

Bankhead-Coley Cancer Research Program

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*Molecular Oncology Program
H. Lee Moffitt Cancer Center & Research Institute*

*2011 Program
Team Science Program
(3-year project)*

Project Title: Targeting the Tumor Microenvironment in Multiple Myeloma

Project Summary: Multiple myeloma (MM) often responds well to standard therapy initially. However, drug resistance inevitably emerges, and all patients eventually die of recurrent disease that is resistant to available treatments. Therefore, identification and validation of novel therapeutic strategies and understanding the evolutionary dynamics of resistance are essential for improving the clinical outcome of patients with MM. In this grant, our group, composed of investigators with expertise in biology of myeloma, mathematical modeling, clinical investigations, pharmacology, and chemistry, will use diverse hypothesis-driven strategies to target MM cells residing in the bone marrow. Our grant consists of 5 projects: Project 1 will focus on pre-clinical development of c-HYD1, a cyclized peptide targeting VLA-4-CD44 containing complexes; Project 2 will test novel CRM1 inhibitors for increasing the efficacy of topoisomerase II inhibitors; Project 3 is based on an interesting observation that Notch inhibitors are devoid of activity in vitro yet have significant anti-MM activity using in vivo models; Project 4 will examine the role of the FA pathway in mediating de novo and acquired resistance using a co-culture model system; and Project 5 will develop evolutionary based models for testing strategies for combining therapeutic agents for maintenance of minimal residual disease.