China – HIV Transcription Activation and Latency Reversal

Functional characterization of novel Tat (Trans-activator of transcriptions) partners key for activation of HIV-1 transcription and exit from latency
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Background: We are interested in elucidating the mechanisms and identifying the host cellular co-factors that control HIV-1 transcription and latency. It was 20 years ago when the human transcription elongation factor P-TEFb was first identified as a host cofactor for activation of HIV-1 transcription by the viral encoded Tat protein. Recruited by Tat to the viral LTR, P-TEFb stimulates RNA polymerase II elongation, a process essential for viral replication. Since 1997, this landmark discovery has provided the basic framework for our understanding of Tat function during the HIV life cycle, and P-TEFb remains the only widely accepted functional Tat partner till this day. However, published data suggest that Tat-transactivation involves more than the interaction between Tat and P-TEFb. A major effort of ours is thus aimed at identifying additional cellular factors that may associate with Tat-P-TEFb to further enhance Tat-transactivation.

Project Description: Recently, our laboratory has successfully identified the first new Tat partners since 1997. These partner proteins join P-TEFb to form a multisubunit complex called the Super Elongation Complex (SEC). The MHIRT research apprentice will use a combination of molecular and biochemical techniques to characterize this complex and determine the mechanism by which it cooperates with Tat to stimulate HIV-1 transcription and exist from latency. A portion of this project will be conducted over the summer in our collaborator's lab, led by Dr. Yuhua Xue, at Xiamen University in China. Dr. Xue is the partner for this project in the School of Pharmaceutical Sciences at Xiamen University, China. The visiting student will first be paired with a senior graduate student or a postdoc in the lab in order to become familiar with the daily operations in the lab. Once becoming more experienced, the student will be assigned an independent research project.

Required qualifications: Advanced undergraduate students in MCB or other biology departments will have the appropriate background to complete this project.