

Bankhead-Coley Cancer Research Program

Cress, Doug

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

*2008 Program
Bridge (1-year project)*

Project Title: Basic Mechanisms of E2F Regulation in Cancer Therapeutics

Project Summary: A recent NIH Think Tank workshop put forth four specific recommendations “to accelerate progress in cancer research.” The third of these reads, “Support further identification of molecular targets for enhancing programmed cell death in response to DNA damage, particularly by investigating p53-independent pathways of DNA damage response (DDR)-induced cell death and by investigating strategies to modulate activity of DDR sensor and mediator proteins to amplify cell death signals.”

In lay terms, this recommendation means that cancer researchers need to focus on improving what we already know works. We know that radiation and chemotherapy work, but we also know that cancer cells find ways to avoid dying during radiation and chemotherapy. Thus, it is very important for us to find new drugs that will block these unwanted survival pathways—at least temporarily—so that standard cancer treatments can be effective.

Over the past five years we have used our basic understanding of the E2F family of transcription factors to develop a new drug (HLM006474) that we expect will help standard cancer therapies work much better and may even have activity on its own. This work focuses on a further characterization of HLM006474 in preclinical studies. It is our goal to better understand how the drug works to kill cancer cells while sparing normal cells, to predict which lung cancers are most sensitive to the drug (based on the mutation they have), and to demonstrate that the drug works in human cancer cells grown in mice. The outcome of these studies will enhance our ability to gain long-term support for development of this novel class of cancer drug.