Science at the Edge Seminar Series

Quantitative Biology Graduate Program/
Gene Expression in Development and Disease

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Using Biophysics to Understand Mechanisms of HIV Replication

Alternative splicing is a key event of the HIV replication cycle; however, little is known about the RNA structures and protein interactions that regulate splice site selection. Acceptor site A7 is one of the better-characterized sites, where its activity along with donor site D4 is required to remove the Rev Responsive Element and produce multiply spliced transcripts encoding *tat, rev,* and *nef*. The activity of A7 is suppressed by an intronic splicing silencer (ISS), a bipartite exonic splicing silencer (ESS3a/b), and activated by an exonic splicing enhancer (ESE3). The hnRNP A1 protein binds the silencer elements to effectively block SRSF1-ESE3 interaction, thereby inhibiting A7 usage. The series of molecular events that result in the competitive displacement of SRSF1 by hnRNP A1 remain poorly defined, however. To gain insight into the molecular mechanisms that regulate ssA7, we have investigated the structural, biophysical, and biochemical basis of hnRNP A1 recognition of the ISS and ESS3 elements. Here, we present solution NMR structures of these RNA elements and described their binding interactions to hnRNP A1. The collective results provide the first structural insights into how hnRNP A1 regulates HIV splicing.

Bio

Prof. Tolbert received his BS in Chemistry from the University of South Carolina in 1999. After a two year break, he went on to complete PhD studies in Biophysics and Structural Biology (2006) at the University of Rochester, where he completed dissertation projects under Ravi Basavappa (protein biophysics/crystallography) and Doug Turner (NMR studies of RNA). Following his PhD, he joined the laboratory of Michael F. Summers as an HHMI postdoctoral fellow. In the Summers' lab, Prof. Tolbert developed NMR methods to study large retroviral RNA elements. In 2009, he accepted a tenure track position in the Department of Chemistry at Miami University of OH and in June of 2012, Prof. Tolbert relocated his research group to the Department of Chemistry at CWRU.

Friday, April 3, 2015 at 11:30a.m.
Room 1400 BPS

Refreshments at 11:15