HOW ALTERNATIVE SPLICING WORKS

While some details of the mechanisms of splicing remain to be worked out, it's known that mature, edited mRNAs result from an interplay between multiple factors within and outside the transcript itself. Among these is the spliceosome, the machinery that carries out the splicing.

Each splicing event requires three components: the splice donor, a GU nucleotide sequence at one end of the intron; a splice acceptor, an AG nucleotide sequence at the opposite end; and a branch point, an A approximately 20–40 nucleotides away from the splice acceptor. These three "splice sites" are recognized by two core small nuclear RNAs (snRNAs) of the spliceosome, U1 and U2, followed by a protein, U2AF. The binding of these molecules to a transcript recruits a complex of three more snRNAs—U4, U5, and U6—which facilitates the splicing reaction.

A variety of factors affect how transcripts from a particular gene are spliced. Exon recognition by the spliceosome can be influenced by RNA binding proteins (RBPs), which bind to enhancer and silencer motifs within the mRNA and help or hinder spliceosome recognition of the splice sites. And because pre-mRNAs are frequently spliced as they're transcribed, the speed of transcription by RNA polymerase II further tunes the window of opportunity for splice site recognition by the spliceosome.