MOLECULAR AND CELLULAR BIOLOGY

INTERDISCIPLINARY GRADUATE PROGRAM IN

MOLECULAR AND CELLULAR BIOLOGY

DISSERTATION SEMINAR

Regulation of Pol II transcription and mRNA capping

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Tuesday, April 12, 2016
1:30 p.m.
Auditorium 2, BSB
Regulation of Pol II transcription and mRNA capping

In humans, RNA polymerases II is the sole source of messenger RNAs and this transcriptional activity is highly regulated. Mechanisms have evolved to control which, when, and to what degree genes are transcribed. Because every cell has the same genome, control of transcription is essential in maintaining cellular identity. Misregulation of Pol II transcription is a hallmark of both cancer and retroviral infection. During my graduate career, I investigated the regulation of Pol II transcription and related co-transcriptional mRNA capping both generally and in response to cellular stress.

I developed a number of sequencing techniques and characterized the occupancies of Pol II, pausing factors, and histone modifications at bidirectional promoters and enhancers. I also uncovered an extremely rapid and global transcriptional response to hydrogen peroxide. In collaboration with Alberto Bosque and Vicente Planelles at the University of Utah, sequencing experiments were performed in a primary T cell model of HIV latency and a role for sequence-specific recruitment of STAT5 was established in HIV reactivation. In contrast, analysis of Myc occupancy in vitro and in cells demonstrated that transcription machinery, rather than DNA sequence elements, played the major role in recruiting the Myc-Max heterodimer to genomic sites.

While not discussed in this seminar, I also performed in vitro assays to identify new roles for Cdk7 and characterized the effects of THZ1, a recently developed covalent inhibitor with anti-cancer properties. Inhibition of Cdk7 caused defects in co-transcriptional capping, promoter proximal pausing, and productive elongation. I discovered that capping is most efficient as the nascent transcript emerges from Pol II and this position is regulated in part by a previously undescribed THZ1-sensitive factor. THZ1 also impacted pausing through a capping-independent block of DSIF and NELF loading. These results suggest that Cdk7 is required for an ordered exchange of factors between initiation and elongation and disruption leads to the formation of defective elongation complexes.

Kyle Nilson
Biographical Sketch

After considering careers in music and statistics, I settled on molecular biology under the guidance of Dr. Dennis Miller at the University of Texas at Dallas, where I graduated with a BS in 2010. During interviews at Iowa, I met Dr. Price and was quickly absorbed by the field of transcription. The Price Lab exposed me not only to biochemistry, but also to competitive motorsports. When I’m not busy in lab, I spend my time racing or repairing my Miata.


