



清华大学高等研究院

Institute for Advanced Study, Tsinghua University

剪接体的三维结构-RNA剪接的分子基础

The 3-D Structure of Spliceosome - the molecular basis for RNA splicing



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The basic principle of all living cells, gene expression, is a process during which the genomic information stored in genome DNA sequences is delivered to pre-mRNAs by transcription and finally to functional proteins by translation. In eukaryotes, pre-mRNAs are intervened by coding sequences containing exons and untranslated introns. The exclusion of introns and ligation of exons is named as pre-mRNA splicing, and executed by spliceosome. This huge molecular machine consists of five small nuclear ribonucleoprotein particles (snRNPs), nineteen complex (NTC), NTC related (NTR), and a number of associated enzymes and cofactors. The involved proteins and RNAs assemble and separate into spliceosome in a strict order during splicing, endowing extreme dynamics and flexibility of the spliceosome. These features guarantee the accomplishment of the complex splicing reaction and at the same time tangling the structural study of spliceosome.

Besides the basic biological importance of spliceosome, numerous diseases are also related to the dysfunction of spliceosomal regulation or the splicing mistakes. Almost 35 percent of genetic disorder is resulted from wrong splicing, exemplified by unusual expression of alternative splicing leading to frontotemporal dementia driven by tau mis-splicing. The mutation of key spliceosomal proteins like Brr2 or Prp8 can lead to the Autosomal Dominant retinitis pigmentosa. Some cancer is also associated with abnormal splicing. Therefore, the structural investigation of spliceosome is regarded as the most expectative one.