



OBRR

Office of Biorepositories
and Biospecimen Research

The NCI Best Practices for Biospecimen Resources



NCI Best Practices: Next Steps

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- NCI Best Practices will be made publicly available on the OBBR Web site.
- NCI Best Practices will be distributed to managers of all NCI-supported intramural and extramural biospecimen resources.
- OBBR will launch a national education and outreach program:
 - Local meeting – NIH campus, June 18, 2007
 - Regional meetings – Fall 2007
 - Boston, MA
 - Chicago, IL
 - Houston, TX
 - Los Angeles, CA
 - Seattle, WA
- OBBR and caBIG™ have developed “caBIG for Dummies”
- OBBR and NCI Biorepository Coordinating Committee are developing a biospecimen resource self-evaluation checklist based on the Best Practices

Systematic and Integrative Approach

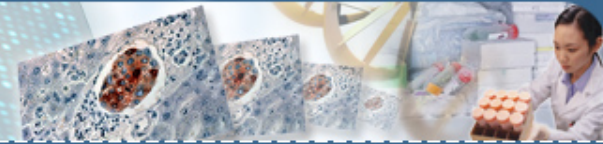
- Best practice recommendations based on current evidence
 - **NCI Best Practices for Biospecimen Resources**
 - **Biospecimen Resource Evaluation Tool**
- Systematic approach to evidence-based biobanking processes
 - **Dry research (existing data) and creation of searchable literature database**
 - **Wet research (new data): Biospecimen Research Network**
- Integration with and support of other NCI strategic initiatives
 - **The Cancer Genome Atlas, Clinical Proteomics, IMAT, et al.**
- External partnerships: expertise, education, implementation
- Harmonization of biobanking practices in NCI enterprises
 - **Clinical trials groups (Group Banking Committee), TRWG, CCR, et al.**
- Facilitation of NIH and international efforts to harmonize biobanking practices



NCI Best Practices: Next Steps

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- Periodic revision of the Best practices will occur with input from researchers, biospecimen resource managers, advocates, policymakers, and related stakeholders as new technologies and clinical practices emerge.
- OBBR's Biospecimen Research Network will conduct research to establish the scientific basis for data-driven standards for specimen collection, processing, and storage.
 - **Develop an extramural program to study the effect of pre- and post-acquisition variables on biomolecular profiles in specimens of different types**
 - **Create a searchable Web-based tool to access biospecimen research data**
 - **Partner with College of American Pathologists to develop evidence-based specimen type-specific and analysis-type specific SOPs**



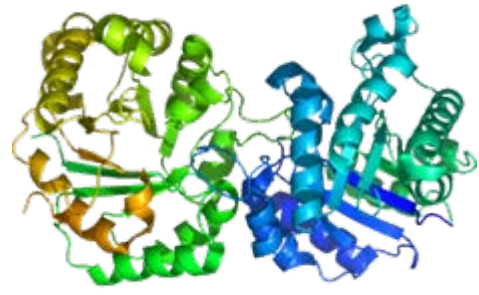
Molecular Research Using Human Analytes

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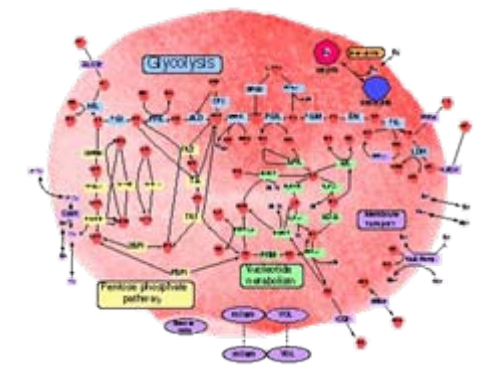
Genomics



Proteomics



Metabolomics



**All Depend
On High-Quality
Human Biospecimens**



Reproducible data is urgently needed to advance molecular medicine

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- **First rule of science: Valid data is reproducible**
 - **Enemy of reproducibility is variation, variation, variation....**
 - **Irreproducible data in research – many possibilities exist:**
 - Hypothesis is wrong
 - Experimental design is flawed
 - Analysis tools are flawed
 - Random noise is present (rare event → unforeseen outcome)
 - Individual variation/biological complexity
- OR –
- **Analyte itself is of poor quality and is the source of variation**

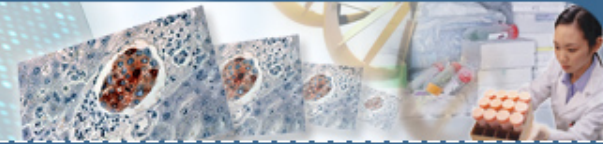


Molecular Research and Analyte Variation

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Pitfalls for translational research using human biospecimens:

- **Varying methods** of collection, processing, and storage can alter the physical/biologic state of the specimen
- **Varying associated specimen data** elements alter what the scientist knows about the character/nature of the specimen
- **Variable clinical information** alters what the scientist knows about the patient (biologic context of the specimen)
- **Variable restrictions** (patient consent; other ethical, legal, and policy issues) alter what the scientist may do with the specimen and/or data



Biospecimen pre-analytical variables

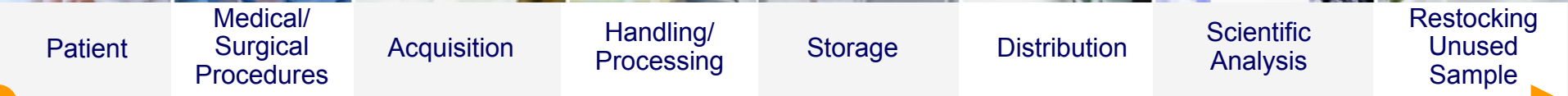
Variables (examples):

- **Antibiotics**
- **Other drugs**
- **Type of anesthesia**
- **Duration of anesthesia**
- **Arterial clamp time**

Time 0

Variables (examples):

- **Time at room temperature**
- **Temperature of room**
- **Type of fixative**
- **Time in fixative**
- **Rate of freezing**
- **Size of aliquots**



Patient

Medical/
Surgical
Procedures

Acquisition

Handling/
Processing

Storage

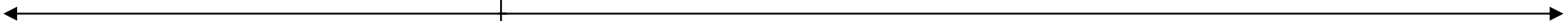
Distribution

Scientific
Analysis

Restocking
Unused
Sample

Pre-acquisition

Post-acquisition





Potential Effects of Biospecimen Variables

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- Effects on clinical outcomes:
 - Morphological artefact confounding diagnosis
 - Skewed clinical chemistry results
 - Potential for incorrect therapy when a therapy is linked to a diagnostic test on a biospecimen (e.g., HER2 in breast cancer)
- Effects on research outcomes:
 - Variations in gene expression data
 - Variations in post-translational modification data
 - Potential for misinterpretation of artefacts as biomarkers



Science of Any Type or Size

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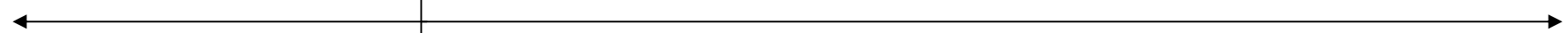
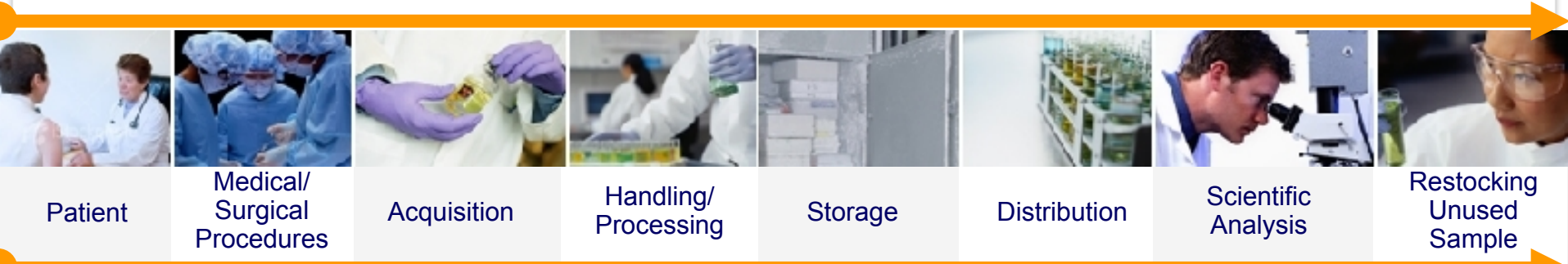
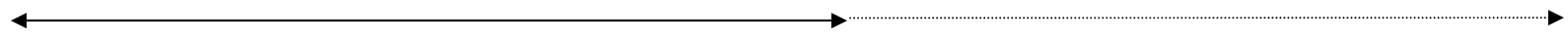
Garbage In ⇒ Garbage Out



Moving forward with Biospecimen Research

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The specimen is viable



Pre-acquisition

Post-acquisition

Time 0

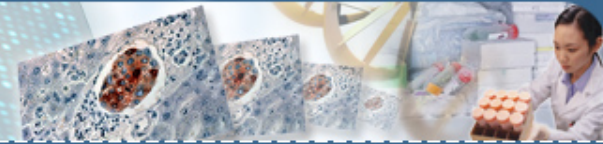
Short list of Biospecimen Variables

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**

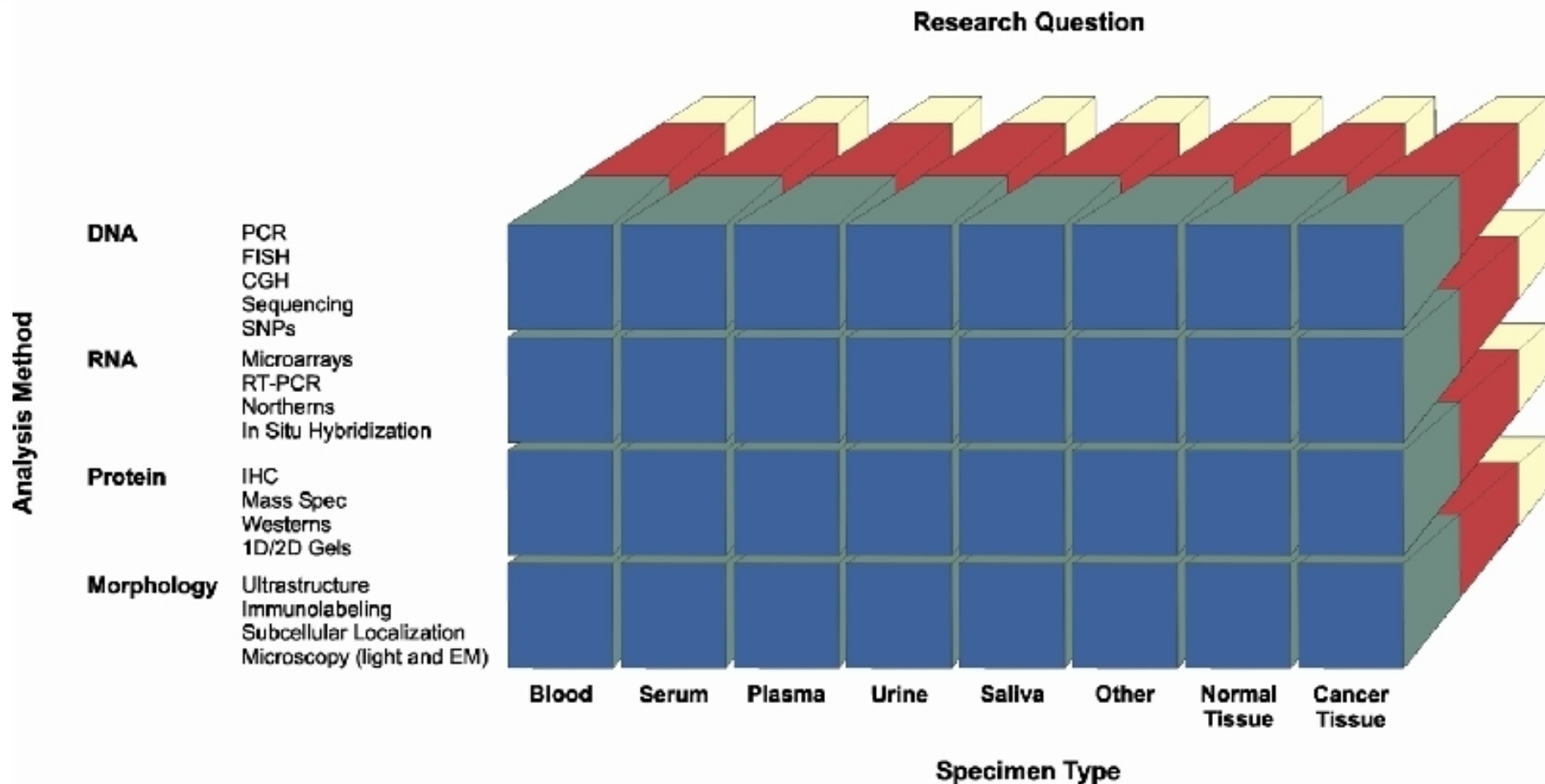
Post-acquisition variables:

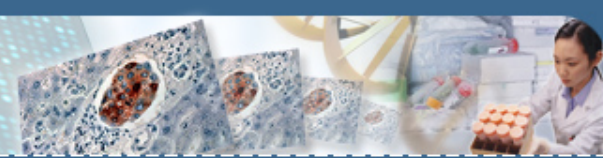
- Time at room temperature
- Temperature of room
- Type of preservative
- Time in preservative
- Rate of freezing
- Size of aliquots
- Type of collection container
- Biomolecule extraction method
- Storage temperature
- Storage duration
- Storage in vacuum



Not one size fits all: the nature of the specimen should be matched to the analysis method

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The Biospecimen Research Network: Central Source, Collaborator, Researcher

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- Produce scientific evidence for guiding development of data-driven SOPs for collection, processing, storage and analysis of specimens.
- Provide leadership to stimulate investment in biospecimen science development.

What needs to be done? Informed by:

- *Summer 2005 NCI workshops on Biospecimen issues*
- *March 2006 OBBR Biospecimen Research Symposium*
 - *Built on several months of individual meetings with more than 100 investigators from the National Institutes of Health (NIH) intramural program and other Government, academic, and commercial research organizations*
 - *Clinicians and scientists from the intramural and extramural community with the collective expertise to carry out complex BRN research projects*



Central Resource: RAND survey

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- **Comprehensive assessment of the existing published and unpublished information on biospecimen research studies**
 - *What important biospecimen research has been done?*
 - *What remains to be done?*
- **Currently developing a literature curation tool and database** to populate a publicly available, searchable biospecimen science website
 - *Central resource for the research and biobanking community*



Additional BRN Projects

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- Pre-acquisition:
 - Effects of surgical clamp time (ischemia) on gene expression patterns (Colon cancer, Renal cell carcinoma)
- Post-acquisition:
 - Effect of different DNA isolation protocols on downstream analysis techniques - Renal cell carcinoma
 - Effect of different tissue fixation protocols on fixed and paraffin-embedded – Breast HER2, ER, PR
 - Recovery of RNA and proteins from differentially fixed tissue
 - Recovery of RNA and proteins from tissue using different laser microdissection platforms



Biospecimen Research Program: Central themes of proposed research

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- “Bridging the gap” between existing clinical practice for biospecimens and emerging technologies for personalized diagnostics and therapies
- Defining the most significant variables for prospective collection of tissues, blood, and body fluids
- Developing evidence-based biospecimen quality indicators for specific analytical platforms



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