

NEW INSIGHT INTO THE SPLICING PROCESS AND MECHANISM OF ITS REGULATION

Summary

In eukaryotic cells many genes are transcribed in the form of pre-mRNA containing coding (exon) and non-coding (intron) sequences. In the splicing process, introns are removed and exons ligated providing thus complete template for protein translation. Despite constitutive splicing there occurs also an alternative splicing within which not all introns are taken out. Splicing leads thus to production of multiple copies of mRNA from a single gene. The splicing as a multi-functional and step-wise process needs to be tightly regulated. Many cellular malfunctions are effected by errors occurring during constitutive and alternative splicing. These malfunctions encompass metabolism, apoptosis and cell cycle control; in some cases they may lead to cancerogenesis.

Splicing could be regulated directly by modifying activity of splicing factors such as SR proteins and RNA-binding proteins (RBPs) by phosphorylation/dephosphorylation and changes in concentration of ATP and ATP-ases Prp involved into conformational changes in of spliceosomal complexes. Indirect pathway of splicing regulation is based on accessibility of snRNP particles and control of the integrity and functionality of Cajal bodies (CB) participating in snRNP biogenesis. The integrity of CB is maintained by mutual interactions between SMN complex, coilin protein and core proteins Sm, the activity of which activity is regulated by phosphorylation and symmetrical arginine dimethylation.