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13. ABSTRACT (Maximum 200) The Breast Tissue Repository at Duke University has completed its fourth year of funding. This resource was designed to: 1.) provide freshly frozen tumor tissue from primary and metastatic sites (lymph nodes) for exploratory research, 2.) collect serum and plasma from patients and controls, and 3.) collect white blood cells from patients and controls. During the past year, we collected tumor tissue from 86 patients, 128 patients donated pre-operative blood samples, and 10 specimens were collected in a sterile fashion for special studies. We provided investigators at Duke and collaborating centers with more than 300 samples of frozen breast tumors. In each case, the quality of the tissue was determined by frozen section analysis and macrodissection done to enhance the fraction of the tissue specimen which contained malignancy. Blood samples were distributed to investigators at Duke and sent to collaborators in other institutions. We have applied for administrative continuation (without funding) to continue the process of serial blood collection from patients already consented and who have already provided a first blood sample. As a partial indication of the success of this bank, we competed for and received a Planning Grant in Breast Cancer from the NCI in 1994. A SPORE in Breast Cancer was awarded in 1995 and a Cancer Genetics Network grant started in 1998.				
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FOREWORD

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NA 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.

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

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

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

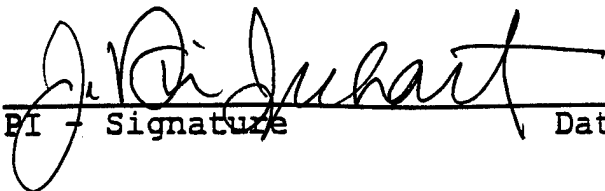

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INTRODUCTION

The Breast Cancer Tissue Repository at Duke University Medical Center is a US Army-funded infrastructure project. Our project began in 1994 and we have just completed our fourth year. We have had continuous Institutional Review Board approval for this project. Informed consent was obtained from each patient and is kept in files within the Multidisciplinary Breast Program office and within the offices of the Principal Investigator. We have more than 500 separate consents for the donation of blood. The donation of tissue is covered by the global informed consent document given to all patients going to surgery at Duke. The IRB approval for tissue acquisition is held by the Chairman of Surgery at Duke Hospital. We have collected specimens from 359 separate patients during the past four years.

The philosophy of our resource was unique. We encouraged the rapid use of our tissues by investigators seeking validation of hypotheses or performing exploratory, hypothesis generating studies. Our Repository was not designed for long-term follow-up studies and did not include an extensive clinical history database. However, we did construct a data management system that was used to inventory the bank and to provide detailed information about pathology. Anonymous linkage to the Cancer Center tumor registry was available for those investigators who requested this information. We were committed to providing large amounts of tissue to investigators with only a brief justification for its use. As the list of our users shows, this was a very mature and productive group of people.

We also provided special services to investigators who needed it. This was particularly true for scientists on the Duke Campus. Blood collection from special groups of patients and tissue collection in special ways was done for several groups of scientists. For instance, we provided "on-call" services to the Duke SPORE for a project concerned with genetic counseling about BRCA1 and BRCA2 testing. Patients were given the option of testing at Duke, for free, and part of the counseling research. In this circumstance, blood needed to be drawn and delivered to the testing laboratory immediately and confidentially. The US Army Repository phlebotomist was available to obtain the blood and deliver it immediately to the testing laboratory.

We have now reached the final year of funding. However, because of the DOD grant, we have been successful in securing continuing funding for this activity. In 1994, we were awarded an NIH Planning Grant in Breast Cancer. In 1995, we received a SPORE in Breast Cancer from the NCI. This year, we won a Cancer Genetics Network grant. These, and other sources, will allow us to continue the invaluable work of collecting, storing and distributing human tissue for cancer research.

BODY

We have collected large numbers of breast cancer tissues from patient undergoing surgery at Duke Hospital. In most cases, more than 5 small samples were obtained from each tumor; in some cases, several grams of tissue were obtained. In 30 cases, we collected both the primary and metastatic tumor from the same patient. In the majority of cases, we collected peripheral WBC's for a sample of germline, normal DNA.

The following is a breakdown of the racial demographics of our bank:

Caucasian.....	263 patients
African American.....	90 patients
Hispanics.....	3 patients
Asian.....	3 patients
TOTAL CONSENTED.....	359 patients

The Repository has provided sterile tumor tissue for attempts at continuous culture. Sterile tissue has also been provided to investigators who have isolated tumor infiltrating lymphocytes and characterized their reactivities. The Repository has provided more than 80 sterile tumor specimens to investigators over the past four years.

Our blood bank has grown to substantial proportions. We now have blood and WBC's from more than 500 patients. This year, we added 128 new entries to the general bank and supported blood drawing for the cancer genetics projects in the Duke SPORE in Breast Cancer. The SPORE projects are noteworthy. The DOD phlebotomy service drew blood from more than 100 patients who choose to have BRCA1 and BRCA2 testing in our research laboratory. This was confidential testing and was done at Duke for no charge. In addition, patients and families testing negative for alterations in BRCA1 or BRCA2 were approached in the SPORE to donate blood for mapping studies (looking for other susceptibility genes). These studies involved blood donations both at Duke, in the field at family reunions or in private homes and through the mail. The DOD phlebotomy service has supported these efforts and our technologist accompanied the SPORE investigators in trips to collect blood from family members. I would estimate that at least 100 bloods were obtained from patients in families entered into the mapping projects.

The following table gives the demographics of 533 patients donating blood to our DOD tissue repository.

Caucasian.....	418
African American.....	96
Asian.....	14
Hispanic.....	5
TOTAL COLLECTION	533 patients (not including blood drawn for special projects)

The use of the Repository has been very brisk. Blood has gone to more than 10 investigators at Duke and several requests have been answered from laboratories outside of Duke. For instance, more than 150 samples went to Dr. Robert Ochs at the Scripps Institute in California. Dr. Ochs and his collaborators are looking at the autoimmune reaction seen frequently in patients with breast cancer. Dr. Alexander Miron at Duke has looked at E2F transcription factor mutations in primary breast cancers and in germline DNA. He has used several hundred samples of both blood and tumor tissue. Finally, Dr. Andrew Futreal has analyzed polymorphisms in candidate genes associated with breast cancer risk and he also collaborated with medical oncologists to look at determinate alleles in response to chemotherapy.

The use of tumor tissue has been equally brisk. Dr. Jeffrey Marks in the Breast Program at Duke has used more than 1000 samples of breast cancer over the past four years for a variety of projects. The most notable were collaborations with Andrew Futreal at the NIEHS and later at Duke to characterize somatic mutations of BRCA1 and BRCA2 in sporadic breast cancers. This work is highly visible and widely quoted. Dr. Marks is currently studying the best way to amplify and preserve cDNA and genomic DNA from microdissected breast cancer tissue. Again, this work depends entirely upon the availability of high quality breast cancer tissue. To date, we have distributed several thousand samples of breast cancer to more than 20 investigators at Duke and to investigators at six outside institutions.

As noted above, the most significant reflection of the quality of the work done by the Repository is its ability to be self-sufficient in the future. We successfully competed for a SPORE in Breast Cancer in 1994 and recently re-competed the SPORE for a supplemental two years of funding. This will provide funds to maintain the tissue bank and hopefully expand the blood and white cell resource. We have sought funding from industrial collaborators for an even more ambitious blood-tissue collection facility at Duke. The Comprehensive Cancer Center at Duke recently completed its competitive review. The tissue collection and banking facilities of the Center were highly rated and funded in their entirety. This will include support for the breast cancer tissue bank. The Cancer Center also added the Breast Program as a standing program of research within the Center. In large measure, this recognition was based upon the infrastructure built up at Duke over the past four or five years.

CONCLUSION

The Breast Cancer Tissue Repository at Duke University has been invaluable to building our program in breast cancer research. This has resulted in a Planning Grant, a SPORE in Breast Cancer, a Cancer Genetics Network grant and funding of a new standing Program of Research in the Duke Comprehensive Cancer Center. Use has been brisk and several seminal contributions have been made to breast cancer biology.