Both Catalytic Steps of Nuclear Pre-mRNA Splicing Are Reversible

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Nuclear pre-mRNA splicing is an essential processing step for the production of mature mRNAs from most eukaryotic genes. Splicing is catalyzed by a large ribonucleoprotein complex, the spliceosome, which is comprised of five small nuclear RNAs and over one hundred protein factors. Despite the overwhelming complexity of the spliceosome, the chemistry of the splicing reaction is fairly simple, consisting of two consecutive transesterification reactions. The presence of introns in spliceosomal RNAs of certain fungi has suggested that splicing may be reversible; however, this has never been demonstrated experimentally. Here, by using affinity-purified spliceosomes, we show that both catalytic steps of splicing can be efficiently reversed under appropriate conditions. These results provide significant insight into the catalytic flexibility of the spliceosome.

A diagram showing both catalytic steps of pre-mRNA splicing are reversible