

Biomarkers of Breast Cancer

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Concerns about adverse health effects associated with exposure to environmental contaminants are increasing globally. These concerns are often focused on the impact of environmental contaminants on fetuses, as insults *in utero* can have life-long health consequences, including an increased risk of breast cancer. Breast cancer risk is associated with total lifetime exposure to estrogens, but most studies have examined the association between breast cancer and exposure to man-made xenoestrogens, ignoring the effect of exposure to dietary phytoestrogens. The objective of this project is to identify biomarkers of breast cancer representative of estrogenic exposures *in utero*. We hypothesized that *in utero* exposure to estrogenic compounds will change the expression of genes involved in mammary tumor development. We predicted that altered gene expression of a suite of genes critical to tumorigenesis in our animal model can also be expressed in human tissues, and are useful as biomarkers for breast cancer. To test our hypothesis, we utilized a transgenic mouse model that closely mimics the human disease state, to study interactions between genes and proteins relevant to human breast cancer and *in utero* exposure to estrogenic agents.

Implications: Successful completion of this project provides context regarding the risk of *in utero* exposure to man-made and dietary estrogenic compounds, and the subsequent development of breast cancer. Our results will inform policy makers, regulators, health care providers, and patients so that evidence-based decisions can be made. Our results also expand the literature by identifying key genes and proteins in breast cancer.

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Presentations:

Foster, W.G. (2003). Environmental chemical exposure and breast cancer. Regional Oncology Rounds, Juravinski Cancer Centre, Hamilton, Ontario, February 25, 2003.

Miller, M.E., Holloway, A.C., and Foster, W.G. (2003). Benzo-[a]-pyrene alters cell invasion in a human breast cancer cell lines MDA-MB-231 and BT-474 through altered prostaglandin E₂ (PGE₂) metabolism. 2nd Annual AACR International Conference, Frontiers in Cancer Prevention Research, Phoenix, AZ, October 26-30, 2003.

Foster, W.G., Wade, M.G., Hughes, C.L., and YoungLai, E.V. (2004). Developmental exposure to a complex mixture of environmental toxicants interacts with postnatal genistein to induce changes in reproductive development of female Sprague Dawley rats. 43rd Annual Meeting, Society of Toxicology, Baltimore, MD, March 21-25, 2004.

Foster, W.G., Mirshokraei, P., Bulk, S., and Holloway, A.C. (2006). Developmental exposure to environmentally relevant concentrations of Dieldrin in BABL/c mice does not affect mammary gland development. 44th Annual Meeting, Society of Toxicology, San Diego, CA, March 5-9, 2006.

Foster, W.G. (2006). Anoikis in estrogen sensitive target tissues and disease. Department of Anatomy and Physiology, Queen's University, Kingston, Ontario, December 7, 2006.

Cameron, H.L. and Foster, W.G. (2007). Developmental and lactational exposure to environmentally relevant concentrations of dieldrin in neu/ErB2 transgenic mice. American Association for Cancer Research Special Conference, Santa Ana Pueblo, NM, May 30-June 2, 2007.

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Peer-reviewed publications:

Foster, W.G., Bouttross-Tadross, O., YoungLai, E.V., Hughes, C.L., and Wade, M.G. (2004). Mammary gland morphology in Sprague Dawley rats following treatment with an organochlorine mixture *in utero* and neonatal genistein. *Toxicological Science* 77: 91-100.

Miller, M.E., Holloway, A.C., and Foster, W.G. (2005). Benzo-[a]-pyrene alters cell invasion in a human breast cancer cell lines BT-474 and MDA-MB-231 through altered prostaglandin E2 (PGE₂) metabolism. *Clinical and Experimental Metastasis* 22: 149-156.

Foster, W.G., Mirshokraei, P., Holloway, A.C., and Zhang, B. (2008). Developmental and lactational exposure to environmentally relevant concentrations of dieldrin does not alter pregnancy outcome and mammary gland morphology in BALB/c mice. *Environmental Research* 108: 21-27.

Cameron, H.L. and Foster, W.G. (2008). Dieldrin promotes resistance of anoikis in breast cancer cells *in vitro*. *Reproductive Toxicology* 25: 256-262.

Cameron, H.L. and Foster, W.G. (2009). Developmental and lactational exposure to dieldrin alters mammary tumorigenesis in Her2/*neu* Tg mice. *Public Library of Science One* 4(1): e4303.

Foster, W.G., Stals, S.I., Zhang, B., and Cameron, H.L. Genistein decreases expression of markers of inflammation and invasion in mammary tumors of FVBN/*neu* transgenic mice. (In preparation).

Other publications: None to date.

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