Project 2: Recognition and masking of putative HIV-1 U1 snRNA binding sites and processing of HIV-1 intron-containing mRNAs

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Abstract
Removing intronic regions from a pre-mRNA is catalyzed by the spliceosome. The spliceosome is formed at the exon-intron boundaries, which are defined by recognition sequences, the so-called splice sites. The excision of the intron sequences from the pre-mRNA has to be performed with nucleotide precision in order to ensure uniformity for the particular protein to be translated. Even more astonishing is the variety of alternative splice site usage in the HIV-1 pre-mRNA. Today over forty different HIV-1 mRNAs have been described, all of which are processed by means of alternative combinations of the HIV-1 splice sites. Among the many different HIV-1 mRNAs are also those in which some splice sites are repressed and therefore still contain the intronic region. The formation of the spliceosome at the exon-intron boundaries is so in spite of their accuracy highly flexible. This flexibility can not lie in the splice sites alone, since the sequence of the pre-mRNA does not change. Rather the flexibility is due to surrounding sequence motifs and splicing regulatory proteins which bind to these motifs promoting or repressing the formation of the spliceosome. Depending on their binding position on the pre-mRNA, relative to a splice site, the splicing regulatory proteins exert partly opposite functions. The aim of this research is to understand the molecular basis which lead to the activation or repression of U1 snRNA binding sequences and the processing of the HIV-1 intron-containing mRNAs encoding the proteins Vif, Vpr, and Env.