CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
R1222

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

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

Principal Investigator:
Wang, Zhigao

Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

Dr. Zhigao Wang received his Ph.D. degree in 2004 at the University of Texas Southwestern Medical Center in Dr. Eric Olson's lab. He then did his post-doctoral training in the lab of Dr. Xiaodong Wang at UT Southwestern. He will become an assistant professor in the Department of Molecular Biology in September, 2012 at the same institute. His lab will investigate the molecular mechanisms of necrotic cell death and apply the knowledge to develop novel pharmacological interventions to treat necrosis-related human diseases, including cancer.

During his Ph.D. training in Dr. Eric Olson's lab, Dr. Wang focused on the transcriptional regulation of muscle gene expression in animals. He demonstrated that a novel transcription factor myocardin is a master regulator for smooth muscle gene expression. A longstanding mystery in the field at the time was how serum response factor (SRF) activates both muscle-specific and growth-regulated genes, which represent opposing transcriptional programs. He solved this puzzle by showing that myocardin and the growth-regulated transcription factor Elk-1 compete for occupancy of a common docking site on SRF. This discovery, published in Nature, became a paradigm in the field for understanding the transcriptional basis of phenotypic plasticity of smooth muscle cells. The graduate training from the Olson lab provided Dr. Wang with the skills and confidence to explore completely new scientific territories.

As a postdoctoral fellow in Dr. Xiaodong Wang's lab, Dr. Wang struck out in a new direction to dissect the molecular pathways of necrotic cell death. Necrosis is a process clearly distinguished from apoptosis and is implicated in many human pathological conditions, including infections, ischemic injuries, neurodegeneration and cancer. However, the molecular mechanisms of necrosis remain largely unknown. Using a combination of chemical genetics and biochemical approaches, Dr. Wang delineated the TNF-a-induced necrotic pathway into distinct steps and identified the mitochondrial protein phosphatase PGAM5 as a central player. PGAM5 also plays key roles in necrosis induced by reactive oxygen species (ROS) and calcium overload. This research brought new insights into necrotic cell death pathways and identified many chemical inhibitors of necrosis, which potentially will lead to therapeutic strategies to treat necrosis-related diseases. Activation of necrotic pathways in tumors that are highly resistant to apoptosis will be a novel direction in cancer treatment.

At UT Southwestern, Dr. Wang will continue investigating the mechanisms of necrotic cell

death, especially the executioners of the process, using unique chemical and biological tools. The in vivo functions of the key components of the necrosis pathways will also be investigated using mouse genetics and chemical biology. The role of necrosis in tumor development and therapy represents an exciting new frontier.