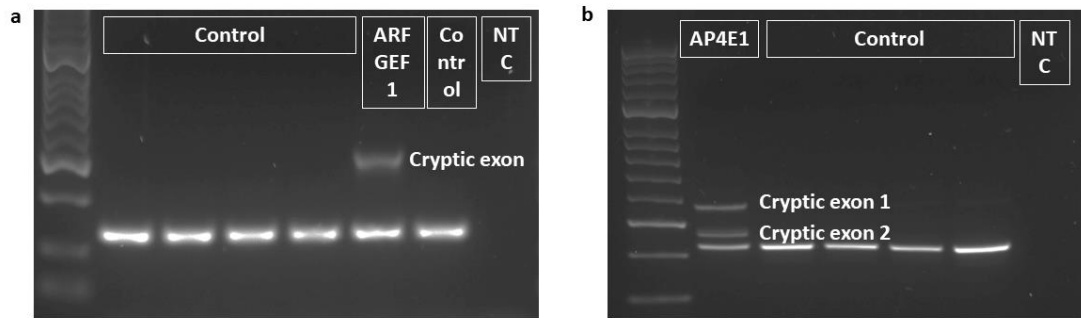
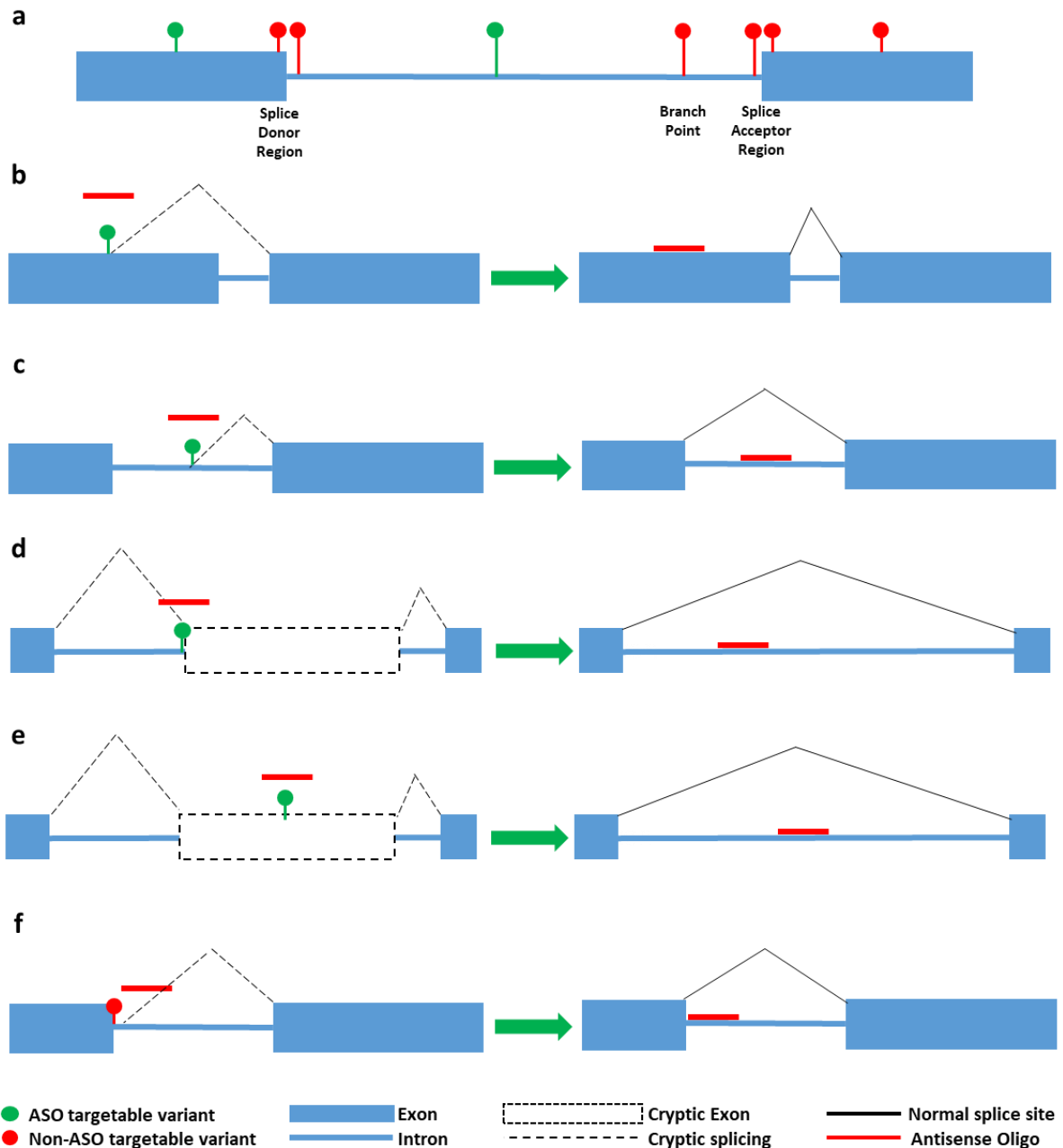
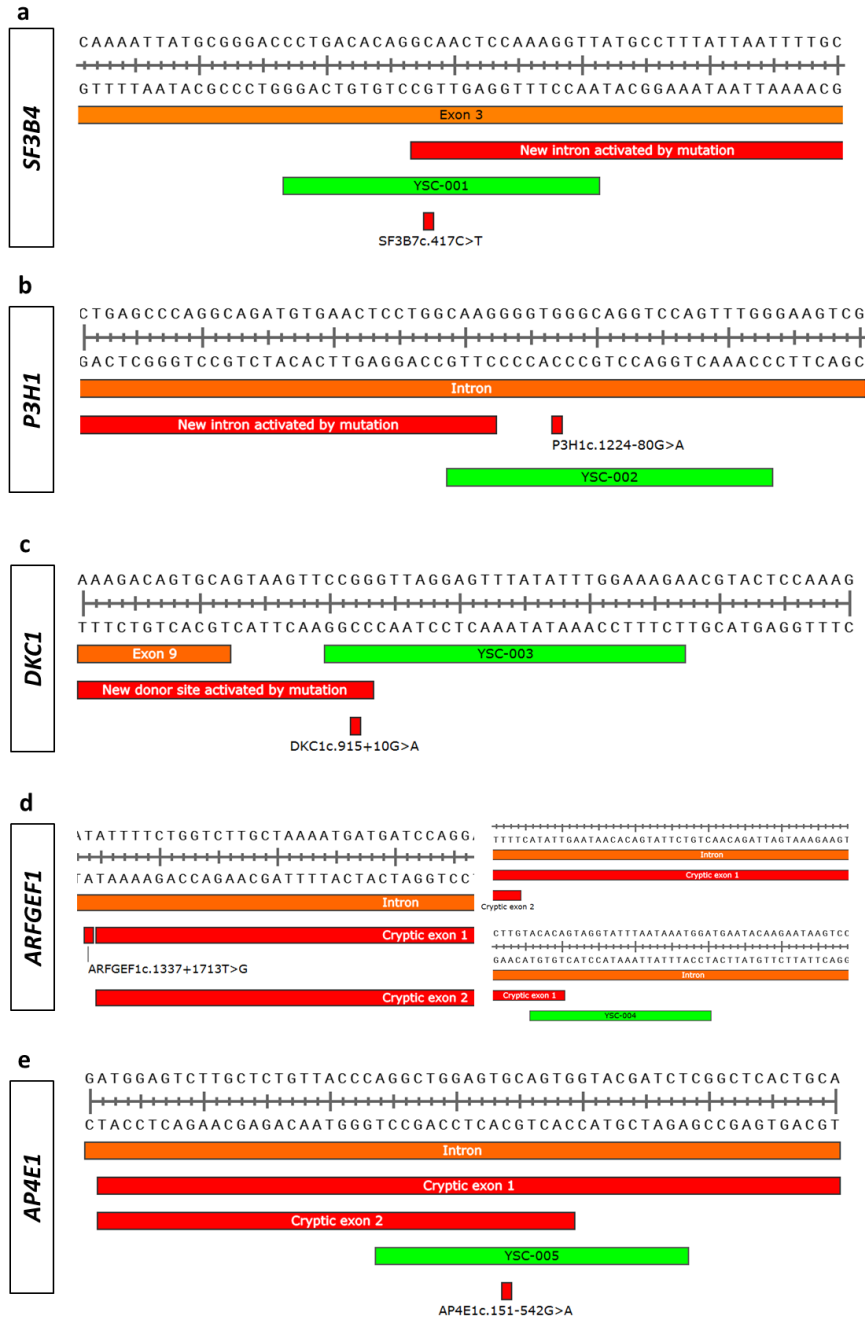




Supplementary figure 1. RT-PCR gel electrophoresis picture of ARFGEF1 c.1337+1713T>G and AP4E1 c.151-542G>A using patient blood samples. (a) ARFGEF1 variant causes the activation of a cryptic exon in the patient blood sample. (b) AP4E1 intronic variant induces two cryptic exons in the patient blood sample.



Supplementary figure 2. Determining ASO targetability of aberrant splicing variants. (a) ASO targetable variants are generally located in the region far away from splice donor and acceptor sites. (b) Cryptic splice site activating exonic synonymous variants can be targeted by ASO to restore the normal splicing. (c) Cryptic splice site activating intronic variant can also be targeted by ASO for splicing correction. (d) Variant activating donor site of cryptic exon can also be targeted by ASO or (e) Cryptic exon activating distant variant can be silenced with ASO by directly masking the variant region without interfering the cryptic exon (f) Variant near the splice donor site can be targeted without interfering the constitutive splice donor site.



Supplementary figure 4. Genomic sequences with mutations, aberrant splicing and ASO target sequence locations. (a) The synonymous exonic mutation of SF3B4c.417C>T activates a new donor site which was targeted with YSC-001 (AACCTTTGGAGTTACCTGTGTCAGG). (b) The P3H1 c.1224-80G>A mutation creates a new donor site which was targeted with YSC-002 (CCAACTGGACCTGCCTACCCCTTG). (c) The intronic DKC1 c.915+10 G>A mutation generates a new donor site near the wild-type constitutive donor site and was targeted with YSC-003 (TCTTTCCAAATATAAACTCCTAACCTGG). (d) This intronic mutation ARFGEF1 c.1337+1713T>G activates a new acceptor site and activates two cryptic donor sites, and one donor site was targeted with YSC-004 (TCCATTTATTAAATACCTACTGTGT). (e) The intronic mutation AP4E1 c.151-542G>A functions as an exonic enhancer, leading to the creation of two cryptic exons. The enhancer site was targeted with YSC-005 (AGATCGTACCACTGTACTCCAGCCT).

Supplementary data 1

pTB Vector Sequence

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Supplementary data 2

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