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GRANT NUMBER: DAMD17-94-J-4024

TITLE: Predoctoral Training Program in Breast Cancer Research

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REPORT DATE: July 1996

TYPE OF REPORT: Annual

PREPARED FOR: Commander
U.S. Army Medical Research and Materiel Command
Fort Detrick, Frederick, Maryland 21702-5012

REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. AGENCY USE ONLY *(Leave blank)*	2. REPORT DATE	3. REPORT TYPE AND DATES COVERED
	July 1996	Annual (1 Jun 95 - 31 May 96)

4. TITLE AND SUBTITLE
Predoctoral Training Program in Breast Cancer Research

5. FUNDING NUMBERS
DAMD17-94-J-4024

6. AUTHOR(S)
Lynn M. Matrisian, Ph.D.

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Vanderbilt University Medical Center
Nashville, TN 37232-2301

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
Commander
U.S. Army Medical Research and Materiel Command
Fort Detrick, MD 21702-5012

10. SPONSORING/MONITORING AGENCY REPORT NUMBER

11. SUPPLEMENTARY NOTES

12a. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for public release; distribution unlimited

12b. DISTRIBUTION CODE

13. ABSTRACT *(Maximum 200*

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 are 1) a monthly journal club to facilitate the exchange of current information related to breast cancer research, 2) a yearly retreat to encourage interactions between trainees and investigators at Vanderbilt University interested in Breast Cancer research, and 3) a special seminar series involving a guest speaker prominent in the field of breast cancer research. Each of these goals were accomplished over the past year. Three trainees were supported for a second year and two new trainees were supported by this training grant; three different departments are represented. Seven abstracts, 5 publications, and 2 submitted manuscripts related to breast cancer resulted from this support.

14. SUBJECT TERMS
Breast Cancer

15. NUMBER OF PAGES
8

16. PRICE CODE

17. SECURITY CLASSIFICATION OF REPORT	18. SECURITY CLASSIFICATION OF THIS PAGE	19. SECURITY CLASSIFICATION OF ABSTRACT	20. LIMITATION OF ABSTRACT
Unclassified	Unclassified	Unclassified	Unlimited

NSN 7540-01-280-5500

Standard Form 298 (Rev. 2-89)
Prescribed by ANSI Std. Z39-18
298-102

FOREWORD

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TABLE OF CONTENTS

INTRODUCTION:

This training grant for 5 predoctoral students 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 are 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 five students were supported by the Breast Cancer Training Grant between June 1, 1995 to May 31, 1996. Listed is the accomplishments in the form of required coursework completed, abstracts, and publications for each student during this time.

L. Renee Bailey. Third/fourth year student in the laboratory of Dr. Fritz Parl, Dept. of Pathology. Reappointed to the training grant for a second year based on excellent progress and high relevance to breast cancer. Progress is demonstrated by an abstract which was presented at the American Association for Cancer Research special conference on "Cancer and the Cell Cycle", two publications, and a first-author manuscript in press in Cancer Research.

Yee, C.J.; Verrier, C.S.; Bailey, L.R.; Roodi, N. and Parl, F.F. Molecular characterization of lobular breast cancer. Proceedings of the American Association for Cancer Research, 36:225, 1995.

Yaich, L.E.; Roodi, N.; Bailey, L.R.; Verrier, C.S.; Yee, C.J.; Cavener, D.R. and Parl, F.F. Analysis of the estrogen receptor (ER) gene, transcript and protein in ER-positive and -negative breast cancer cell lines. Endocrine-Related Cancer, 2(4), 293-309, 1995.

Roodi, N.; Bailey, L.R.; Kao, W.-Y; Verrier, C.S.; Yee, C.J.; Dupont, W.D.; Parl, F.F. Estrogen receptor gene analysis in estrogen receptor-positive and receptor-negative primary breast cancer. Journal of the National Cancer Institute, 87(6), 446-451, 1995.

Bailey, L.R.; Roodi, N.; Verrier, C.S.; Yee, C.J.; Dupont, W.D.; and Parl, F.F., "Combination of Cytochrome P450IA1 Polymorphism with Glutathione S-Transferase T1 Null Genotype is Associated with Increased Breast Cancer Risk." Cancer Research (in press).

Heather Joseph. Second/third year student, laboratory of Dr. Harold Moses, Dept. of Cell Biology. Successfully completed 4 credit hours of course work in "Cancer Biology", CBIO 342. Progress is summarized by an abstract presented at a Keystone Conference entitled "Breast and Prostate Cancer: Basic Mechanisms"

Joseph, H.; Serra, R. and Moses, H.L. TGF-β Signaling in the Mammary Gland: Studies in Organ Culture and Transgenic Mice. Keystone Symposia on Molecular and Cellular Biology, Breast and Prostate Cancer: Basic Mechanisms.

Laura J. Niedernhofer. MSTP student, third/fourth year of graduate training, laboratory of Dr. Larry Marnett, Dept. of Biochemistry. Reappointed to training grant for a second year based on excellent progress in cancer research relevant to breast cancer. Progress is summarized by an abstract presented at the Gordon Conference on Mutagenesis, an abstract presented at the Keystone Conference on Cancer Susceptibility Genes and Molecular Carcinogenesis, and two first-author manuscripts which have been submitted.

Niedernhofer, L.J.; Chaudhary, A.K.; Reddy, G.R. and Marnett, L.J. The endogenous product, malondialdehyde, forms interstrand crosslinks and induces mutations in human cells. Poster presented at the Gordon Conference in Mutagenesis, Plymouth State College, June 23-28, 1996.

Niedernhofer, L.J.; Reddy, G.R. and Marnett, L.J. Malondialdehyde, an endogenously produced mutagen, forms DNA interstrand crosslinks. Poster presented at the Keystone Conference: Cancer susceptibility genes and molecular carcinogenesis, Keystone Colorado, February 19-25, 1996.

Niedernhofer, L.J.; Rouzer, C.A.; Greene, R.A. and Marnett, L.J. Mutagenicity of the endogenous metabolite malondialdehyde in human cells: Induction of frameshifts and GC->AT transitions via interstrand crosslinks. Submitted.

Niedernhofer, L.J.; Schnetz-Boutad, N.; Riley, M.; Sanduwaran, G.; Chaudhary, A.K.; Reddy, G.R. and Marnett, L.J. Isolation and identification of crosslinks between malondialdehyde-deoxynucleoside adducts and the buffer, Tris[hydroxmethyl]aminomethane. Submitted.

Suzanne Szak. Second/third year student, laboratory of Dr. Jennifer Pietenpol, Dept. of Biochemistry. Successfully completed 4 credit hours of course work in "Cancer Biology", CBIO 342. Progress is summarized by an abstract presented at the American Association of Cancer Research meeting.

Yang, J-L.; Szak, S.T.; Dixit, M.; Pietenpol, J.A. and Arteaga, C.L. TGF alpha induces p53-independent apoptosis and p21WAF1/CIP1 mRNA and protein in EGF receptor (R)-overexpressing human breast cancer cells. Proceedings of the AACR 37: 593, 1996.

Cindy J. Yee. Third/fourth year student, laboratory of Dr. Fritz Parl, Dept. of Pathology. Reappointed to training grant for a second year based on excellent progress in areas highly relevant to breast cancer. Progress on this grant is demonstrated by an abstract presented at the American Association of Cancer Research's workshop on the "Histopathobiology of Neoplasia", an abstract presented at the Endocrine Society meeting, a publication, and a manuscript in press in Cancer Research.

Yee, C.J.; Verrier, C.S.; Bailey, L.R.; Roodi, N. and Parl, F.F. "Isolation of Genes Differentially Express in Breast Cancer Subtypes." Histopathobiology of Neoplasia Workshop, Keystone, Colorado, July 9-16, 1995.

Bailey, L.R.; Yee, C.J.; Verrier, C.S.; Roodi, N. and Parl, F.F. "Estrogen Induction of WAF1/Cip1 in MCF-7 Breast Cancer Cells by a p53-Independent Pathway." The 77th Annual Meeting of the Endocrine Society, Washington, D.C., 1995.

Yaich, L.E.; Roodi, N.; Bailey, L.R.; Verrier, C.S.; Yee, C.J.; Cavener, D.R. and Parl, F.F. "Analysis of Estrogen Receptor Gene, Transcript and protein in ER-Positive and -Negative Breast Cancer Cell Lines." Endocrine-Related Cancer 2:293-309, 1995.

Bailey, L.R.; Roodi, N.; Verrier, C.S.; Yee, C.J.; Dupont, W.D. and Parl, F.F., "Combination of Cytochrome P450IA1 Polymorphism with Glutathione S-Transferase T1 Null Genotype is Associated with Increased Breast Cancer Risk." Cancer Research (in press).

Journal Club

The Breast Cancer Trainees meet monthly in the Vanderbilt Cancer Center Conference room. Topics of particular relevance to breast cancer research were selected by the Principal Investigator of the Training Grant (Lynn Matrisian) and appropriate faculty invited to lead the discussion. Relevant papers were distributed two weeks before the meeting, and in several cases, each student was asked to prepare a brief presentation describing a particular aspect of the topic. This format was highly praised by the trainees as an excellent mechanism for learning complex material and as an opportunity to discuss relevant topics in detail with faculty and local experts in the field. Topics included breast cancer risk factors, hormone replacement therapy, Her2/neu and family, p53, hereditary breast cancer, BrCa1, estrogen, and the estrogen receptor. Meetings were well attended and discussion was lively.

Retreat

The Breast Cancer Retreat was held Sept. 9th, 1995 at Montgomery Bell State Park. The retreat included all members of the Breast Cancer Program of the Vanderbilt Cancer Center. Each of the Army Breast Cancer Trainees were expected to attend and present a poster. Two students, however, were unable to participate due to extenuating circumstances and were excused from the retreat. The program included 8 presentations of ongoing research in Breast Cancer at Vanderbilt University, numerous posters, and ample time for discussion and

interaction with program members. Trainees were provided the opportunity to stay overnight and continued discussions with a small number of faculty throughout dinner and into the evening. The retreat was successful in its goal to introduce trainees to the investigators involved in breast cancer research on the Vanderbilt campus and to obtain their input on the student's research projects.

Seminar Speaker

The Breast Cancer Training Grant supported the visit of Dr. Mary Claire King, University of Washington, on March 11, 1996. Dr. King was featured in a minisymposium during which new information from her laboratory and the laboratories of Drs. Jeffrey Holt and Roy Jensen of Vanderbilt University on the effects of BrCa1 overexpression on inhibition of growth in breast and ovarian cancer cells and the localization of the BrCa1 protein in the secretory pathway was highlighted. The trainees were exposed to the latest results in this fast-moving field from one of the most distinguished experts in the area of hereditary breast cancer.

CONCLUSIONS:

The second year of the Breast Cancer Training Grant supported 2 new students and 3 students for a second year from the Departments of Cell Biology, Pathology, and Biochemistry. Select students were reappointed to the training grant based on excellent research productivity in areas highly relevant to breast cancer. Research productivity is demonstrated by a total of 7 abstracts and 7 manuscripts during this period. The Breast Cancer Retreat provided the trainees with an opportunity to meet and discuss their research with Vanderbilt investigators interested in breast cancer. The Breast Cancer Journal Club provided an excellent forum for discussing current literature on topics of particular relevance to breast cancer research with local experts. The invitation of Dr. Mary Claire King to Vanderbilt provided the opportunity to hear the latest results on BrCa1 from a prominent investigator in the field. Training of these students was therefore enhanced at multiple levels contributing to their scientific development.