

## **Vitamin D and Breast Cancer**

### **Project Summary and Progress**

Over the past year we have greatly benefited from the generous funding provided by *A Sister's Hope*. The funds have been used to support two graduate students project which focus on dietary effects on breast cancer. One project is testing how energy metabolism alters breast cancer cell growth and whether vitamin D disrupts the abnormal metabolism of the tumor cells. The other project is testing how breast cancer cells interact with inflammatory mediators and whether vitamin D affects these interactions. The results we have obtained are further discussed here.

As described in last years progress report, our initial studies compared genomic profiles in normal breast cells and in breast cancer cells treated with vitamin D. These studies demonstrated that vitamin D had completely different cellular and molecular effects in these two cell lines. These data suggested that the mechanisms by which vitamin D acts to prevent cancer in normal cells are likely very different than the mechanisms by which it triggers anti-proliferative and pro-apoptotic effects in cancer cells. From this genome-wide approach, we have chosen to focus on two pathways (metabolism and inflammation) that were specifically regulated by vitamin D in normal cells. Our work is geared at determining the differences in these pathways in efforts to identify breast cancer patients who would most benefit from optimizing vitamin D nutrition.

***Project 1. Anti-inflammatory effects of vitamin D in breast cancer.*** Based on enrichment of GO terms "inflammatory response" and "response to liposaccharide" we identified genes altered by vitamin D in breast cells that play a role in the immune response. We confirmed these changes and demonstrated that the predominant effect of vitamin D is to promote anti-inflammatory signaling in the tissue environment. These effects are elicited by physiological concentrations of the circulating form of vitamin D that correlates with vitamin D status.

***Project 2. Vitamin D regulation of tumor cell metabolism.*** Based on enrichment of GO terms related to energy metabolism, our second project focuses on regulation of metabolic genes by vitamin D in breast cells. It is well characterized that cancer cells adjust their energy metabolism to fuel rapid cell growth and proliferation, and this often involves changes in metabolism of the amino acids glutamate and glutamine. We found that vitamin D has profound effects on two genes critically involved in cellular uptake and metabolism of glutamate (SLC1A1 and GLUL). Glutamine has recently been identified as a critical driver of triple negative breast cancers which represent a highly aggressive subset of breast cancers. Our most recent studies demonstrated that vitamin D reduces the ability of breast cells to adapt to glutamine deprivation. Our next steps will utilize cell and animal models to examine how vitamin D interacts with the oncogene myc and the tumor suppressor p53 (known genetic regulators of tumor cell metabolism) in breast cancer development and progression.

### **Funding updates:**

- In Sept 2012, graduate student Katrina Simmons was awarded a two year NIH fellowship from the National Center for Complementary and Alternative Medicine (NCCAM) to pursue Project 1 in Dr. Welsh's lab at the Cancer Research Center of the University at Albany. This work will constitute her doctoral research in the Department of Biomedical Sciences. [USPHS, NATIONAL CENTER FOR COMPLEMENTARY AND ALTERNATIVE MEDICINE, F31 AT007276 NRSA Award for K Simmons, Mentor: JE Welsh. 2012 – 2014]

- Dr. Welsh was recently awarded a two year NIH R21 grant from the National Cancer Institute (NCI) for Project 2. The award will begin January 2013 and will support graduate student Sarah Beaudin who has been pursuing the metabolism project as the basis for her doctoral degree. [USPHS NCI R21 CA166434 (PI: JE Welsh) "Vitamin D, Metabolic Flux and Breast Cancer" The aims are to study the interactions between vitamin D and energy metabolism in cells and tumor models. 2013 - 2015]

In summary, we have greatly benefited from the funding received from A Sister's Hope. The money was used to develop new projects related to vitamin D prevention and treatment of breast cancer and to support the research of two graduate students. Again, we all thank you for your generous support over the last few years, as it has allowed us to keep the projects going when other avenues of funding were so scarce.

JoEllen Welsh, PhD  
Empire Innovations Professor  
University at Albany Cancer Research Center  
1 Discovery Drive Suite 340D  
Rensselaer, NY 12144  
518 591-7232 office  
518 591-7201 fax