CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
R1201

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

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

Principal Investigator:
Nakada, Daisuke

Entity:
Baylor College of Medicine

Lay Summary:

Dr. Daisuke Nakada received his Ph.D. degree from Nagoya University Graduate School of Science in 2005, and completed his postdoctoral research in stem cell biology at University of Michigan in 2011. In November 2011, Dr. Nakada joined the Department of Molecular and Human Genetics at Baylor College of Medicine. He will apply his background in genetics and stem cell biology to understand how cancer cells gain unlimited proliferation capacity.

During his Ph.D. research in the laboratory of Dr. Kunihiro Matsumoto, Dr. Nakada studied how DNA damage sites are recognized by ATM-related kinases using budding yeast. Understanding how cells recognize DNA damage is fundamental for cancer prevention, because cells need to respond to DNA damage and elicit cell cycle arrest, DNA repair, or apoptosis, to prevent propagation of the damaged cells. He demonstrated that the Mre11 complex recruits both ATM and ATR related kinases to DNA damage sites through distinct mechanisms. These were the first evidence that the Mre11 complex functions upstream of ATM and ATR related kinase to control recruitment of these kinases to DNA damage sites.

Dr. Nakada then moved to the laboratory of Dr. Sean Morrison at University of Michigan. During his postdoctoral research, he studied how tumor suppressor genes control stem cell maintenance and tumorigenesis. He discovered that deletion of Pten, a tumor suppressor gene that negatively regulates the phosphoinositide 3-kinase (PI3K) pathway, from the hematopoietic system activated mTOR and induced the expression of several tumor suppressor genes. The induction of tumor suppressor genes depleted hematopoietic stem cells but inhibited leukemogenesis. The tumor suppressor gene Lkb1, which is mutated in Peutz-Jeghers syndrome, also regulates the mTOR pathway by activating AMP-dependent kinase (AMPK). The Lkb1-AMPK pathway governs metabolic responses upon stress, but little was known about metabolic regulation in stem cells. Dr. Nakada demonstrated that Lkb1 plays a critical role in maintaining hematopoietic stem cells by controlling energy homeostasis of stem cells. Unexpectedly, Lkb1 not only regulated energy homeostasis, but also regulated chromosome stability of hematopoietic stem cells.

At Baylor College of Medicine, Dr. Nakada will investigate how stem cell maintenance and tumorigenesis are controlled by mechanisms that regulate chromosome stability and energy metabolism. Since stem cells persist throughout life and may accumulate

deleterious mutations that initiate cancer, studying the mechanisms that regulate stem cells and tumor suppression in parallel will lead to a better understanding of tissue homeostasis and may yield new therapeutic strategies for cancer.