2015 Irving H. Wiesenfeld Fellow

Zichong Li, UC Berkeley PhD Candidate in Molecular and Cell Biology, Zhou Lab

Zichong Li is a graduate student in Dr. Qiang Zhou's lab, where he is studying the host factors that regulate HIV latency and reactivation. In 2012, Zichong was among the first to Identify human bromodomain protein Brd4 as a major restriction factor for latent HIV reactivation at the transcription elongation stage, and that a new epigenetic drug, JQ1, can antagonize Brd4 to reactivate latent HIV. Zichong received his Bachelor of Science degree from Laiyang Agricultural College and his M.S. degree from Xiamen University.

Fellowship Proposal

Although anti-retroviral therapy has made a huge impact on HIV treatment, those with HIV must remain on these drugs for the rest of their lives due to the potential for the virus, once cleared from the body, to reemerge from its latent provirus reservoir within the DNA of the patient's T-cells. Thus, a fundamental challenge in the HIV research is how to reactivate the latent viral reservoirs for clearance by anti-retroviral drugs.

HIV latency depends critically upon the host factors that restrict the transcription of the provirus. There are now multiple of these host restriction factors (HRFs) known. However, efforts to reactivate the virus through antagonizing multiple HRFs simultaneously have not been wholly successful. Additional host factor mechanisms may exist that will need to be overcome to allow efficient and complete HIV transcription.

Zichong intends to identify novel HRFs by conducting a CRSIPR/Cas 9 based whole genome screen to identify all genes related to HIV transcription suppression in a well-known mammalian cell line model of HIV latency. The CRISPR system will be used to "knock out" each gene in the chromosome through disruption of the DNA code within the gene. Those cells which remain viable will be tested for their ability express HIV provirus, marked by the co-expression of a green fluorescent protein also integrated into the cell's genome with the provirus. Genome sequencing will identify the knocked-out HRF genes. In a parallel approach, Zichong plans to use a lentiviral short hairpin (sh) RNA library that will interfere with, and thus "knock down," the expression of the cell's genes as an alternative mechanism for identifying the HRFs. The HRFs identified by these approaches will be verified and their specific mode of action characterized through a variety of methods.

Zichong hopes that the identification of novel HRFs and their thorough characterization will provide additional avenues to allow more efficient reactivation of latent HIV for subsequent eradication, and achieving a sustained cure of HIV/AIDS in the treated patient.