

OBBR

Office of Biorepositories
and Biospecimen Research

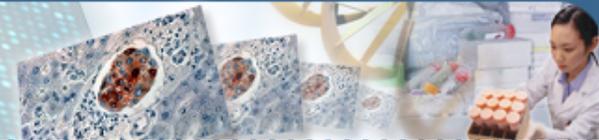
Next Steps for NCI's Best Practices: Biospecimen Research for Molecular Medicine

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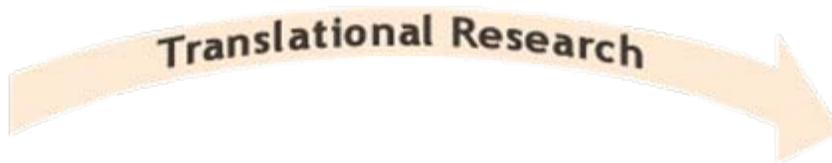
Translational Research Promises to Advance Molecular Medicine for Cancer Patients

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Molecular Data

Diagnosis / Therapy



PERSONALIZED CANCER CARE

Biospecimen Distribution

Biospecimen Collection



Biospecimen Processing and Banking



OBBR's Strategic Efforts

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- Optimize and standardize the quality of human specimens for the research that will drive the development of personalized cancer medicine
- Remove the barriers to cancer research represented by the limited availability of high-quality, platform-appropriate human biospecimens
- Lay the foundation for tomorrow's standard of care



**Developing and implementing
state-of-the-science processes that insure
the molecular integrity and clinical relevance
of human biospecimens
used in cancer research and clinical medicine**



Biospecimen Science

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What is biospecimen science*?

- A **multidisciplinary** field of study
- Goal: develop **tested and proven** biospecimen resource-related procedures based on experimentation in the areas of specimen collection, processing, shipping, and storage

Why is it needed?

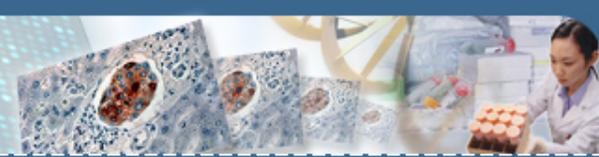
*Source: <http://biospecimens.cancer.gov/sciences/symposium.asp>

- Biospecimens are composed of active and reactive living cells or cell products, making them highly complex
- Collection, handling, and storage processes can profoundly alter the molecular profiles and quality of biospecimens
- Such alterations, though artificial, can be misinterpreted as disease-related or disease-specific
- High degrees of sensitivity and specificity in new molecular techniques raise the bar for analyte (specimen) data and quality



The Premise of Biospecimen Science

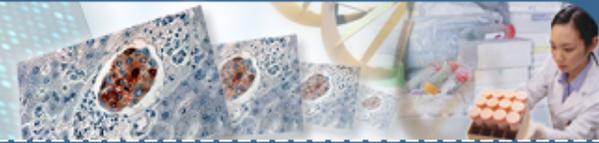
- Quality is not a generic concept.
- Quality of human biospecimens is multifactorial and is determined by the:
 - Type of specimen: normal tissue, tumor tissue, serum, plasma
 - Physical state of the specimen
 - Amount and type of specimen characterization data
 - Amount and type of quality control exercised
 - Amount and type of clinical data
 - Permitted use of the specimen
 - Analysis platform to be used; the biomolecules targeted by the analysis
 - The goal of the research (application of the data)



Pathway to Improving Biospecimen Quality: Systematic, Comprehensive Approach

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- **Biology**
 - Dry research (gather existing data)
 - Make data more accessible: searchable literature database (RAND)
 - Wet research (create new data)
 - OBBR's Intramural Biospecimen Research Network (BRN)
 - NCI Gaithersburg, NCI Frederick, NCI Bethesda, Walter Reed Army Medical Center
 - New extramural Programs: RFI, RFP, BAA approved and coming soon
- **Technology Development**
 - IMAT Program – Innovative technologic solutions for biospecimens (RFA)
- **Strategic Partnerships**
 - The College of American Pathologists (CAP)
 - Data-driven, specimen-specific, platform-appropriate SOPS
 - Implementation and monitoring: Laboratory Accreditation Program



Pre-analytical Variables Alter the Physical State/ Molecular Composition of the Specimen

Time 0

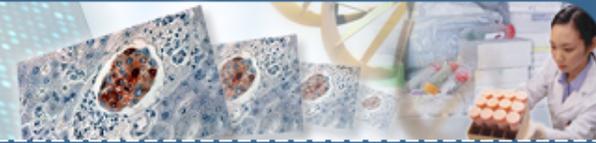
**Specimen is viable
and biologically reactive**

**Molecular composition subject to
further alteration/degradation**



Pre-acquisition

Post-acquisition



Key Variables: Biospecimen Research

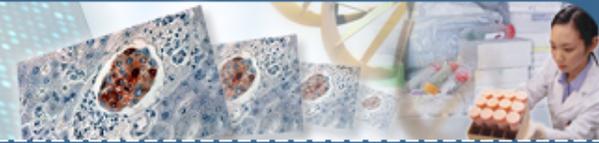
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Pre-acquisition variables:

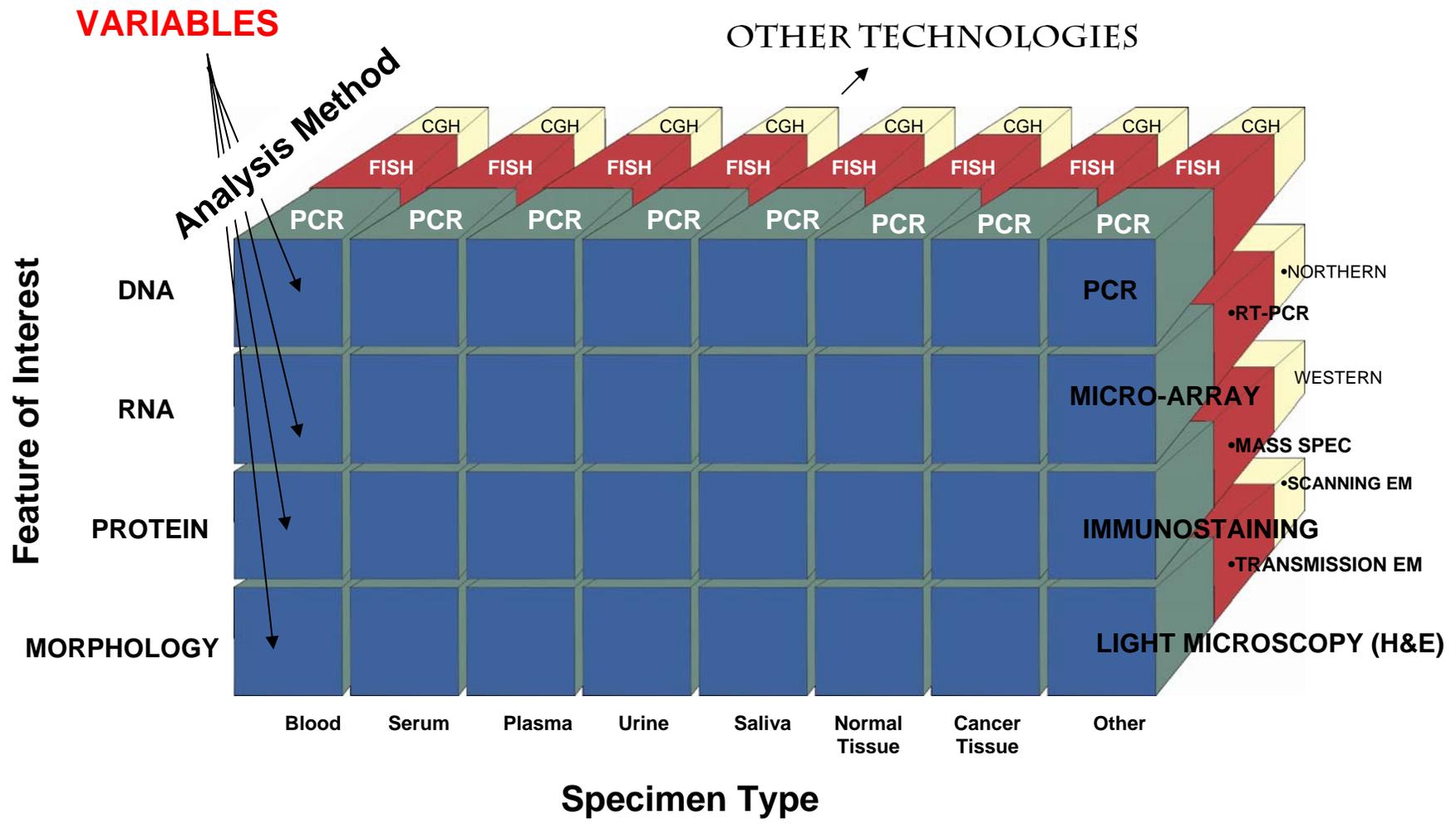
- Antibiotics
- Other drugs
- Type of anesthesia
- Duration of anesthesia
- Arterial clamp time
- Blood pressure variations
- Intra-op blood loss
- Intra-op blood administration
- Intra-op fluid administration
- Pre-existing medical conditions
- Patient gender

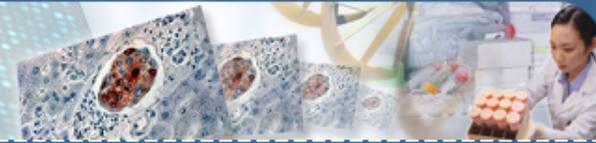
Post-acquisition variables:

- Time at room temperature
- Temperature of room
- Type of fixative
- Time in fixative
- Rate of freezing
- Size of aliquots
- Type of collection container
- Biomolecule extraction method
- Storage temperature
- Storage duration
- Storage in vacuum



Framework for Development of Evidence-Based Standards Operating Procedures

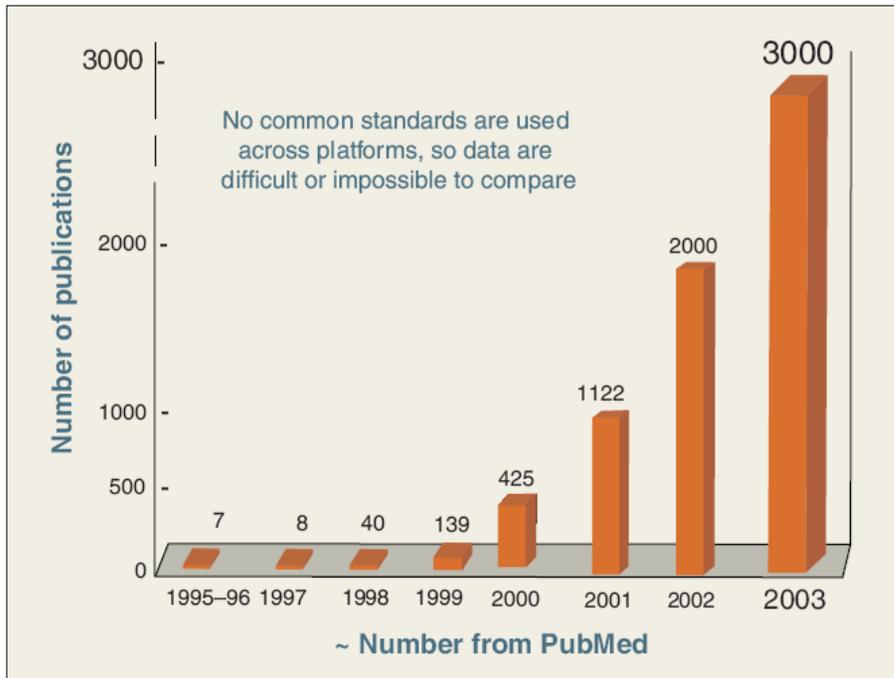




Technical Variation? Analyte Variation? Both?

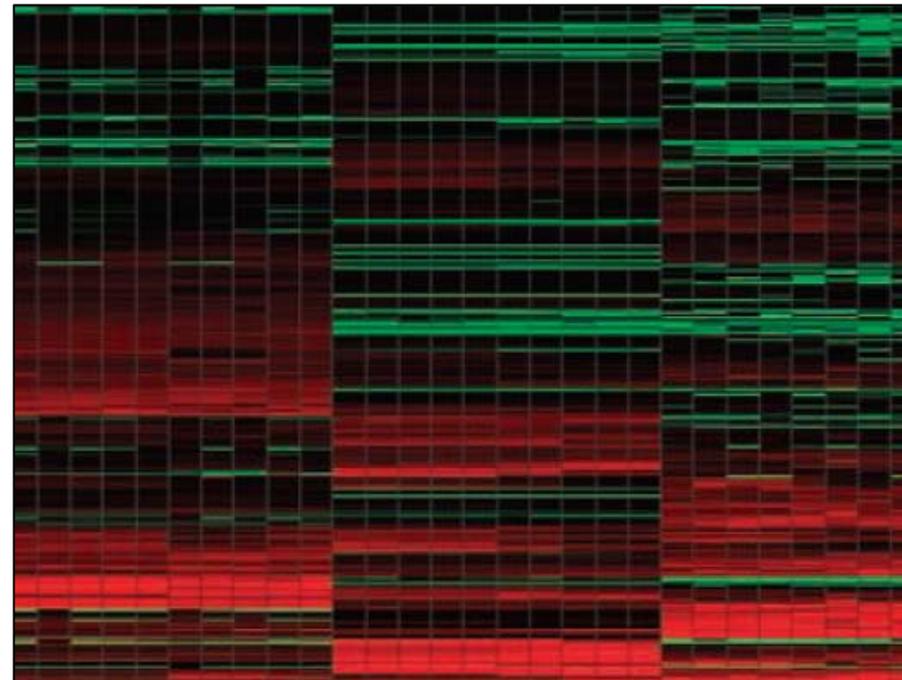
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Rapid Increase in Microarray Publications



Source: SCIENCE, 22 OCT 2004,
“Getting in the Noise Out of Gene Arrays”

Results Vary



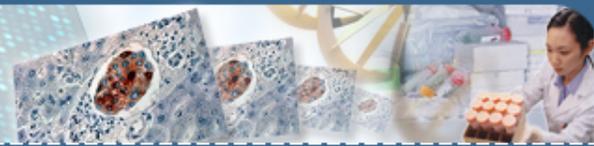
Map of discordance. An experiment at NIH found that three commercial devices rated different genes as being turned on (red) and turned off (green) in a single batch of pancreatic cells



Potential Effects of Biospecimen Variables

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- **Detrimental effects on technology development**
 - **Comparing same technology from day to day, lab to lab**
 - **Standardizing existing technology for clinical application**
 - **Comparing new technologies to existing technologies**



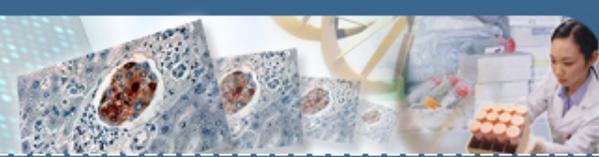
- **Effects on Clinical Outcomes**
 - **Potential for incorrect diagnosis**
 - Morphological/immunostaining artifact
 - Skewed clinical chemistry results
 - **Potential for incorrect treatment**
 - Therapy linked to a diagnostic test on a biospecimen (e.g., HER2 in breast cancer)
- **Effects on Research Outcomes**
 - **Irreproducible results**
 - Variations in gene expression data
 - Variations in post-translational modification data
 - **Misinterpretation of artifacts as biomarkers**



Biospecimen Research

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- **Evidence base for SOPs**
 - What we need to control
 - What we don't need to worry about
- **Elucidate the effect of what can't be controlled, allowing for appropriate correction of analysis data**



Defining the Problems and Refining the Solutions: Due Diligence

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- **National Forums: Boston, Chicago, Seattle**
- **Symposia on timely topics: Custodianship**
- **RFI, RFP, Broad Agency Announcement**
- **IMAT: Innovations in Sample preparation**
- **2008: Second OBBR Biospecimen Research Symposium**
 - In development for early spring
- **OBBR continued collaboration on key NCI initiatives**
 - NCI Community Cancer Centers Program (NCCCP)
 - The Cancer Genome Atlas (TCGA)
 - Clinical Proteomics Technologies Assessment for Cancer (CPTAC)
 - Alliance for Nanotechnology in Cancer
 - Interagency Oncology Task Force (FDA/NCI/CMS)
 - Cancer Biomarkers Collaborative (AACR/NCI/FDA/academia/industry)
 - SPOREs
 - Group Banking Committee
- **OBBR collaboration on international initiatives**
 - ISBER, IARC, P3G, Marble Arch Group, EORTC



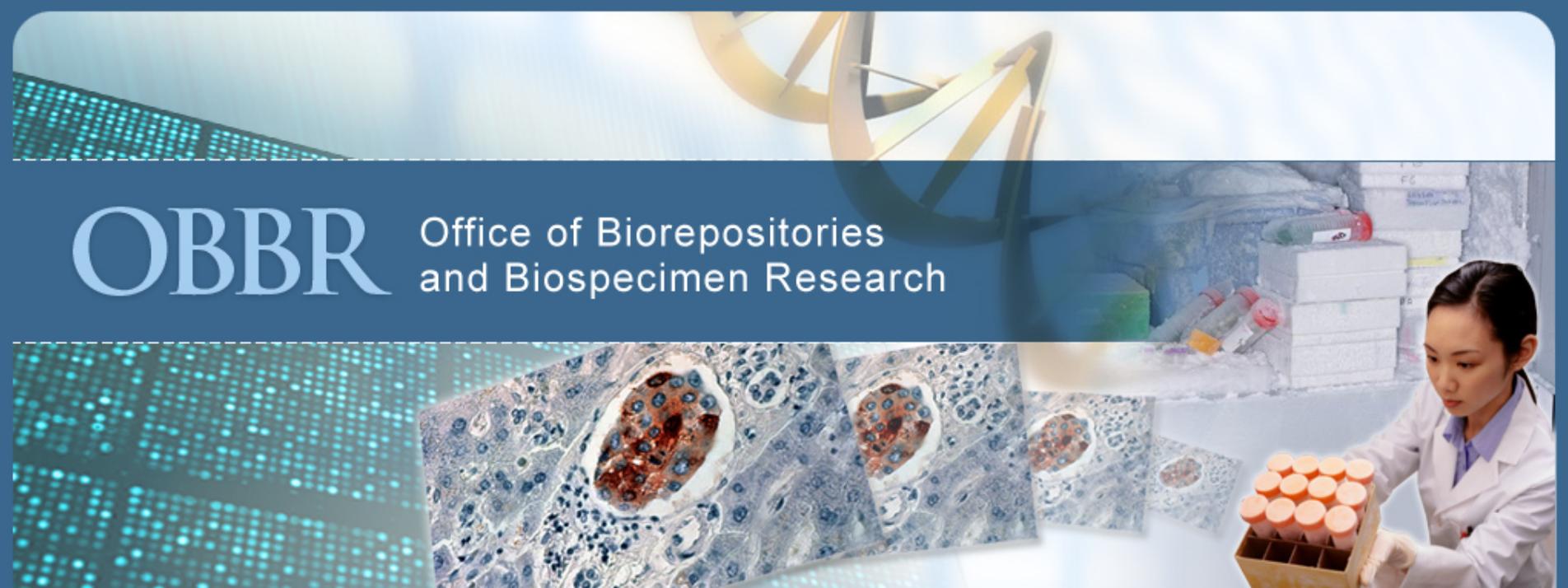
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- **Listening to YOU!!!**

<http://biospecimens.cancer.gov>

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