

“Dissecting Molecular Mechanisms Of Transcription Regulation In Cells & Genome-wide”

Prof John T. Lis
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Date : 4 April 2018

Time: 11:00am to 12:30pm

**Venue: Peter Ho Lecture Theatre (LT-10),
Yeung Kin Man Academic Building**

Abstract

RNA Polymerase II (Pol II) is the molecular machine that transcribes all the protein-encoding mRNAs as well as a spectrum of non-coding regulatory RNAs. The distribution of Pol II reveals not only location and levels of transcription of these transcribed genes, but also, the distinctive patterns of divergent transcription that can be used to identify the active promoters and enhancers that regulate these genes. Moreover, by monitoring changes in the distribution of Pol II across genomes in response either to regulatory signals and to directed perturbations of transcription factors, the distinct steps in transcription that are regulated can be elucidated. With increasing positional and temporal resolution provided by new, genome-wide nuclear run-on and chromatin assays, like GRO-seq, PRO-seq, and GRO-cap, we are able to gain critical insights into the mechanisms governing how RNA polymerases initiate and elongate through transcription units and how these processes are regulated. Moreover, the genome-wide patterns of regulated transcription provide insight to the networks of gene regulation and the biology of the stress response. In this presentation, I will provide a genome-wide view of the rapid and dramatic changes in transcription that accompany the heat shock stress response in both *Drosophila* and mammals. The heat shock model for studying transcription regulation has provided seminal insights into regulatory mechanisms in earlier, focused-gene studies. Our highly-sensitive, genome-wide assays, which produce an immediate readout of transcription, have provided a host of new insights to stress regulation at the transcriptional level. We find that promoter-proximal paused Pol II has a critical role for genes activated immediately upon heat shock and specific factors, such as GAGA Factor (GAF), are required for the earliest steps in transcription of generating the promoter-proximal paused Pol II. The step of release of this paused Pol II into productive elongation is in turn upregulated by transcription factors, such as HSF1, that bind to promoters and enhancers. We also are evaluating the structure and function of promoter and enhancer regulatory elements in the stress response and more broadly across the genome. The general implications of these studies indicate that the action of distinct transcription factors at separate steps in the transcription cycle provide a means to integrate cell signaling pathways, producing specific and dynamically-regulated patterns of gene expression.

Biography

John T. Lis is the Barbara McClintock Professor of Molecular Biology and Genetics at Cornell University. He did his undergraduate studies at Fairfield University and his graduate research at Brandeis University, receiving his Ph.D. in Biochemistry in 1975. His postdoctoral work focused on *Drosophila* gene regulation and chromosome structure at Stanford University, during which time he was supported by a fellowship from the Helen Hay Whitney Foundation. Dr. Lis joined the faculty at Cornell in 1978. His research program has been supported by the National Institutes of Health, including a MERIT Award, the National Science Foundation, The March of Dimes, American Cancer Society, Cornell Biotechnology Institute, and a Proctor and Gamble University Exploratory Research Grant. Dr. Lis was elected to the National Academy of Arts & Sciences in 2013, and was inducted into the National Academy of Science in 2015.

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All are welcome !