

Bankhead-Coley Cancer Research Program

Cai, Jun

*Anatomy and Cell Biology
University of Florida*

*2009 Program
New Investigator (3-year project)*

Project Title: Role of Alpha-B-Crystallin (CRYAB) and the Unfolded Protein Response in Tumor Vascularization

Project Summary: The integration of host blood vessels into a developing tumor is critical for tumor survival, growth, and metastasis of cancer to other tissues and organs. Tumor cells secrete a number of factors, including vascular endothelial growth factor (VEGF) that stimulates blood vessel growth and expansion within the tumor. We have recently identified alpha-B-crystallin (CRYAB), a chaperone protein, as a critical component in tumor-induced angiogenesis. We have observed that a) CRYAB is upregulated by factors released by tumor cells, b) breast tumors' biopsies exhibit elevated levels of CRYAB, c) CRYAB is strongly associated with intracellular VEGF, and d) inhibition of CRYAB blocks in vitro angiogenesis. Our data suggests that CRYAB sustains tumor angiogenesis by activating the internal autocrine VEGF signaling loop, which is unresponsive to current anti-angiogenesis therapies. This project will characterize the pathways that upregulate CRYAB, identify potential inhibitors of CRYAB, and then translate these inhibitors into animal tumor models to determine their efficacy in slowing or halting tumor progression. The results of our research will provide an alternative intervention strategy in the treatment of a range of cancers including breast cancer.