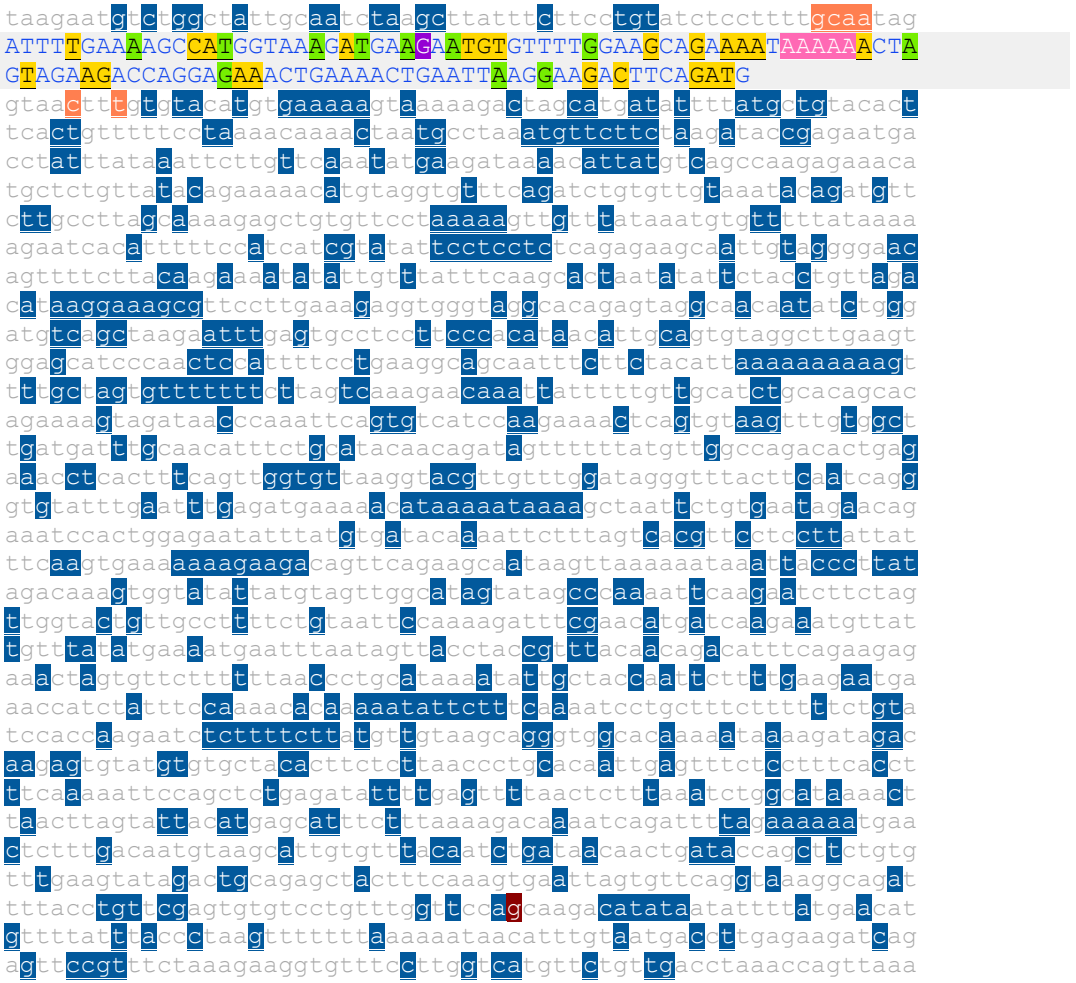
Ejemplo comparación de resultados predictores in sillico

Cambio de estudio BCAP29 c.589+1714G>T (chr7:107602219 G/T, COSV50051686 o NM_001008405.4: c.589+1714G>T)

Exón 5 e intrones adyacentes:



El cambio se encuentra en la antepenúltima línea del intrón 5 (la **g** en color rojo).

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'
170	1	+	0.55	ACTTCAGATG^GTAACTTTGT
373	2	+	0.32	AGAAAAACAT^GTAGGTGTTT
616	1	+	0.53	CTTGAAAGAG^GTGGGTAGGC
876	1	+	0.64	AAAACTCAGT^GTAAGTTTGT
976	2	+	0.62	TGGTGTTAAG^GTACGTTGTT
1838	2	+	0.54	TAGTGTTCAG^GTAAAGGCAG

Donor splice sites, complement strand

pos 3'->5'	pos 5'->3'	phase	strand	confidence	5' exon intron 3'
1854	176	1	-	0.44	ACTCGAACAG^GTAAAATCTG
1343	687	1	-	0.47	GTTGTAAACG^GTAGGTAACT
1339	691	2	-	0.37	TAAACGGTAG^GTAACTATTA

Acceptor splice sites, direct strand

pos 5'->3'	phase	strand	confidence	5' intron exon 3'
60	0	+	0.00	TTTGCAATAG^ATTTTGAAAA
103	1	+	0.19	GTTTTGGAAG^CAGAAAATAA
106	1	+	0.19	TTGGAAGCAG^AAAATAAAAA
509	2	+	0.53	CTCCTCTCAG^AGAAGCAATT

Acceptor splice sites, complement strand

pos 3'->5'	pos 5'->3'	phase	strand	confidence	5' intron exon 3'
819	1211	2	-	0.33	TGCTGTGCAG^ATGCAACAAA
751	1279	1	-	0.25	TTTAATGTAG^AAGAAATTGC
748	1282	1	-	0.23	AATGTAGAAG^AAATTGCTGC
582	1448	2	-	0.25	TGTCTAACAG^GTAGAATATA
354	1676	0	-	0.25	TGTATAACAG^AGCATGTTTC
242	1788	2	-	0.25	TTTGTTTTAG^GAAAAACAGT

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Splice Site Prediction by Neural Network (NNSplice)

Donor site predictions for wt :

Start	End	Score	Exon	Intron
70	84	0.77	agccatg	gtaaagat
163	177	0.64	tcagatg	gtaacttt
366	380	0.67	aaaacat	gtaggtgt
609	623	0.93	gaaagag	gtgggtag
869	883	0.99	actcagt	gtaagttt
969	983	0.99	tgttaag	gtacgttg
1510	1524	0.63	ttatgtt	gtaagcag
1735	1749	0.98	tgacaat	gtaagcat
1831	1845	0.93	tgttcag	gtaaaggc

Donor site predictions for mut :

Start	End	Score	Exon	Intron
70	84	0.77	agccatg	gtaaagat
163	177	0.64	tcagatg	gtaacttt
366	380	0.67	aaaacat	gtaggtgt
609	623	0.93	gaaagag	gtgggtag
869	883	0.99	actcagt	gtaagttt
969	983	0.99	tgttaag	gtacgttg
1510	1524	0.63	ttatgtt	gtaagcag
1735	1749	0.98	tgacaat	gtaagcat
1831	1845	0.93	tgttcag	gtaaaggc

Acceptor site predictions for wt :

Start	End	Score	Intron	Exon
40	80	0.95	ctgtatctccttttgcaat	agattttgaaaagccatggtaa
489	529	0.88	atcgtatattcctcctctc	agagaagcaattgtaggggaac
568	608	0.82	ctaatatattctacctgtt	agacataaggaaagcgttcctt
717	757	0.59	cccaactccattttcctga	aggcagcaatttcttctacatt
771	811	0.86	ttgctagtgttttttcttt	agtcaaagaacaaattattttt

Acceptor site predictions for mut :

Start	End	Score	Intron	Exon
40	80	0.95	ctgtatctccttttgcaat	agattttgaaaagccatggtaa
489	529	0.88	atcgtatattcctcctctc	agagaagcaattgtaggggaac
568	608	0.82	ctaatatattctacctgtt	agacataaggaaagcgttcctt
717	757	0.59	cccaactccattttcctga	aggcagcaatttcttctacatt
771	811	0.86	ttgctagtgttttttcttt	agtcaaagaacaaattattttt

Spliceman

Point mutation	Wildtype (wt)	Mutation (mt)	L1 distance	Ranking (L1)
ttcca(g/t)caaga	ccagca	ccatca	28230	63%

Human Splicing Finder

No significant impact on splicing signals.	No significant impact on splicing signals.

SVM-BPfinder

seq_id	agez	ss_dist	bp_seq	bp_scr	y_cont	ppt_off	ppt_len	ppt_scr	svm_scr
wt	22	15	atataatat		-1.2551519652	0.6	1	8	14	0.17123247
mut	22	25	ccatcaaga		-3.03704966887	0.45	11	8	14	-1.2078935
mut	22	15	atataatat		-1.2551519652	0.6	1	8	14	0.17123247

Aparece un BP en la secuencia mutante, pero tiene puntuación negativa, por lo que no se tendrá en cuenta.

Variant Effect Predictor tool

ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	intron_variant	BCAP29	ENSG00000075790	Transcript	ENST00000005259.9	protein_coding	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	intron_variant	BCAP29	ENSG00000075790	Transcript	ENST00000379117.6	protein_coding	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	intron_variant	DUS4L-BCAP29	ENSG00000288558	Transcript	ENST00000379119.6	protein_coding	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	intron_variant	BCAP29	ENSG00000075790	Transcript	ENST00000436699.2	protein_coding	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	intron_variant, NMD_transcript_variant	BCAP29	ENSG00000075790	Transcript	ENST00000442065.5	nonsense_mediated_decay	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	intron_variant	BCAP29	ENSG00000075790	Transcript	ENST00000445771.6	protein_coding	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	intron_variant	BCAP29	ENSG00000075790	Transcript	ENST00000457837.5	protein_coding	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	upstream_gene_variant	AC004839.1	ENSG00000238832	Transcript	ENST00000459477.1	snoRNA	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	intron_variant	BCAP29	ENSG00000075790	Transcript	ENST00000465919.5	protein_coding	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	downstream_gene_variant	BCAP29	ENSG00000075790	Transcript	ENST00000479917.5	protein_coding	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	intron_variant, NMD_transcript_variant	BCAP29	ENSG00000075790	Transcript	ENST00000482371.5	nonsense_mediated_decay	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	downstream_gene_variant	BCAP29	ENSG00000075790	Transcript	ENST00000490060.1	retained_intron	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	intron_variant	BCAP29	ENSG00000075790	Transcript	ENST00000491150.5	protein_coding	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	intron_variant, non_coding_transcript_variant	BCAP29	ENSG00000075790	Transcript	ENST00000494086.5	processed_transcript	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	intron_variant	DUS4L-BCAP29	ENSG00000288558	Transcript	ENST00000673665.1	protein_coding	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	intron_variant	DUS4L-BCAP29	ENSG00000288558	Transcript	ENST00000673689.1	protein_coding	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	intron_variant, NMD_transcript_variant	DUS4L-BCAP29	ENSG00000288558	Transcript	ENST00000673709.1	nonsense_mediated_decay	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	intron_variant	DUS4L-BCAP29	ENSG00000288558	Transcript	ENST00000673720.1	protein_coding	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	intron_variant	DUS4L-BCAP29	ENSG00000288558	Transcript	ENST00000673757.1	protein_coding	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	intron_variant	DUS4L-BCAP29	ENSG00000288558	Transcript	ENST00000673780.1	protein_coding	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	intron_variant, NMD_transcript_variant	DUS4L-BCAP29	ENSG00000288558	Transcript	ENST00000673784.1	nonsense_mediated_decay	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	intron_variant	DUS4L-BCAP29	ENSG00000288558	Transcript	ENST00000673970.1	protein_coding	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	intron_variant, NMD_transcript_variant	DUS4L-BCAP29	ENSG00000288558	Transcript	ENST00000673992.1	nonsense_mediated_decay	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	intron_variant, NMD_transcript_variant	DUS4L-BCAP29	ENSG00000288558	Transcript	ENST00000674049.1	nonsense_mediated_decay	-	-	-	-	-	-	COSV50051686
ENST00000379119.6:c.589+1714G>T	7:107602219-107602219	T	intron_variant, NMD_transcript_variant	DUS4L-BCAP29	ENSG00000288558	Transcript	ENST00000674062.1	nonsense_mediated_decay	-	-	-	-	-	-	COSV50051686
ENST00000381652.3:c.1849G>T	9:5073770-5073770	T	missense_variant	JAK2	ENSG00000096968	Transcript	ENST00000381652.4	protein_coding	14/25	2316	1849	617	V/F	GTC/TTC	rs77375493, CM123094,

ESEfinder

Para los resultados que contienen la posición de interés, se observa que, para la secuencia WT (arriba), 1869 tiene puntuación positiva y 1873 negativa, mientras que, para la secuencia mutante (abajo), ocurre justo al revés para las matrices 3'. Esto es una contradicción, dado que significaría que se está perdiendo y activando un sitio *acceptor* en esa región, lo que no tiene mucho sentido, por lo que no se tendrá en cuenta:

1869 (-161)	cctgtttggttccagcaagacatataatat	-22.77080	1869 (-161)	cctgtttggttccagcaagacatataatat	6.37690	1869 (-161)	cctgtttggttccagcaagacatataatat	-19.70470	1869 (-161)	cctgtttggttccagcaagacatataatat	6.31190
1870 (-160)	ctgtttggttccagcaagacatataatatt	-30.00420	1870 (-160)	ctgtttggttccagcaagacatataatatt	-23.94990	1870 (-160)	ctgtttggttccagcaagacatataatatt	-27.07280	1870 (-160)	ctgtttggttccagcaagacatataatatt	-21.65660
1871 (-159)	tgtttggttccagcaagacatataatattt	-29.07240	1871 (-159)	tgtttggttccagcaagacatataatattt	-32.36300	1871 (-159)	tgtttggttccagcaagacatataatattt	-28.07440	1871 (-159)	tgtttggttccagcaagacatataatattt	-33.78380
1872 (-158)	gtttggttccagcaagacatataatatttt	-17.97170	1872 (-158)	gtttggttccagcaagacatataatatttt	-9.38330	1872 (-158)	gtttggttccagcaagacatataatatttt	-15.05790	1872 (-158)	gtttggttccagcaagacatataatatttt	-12.62220
1873 (-157)	tttggttccagcaagacatataatatttta	-13.02520	1873 (-157)	tttggttccagcaagacatataatatttta	-0.92280	1873 (-157)	tttggttccagcaagacatataatatttta	-14.42660	1873 (-157)	tttggttccagcaagacatataatatttta	-0.81980

1869 (-161)	cctgtttggttccatcaagacatataatat	-26.74060	1869 (-161)	cctgtttggttccatcaagacatataatat	-5.71070	1869 (-161)	cctgtttggttccatcaagacatataatat	-23.62790	1869 (-161)	cctgtttggttccatcaagacatataatat	-6.64150
1870 (-160)	ctgtttggttccatcaagacatataatatt	-30.07240	1870 (-160)	ctgtttggttccatcaagacatataatatt	-19.38200	1870 (-160)	ctgtttggttccatcaagacatataatatt	-27.07750	1870 (-160)	ctgtttggttccatcaagacatataatatt	-19.99810
1871 (-159)	tgtttggttccatcaagacatataatattt	-30.16970	1871 (-159)	tgtttggttccatcaagacatataatattt	-25.94350	1871 (-159)	tgtttggttccatcaagacatataatattt	-29.10130	1871 (-159)	tgtttggttccatcaagacatataatattt	-26.84880
1872 (-158)	gtttggttccatcaagacatataatatttt	-18.43090	1872 (-158)	gtttggttccatcaagacatataatatttt	-9.31690	1872 (-158)	gtttggttccatcaagacatataatatttt	-15.55170	1872 (-158)	gtttggttccatcaagacatataatatttt	-12.61780
1873 (-157)	tttggttccatcaagacatataatatttta	-13.14810	1873 (-157)	tttggttccatcaagacatataatatttta	1.75940	1873 (-157)	tttggttccatcaagacatataatatttta	-14.46190	1873 (-157)	tttggttccatcaagacatataatatttta	1.92710