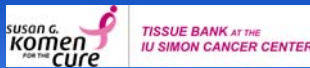


The Susan G. Komen Tissue Bank at the IU Simon Cancer Center

A Prelude to Understanding the Biology and Developmental Genetics of the Normal Mammary Gland



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Abstract

In 1998, the Breast Cancer Progress Review Group of the National Cancer Institute identified the limited understanding of the biology and developmental genetics of the normal mammary gland as a significant barrier to progress in preventing and treating breast cancer. This challenge went unmet until 2005 when an unprecedented collaboration among patient advocates, clinicians, basic scientists and volunteers was organized under the auspices of the Indiana University Breast Program and underwritten by the Catherine Peachey Fund, Inc. This collaboration has produced the first in the world (to our knowledge) bank of breast tissue and biomolecules from donors **without** cancer.

Using guidance from a number of sources including the First-Generation Guidelines for NCI-Supported Biorepositories, the RAND Report, the Nina Holland Lab, and CTEP, Standard Operating Procedures were developed for the collection, processing, storage, retrieval and dissemination of the specimens. The Bank has collected over 2,500 specimens including whole blood, DNA, serum, and breast core biopsies from over 200 women without clinical evidence of breast cancer. Each specimen is annotated with detailed information about the donor including menstrual status, reproductive history, health history, medications, and family history. All data is available in a searchable Web-accessible, HIPAA-compliant Oracle database. There has been active outreach to minority communities which has enabled 14% of the Bank to be populated with specimens from African-Americans. The goals of the Bank are to acquire specimens from the entire continuum of breast development: puberty to menopause, and to make these specimens or the digital data derived from them available and accessible to researchers across the Globe. Susan G. Komen for the Cure awarded the Bank 1 million dollars in April of 2007 in recognition of its research potential and the Bank has named the Susan G. Komen for the Cure Tissue Bank at the IU Simon Cancer Center.

Background

REPORT OF THE BREAST PROGRESS REVIEW GROUP¹

In 1997, the Breast Cancer Progress Review Group (BC-PRG), a group of basic and clinical researchers from academia, industry and government, and representatives from the patient advocacy community, were charged by the NCI with developing a "national plan for the next decade of breast cancer research". The BC-PRG identified 13 critical areas in which greater emphasis was considered to be "imperative". One of these critical areas was the following:

Our limited understanding of the biology and developmental genetics of the normal mammary gland is a barrier to progress. Much of our biological research in breast cancer has focused on understanding the initiation and development of the disease. This research has been fruitful, but it is now clear that a more complete understanding of the normal mammary gland at each stage of development—from infancy through adulthood—will be a critical underpinning of continued advances in detecting, preventing, and treating breast cancer. This focus represents a major shift in breast biology research and requires increased support for these studies and the materials needed to conduct them.

In 2003, a researcher at Indiana University identified lack of normal breast tissue as a major impediment to her research. Patient advocates viewed this as an unmet challenge in breast cancer research and they organized a collaboration among patient advocates, clinicians, basic scientists and volunteers under the auspices of the Indiana University Breast Program and underwritten by the Catherine Peachey Fund, Inc. to address this need. This was the germination of Mary Ellen's Tissue Bank and its successor, the Susan G. Komen for the Cure Tissue Bank at the IU Simon Cancer Center.

Objectives

- Identification of women and men at risk for breast cancer
- Insight into how the cancer process begins
- Identification of new targets for prevention

Materials & Methods

Prior to embarking on this endeavor, two overarching considerations were addressed:

1. Ethics
2. Quality assurance

Initial Ethical Considerations

Institutional Review Board: These are "normal", healthy subjects

- Risks to subjects: are they acceptable?
- Protection of privacy
- "Fishing expedition": Collecting tissue without a pre-specified research question

Donors

- Identified versus anonymous
- Tiered access to "identified" information (see database)
- Broad vs. limited usage
- Permission for future contact
- Right to personal results

Quality Control STANDARDIZATION Best Practices

A number of resources were consulted to compile a compendium of best practices. These resources included, but were not limited to, the following:

RAND Report

http://biospecimens.cancer.gov/nbn/RAND_REPORT.pdf

First-Generation Guidelines for NCI-Supported Biorepositories

http://biospecimens.cancer.gov/biorepositories/guidelines_full_formatted.asp

TuBaFrost 2: Standardising tissue collection and quality control procedures for a European virtual frozen tissue bank network.

Eur J Cancer. 2006 Nov;42(16):2684-91

Nina Holland Lab

Biological sample collection and processing for molecular epidemiological studies. Mutat Res. 2003 Jun;543(3):217-34

Molecular epidemiology biomarkers—sample collection and processing considerations. Toxicol Appl Pharmacol. 2005 Aug 7;206(2):261-8
<http://ehs.sph.berkeley.edu/holland/protocollibrary.html>

CTEP

http://ctep.cancer.gov/forms/guidelines_blood_collection_n.pdf
http://ctep.cancer.gov/forms/guidelines_fresh_tissue.pdf

Standard Operating Procedures (SOPs) were developed for all aspects of banking in order to minimize bias and to enable bias to be recognized²

- Collection
- Processing
- Storage
- Retrieval
- Dissemination



Examples include:

- Collection tube/container
- Anticoagulant choice
- Temperature during processing and storage
- Standardized concentration of aliquots
- Storage/stabilization medium, if applicable
- Special considerations:
 - e.g., presence or absence of protease inhibitors

THE DATABASE

- HIPAA compliant
- Tiered access
- Web accessible
- Searchable
- Oracle

	Admin- istrator	Super User	Data Manager	Specimen Manager	User
Manages users (create + edit)					
Manages donor info (create + edit)					
Manages sample info (create + edit)					
Views identified donor data					
Views identified sample data					
Views identified donor report					
Views identified sample report					
Searches donors with identified data					
Searches samples with identified data					
Views de-identified sample report					
Searches donors with de-identified data					
Searches samples with de-identified data					
Views statistics report					
Edits teacher demographics profile					

www.komentissubank.iu.edu

Mary Ellen's: https://iubcr.uiupui.edu/ffl_admin/login.jsp

Specimen annotations include:

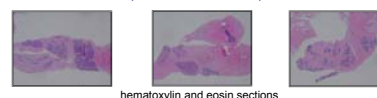
- age
- menstrual status
 - luteal or follicular phase of the menstrual cycle
- reproductive history
- health history
- medications
- hormone replacement therapy
- family history

Results

The Collection

Date	Venue	Type	#
April 16, 2005	Susan G. Komen Race for the Cure/Indianapolis	Blood	1220
April 22, 2006	Susan G. Komen Race for the Cure/Indianapolis	Blood	684
June 17, 2006	Indiana University Cancer Center	Breast Tissue + Blood	10
July 15, 2006	Indianapolis Black Expo	Saliva	155
July 20-21, 2006	Columbia City, Indiana	Saliva	113
September 16, 2006	Indiana University Cancer Center	Breast Tissue + Blood	7
October 13, 2006	Eli Lilly and Company	Blood	122
November 4, 2006	Clarian North Hospital/Spa Day	Breast Tissue + Blood	32
January 20, 2007	Clarian West Hospital/Spa Day	Breast Tissue + Blood	32
February 17, 2007	Indiana University Cancer Center	Breast Tissue + Blood	14
July 19-22, 2007	Indianapolis Black Expo	Blood	76
August 11, 2007	Indiana State Fair	Blood	51
September 22, 2007	Citizens Health Fair	Saliva	36
November 17, 2007	Indiana University Cancer Center	Breast Tissue + Blood	32
January 12, 2008	Indiana University Cancer Center	Breast Tissue + Blood	31
February 16, 2008	Clarian North Hospital/Spa Day	Breast Tissue + Blood	28

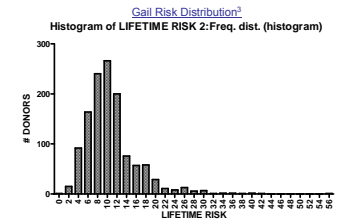
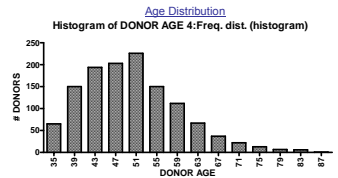
Representative Core Biopsies



THE COLLECTION: DIVERSITY

Race	
%	Number
2656	
Black or African American	14 373
White	80 2135
American Indian or Alaska Native	<1 6
Asian	1 34
> 1	1 23
Other	1 21
Unknown	2 64

Ethnicity		
	%	Number
2656		
Hispanic/Latino	2	56
Not Hispanic/Latino	94	2500
Unknown	4	100



PUBLICATIONS/PRESENTATIONS

Bryan P. Schneider, Milan Radovich, George W. Sledge, Jason D. Roberge, Lang Li, Anna M. Storniolo, Suzanne Lemler, Anne T. Nguyen, Bradley A. Hancock, Michael Stout, Todd Skaar and David A. Flockhart. *Association of polymorphisms of angiogenesis genes with breast cancer*. Breast Cancer Res Treat. 2007 Sep 20 [Epub ahead of print]

San Antonio Breast Cancer Symposium

[S084] Exploratory study evaluating the association of polymorphisms of angiogenesis genes with hot flashes
— Schneider BP, Radovich M, Flockhart DA, Carpenter J, Li L, Roberge J, Storniolo AM, Lemler S, Nguyen A, Skaar T, Sledge GW.
[S085] Association of genetic polymorphisms of angiogenesis genes and breast cancer risk.
— Schneider BP, Radovich M, Sledge GW, Li L, Roberge JD, Skaar T, Storniolo AM, Flockhart DA.

[S084] Creating a DNA bank for pharmacogenomic epidemiology: the Friends for Life study
— Lemler S, Rufenbarger C, Skaar T, Murphy V, Rush Taylor A, Garvey J, Thompson B, Christman D, Coleman N, Rosenberg L, Schneider B, on behalf of the Friends for Life Volunteers

American Society for Clinical Pharmacology & Therapeutics 2007 Meeting

A. Taraska, S. Borges, M. Radovich, S. Phillips, A. Nguyen, L. Li, J. Roberge, S. Lemler, B. Schneider, D. Flockhart, T. Skaar. *Effect of CYP2D6 genotype on antidepressant use patterns*.

References

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²Ransohoff, D.F. Bias as a threat to the validity of cancer molecular-marker research. Nat Rev Cancer. 2005 Feb;5(2):142-9.
³Galil, M.H., et al., Projecting individualized probabilities of developing breast cancer for white females who are being examined annually. J Natl Cancer Inst. 1989. 81(24):1879-86.