The NCI Best Practices for Biospecimen Resources
NCI Best Practices: Next Steps

- 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
- 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

- 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
<table>
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<tr>
<th>Genomics</th>
<th>Proteomics</th>
<th>Metabolomics</th>
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All Depend On High-Quality Human Biospecimens
Reproducible data is urgently needed to advance molecular medicine

- 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
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

Variables (examples):
- Time at room temperature
- Temperature of room
- Type of fixative
- Time in fixative
- Rate of freezing
- Size of aliquots

Pre-acquisition

Post-acquisition
Potential Effects of Biospecimen Variables

- 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

Garbage In $\Rightarrow$ Garbage Out
Moving forward with Biospecimen Research

The specimen is viable

- Patient
- Medical/Surgical Procedures
- Acquisition
- Handling/Processing
- Storage
- Distribution
- Scientific Analysis
- Restocking Unused Sample

Pre-acquisition

Post-acquisition

Time 0

The specimen is viable
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.
The Biospecimen Research Network: Central Source, Collaborator, Researcher

- 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

- 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

- **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

- “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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