

Title: Spatial organization of co-transcriptional pre-mRNA splicing

Synopsis:

Splicing of pre-mRNAs is a fundamental process for gene expression in eukaryotic cells and its mis-regulation is a hallmark of many human diseases. Understanding the processes involved in splicing regulation is essential to deciphering disease mechanisms and to developing new targeted treatment strategies.

The molecular mechanisms of the splicing reactions have been extensively characterized, and proteins that bind to the pre-mRNA (RNA-binding proteins, RBPs) are known to influence splicing decisions. However, the principles governing splicing regulation remain elusive. It has been proposed that Pol II assembles with splicing factors into local higher-order complexes that control the efficiency of the splicing process, but currently very little is known about the higher-order organization of pre-mRNA in the nucleus.

Recently, methods were developed to measure higher-order RNA and protein contacts within 3D structures. This project aims to explore the potential application of these methods to test the hypothesis that nascent transcripts are organized in 3D territories where splicing-related RBPs and their binding sites are highly enriched.

We are seeking highly motivated students, with strong background on biochemistry and molecular biology.

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