COH BrTM Registry, A Biospecimen Resource for Translational Research

Michelle Banzet, M.A.[1]; Jacob Justus[2]; Liton Francisco[1]; Melanie R. Palomares, MD, MS[1]

[1]City of Hope; [2]California State University San Bernardino

INTRODUCTION

The NCI has cited several challenges with biorepositories, including clinical and pathologic data annotation, tracking of preanalytic variables that influence assay measurement error, and common terminology for each.[1] The City of Hope (COH) Circulating Breast Tumor Marker (BrTM) Registry has collected peripheral blood samples from over 500 women with a spectrum of breast disease since November 2005.[2] The samples were separated into blood components and stored for analysis by outcomes ascertained after long-term prospective follow-up. This project aims to evaluate the compliance with standard operating procedures (SOPs) that were set forth at initiation of the project for the collection and processing of biospecimens. This project also describes the creation of a database and querying system that combines clinical data and biospecimen data.

METHODS

Dataset Creation:

Biospecimen tracking data for the BrTM and matching clinical data for registry participants are currently housed within COH Population Sciences data resources. Specimen tracking data recorded include preanalytic variables such as date and time of blood collection, centrifugation, and storage at -80C, which allow for evaluation of the quality of specimen processing performed over the duration of the study. Tumor and treatment data are extracted onto standardized clinical data forms by Clinical Research Associates and reviewed with a clinician on the study team prior to database entry. Up to date demographic and follow-up data are obtained from the COH electronic medical record (CIS). Medical record number (MRN) and research participant number (RPN) were used to link data across data sources.

Evaluation of Specimen Processing Quality:

Elapsed time between blood collection and centrifugation and placement into the freezer was calculated for all blood components. These data were compared to the specimen processing SOPs for this study, summarized here:

Serum

- must be allowed to clot for 1 hour after collection.
- must be centrifuged and harvested within 2 hours of clotting, and immediately placed into a -80° C freezer.

Plasma

- must be centrifuged, harvested and frozen within 4 hours of collection.

Lymphocytes

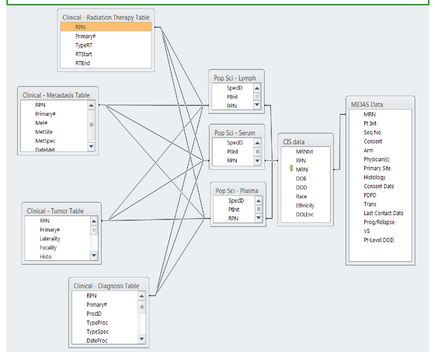
- must be centrifuged and harvested within 4 hours of collection.
- must be frozen within 24 hours of collection.

For the purposes of this study, samples that were not time tracked properly were deemed to be out of compliance. Adequate specimen processing quality was defined as >80% compliance with each of the above measures.

Figure 1.

DATABASE DESIGN

RPN is used to join clinical data (left) with biospecimen data stored in Population Sciences (left center), and to demographic and follow up data in the CIS system (right center). MRN is then used to join clinical, biospecimen, and CIS data to histological data stored in the BrTM database (right).



RESULTING DATASET:

As of February 14, 2012, the COH Circulating Breast Tumor Marker Registry includes 666 women who have consented onto the study. Of these, 548 have donated blood samples. Linkage to demographic data on CIS was feasible for 560 of these individuals. These data are summarized in Table 1.

Table 1.

DESCRIPTION OF PATIENT COHORT

		N	%
N		560	100.0%
Age	<40	27	4.7%
	40-49	104	18.7%
	50-59	165	29.4%
	60-69	162	28.9%
	70-79	75	13.5%
	80+	27	4.8%
Race	Caucasian, Non-Hispanic	242	43.1%
	Hispanic	108	19.3%
	African American	25	4.5%
	Asian/Pacific Islander	58	10.4%
	Other	113	20.2%
	Unknown	14	2.5%
Histo-logy		151	27.1%
		65	11.6%
	Benign Breast Disease		
	Ductal Carcinoma In-Situ (Stage 0)	284	50.8%
	Invasive Breast Cancer, Stage I-III		
	Invasive Breast Cancer, Stage IV	59	10.5%

Table 2.

TOTAL NUMBER OF BIOSPECIMENS

# of Samples	Sample Type	# of Patients	# of Time Points
4047	Serum samples	557	1350
7924	Plasma samples	560	1366
3647	Lymphocyte samples	560	1366
15618	TOTAL # OF SAMPLES		

Table 3.

SPECIMEN PROCESSING COMPLIANCE

SERUM

Draw to Spin			Draw to Freeze		
TIME (Hr)	Number of Aliquots	Percent Compliance	TIME (Hr)	Number of Aliquots	Percent Compliance
Complete Documentation	1225	99%	Complete Documentation	1229	99%
< 1	183	82%	< 1	77	91%
>= 1	1018		>= 1	1128	
> 3	24		>24	24	

PLASMA

Draw to Spin			Draw to Freeze		
TIME (Hr)	Number of Aliquots	Percent Compliance	TIME (Hr)	Number of Aliquots	Percent Compliance
Complete Documentation	1184	95%	Complete Documentation	1227	98%
< 4	1183	94%	< 4	1203	96%
>= 4	1		>= 4	24	

LYMPHOCYTES

Draw to Spin			Draw to Freeze		
TIME (Hr)	Number of Aliquots	Percent Compliance	TIME (Hr)	Number of Aliquots	Percent Compliance
Complete Documentation	1178	94%	Complete Documentation	1199	96%
< 4	1175	94%	< 24	1179	94%
>= 4	3		>= 24	20	

Table 4.

BIOMARKER STUDIES

- K19 mRNA vs EPCAM for detection of circulating tumor cells (*DOD funded; laboratory: D. Sabath, UW*)
- MALDI-TOF proteomics pilot project (*CreFF funded; laboratory: T. Lee, COH*)
- Epigenomics study (*Komen funded; laboratory: P. Laird, USC*)
- Deep sequencing miRNA marker discovery project (California Breast Cancer Research Program; *laboratory: S.E. Wang, COH*)

CONCLUSIONS

Objective 1: Evaluate compliance with study specimen processing SOPs

We demonstrated that adherence to all specimen processing protocol requirements occurred >80% of the time over the 5.7 years that the COH Breast TM Registry has been in operation. The biggest challenge was adherence to the strict clotting time of 1 hour for serum processing. Adherence to all other processing quality measures was >90%.

Objective 2: Create a database and querying system that combines clinical data and biospecimen data

To carefully select samples by histologic and outcome group and exclude those in which processing was not optimally performed, it is imperative to be able to link clinical information with biospecimen information related to the study participants. We have demonstrated that such linkage is feasible within existing COH shared resources.

In summary, the COH TM Registry is a high quality resource that links biospecimens with demographic and clinical data that will enable basic and clinical researchers come together to discover and validate diagnostic, prognostic, and predictive biomarkers for breast cancer.

References/Footnotes:

1. JNCI (2005) 97:4, 247-248.

2. COH IRB# 04125 was funded by the Department of Defense Grant # DAMD17-99-9439 and the Stop Cancer Foundation.