Cancer Biobanking: The American Perspective

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At current incidence rates, 1 in 2 men and 1 in 3 women will develop cancer within their lifetime.
Cancer Burden Will Increase as Baby Boomers Age

Projected New Cancer Cases, United States

Sources:
The Value of Early Screening

The need for relevant and valid biomarkers is obvious, and applies to all diseases

Source: Canary Foundation
Translational Research Promises to Advance Molecular Medicine for Cancer Patients

PERSONALIZED CANCER CARE

Molecular Data → Diagnosis / Therapy

Biospecimen Distribution → Biospecimen Processing and Banking

Biospecimen Collection
### Future of Personalized Medicine: Molecular Oncology/Molecular Medicine

**Advances in Molecular Research and Technologies**

<table>
<thead>
<tr>
<th>The Past Century</th>
<th>21st Century</th>
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<tbody>
<tr>
<td>Treatment of established symptomatic disease</td>
<td>Targeted treatments, early detection and prevention</td>
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<tr>
<td>Morphologic diagnosis and phenotypic tumor classification</td>
<td>Genotypic tumor classification and molecular characterization of pathways and processes</td>
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<td>Generic therapeutic regimens not effective for all tumors of same class</td>
<td>Pharmacogenomics defines host response to drug therapies</td>
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<td>Treatments have unpredictable adverse effects on patients</td>
<td>Emphasis on specific biology of host and disease</td>
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A Future Dependent on Quality Biospecimens
Understanding Cancer -- or Any Disease --
Means Confronting Biological Complexity

Genomics

Proteomics

Metabolomics
Understanding Cancer -- or Any Disease -- Means Confronting Biological Complexity

All Depend On High-Quality Materials and Technologies
The Discovery “Pipeline”: Potential Sources of Variation

- Hypothesis is wrong
- Experimental design is flawed
- Experimental materials, e.g., biospecimens, are highly variable in quality
- Analytical tools are inadequate to complexity of data or flawed at core
- Tools are inadequate, not applicable to experimental design, or even broken
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“Quality” of human biospecimens is multifactorial

Defined by:

- Physical (biologic) state of the analyte
- 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 (ethical, legal, policy issues)
The challenges:

- **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
OBBR: NCI Best Practices for Biospecimen Resources

- Process built on intensive due diligence over 5 years
  - Rand reports on existing biorepositories and practices
  - National Biospecimen Network Blueprint
    - NBN pilot project with Prostate Cancer SPOREs
  - NCI Biorepository Coordinating Committee
  - National workshops
    - Collection, processing, storage aspects
    - Ethical, legal, policy aspects
  - Approval by NCI’s National Cancer Advisory Board (NCAB) and Board of Scientific Advisors (BSA)
  - First published April 2006
  - Public comment period from April to July 2006
  - Final version approved by NCAB and BSA in June 2007
  - 3 National Educational Forums: Boston, Chicago, Seattle
Includes recommendations for:

- Common best practices for research biorepositories
- Quality assurance and quality control programs
- Implementation of enabling informatics systems
- Addressing ethical, legal, and policy issues
- Establishing reporting mechanisms
- Providing administration and management structure

- Informed consent
- Access to biospecimens and data
- Privacy protection – HIPAA
- Ownership/custodianship
- Intellectual property
Many Standards Around the World: Which Are the Best?

- Impossible to call any set of standards “the best” (even NCI’s)
  - All have strengths and weaknesses
  - No single set of SOPs are applicable to all clinical and research analytical platforms
  - Very few SOPs are based on scientific evidence
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Where we need to go
Biospecimen Research: What Needs to Be Understood?

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
Pre- and Post- Acquisition Variables Impact Clinical and Research Outcomes

**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
BRN research addresses the following challenges in biospecimen science:
• Bridging gaps between existing clinical practice and emerging technologies
• Defining significant variables for prospective collections
• Developing evidence-based biospecimen quality indicators

Activities of the BRN program to date:
• Public outreach to define issues and needs in biospecimen standardization
• Consulting on biospecimen issues for programs within NCI/NIH
• BRN laboratory: research studies with intramural and extramural collaborators
• Development of the Biospecimen Research Database
  • Searchable web tool for biospecimen literature/published data
• Extramural research programs to define pre-analytical variables approved
A New Extramural Research Program: $20.5 M

An ordered approach to filling the knowledge gaps: RFP

- Studies to assess effects of pre-analytical variables in human specimens on genomic, epigenomic, and proteomic analyses
- Model of variable-controlled and/or variable-annotated biospecimen acquisition and invariable molecular analysis
- Trans-disciplinary and highly collaborative design
  - Addresses the many operational factors that influence specimen variation

A creative approach to meeting existing challenges: BAA

- Solicitation of solutions to address unmet needs and difficult issues
Framework for Development of Evidence-Based Standards Operating Procedures

- **VARIABLES**
  - **Feature of interest**
    - DNA
    - RNA
    - PROTEIN
    - MORPHOLOGY
  - **Analysis Method**
    - PCR
    - FISH
    - CGH
    - MICRO-ARRAY
    - IMMUNOSTAINING
    - LIGHT MICROSCOPY (H&E)
  - ** OTHER TECHNOLOGIES**
    - RT-PCR
    - NORTHERN
    - WESTERN
    - MASS SPEC
    - TRANSMISSION EM

- **Specimen Type**
  - Blood
  - Serum
  - Plasma
  - Urine
  - Saliva
  - Normal Tissue
  - Cancer Tissue
  - Other
Expected Program Outcomes

- Published data on the effects pre- and post-acquisition variables on downstream molecular analysis
- Raised awareness of the importance of biospecimen research
- Increased attention to specimen QA/QC issues by manufacturers of consumables, reagents, and robotics
- College of American Pathologists guidelines based on new data with implementation in the clinical arena
- Implementation of data-driven standards for specimen handling in new venues: Inclusion of biospecimen handling parameters in clinical trials and in research, development, and regulation of cancer biomarkers
- GREATER REPRODUCIBILITY OF RESEARCH AND CLINICAL RESULTS
NCI’s Efforts Towards Evidence-Based Standards: Preparing the Way for Personalized Medicine

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