MBG FOCUS TALK

hosted by Torben Heick Jensen

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Building1531-215 Auditorium D3

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Visualizing chromatin-mediated genome transcription at nucleotide resolution in human cells

Major features of chromatin-mediated genome transcription by RNA polymerase II (Pol II) remain poorly defined due to the lack of quantitative approaches for visualizing RNA synthesis at nucleotide resolution in vivo. We developed a simple and robust approach for performing native elongating transcript sequencing (NET-seq) in human cells that exploits a quantitative biochemical purification of transcriptionally engaged Pol II along with the associated nascent RNA. This approach allows the genome-wide profiling of Pol II density in a strand-specific manner and at single-nucleotide resolution. Application of NET-seq exposes novel features of the topography and regulatory complexity of human gene expression. For instance, we uncover an unappreciated mode of antisense transcription at lower expressed genes and pervasive Pol II pausing at the majority of active genes. Recently, we have started to analyze the role of BET chromatin proteins in the regulation of global Pol II gene transcription by in vivo target protein degradation. These mechanistic studies are performed in translational models of T-cell acute lymphoblastic leukemia.

In my talk, I will (i) introduce the human NET-seq approach, (ii) highlight selected key aspects of Pol II transcription as revealed by NET-seq and (iii) will describe new insights into the regulatory role of BET chromatin proteins in Pol II genome transcription.