

Briegel, Karoline

*Department of Biochemistry and Molecular Biology
University of Miami*

*2005 Program
New Investigator (3-year project)*

Project Title: Molecular Mechanisms of Breast Cancer and Development

Project Summary: Smoking as well as passive exposure to smoking increases the risk of breast cancer in pre-menopausal women by > 3 - 7 fold. The majority of breast cancer results from the uncontrolled growth of cells that are part of the milk-secreting glands. These breast cells are prone to accumulate genetic mutations caused by environmental carcinogens (e.g. Tobacco) over time, because they are rather long-lived. Another cancer-predisposing factor is that breast cells have a higher growth potential than most other cells in the human body. Full maturation of breast cells is achieved only by hormone induction during pregnancy and lactation periods.

A hallmark of breast cancer is that carcinogen-induced mutations activate genetic programs, which exploit the growth potential of breast cells by promoting cell growth and blocking cell maturation. Recent studies suggest that many of these genetic programs normally regulate similar processes during embryonic development. Despite the high incidence of mutational activation of embryonic genes in cancer, the role of these genetic programs in normal and cancerous breast development remain poorly understood.

One genetic program that is of key importance to both embryonic as well as cancer development is the Wnt signal transduction pathway. This signaling pathway activates growth-promoting genes, which are largely unknown. Our previous work has identified a Wnt-regulated growth-promoting gene, Lbh, which is expressed at elevated level in breast tumor cells in mice. Lbh controls gene expression and has been shown to be an important regulator of embryonic development. This research uses tissue culture model systems and transgenic mouse models to confirm that Lbh is a target of the Wnt signaling pathway in breast cells. Moreover, the potential role of Lbh in breast cancer and development will be determined in these model systems. As the Wnt pathway and Lbh have demonstrated oncogenic (cancer-causing) potential, the results of our research will provide new insights into the development of breast cancer diagnostics and treatments.