Award ID:
R1115

Project Title:
Recruitment of First-Time, Tenure-Track Faculty Members

Award Mechanism:
Recruitment of First-Time, Tenure-Track Faculty Members

Principal Investigator:
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Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

While attending the Beijing Medical University (the current Peking University Health Science Center) in China, I developed a strong interest in biomedical science. I was fascinated by the idea of studying something that no one had ever really investigated before and discovering facets, especially at the molecular level, of the world around us. Although my major was Clinical Medicine, I found myself more and more drawn to basic biomedical research. To pursue a scientific career, I came to US and enrolled in the Ph.D. program at Baylor College of Medicine in 1999. During my doctoral studies, my exposure to scientific and my knowledge base was significantly expanded. Attracted by the newly developed field of epigenetics and chromatin remodeling, I joined Dr. Mitzi Kuroda's laboratory to study chromatin regulation using X-chromosome dosage compensation in Drosophila as the model system. Utilizing the powerful genetic tools in Drosophila, I studied the mechanism by which the dosage compensation complex (DCC) binds to the single male X chromosome to upregulate transcription. I also discovered a functional antagonism between DCC and NURF, a SWI/SNF complex, in regulating chromatin structure.

These experiences developed in me both a fascination with epigenetic gene regulation and a desire to apply my knowledge to a disease-related model using a robust genetic system. The zebrafish model allows me to merge all of these interests. In Spring 2005, I joined the laboratory of Dr. Leonard Zon, a prominent leader using the zebrafish model to study blood development and cancer biology. His group had previously identified several novel regulators of embryonic hematopoiesis using a genetic screening approach. One of the regulators is the TIF1? gene, which causes loss of blood production during development when mutated, but the underlying molecular mechanism was not clear. I wanted to study TIF1? using a genetic modifier screening approach. Such strategies have proven to be very powerful in identifying novel genetic interactions in invertebrate models, but are difficult to apply in vertebrate systems. With my training in Drosophila genetics, I conducted the first genetic modifier screen in zebrafish and successfully identified two recessive suppressor mutants that could restore the blood in TIF1? mutants. Characterizing these suppressor mutants revealed unexpected roles of TIF1? in regulating transcriptional elongation and chromatin remodeling. In addition, I have begun exploring the function of TIF1? in mammalian hematopoiesis using a conditional knockout mouse model and discovered a potential tumor suppressor function of TIF1? in human myeloid leukemia.

At UT Southwestern, I will continue to take the advantage of the zebrafish as an experimental system for developmental biology, as well as a model for cancer and a tool for genetic and chemical screening to study fundamental questions related to normal and malignant blood development. My goal is to discover novel pathways involved in chromatin regulation that contribute to hematological malignancies such as leukemia and lymphoma.