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"Transcriptional Repression by Maf1: Implications for Cancer and Obesity"

Dr. Ian M. Willis

Professor

Albert Einstein College of Medicine
Departments of Biochemistry
and Systems and Computational Biology

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Donnelly Centre James Friesen |
Cecil Yip Red Seminar Room

Abstract:

Gene transcription by RNA polymerase (pol) III drives cell growth through the synthesis of 5S rRNA and tRNAs and is under coordinate transcriptional control with the other components of the ribosome. We identified the Maf1 protein as a master regulator of pol III gene transcription in yeast and demonstrated its involvement in the Ras/PKA, TOR and other signaling pathways that control ribosome and tRNA synthesis. Our recent work on Maf1-dependent repression identified a new branch of the TORC1 signaling pathway and two conserved protein kinases that were not previously implicated in transcriptional control of ribosome and tRNA synthesis. We identified RNA pol III as a specific target of these kinases and proposed a mechanism of repression in which posttranslational changes to functions of both Maf1 and RNA pol III are required to inhibit transcription initiation. Prompted by these findings we have recently completed a systematic study of phosphoregulation of the pol III machinery. This work has identified another regulatory target and has expanded the signaling network to include an additional protein kinase. The findings have been integrated into a mechanistic model of Maf1-dependent repression. In addition, based on the role of Maf1 as a conserved terminal effector of TOR signaling and mounting evidence linking disregulated TOR signaling to cancer, metabolic diseases and aging, we generated a Maf1 knockout mouse to assess its involvement in these processes. Our characterization of these mice will be presented.

Host: Dr. Brenda Andrews