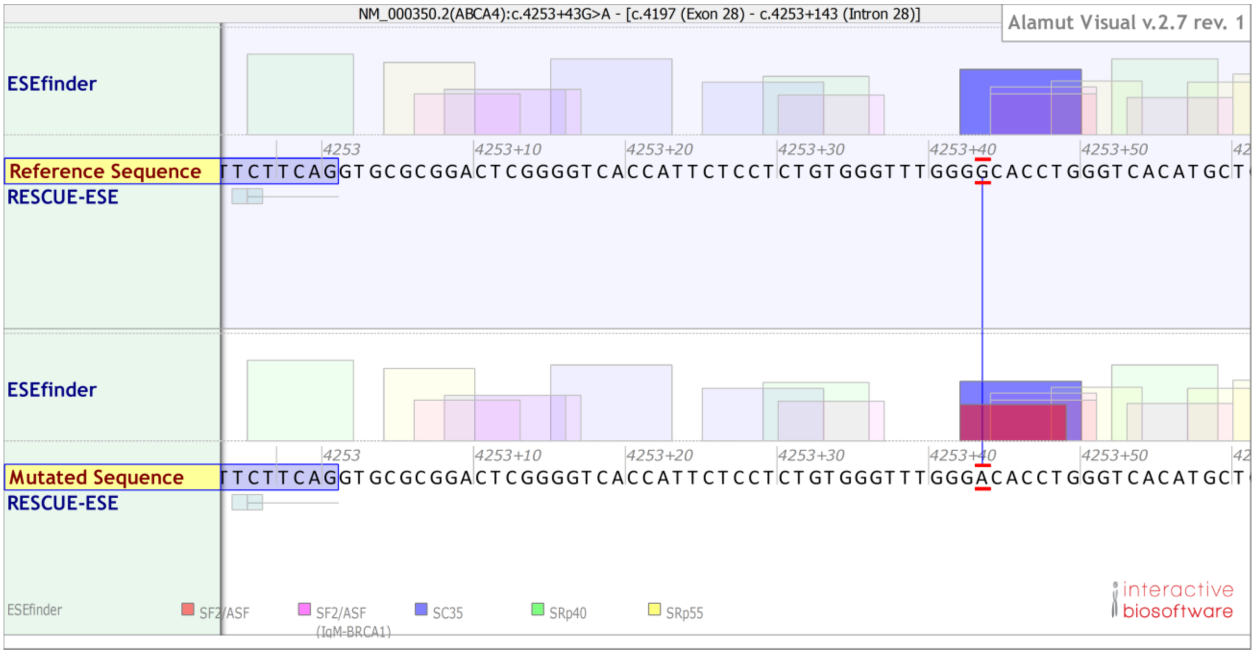
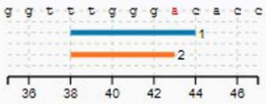
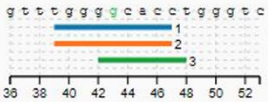
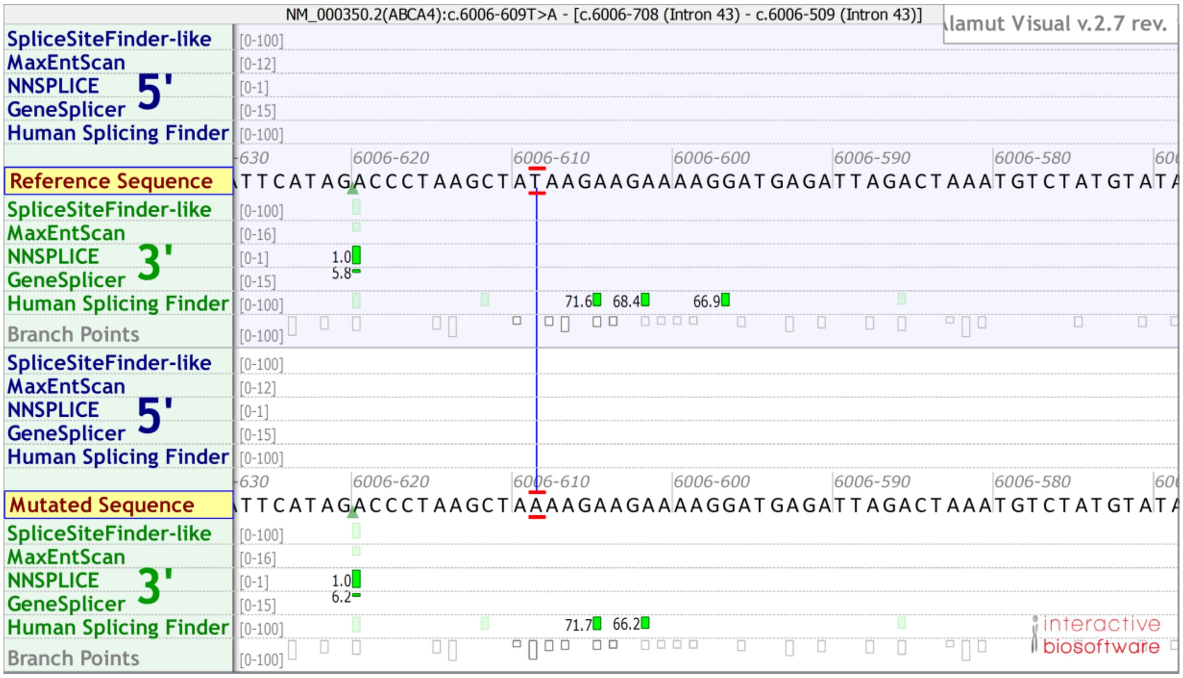
A **c.4253+43G>A**



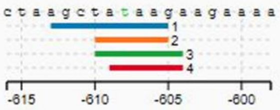
Changes: SC35 motif 3.75>3.39, and new SF2/ASF motif 2.09

Predicted signal	Prediction algorithm	cDNA Position	Interpretation
ESS Site broken	1 - Sironi et al. - Motif 2		Alteration of an intronic ESS site. Probably no impact on splicing.
	2 - Fas-ESS hexamers		
New ESE Site	1 - HSF Matrices - 9G8		Creation of an intronic ESE site. Probably no impact on splicing.
	2 - EIEs from Zhang et al.		
	3 - ESE-Finder - SF2/ASF		

B c.6006-609T>A

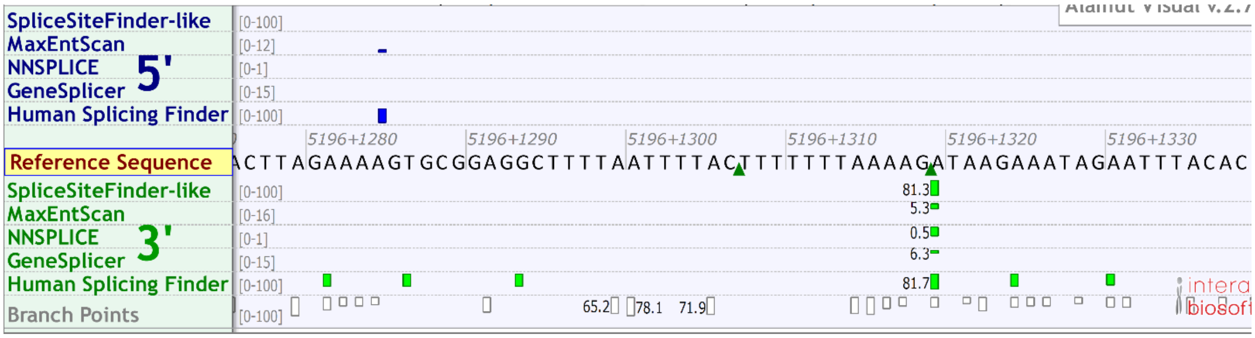


Changes: SRp40 motif 2.71>3.53

Predicted signal	Prediction algorithm	cDNA Position	Interpretation
New ESE Site	1 - EIEs from Zhang et al.		Creation of an intronic ESE site. Probably no impact on splicing.
	2 - HSF Matrices - Tra2-β		
	3 - RESCUE ESE Hexamers		
	4 - ESR Sequences from Goren et al.		

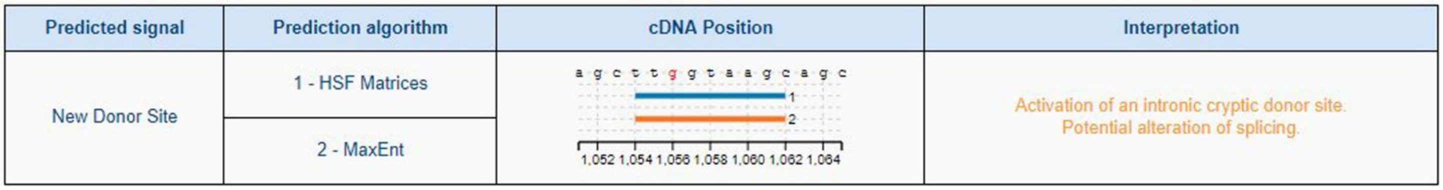
C **c.5196+1056A>G**

Cryptic donor strongly activated

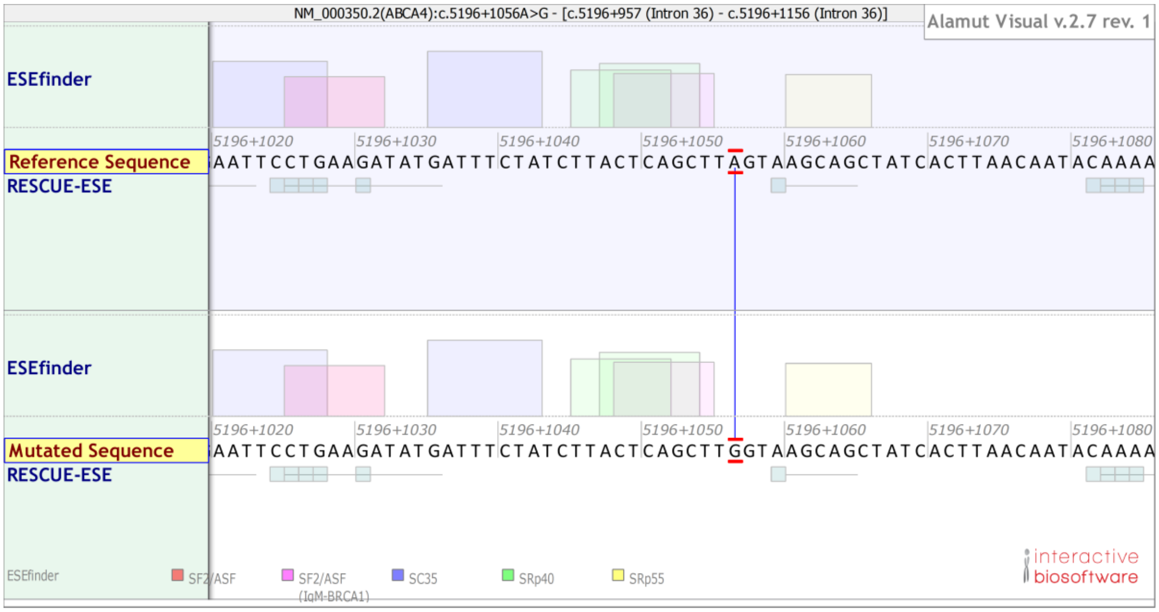


Probable nearest downstream cryptic splice acceptor at c.5196+1318

Splicing from these cryptic sites would result in a 262 bp pseudoexon and frameshift.



Predicted signal	Prediction algorithm	cDNA Position	Interpretation
New Donor Site	1 - HSF Matrices	a g c t t g g t a a g c a g c 1 2 1,052 1,054 1,056 1,058 1,060 1,062 1,064	Activation of an intronic cryptic donor site. Potential alteration of splicing.
	2 - MaxEnt		



Supplemental Figure 1. Predicted effects of the three non-coding *ABCA4* variants on splicing and exonic splicing enhancers and silencers (ESE and ESS). Assessed using 5 different algorithms (SpliceSiteFinder, MaxEntScan, NNSPLICE, GeneSplicer, Human Splicing Finder) via Alamut software (http://www.interactive-biosoftware.com).