

Bankhead-Coley Cancer Research Program

Fang, Jia

Molecular Oncology

H. Lee Moffitt Cancer Center & Research Institute

2008 Program

New Investigator (3-year project)

Project Title: Role of Novel Methyl-H3K9 Binding Protein MPP8 in Transcription Silencing and Tumorigenesis

Project Summary: Epigenetic modifications, including DNA methylation and histone modifications, occur within a larger context of chromatin and influence a variety of cellular processes from regulation of gene transcription to proper chromosome segregation. Altered epigenetic regulation could result in aberrant gene function or a gene expression pattern that could lead to carcinogenesis. As one of the best-studied epigenetic modifications, histone H3K9 methylation is catalyzed by several histone methyltransferases and has been linked to transcription regulation of heterochromatic and euchromatic genes. To further dissect the function of this modification, we have identified and characterized a novel methyl H3K9 binding protein MPP8. Our preliminary data argue for a model by which MPP8 is a key regulator in methyl-H3K9 mediated euchromatic gene silencing and in turn plays an important role in tumorigenesis by epigenetically silencing tumor suppressor genes. To extend our studies, we are using a combination of approaches to further characterize H3K9 methylation, recognition, and transcription regulation cooperated by histone methyltransferases and MPP8. We are also determining the role of MPP8 in the repression of tumor suppressor genes and in breast cancer metastasis. Since the overall disruption of the epigenetic landscape is the most common feature of all human tumors, advances in our understanding of the functional significance has a major impact on issues related to human cancer.