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Non-coding functions of alternative pre-mRNA splicing in development

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Abstract
A majority of messenger RNA precursors (pre-mRNAs) in the higher eukaryotes undergo alternative splicing to generate more than one mature product. By targeting the open reading frame region this process increases diversity of protein isoforms beyond the nominal coding capacity of the genome. However, alternative splicing also frequently controls output levels and spatiotemporal features of cellular and organismal gene expression programs. Here we discuss how these non-coding functions of alternative splicing contribute to development through regulation of mRNA stability, translational efficiency and cellular localization.

Keywords
Alternative pre-mRNA splicing; mRNA stability; translational regulation; mRNA localization; development

Keywords
A3E lternative 3' terminal exon,APA lternative cleavage and polyadenylation, ARE AU-rich element, AS alternative splicing, IR intron retention, NMD nonsense-mediated decay, NMTR nonsense-mediated translational repression, NRE nuclear retention and elimination, nt nucleotide, PTC premature termination codon, RUST regulated unproductive splicing and translation, uORF upstream open reading frame

1. Introduction

Eukaryotic genomes contain a large number of intronic sequences that "split" gene-encoded messages at the level of DNA and mRNA precursor transcripts (pre-mRNAs) but are spliced out from the mature mRNAs [1]. A large ribonucleoprotein complex called the spliceosome catalyzes this reaction either co-transcriptionally or following the release of a nascent transcript from the RNA polymerase complex [2-5].

Soon after the discovery of split genes [6, 7] it became obvious that some pre-mRNAs can be spliced in more than one way to give rise to distinct mature products [8, 9]. Subsequent studies showed that such alternative splicing (AS) events are extensively controlled by *cis*-regulatory RNA sequences and *trans*-acting splicing factors [3, 10, 11]. Moreover, a number of AS topologies have been described including selection between alternative 5' or 3' splice sites, cassette exons, mutually exclusive exons, alternative 5' or 3' terminal exons (A5Es and