Bankhead-Coley Cancer Research Program

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Cancer Biology — *2009 Program*
The Scripps Research Institute — *Bridge (1-year project)*

Project Title: The Kinase-Independent Function of IKKalpha Protein in Breast Cancer

Project Summary: The dramatic differences between loss of Ikka protein and inactive Ikka kinase on tumorigenesis suggest that the enzyme-dependent and independent functions of IKKa play opposite roles in breast cancer development. Inhibition of IKKa kinase activity suppresses breast cancer development whilst inhibition of IKKa protein expression augments tumorigenesis. Given the widespread involvement of this pathway in breast cancer, it is very important to confirm that selective inhibition of IKKa kinase activity, rather than complete ablation of IKKa protein, is a safe and effective means of blocking breast tumor development.

To accomplish this work, we plan to first address the following questions:
1) Does IKKa loss affect mammary gland development?
2) Does IKKa loss augment carcinogen-induced transformation of mammary epithelial cells?
3) How do IKKa kinase- dependent and independent functions regulate breast cancer stem cells (CSCs) self-renewal and differentiation?
4) Are IKKa expression and kinase activity augmented in human breast cancer?

We believe these experiments will help us to achieve the research goals that will lead to the development of IKKa agents that selectively inhibit its kinase activity as cancer therapeutics.