



Beyond The Promoter: Regulating Gene Activation Through Transcriptional Pausing

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Abstract:

One of the great mysteries of biology is how the human genome is programmed in every cell to activate only the relevant genes. In search of a solution to this overarching problem, researchers explore regulation of gene transcription by epigenetic mechanisms. My laboratory has set out to tackle the opposite question, of whether gene transcription itself can actively drive epigenetic reprogramming. RNA polymerase II (Pol II) is the enzyme responsible for mRNA gene transcription. My lab focuses on the phenomenon of promoter-proximal Pol II pausing, which takes place within the first 100 nucleotides after the start of gene transcription and results in production of short RNAs from mRNA gene promoters. Here we characterize the dynamics of Pol II pausing during transcriptional responses. We find that responses of human MCF-7 breast cancer cells to stimuli, including heat shock and histone deacetylase inhibitors, involve changes in Pol II pausing that are not reflected in mRNA production. The work suggests that activation of a promoter, and possibly epigenetic changes, can take place without mRNA production. The current work mechanistically connects cell state transitions to transcriptional responses and suggests that systems biology approaches describing transcriptional networks may need to consider Pol II pausing.

CV:

EDUCATION:

- B. Sci. equivalent, Molecular Biology, Moscow State University, 1996.
- M. Sci. equivalent, Biochemistry, Moscow State University, 1997.
- Ph.D., Molecular Biology, Institute of Genetics and Selection of Industrial Microorganisms, Moscow, Russia, 10/2001.

PROFESSIONAL EXPERIENCE:

- Assistant Professor (2012-present). Department of Basic Sciences, University of North Dakota School of Medicine and Health Sciences, Grand Forks, ND
- Postdoctoral training. Center for Molecular Genetics, University of California, San Diego, California (2002-2006) (Advisor: E. Peter Geiduschek).
- Postdoctoral training, Laboratory of Molecular Carcinogenesis (LMC), NIEHS/NIH, RTP, North Carolina (2006-2011) (Advisor: Karen Adelman).