Bankhead-Coley Cancer Research Program

Ishov, Alexander

Department of Anatomy and Cell Biology — *2007 Program*
University of Florida — *Bridge (1-year project)*

Project Title: Function of Daxx in Mitosis That Determines Paclitaxel Sensitivity in Breast Cancer

Project Summary: Taxanes are among the most powerful drugs for breast cancer treatment; however, a large number of patients are resistant to this therapy for unknown reasons. Therefore, it is essential to develop prognostic tools and predictive markers to differentiate patient population for appropriate chemotherapy selection. This grant aims to evaluate function of protein Daxx as a predictive marker for taxane response and is based on our observation that sensitivity to paclitaxel treatment, in breast cancer cell lines and mouse cells, correlates with the level of Daxx. Our central hypothesis is that Daxx deficiency can determine resistance to paclitaxel-induced mitotic catastrophe in breast cancer patients by reversibly blocking cells in prometaphase upon treatment. The purpose of this bridge proposal is to elucidate Daxx function in mitotic progression as a mechanism of Daxx-dependent paclitaxel response. We found that Daxx participates in mitotic progression interacting with one of mitotic checkpoint proteins. We are analyzing checkpoint release function of Daxx as a sensor for paclitaxel-induced cell death. Identification of Daxx as a novel mitotic checkpoint protein that determines resistance for taxanes, chemotherapeutic drugs commonly used in the breast cancer treatment, will aid in proper selection of breast cancer patients to receive this therapy and add to understanding of mechanisms that connect cell division, genome instability, and breast cancer progression.