

Bankhead-Coley Cancer Research Program

Lu, Jianrong

Biochemistry and Molecular Biology
University of Florida

2009 Program
New Investigator (3-year project)

Project Title: Snail-mediated Epigenetic Regulations in Cancer Metastasis

Project Summary: The most deadly aspect of cancer is its ability to spread, or metastasize. Most human cancer cells are derived from epithelial cells. Through a process termed *epithelial-mesenchymal transition* or EMT, epithelial cancer cells quickly lose epithelial features and acquire increased capability of invasion and migration. Snail, a DNA-binding protein, is known as a master regulator of EMT. Snail promotes tumor invasion and metastasis, and its expression in human cancer is associated with poor clinical outcome. Snail can inhibit expression of epithelial genes; however, the mechanism underlying Snail's action is unclear. The goal of this grant is to define the biochemical basis by which Snail inhibits epithelial genes and drives EMT.

Human DNA is wrapped around proteins to form chromatin, whose modification and structure are critical for gene expression. It was found in the grantee's laboratory that Snail physically interacts with LSD1, an enzyme capable of modifying chromatin. We hypothesize that Snail may induce multiple chromatin modifications during EMT. Here we plan 1) to characterize Snail-induced chromatin modifications at its target genes; and 2) to determine the function of Snail-induced chromatin modifications in cancer metastasis. This grant will shed light on how a specific combination of multiple chromatin modifications is achieved and its contribution to cancer metastasis. Since chromatin modifications are reversible and many key regulators are enzymatic proteins that can be targeted by small molecule drugs, the study may identify therapeutic targets for cancer treatment.