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TITLE: Predoctoral Training Program in Breast Cancer Research

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those of the author(s) and should not be construed as an official
Department of the Army position, policy or decision unless so
designated by other documentation.
This training grant for 5 predoctoral students was designed to integrate students in diverse disciplines with a common interest in understanding breast cancer. The training features of this program were 1) a monthly journal club to facilitate the exchange of current information related to breast cancer research, 2) participation in a yearly retreat to encourage interactions between trainees and investigators at Vanderbilt University interested in Breast Cancer research, and 3) a special seminar involving a guest speaker prominent in the field of breast cancer research. Twelve individual students were supported throughout the four year funding period, and this work resulted in 22 publications or submitted manuscripts that were supported at least in part by this program. Two students have received Ph.D. degrees, one a M.D./Ph.D. degree, and two M.S. degrees. The remaining students are still matriculated in Ph.D. or M.D./Ph.D. programs. The research performed was highly focused on topics relevant to cancer research, for example growth factor regulation and processing, cell:cell interactions, and oncogene signaling pathways, as well as topics directly related to breast cancer, including estrogen receptor regulation, mammary gland development, and polymorphisms associated with breast cancer risk. The program has therefore met the goal of training investigators for careers in breast cancer research.
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In conducting research using animals, the investigator(s) adhered to the "Guide for the Care and Use of Laboratory Animals," prepared by the Committee on Care and Use of Laboratory Animals of the Institute of Laboratory Resources, National Research Council (NIH Publication No. 86-23, Revised 1985).

For the protection of human subjects, the investigator(s) adhered to policies of applicable Federal Law 45 CFR 46.

In conducting research utilizing recombinant DNA technology, the investigator(s) adhered to current guidelines promulgated by the National Institutes of Health.

In the conduct of research utilizing recombinant DNA, the investigator(s) adhered to the NIH Guidelines for Research Involving Recombinant DNA Molecules.

In the conduct of research involving hazardous organisms, the investigator(s) adhered to the CDC-NIH Guide for Biosafety in Microbiological and Biomedical Laboratories.
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INTRODUCTION:

This training grant for 5 predoctoral students/year was designed to integrate students in diverse disciplines with a common interest in understanding breast cancer. The special features of the training grant were a monthly journal club, a yearly retreat, and the invitation of a seminar speaker prominent in the field of breast cancer research. These mechanisms were designed to provide students with opportunities to enhance their own research by stimulating communication with investigators at Vanderbilt interested in Breast Cancer research, increasing their knowledge of current literature in the field, and exposing them to the latest research from prominent investigators at other institutions. Trainees were required to successfully complete the Cancer Biology course (4 credits, CBIO 342). Progress is measured by the presentation of original research in the form of abstracts and publishable manuscripts.

PROGRESS:

Students:

The following table summarizes the students supported by the Breast Cancer Training Grant (BCTG) over the four-year funding period for the grant. Their name, departmental affiliation, and years supported by the training grant are indicated. In addition, if the student has received an advanced degree from Vanderbilt University by the time of this final report, that degree is indicated. Two of the three students who have received Ph.D. degrees are currently postdoctoral fellows in highly-respected cancer biology laboratories. The third student, Dr. Renee Bailey, is pursuing additional training in Biostatistics and is planning a career in population-based research dealing specifically with breast cancer. Two students received M.S. degrees and are pursuing teaching careers. All students listed who have not yet received degrees are still matriculated in the Ph.D. or M.D./Ph.D. (M.S.T.P.) Program.
The Progress of each student supported by the Breast Cancer Training Grant is measured by presentation of abstracts at national meetings and publications. The following is a list of publications produced by each student which represent work performed, at least in part, during their tenure on the BCTG. In addition, abstracts presented during the time they were funded by the BCTG are listed. In the case of several first year students who were supported for a limited time on this grant, their research accomplishments thus far are presented in paragraph form.

Mark Alexandrow


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**Renee Bailey**


Meetings:

Presentation as a New Investigator at the Era of Hope Breast Cancer Meeting, October 1997.

**Mike Engel**


Laura Niedernhofer


Cindy Yee

Yee, C.J., C.S. Verrier, L.R. Bailey, N. Roodi, and F.F. Parl, "Molecular characterization of lobular breast cancer". Abstract presented at the 86th Annual Meeting of the American Association for Cancer Research, Toronto, Canada


Heather Joseph

Suzanne Szak
Rebecca Townsend
Rebecca was supported for her first year as a Cell Biology graduate student by this training mechanism. Her project involved generating transgenic mice containing a naturally occurring splice variant of the human BRCA1 gene under the control of the mouse mammary tumor virus (MMTV) promoter/enhancer, which directs expression to the mammary gland. Expression of this human BRCA1 splice variant results in a hyperplasia of the ductal system, which is opposite of the effect of other tumor suppressors on the mouse mammary gland.

Christa Brown


Molly Thoreson


Paul Ruest
Paul Ruest is a first year Cell Biology graduate student supported to investigate the mechanism by which focal adhesion kinase contributes to cell invasion and metastasis. He is currently investigating the mechanisms by which the protooncogene Src and FAK cooperate to mediate the phosphorylation of p130Cas, a protein present in focal adhesions. Cas has been reported to be a positive effector of cell migration. His studies have revealed that Fak activation loop phosphorylation is a critical step leading to efficient autophosphorylation and signalling, and that recruitment of Src to the FAK autophosphorylation site is a key step leading to Cas phosphorylation.

Tracy Vargo-Gogola
Tracy is a first year Cell Biology graduate student supported to investigate the expression of the metalloproteinase matrilysin in breast cancer cells and the role it plays in tumor progression. The expression of matrilysin in the mammary gland of transgenic mice results in accelerated development of tumors induced by the oncogene neu. Matrilysin is expressed in MDA MB468
cells but not in “normal” HBL100 breast cells. One difference between these cell lines is the absence of alpha-catenin in MDA MB468 cells. Restoring alpha-catenin by fusion with HBL 100 cells, or by direct transfection of alpha-catenin expression construct, results in a reduction in matrilysin levels. The possibility that modulation of the actin cytoskeleton and cell:cell interactions are responsible for the induction of matrilysin is being investigated.

Journal Club

The Breast Cancer Journal/Research Club has met the first Tuesday of every month at 5:00 for the duration of the funding period of this grant. All students supported by the grant were required to attend, and the sessions were also attended by faculty, post-doctoral fellows, residents, and other students interested in breast cancer research. The format varied and included presentations by students, faculty, and outside guest speakers. In particular, an attempt to provide basic and more advanced talks on topics such as the early detection of breast cancer, current treatments for breast cancer, and diagnosis of malignant and premalignant disease was made by inviting investigators from the departments of Surgery, Radiology, Oncology, and Pathology to present in this format. This forum provided the opportunity for informal discussions and interactions between individuals with a varied scientific background and served the purpose of expanding the interest and interaction of the students to more diverse areas, including in clinical arenas.

Retreat

A Breast Cancer Program retreat was held the first two years of the grant period. At that time, the institution of a Vanderbilt Cancer Center-wide retreat and changes in the leadership of the Breast Cancer Program resulted in the incorporation of the annual retreat into the VCC retreat. Students supported by the training grant actively participated in both forums, presenting posters and interacting with other Breast Cancer Program and VCC members.

Seminar speakers

Seminar speakers with a specific interest in Breast Cancer were invited each year of the retreat. Students supported by the training grant attended the seminar and then had time for informal interactions with the speaker over lunch. The speakers supported for the four years of this grant were Dr. William Muller of McMaster Univ., Dr. Mary Claire King of the Univ. of Washington, Dr. Allen Oliff of Merck Pharmaceuticals, and Dr. Malcolm Pike of U.S.C.

CONCLUSIONS

The Breast Cancer Training Grant has supported 5 predoctoral students for each of the four years of support. Research productivity of each student has been excellent, with a total of 22 publications or submitted manuscripts and many abstracts attributed to work carried out with the support of this training mechanism. The research has been in most cases highly focused on breast
cancer, including topics on estrogen receptor regulation, mammary gland development, and cytochrome polymorphisms as they relate to breast cancer risk. In other cases, basic cancer research problems of considerable relevance to breast cancer were addressed, including studies on growth factor regulation and processing, cell:cell interactions, and oncogene signalling pathways. Students have had the opportunity to interact on a regular basis with faculty and others interested in breast cancer through the monthly Breast Cancer Journal Club. This forum has been particularly helpful in exposing these students to the clinical aspects of breast cancer research and allowing them the opportunity to interact with surgeons, oncologists, radiologists, and pathologists involved in the treatment of breast cancer patients. The exposure to outside speakers who are well known in the field of breast cancer research, including Drs. Mary Claire King and Malcolm Pike, provided the opportunity to hear the latest information in the field and interact on a personal level with these distinguished investigators. These students either have or will receive advanced degrees and are pursuing careers related specifically to cancer research, and in most cases, directly to breast cancer research. This training program has therefore been successful in meeting its goals of training the next generation of investigators interested in this disease.

REFERENCES: NA

APPENDICES: NA