Department of Pharmaceutical Sciences
COLLEGE OF PHARMACY

SUMMER RESEARCH OPPORTUNITIES
FOR UNDERGRADUATE WOMEN

APLICATION DEADLINE: March 1, 2007

The Department of Pharmaceutical Sciences in the College of Pharmacy is pleased to offer the following research project for the summer of 2007. Interested students are urged to contact the faculty member(s) directing the project that most interests them. By contacting the faculty member, you can discover more about the project, learn what your responsibilities will be and if possible, develop a timetable for the twelve-week research period.

Human-Compatible Animal Models for Preclinical Research on Hormones in Breast Cancer

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Project Description

We are working on the development of research models for preclinical studies of hormones in breast cancer. We are creating, through genetic manipulation, a set of mouse strains that will have been "humanized" with regard to the structural gene, tissue expression and secretory patterns of prolactin (PRL), and to characterize their responses to transgene-expressed human PRL (hPRL). The ultimate goal of these maneuvers is to have mice that will serve as superior hosts for xenograft studies with human cancer cells and human neoplastic cell lines. There is an acute need for such models. Xenografting of human breast cancers has been a particularly important tool for the preclinical studies of hormone sensitive breast cancers. These models allow *in vivo* study of tumor growth, invasion and metastasis in response to the host's endogenous hormones. Such studies were essential in defining the role of estrogen in breast cancer and contributed to therapy development through the testing of anti-estrogens (eg., tamoxifen).

Two major prospective studies in humans have identified elevated serum PRL to be a major risk factor for postmenopausal breast cancer. This PRL-associated risk was *equal to but independent of* that associated with estrogen levels. However, there is no good *in vivo* preclinical model for study of PRL in breast cancer. This is due to the fact that the structure of mouse PRL differs significantly from that of human PRL and, in fact, does not activate the human PRL receptor. Thus, the human cancer grafts do not recognize PRL produced by the mouse and cannot respond to it. This was not a problem in the study of estrogen, a steroid, which has identical structure in both mice and humans. The mouse models that we are creating will be compatible for the study of PRL in human breast cancers because these mice will make and secrete PRL that is structurally identical to human PRL. These models will fill a void in the repertoire of research tools currently available for the study of PRL in human breast cancer. They will have broad utility in preclinical research of human cancers – both in the elucidation of the mechanisms by which

prolactin stimulates tumor growth and/or metastases and in the development of safe and effective therapies for prolactin-sensitive breast cancers. Such a translational tool (from basic to clinical research) will have a significant impact on future diagnosis, prognosis and treatment of hormone-dependent breast cancers.

Students participating in this study will be involved in the characterization of these animal models. The work will include some animal handling. The student will learn genotyping and mRNA analysis, as well as cell preparation and culture procedures and, potentially, some small animal surgery.