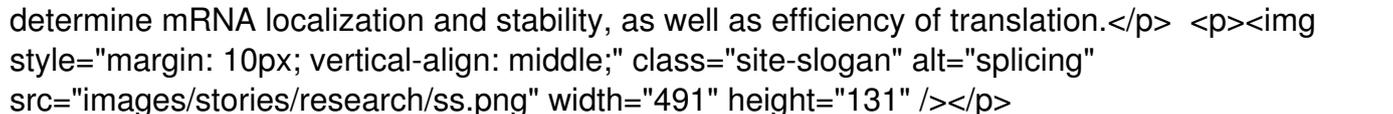


Introduction to Splicing

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Splicing is the process by which introns are removed from an mRNA precursor (pre-mRNA) and exons are ligated to form a mature mRNA. Most types of splicing, in organisms ranging from yeast to human, take place within the spliceosome—a large complex comprised of five ribonucleoproteins (RNPs) containing the small nuclear RNAs (snRNAs) U1, U2, U4, U5, and U6 and as many as 150 proteins. The splicing machinery recognizes exons and introns by using multiple signals, which presumably results in a network of interactions across exons and/or introns; this recognition is known as exon definition and intron definition, respectively. The four main splice signals that delineate the proper exon-intron boundaries are the 5' and 3' splice sites (5'ss and 3'ss), located at the upstream and downstream exon-intron junctions, respectively; the branch site (BS); and the polypyrimidine tract, which is located upstream of the 3'ss (Figure 1A). In metazoans, these four splice signals are not sufficient for the recognition of exons and introns by the splicing machinery; it has been estimated that these splicing signals provide only one-half of the information required. So what other factors assist the splicing machinery in precisely recognizing the exon-intron junctions? Studies of the molecular basis of splicing revealed the existence of exonic and intronic cis-acting regulatory sequences that bind trans-acting factors and thus influence splice-site selection. These cis-acting elements are relatively short, usually 4–18 nucleotides, and are classified as exonic or intronic splicing enhancers or silencers. These regulatory elements are required for constitutive splicing and for the regulation of alternative splicing. Specific binding of splicing regulatory proteins (such as SR and hnRNP proteins) to these splicing regulatory elements assists in the placement of the spliceosome on the appropriate splice sites. Alternative splicing is a mechanism, by which more than one mRNA transcripts are generated from the same mRNA precursor due to variations in the incorporation of coding regions, giving rise to functionally different proteins. Alternative splicing of untranslated (UTR) regions can also determine mRNA localization and stability, as well as efficiency of translation.

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