

Day one-presentation-session II
Carolyn Compton

Rare Disease Biospecimens: Quality and Accessibility Challenges

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Human biospecimens are both the foundation of personalized medicine and the fuel that drives the basic and translational research needed to achieve that vision. Biospecimens are the principal sources of the molecular data used to describe the biology of the patient and the biology of his or her disease. As such, they must be collected and processed following standards that safeguard quality, and annotated with the appropriate clinical and biospecimen information. Both direct experience with NCI initiatives as well as broader input from the scientific community have indicated a striking unmet need for high-quality human biospecimens. To address these issues, the NCI Office of Biorepositories and Biospecimen Research (OBBR) was established in 2005. In addition to the general challenges encountered by biospecimen resources, the acquisition of high-quality rare disease biospecimens presents special difficulties. Patients with rare diseases may present anywhere in the medical system in an unpredictable fashion. This widespread distribution of patients with rare diseases poses a challenge to the implementation of standardized SOPs for specimen collection in the clinical setting. In addition, diagnosis may follow specimen procurement (for example, diagnostic biopsy or tumor resection), making prospective standardization of specimen handling impossible in many cases. And there is no existing central diagnostic verification, specimen quality control, storage, and distribution infrastructure to assure the quality and accessibility of biospecimens. Finally, the diagnostic work-up and/or treatment of some rare diseases may yield no tissue specimens or the specimens may be completely consumed for diagnostic purposes, and therapy may be immediately implemented, precluding further acquisition of specimens reflecting native (untreated) disease. For some cases blood samples may be the only common denominator, but even they should be acquired in a standardized, evidence-based fashion. Although specimen procurement issues related to rare diseases are in some ways unique, they overlap broadly with the universal issues of standardized, evidence-based specimen collection being addressed by OBBR. As part of

the solution for the human biospecimen needs of the translational research community, the OBBR is planning for the implementation of a national biobank called the cancer Human Biobank (caHUB). No centralized resource of this type exists at this time. This initiative will take advantage of resources already developed by the NCI, including the Biospecimen Research Network (BRN) and the *NCI Best Practices for Biospecimen Resources*. The caHUB also will be an opportunity to implement concepts from the National Biospecimen Network (NBN) Blueprint. The NBN concept was the product of an NCI-led effort to define an innovative, comprehensive framework for a national biospecimen resource that would meet the nation's existing and emerging scientific needs. As caHUB is developed there will be opportunities to address some of the issues encountered in the rare diseases research community, as the program casts a wide net to acquire biospecimens from patients with a wide variety of diseases. As caHUB is developed, it is important to note that OBBR and ORDR are working together on several other important biospecimen initiatives, including updating the Specimen Resource Locator; developing a Common Biorepository Model to expand usage of the Specimen Resource Locator; promoting biospecimen research publications; and jointly planning a workshop for the 2010 ISBER annual meeting.



Unifying Rare Diseases



***Advancing Rare Disease Research:
The Intersection of Patient Registries, Biospecimen Repositories
and Clinical Data***

***Session II
Biospecimens/Biorepositories***

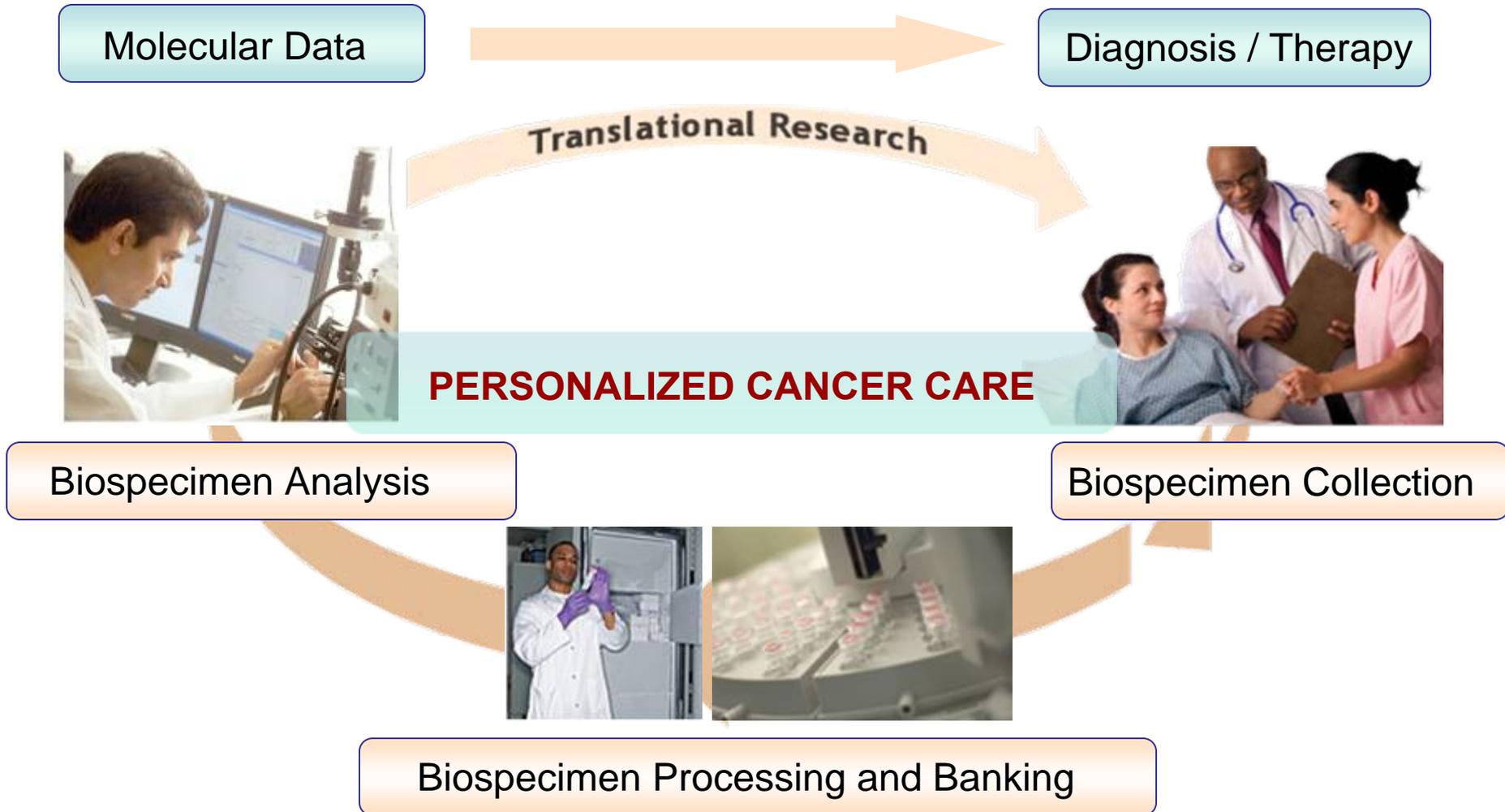
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Rare Disease Biorepositories: Quality and Accessibility



Translational Research Promises to Realize the Vision of Personalized Medicine



Biospecimens and Personalized Medicine

- Biospecimens are the basis of:
 - **Molecular characterization of the disease**
 - Molecular classification of tumor
 - Characterization of tumor heterogeneity/therapeutic targets
 - **Molecular characterization of the host**
 - Disease susceptibility
 - Treatment efficacy (e.g., pharmacogenomics)
- Personalized medicine will depend on accurate, reproducible data derived from patient samples in the clinical setting

Powerful Tools Are Now Available for Analysis, Accompanied by Powerful Risks

- The technological capacity exists to produce low-quality data from low-quality analytes with unprecedented efficiency
- We now have the ability to get the wrong answers with unprecedented speed
- We now desperately need technologies that assure the quality of human analytes used in translational research and ultimately, personalized molecular medicine

Fundamental Risk for All Science

Garbage in...



...Garbage out



Diamonds in.....

Modified from Jerry Thomas

Why Is It Difficult to Acquire High-Quality Specimens and Data?

- Collection, procession, storage procedures differ
 - Degree and type of data annotation varies
 - Scope and type of patient consent differs
 - Access policies are lacking or unknown to potential users
 - Materials transfer agreement conditions differ
 - Supporting IT structures differ in capacity and functionality
- **WIDE VARIATION IN QUALITY OF SPECIMENS AND DATA**

Case Study from The Cancer Genome Atlas (TCGA): Lessons Learned About Specimens Banked for Research

- **Quality of existing samples is typically overestimated by biobanks**
 - **No quality control up front**
- **Collection of normal control samples is not routine**
- **Histological quality does not guarantee molecular quality**
- **Other important factors exist that challenge the science:**
 - **IRB, HIPAA, consent issues**
 - **Intellectual Property, Authorship, Incentives issues**
 - **Informatics needs**
 - **Extraction and transfer of associated clinical data laborious**
 - **Costs**

NCI's Clinical Trials Network of Cooperative Groups: Lessons Learned About Specimens Procured from Clinical Systems

- **All of the foregoing PLUS**
 - **No protocols for specimen acquisition processing and storage**
 - **No requirement to record actual events/conditions**
- **Medical (Pathology) standard of care for specimens is very low**
 - **Practices are highly variable within an institution and among institutions**
 - **The quality of the specimens is set by the medical system and cannot be controlled by the scientific user**
 - **The greater the number of institutions involved in providing specimens, the greater the problem**

NCI's Clinical Trials Network of Cooperative Groups: Lessons Learned About Specimens Procured from Clinical Systems

- **Ever increasing resistance of medical institutions to relinquish specimens for research**
 - **Policy to retain for downstream use related to patient care**
 - **Medical-legal risk**
 - **Non-reimbursable associated professional activities**
 - **Primary custodianship responsibility of the institution**

Additional Issues, Especially Pertinent To Rare Diseases

- Diagnosis may not be known until pathology assessment has been performed, compromising the chance to bank for research prospectively
- Miniaturization of diagnostic samples is the overall trend
 - The more difficult the diagnosis, the greater the depletion of the sample for testing and the less remaining for science
- For cancers, neoadjuvant therapy may be standard of care
 - The surgical resection specimen is irrevocably altered

Crisis in Biospecimens Common to All Diseases, Cancer, Non-Cancer, Rare, Common

Challenge: Lack of availability and standardization of human biospecimens compromises the molecular research dependent on them.

Consensus of the Broad Scientific Community: The lack of high-quality human specimens has become the limiting factor for post-genomic biomedical science.

- ***The #1 roadblock to translational research!!***



Market Survey: Researchers Are Working in Silos Little Specimen Sharing Exists

What percentage of your biospecimens come from each of these sources?

	% Get <u>any</u> from source	Mean % from each
My patients/volunteers	42%	25%
Other patients in my org	55%	31%
Other research institutions	41%	17%
Other medical care facilities	23%	8%
Commercial U.S. biobank	18%	6%
Non-profit biobank	12%	4%
NCI CHTN	12%	4%
Sources outside the U.S.	4%	1%
Other sources	1%	1%

56%

- **Collaborative agreements are not widespread**

55% None/Few (0-25%)

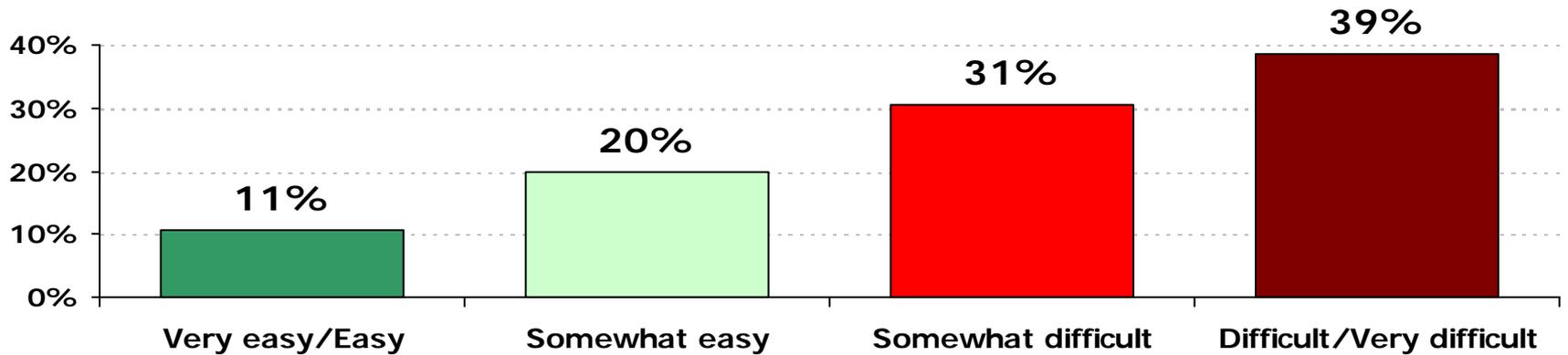
23% Some/Many (26-75%)

22% Most/All (76-100%)

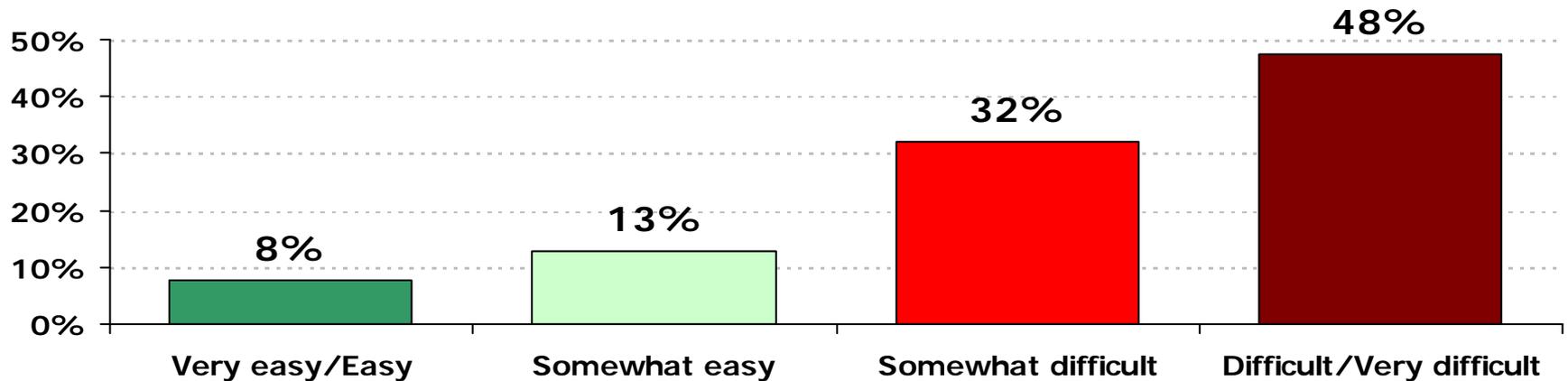
Question: What proportion of your biospecimens come from individuals or organizations who are your research collaborators?

Can Investigators Get What They Need?

Ease of Acquiring the Quantity of Biospecimens Needed

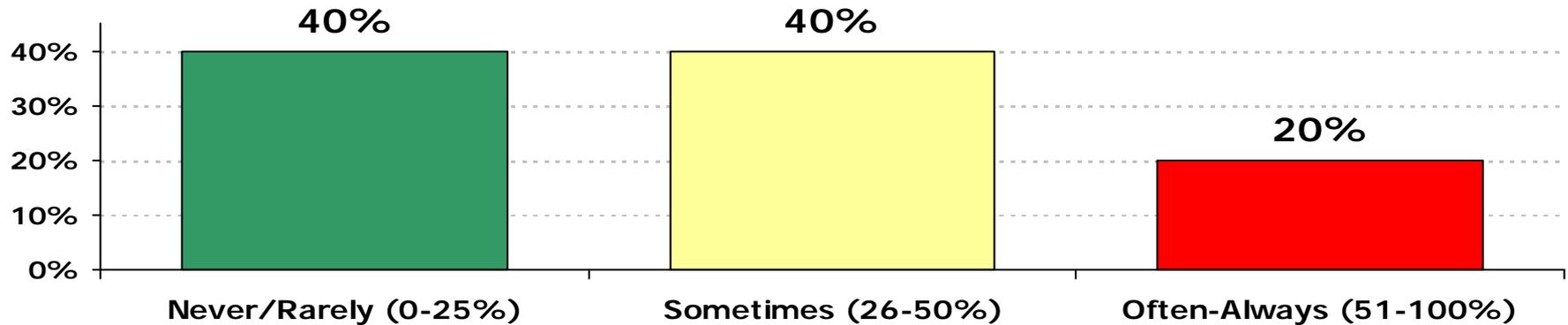


Ease of Acquiring the Quality of Biospecimens Needed

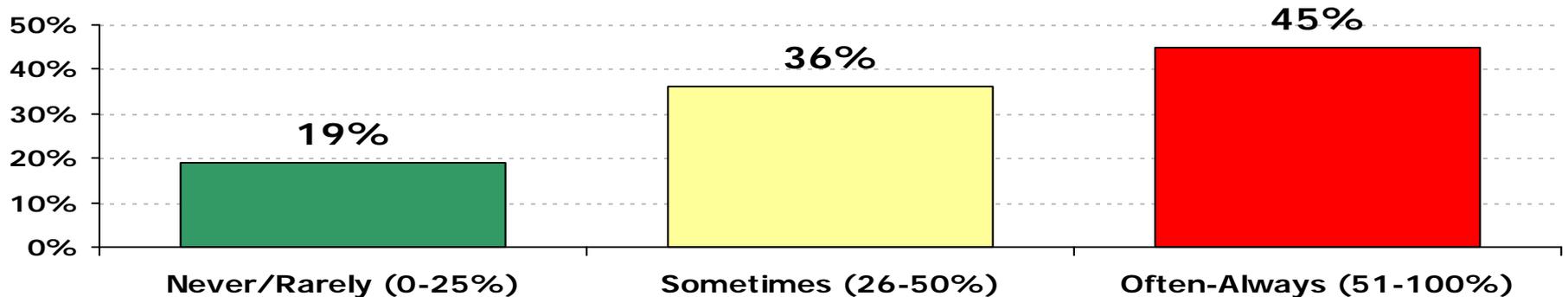


Consequences for Investigators (and the NIH): The Science Suffers

Question Their Data Because of the Quality of Biospecimens



Limit Their Scope of Work Due to the Shortage of Quality Biospecimens



OBBR's Most Recent Undertaking

Development of key national infrastructure for translational research:

The Cancer Human Biobank (caHUB)

What Is caHUB?

A unique, centralized, non-profit public resource that will ensure the adequate and continuous supply of human biospecimens and associated data of measurable, high quality acquired within an ethical framework.



8. Biobanks

By ALICE PARK



Inside Huntsman Cancer Institute's vaults: Pancreatic tumors on ice. Lance W. Clayton for TIME

Folks at the National Cancer Institute (NCI) are heading up an effort to establish the U.S.'s first national biobank — a safe house for tissue samples, tumor cells, DNA and, yes, even blood — that would be used for research into new treatments for diseases.... By fall, the group hopes to have mapped out a plan for a national biobank; the recent stimulus showered on the government by the Obama Administration might even accelerate that timetable.

caHUB Key Concepts

- Scientifically designed, evidence-based collection strategies
- Multiple aliquots of every specimen
- Standardized, annotated collection, processing of all specimens
- Centralized QC and pathology analysis of every specimen
- Rich, standardized data profile for each sample
- Centralized source of normal human specimens
- Provision of tools, resources, training for U.S. biospecimen resources

Linking Biobanks Through Benefits from the Operating and Data Standards Medicine

- Links cancer institutions, researchers, and scientific initiatives
- Benefits (not competes with) other biobanking programs
- Facilitates rapid development and regulatory approval of medical products
- Facilitates standardization and medical implementation of approved products
- Allows direct performance comparisons of different technologies
- Increases efficiency of scientific innovation and knowledge maturation

caHUB Vision: Progress Enabled in Unprecedented Ways

- **Centralized source of standardized human samples**
 - Duplicate samples (aliquots of same tumor) allow direct comparisons of data from different scientific initiatives
 - “Big science” data linked through the specimens (genomic, epigenomic, transcriptomic, and proteomic data on same specimens)
 - Product (therapeutic; diagnostic) and technology development /standardization/regulatory approval all streamlined
 - Direct product-to-product (technology-to-technology) performance comparisons enabled
 - Standardized “benchmark” specimens (“yardstick of truth”) for FDA approval / medical implementation/calibration/proficiency testing

Opportunities for Partnership with ORDR

- caHUB
 - Protocols for collection of rare disease cases in caHUB centers and affiliates
 - “Bench mark” quality of existing samples against those collected under standardized protocol
 - Biospecimen Research Network: develop data for evidence-based protocols
 - Make samples available through public system of access
- Specimen Locator System
 - caHUB and caBIG to expand and increase functionality of existing system to make information about existing specimen inventories publicly available
- Patient Advocacy
 - Synchronize biobanking efforts driven by the advocacy community



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