Genomic punctuation: epigenetic processes and the regulation of splicing

Underestanding the rools of reading the commaless genetic code is a principle issue in the metagenomic era. DNA methylation is one of the principle regulatory mechanisms of gene expression. The DNA methylation profile is orchestrated by the timely modification of cytosine residues in CpG dinucleotides which exhibit a characteristic spatial distribution through the genome. Thus, promoter methylation inhibits their accessibility to the transcriptional machinery, and blocks the initiation of the transcriptional process. However, recent evidence reveals that DNA methylation, which is principally intragenic (exonic), also plays a catalytic role in the regulation of splicing and transcript inclusion, a process critical for cellular development and differentiation. Alternative splicing is strongly related to densely methylated sequences, and specific methylDNA-binding proteins can alter the splicing process. These findings provide revolutional information with respect to the association of two processes which, until recently, were thought to be completely independent. Most importantly however, this data elucidates the yet mostly unresolved mechanisms involved in the regulation of splicing and contributes greatly to the understanding of «epigenetic diseases» such as cancer, aging and neurodegeneration which are also very frequently characterized by splicing deregulation.