Tissue Issue Think Tank
Meeting Summary

Background

When asked what the most important hurdle is facing them today, researchers respond "access to highly annotated tissue." Tissue research is critical to gaining a better understanding of the mechanisms involved in disease development and drug interactions. Because without willing participants in tissue research, scientists will lack the necessary tools and will be unable to find the keys to personalized medicine – the right drug for the right person at the right time. Advocates are in a unique position to help advance scientific issues. Advocates can, help engage the community in understanding what answers may be found in the biology of both the tumor and the host, answers that will not be found through other sources. Advocate organizations that have created biorepositories are addressing some of the storage, collection and data sharing issues.

On Feb 10, 2012 a group of invited stakeholders, advocates and physician-scientists met at the DFW airport Grand Hyatt with the purpose of determining the most effective utilization of advocates in addressing an important hurdle facing the research community -- access to tissue and biospecimens for research.

The meeting was hosted by Research Advocacy Network and structured as a "Think Tank" to identify the "Tissue Issues" and ways advocates and researchers can best work together to address these issues. Unrestricted grant funds from Genentech and Celgene funded the travel and meeting expenses.

Participants

A diverse group of scientists and advocates were invited to come to the table to discuss these issues. Some people who were invited were unable to attend due to scheduling conflicts. All invitees expressed interest in the topic and support for this type of discussion, of those who were unable to attend many offered comments for consideration by the group.

- **Cynthia Chauhan,** Patient Advocate, Mayo Clinic Breast SPORE
- **David Eberhard MD, PhD,** Associate Professor, University of North Carolina
- **Liz Frank, Ed.M.,**Lead Patient Advocate, Dana Farber/Harvard Cancer Center Breast Program
- **Charles E.Geyer, Jr. MD, FACP,** President and Chief Medical Officer, CTNeT - Statewide Clinical Trials Network of Texas
- **Andy Godwin PhD,** Director, Biospecimen Shared Resource; Associate Director for Translation Research; Professor, and Director of Molecular Oncology, Department of Pathology & Laboratory Medicine, University of Kansas Medical Center
- **Daniel F. Hayes M.D.** Clinical Director, Breast Oncology Program; Stuart B. Padnos Professor in Breast Cancer University of Michigan Comprehensive Cancer Center

- **Liz Horn Ph.D., M.B.I.,** Director, Genetic Alliance Registry and BioBank, Genetic Alliance
- **Linda House RN,** Executive Vice President, External Affairs, Cancer Support Community
- **Kay Kays,** Research Advocate, ALLIANCE Cooperative Group; University of Arizona GI SPORE External Advisory Board; AzMN Tissue Donor Awareness Project (TDAP)
- **Joshua LaBaer MD, PhD,** Director, Virginia G. Piper Center for Personalized Diagnostics, Professor of Chemistry and Biochemistry, Biodesign Institute at Arizona State University
- **Ginny Mason RN,** Executive Director, Inflammatory Breast Cancer Research Foundation
- **John Minna MD,** Professor, Hamon Center for Therapeutic Oncology, Internal Medicine, Pharmacology, University of Texas Southwestern Medical Center
- **Christie Pratt Pozo MA DHSc,** Patient Advocacy Program Coordinator, Thoracic Oncology, Moffitt Cancer Center
- **Elda Railey,** Co-Founder, Research Advocacy Network
- **Connie Rufenbarger,** Consumer Representative/Executive Committee, Susan G. Komen for the Cure Tissue Bank at the IU Simon Cancer Center
- **Mary Lou SmithJD, MBA,** Co-Founder, Research Advocacy Network
- **Kemp Battle,** Meeting facilitator and Board Member, Genetic Alliance
- **Misty Shields, PhD,** Meeting notetaker, Postdoc, UT Southwestern Medical Center

Current Environment

The group felt that currently the cancer research enterprise is in need of a paradigm shift to maximize the potential of research utilizing biospecimens. New models that are feasible and include novel collaborations with multiple stakeholders will be necessary for success.

The "Middle" Problem

Collecting biospecimens is a complex enterprise, requiring many steps to ensure high-quality, well-annotated biospecimens. Best practices must also be followed to ensure samples that are useful for future research. These collection practices can be both expensive and resource intensive. In our current system, there seems to be a "Middle Problem" where there are considerable resource costs for time, equipment and appropriate protocols for collection. In addition to collection, resources are needed for annotation, storage, and distribution to researches. Tissues, more broadly referred to as biospecimens, are available but are often not properly annotated, collected or stored properly to maintain quality. Ensuring best practices are followed is resource intensive.

Contributing to the "middle problem," IRBs often restrict research in their effort to protect and ensure ethical treatment of patients or to limit sharing with competitors at other Universities. IRBs are very concerned with risks of identifiability, without taking into account that certain

patient populations are willing to shoulder more risk in order to advance research. A universal informed consent form developed by the NCI for tissue has been in place since the early 90's and has helped contribute to successful tissue collections in breast cancer. However, the increasing use of Next Gen sequencing raises concerns about the validity of this document for future uses and the possible need to re – consent participants for use of their tissue. Programs to keep institutions compliant with protocols and regulations are adding to the complexity and cost of biospecimen banking. Problems with sharing tissue or data exist due to institutional constraints. New models need to incorporate innovative methods of funding for the considerable costs associated with biospecimen collection, annotation and storage. These models must also promote a culture of sharing.

Communication about the need for tissue

A myth exists that patients will not donate their tissues for research has driven the behavior of some scientists. Scientists often communicate linearly to the scientific community but not to patients and the greater community about their need for tissue and the value of tissue research. Malone, et al[1] reported a high rate of consent for future research use of stored biologic samples among cancer patients participating in clinical trials. Education of the community and the public about the need for high-quality biospecimens is essential. An effort to educate physicians and others engaged in the development of clinical trials on the willingness of patient to provide tissue also needs to take place.

Current Challenges of Biorepositories

Currently most biorepositories are disease site specific. There are challenges when collecting patient-associated clinical and outcomes data as well as issues around how samples and clinical data can be accessed and used. There are also issues with sample anonymization and de-identification. Few banks are collecting normal tissue, due to challenges surrounding acquiring normal tissue. This is further complicated by not having a standard definition of "normal" tissue.

Aggregate results are not routinely provided to participants. Many participants want to know how their samples are being used – and how the science is progressing. They have a stake in this – and many may want continued involvement. Offering aggregate results to clinical trial

[1]Malone T, Catalano PJ, O'Dwyer PJ, Giantonio B.High rate of consent to bank biologic samples for future research: the Eastern Cooperative Oncology Group experience. J Natl Cancer Inst. 2002 May 15;94(10):769-71.

results should be done on a routine basis. There is controversy concerning protocols requiring mandatory vs. voluntary participation. In addition most biorepositories do not collect tissue and data longitudinally. Biorepositories are only gaining a snapshot of an individual and a disease, when we know life is a movie. Currently most biorepositories are under the control of individuals within institutions, whose task is to preserve the tissue and share it chiefly within their own institutions, and not promote broader sharing.

Emerging Themes

The group felt that new models will need to be developed to address these themes. Our current systems do not adequately address these challenges.:

- The "Middle" problem
    - Compliance
    - IRB
    - Regulatory - Better defined regulatory pathways for biomarkers/assays
    - Informed consent
        - Protocol specific
        - Perpetual consent forms
        - Issues related to new technologies that may necessitate re-consenting
    - Returning results (aggregate results and dealing w/ incidental findings and individual research results)
    - CLIA certified laboratory tests
    - Clinical utility of tests
    - Access
        - Patients willing to donate but not always released by pathologists
        - Annotated samples and access to DATA
        - Current practices of specimen collection, preparation and storage vary. As a result, significant diversity exists in the quality. Need for standardization
    - Mandatory vs. voluntary participation
    - Funding burden and data sharing
    - Need for consolidation of banks
    - Procurement and collaboration- need for a generic/universal tissue biospecimen procurement protocols (i.e., SOPs) and more user friendly MTAs
- Community Bank(s) – "reversing the arrows" by having community / advocate driven banks
    - Normal to metastatic
    - Longitudinal collection
    - Serial biopsies and data collections over time

  - Ownership
  - Informed consent
  - Consider successful and unsuccessful models
  - Providing aggregate results to participants could be a way of engaging patients and the public
  - Stewardship
- Awareness Campaign - targeted approach to connect the scientist, pathologist, oncologist and primary care physicians and team with the patient and the general public.
  - Public Awareness Campaign - A community tissue bank driven by the community, patients and advocates, and all who have a stake
    - Modeled after the Red Cross Blood Drive Model.
    - Concern about quality of tissue and data in this model
  - Physician (oncology and primary care) awareness campaign
    - Collecting tissue and data over time could be part of this type of campaign.
    - Need to address - Right person, right message, right time.

Other needs and questions for the group to consider:

- Need for common vocabulary and terminology, e.g., biospecimen instead of tissue
- Need to have pilots to try new approaches, CTNET could be one
- Will the Cooperative Group move to 5 banks be an opportunity for advocate involvement?
- Will CAP guidelines and letter from Cooperative Group Intergroup solve the problem of pathologists/institutions not releasing the tissue?
- How can clinically relevant results be provided to participants?
- Need to develop guidelines or best practices for informed consenting of participants and the release of aggregate results.
- Transparency, analysis and reproducibility of results
- Need for development of processes that ensure accurate stewardship of specimens
- Need for a centralized database and methods to list trials with categories to "map" current and completed studies with biospecimens. (DanOGram graphic and listing matrix available for download at: http://tbf.me/a/b2qGC)
- Questions around funding for longer term follow up linking tissue with outcomes
- Consenting process that avoids the need for re-consent whenever possible.
- What types of individual results will patients come to expect?
- What results can tumor banks reasonably commit to providing?
- Ownership of samples
- Stewardship of samples
- Promoting a culture of sharing samples

Additional reading/ links

- Nat Biotechnol. 2012 Feb 8;30(2):141-7. doi: 10.1038/nbt.2116. Personal medicine-the new banking crisis. Scott CT, Caulfield T, Borgelt E, Illes J. Available at: http://www.ncbi.nlm.nih.gov/pubmed/22318029 (or contact Elda for full reprint)- recommended by Connie Rufenbarger
- J Oncol Pract. 2011 Sep;7(5):334-7. Donating tissue for research: patient and provider perspectives. Baer AR, Smith ML, Bendell JC.
- OBBR Workshop report on providing results to participants in biospecimen research: http://biospecimens.cancer.gov/global/pdfs/NCI_Return_Research_Results_Summary_Final-508.pdf
- Research Advocacy Network
    - Results survey PDF version
    - Tissue Education Booklets (available at www.researchadvocacy.org)
    - Tutorial on Pathology and Tissue Research for Advocates PDF version
- Genetic Alliance Registry and Biobanking (GARB) Resources:
    - The GARB toolbox http://www.biobank.org/english/View.asp?x=1432
    - Weekly tips series http://www.biobank.org/english/View.asp?x=1426
    - Monthly registry and biorepository bulletin - http://www.geneticalliance.org/biobank.bulletin