

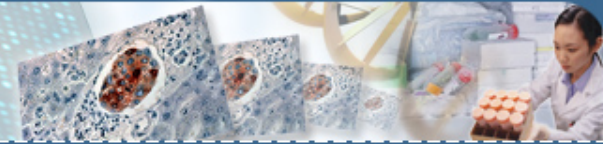


OBRR

Office of Biorepositories
and Biospecimen Research

Cancer Biobanking: The American Perspective

Carolyn Compton
Director, Office of Biorepositories and Biospecimen Research
U.S. National Cancer Institute



The Burden of Cancer

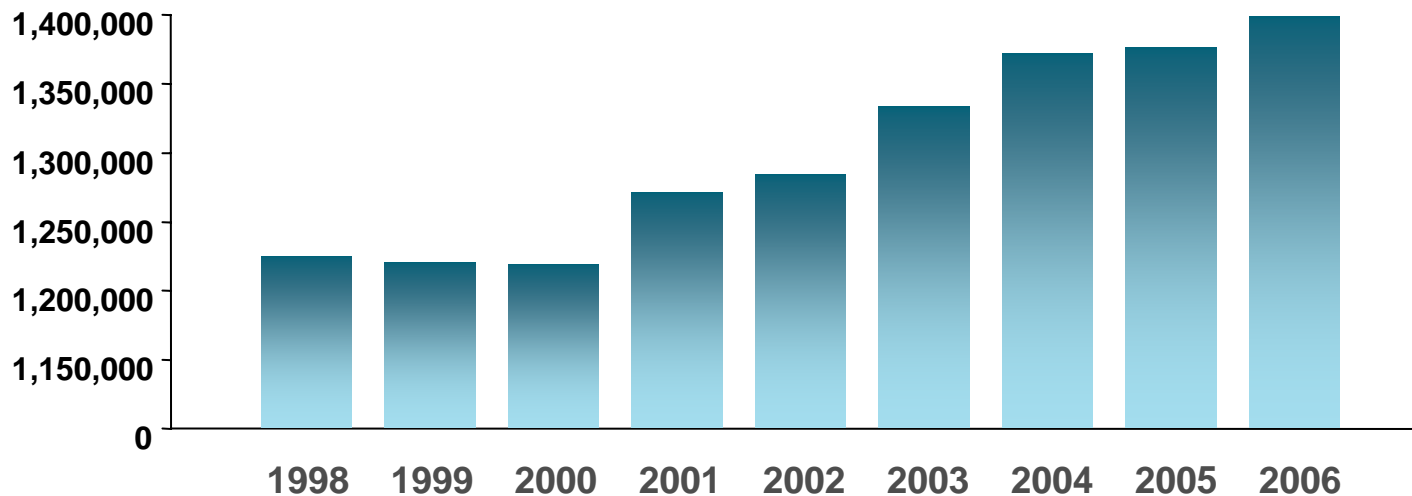
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Sources:

Cancer Facts and Figures, American Cancer Society, 1997-2006.

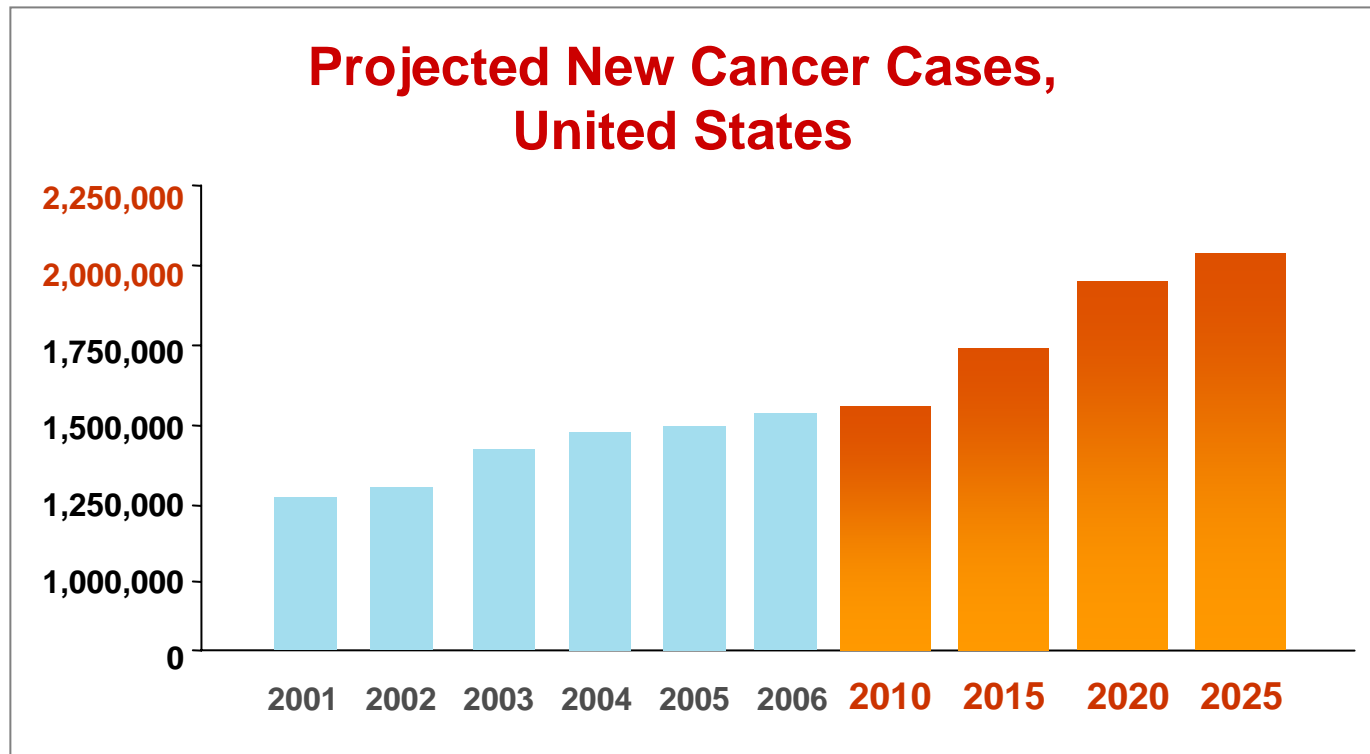
Jemal A, Siegel R, Ward E, Murray T, Xu J, Smigal C, and Thun MJ. Cancer Statistics, 2006. CA Cancer J Clin 2006; 56:106-130.

Estimated Number of New Cancer Cases, United States



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

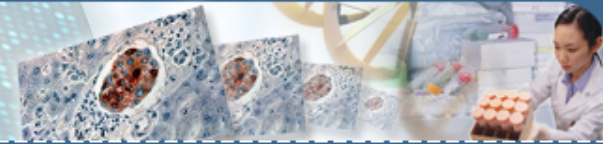


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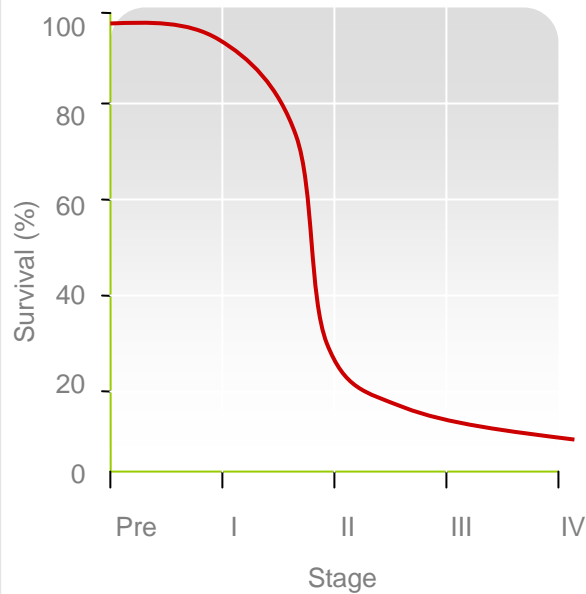
Jemal A, Siegel R, Ward E, Murray T, Xu J, Smigal C, and Thun MJ. Cancer Statistics, 2006. CA Cancer J Clin 2006; 56:106-130.

Edwards BK, Howe HL, Ries LAG, Thun MJ, Rosenberg HM, Yancik R, Wingo PA, Jemal A, Feigal EG, Annual Report to the Nation on the Status of Cancer, 1973-1999, Featuring Implications of Age and Aging on U.S. Cancer Burden, Cancer; May 15, 2002, vol 94. no. 10; pp 2766-2792.

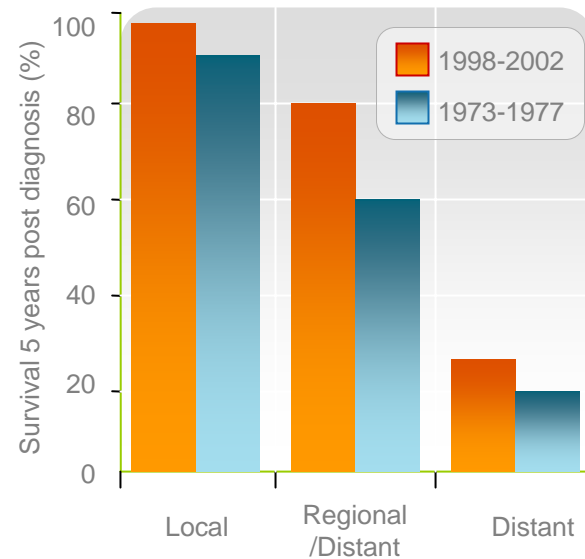


The Value of Early Screening

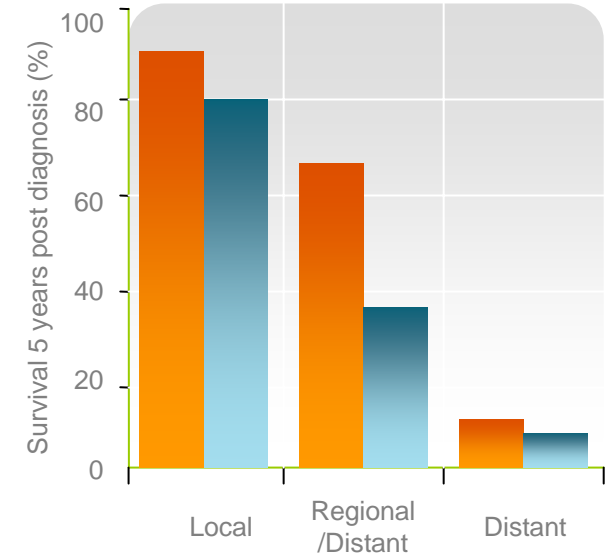
The Value of Early Screening



Breast



Colorectal

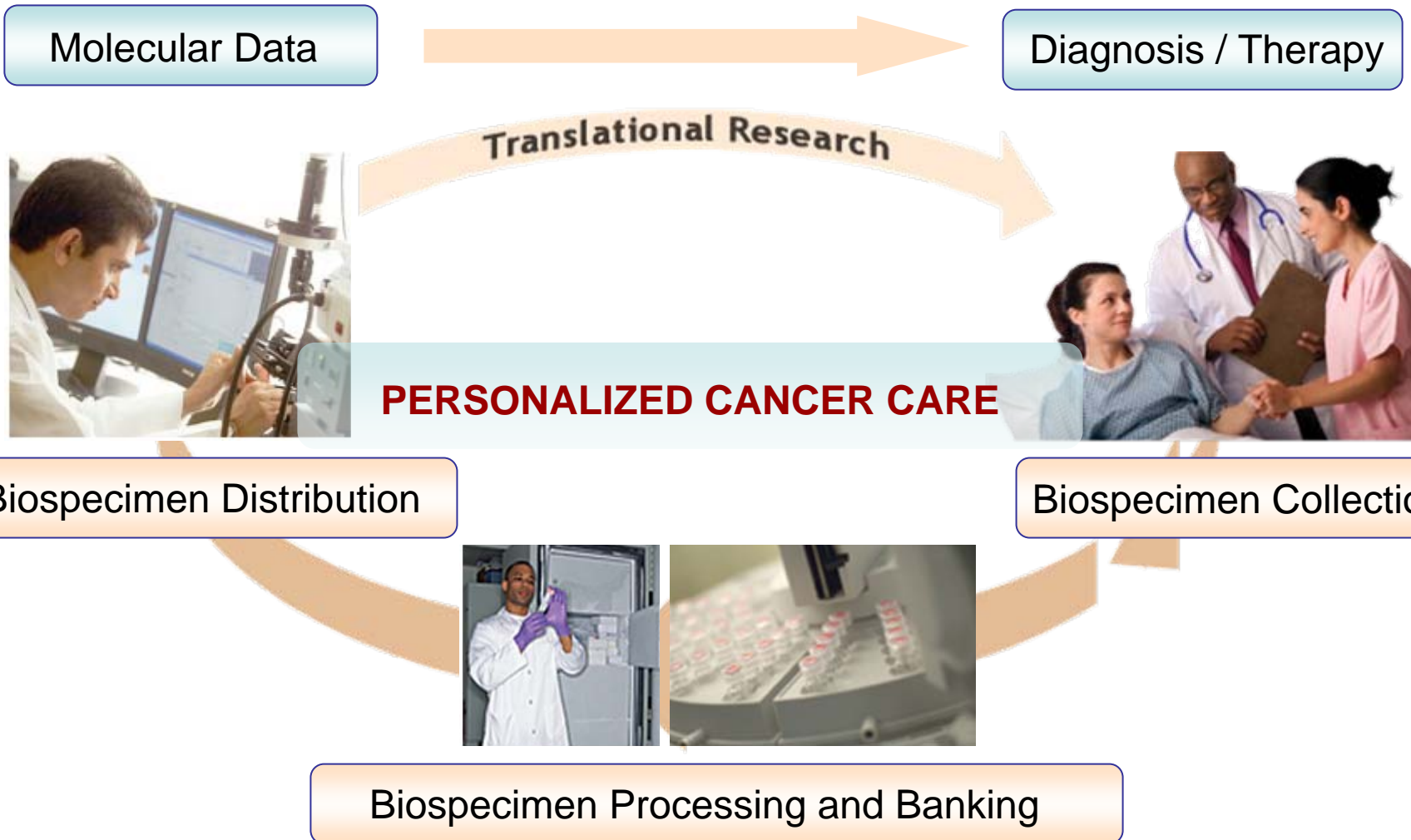


The need for relevant and valid biomarkers is obvious, and applies to all diseases

Translational Research Promises to Advance Molecular Medicine for Cancer Patients



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Molecular Data

Diagnosis / Therapy

Translational Research

PERSONALIZED CANCER CARE

Biospecimen Distribution

Biospecimen Collection

Biospecimen Processing and Banking



Future of Personalized Medicine: Molecular Oncology/Molecular Medicine

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Advances in Molecular Research and Technologies

The Past Century

21st Century

Treatment of established symptomatic disease

Morphologic diagnosis and phenotypic tumor classification

Generic therapeutic regimens not effective for all tumors of same class

Treatments have unpredictable adverse effects on patients

Targeted treatments, early detection and prevention

Genotypic tumor classification and molecular characterization of pathways and processes

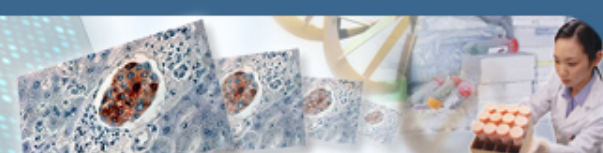
Pharmacogenomics defines host response to drug therapies

Emphasis on specific biology of host and disease

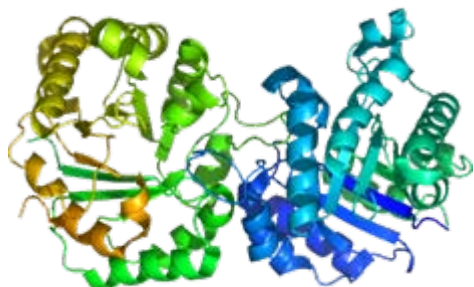
A Future Dependent on Quality Biospecimens

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

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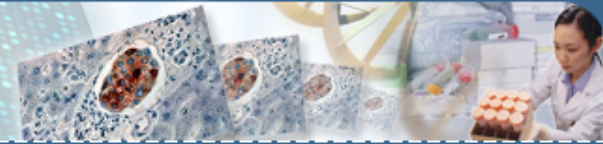
Genomics



Proteomics



Metabolomics

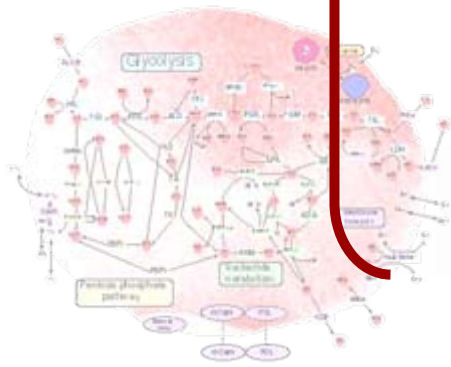


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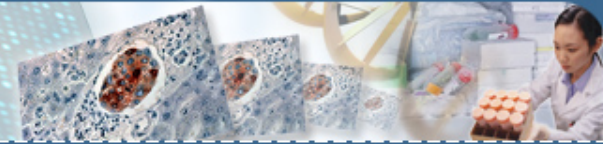
**All Depend
On High-Quality
Materials and
Technologies**



Genomics

Proteomics

Metabolomics



The Discovery "Pipeline": Potential Sources of Variation

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Hypothesis
is
wrong

Experimental materials,
e.g., biospecimens, are
highly variable in quality

Analytical tools are
inadequate to
complexity of data or
flawed at core

Experimental
design is
flawed

Tools are inadequate,
not applicable to
experimental design,
or even broken

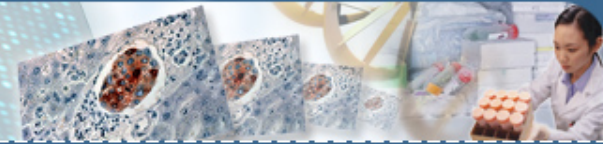
Hypothesis

Experimental
Design

Experimental
Materials

Experimental
Technologies

Data Collection
and Analysis



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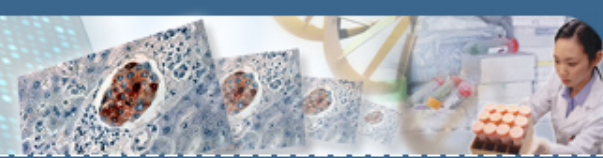
Hypothesis

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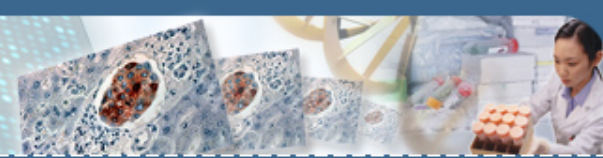
Data Collection
and Analysis



Human Analytes Quality Determined by Multiple Factors

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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)



Molecular Research and Analyte Variation

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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

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- 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

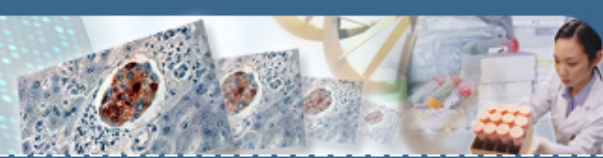


NCI Best Practices for Biospecimen Resources: Contents

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Includes recommendations for:

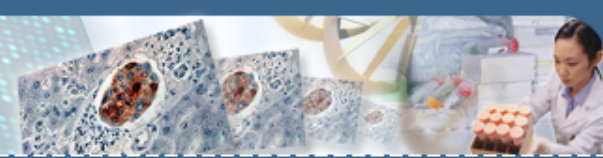
- Common best practices for research biorepositories
- Quality assurance and quality control programs
- Implementation of enabling informatics systems
- Addressing ethical, legal, and policy issues
- Establishing reporting mechanisms
- Providing administration and management structure
- Informed consent
- Access to biospecimens and data
- Privacy protection – HIPAA
- Ownership/custodianship
- Intellectual property



Many Standards Around the World: Which Are the Best?

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and Biospecimen Research

- 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**



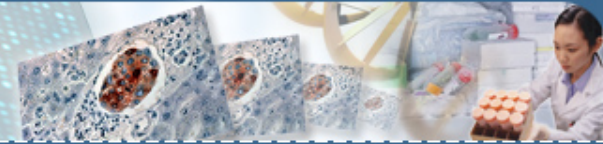
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Where we need to go



Biospecimen Research: What Needs to Be Understood?

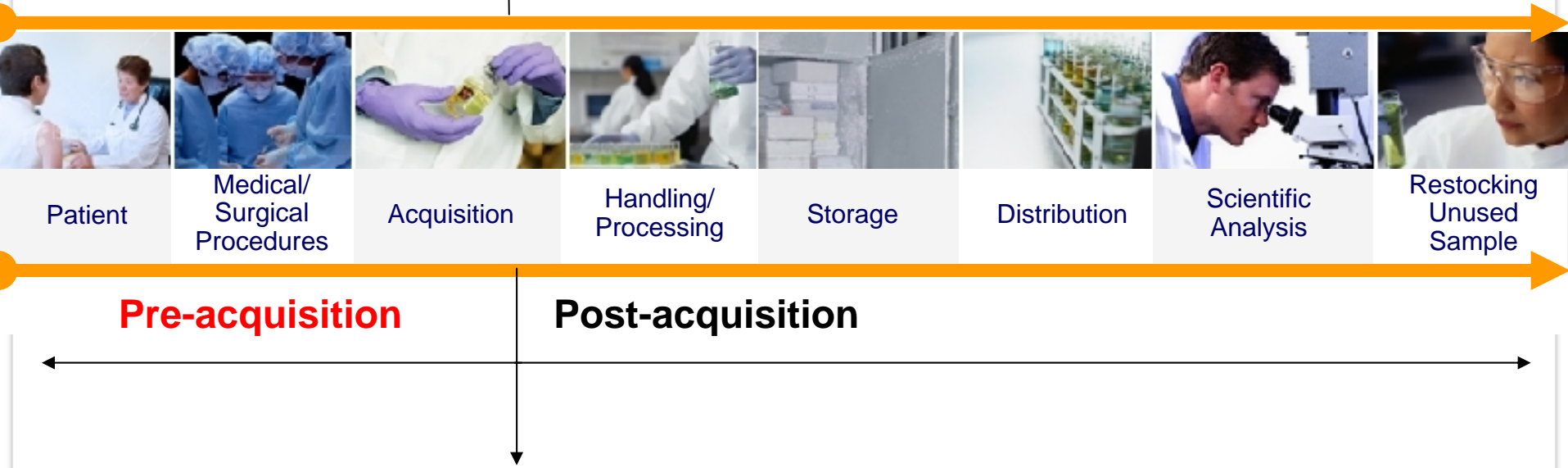
Variables (examples):

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

Time 0

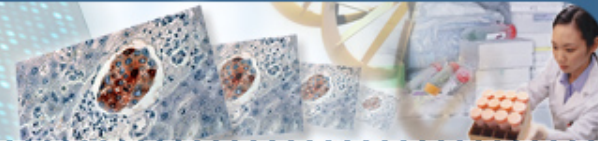
Variables (examples):

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



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

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- **Effects on Clinical Outcomes**

- **Potential for incorrect diagnosis**

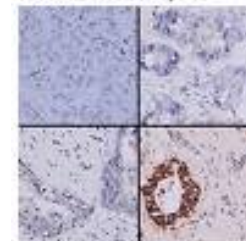
- Morphological/immunostaining artifact
- Skewed clinical chemistry results

- **Potential for incorrect treatment**

- Therapy linked to a diagnostic test on a biospecimen (e.g., HER2 in breast cancer)



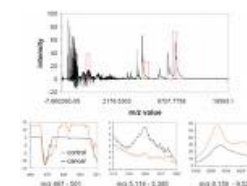
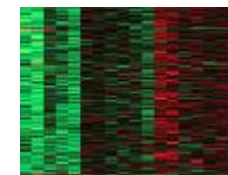
HER-2 as assessed by IHC



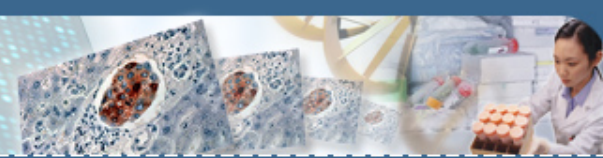
- **Effects on Research Outcomes**

- **Irreproducible results**

- Variations in gene expression data
- Variations in post-translational modification data



- **Misinterpretation of artifacts as biomarkers**



Biospecimen Research Network: Defining the Influence of Acquisition Variables on Downstream Molecular Analysis

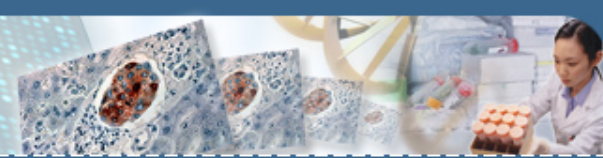
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BRN research addresses the following challenges in biospecimen science:

- 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**



New Extramural Research Program: \$20.5 M

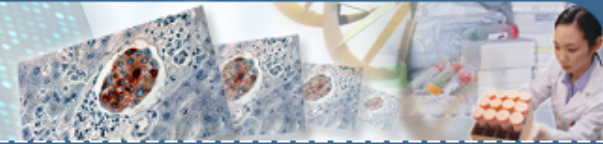
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An ordered approach to filling the knowledge gaps: RFP

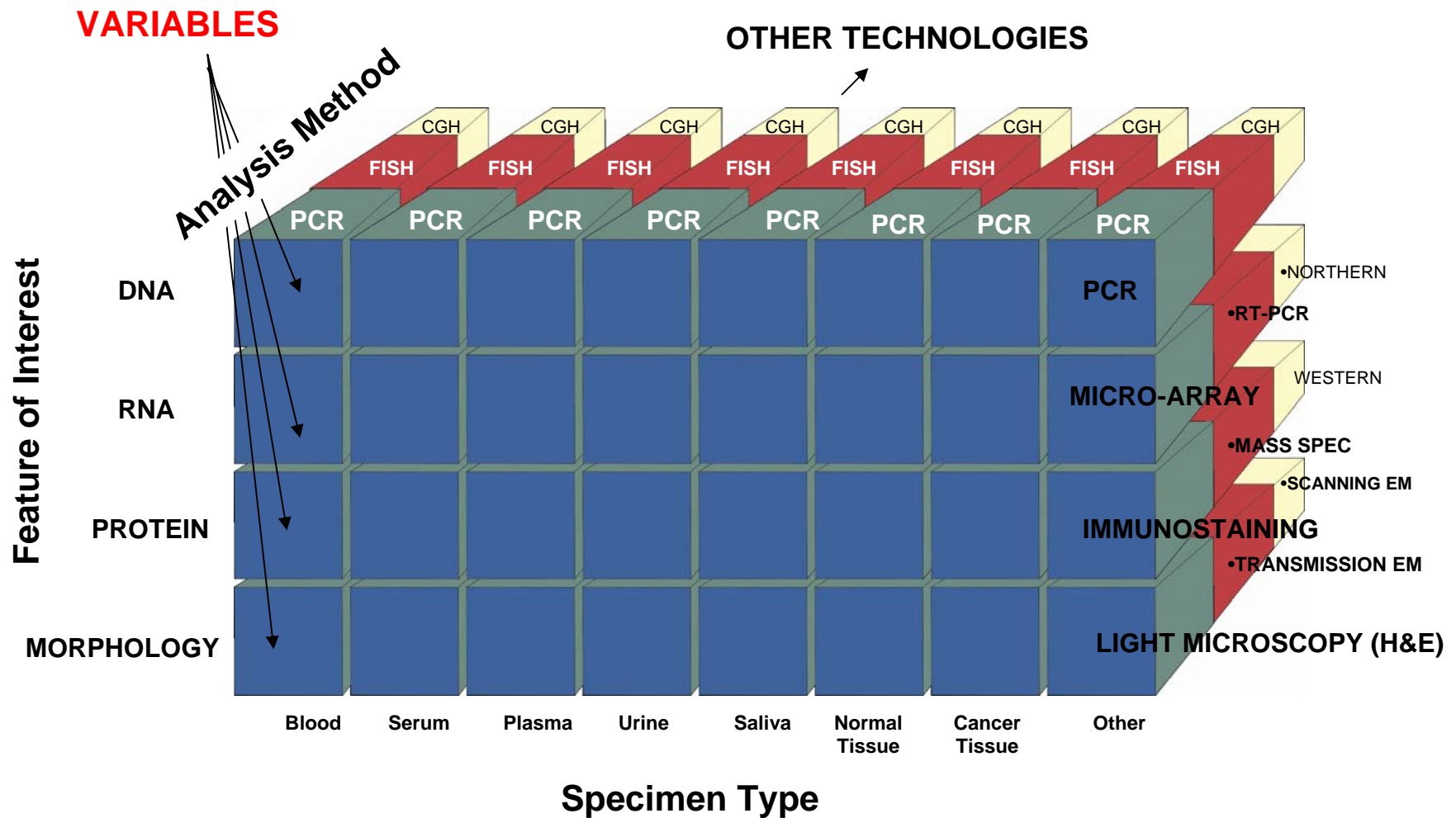
- Studies to assess effects of pre-analytical variables in human specimens on genomic, epigenomic, and proteomic analyses
- Model of variable-controlled and/or variable-annotated biospecimen acquisition and invariable molecular analysis
- Trans-disciplinary and highly collaborative design
 - Addresses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





Expected Program Outcomes

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- ✓ **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**



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NCI's Efforts Towards Evidence-Based Standards: Preparing the Way for Personalized Medicine

Carolyn Compton
Director, Office of Biorepositories and Biospecimen Research
U.S. National Cancer Institute