NCI's Best Practices Forum: Why Do We Need Biospecimen Best Practices?

Seattle, Washington
January 28, 2008

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Cancer: Our #1 Health Problem

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- **Cancer is the #1 killer of Americans under the age of 85**
- **1 American dies of cancer every minute**
- **Nearly 600,000 will die of cancer this year**
- **1.4 million will develop cancer this year**
- **1 of 3 females will develop cancer in their lifetime**
- **1 of 2 males will develop cancer in their lifetime**
- **$189 billion/year on healthcare costs for cancer alone**
- **NCI Budget = $4.8 billion/year**
  - advertising budget for cigarettes = $16 billion/year

A New Era: Molecular Technology Promises to Transform Oncology

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MOLECULAR MEDICINE

Beating cancer

Oct 14th 2004
From The Economist print edition

The war on cancer is entering a new phase

"CANCER" is one of those words that sends shivers down the spine. The phrase "battle with cancer" is a headline writer's cliché. And the military metaphor was widened in 1971, when Richard Nixon, then president of the United States, announced an initiative that later became known as the "war on cancer". Cancer, however, has not been beaten. Indeed, by some measures the problem is worse than it was three decades ago. It is true that treatments have improved somewhat, and prognoses with them, and that a few forms of the disease, particularly in children, can be cleared up altogether. But the biggest success has been due to people giving up smoking, rather than to new treatments. And despite that success, the likelihood that a person will get cancer at some point in his life has actually risen since Nixon's speech.

...the past three decades of effort have seemed a disappointment, the next ...ecade could prove to be one of rapid progress. The battle against cancer is at a ...rning point. Because of recent advances, it is becoming possible to imagine a ...me in the not-too-distant future when new medical treatments will be able to ...me the disease, transforming it from a potent killer into something akin to a ...ronic complaint. The day when cancer no longer strikes terror in the heart of ...se diagnosed with it may not be far away (see article).

...esearchers have unravelled much of the basic molecular biology of cancer and, ...ed by the outpouring of knowledge that the Human Genome Project has ...ded over the past ten years, they have come to understand how the disease ...gresses. Indeed, they have come to understand far more clearly than before ...the term "cancer" properly refers not to a single disease, but rather to a whole ...e of diseases that have in common only the fact that they are caused by cells ...do not know when to stop dividing. That understanding has now reached the ... where it can be turned into action. The next few years should see an array of ...reatments that will add up to a big change in the way that cancer is viewed ...alt with by society.

Unprecedented Potential for Progress

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- **Technological change is exponential, not linear**
  - "We won't experience 100 years of progress in the 21st century – it will be more like 20,000 years of progress (at today's rate)."
    - **Ray Kurzweil, *The Law of Accelerating Returns***
- **Scientific knowledge will double in the next 3 years**
- **Biologic knowledge will double in the next 5 years**
- **The sum of all human knowledge is just 1% of what it will be in the year 2050**

Cancer Research at an Inflection Point

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- **The goals of analysis are broadening**
- **The analysis tools are increasing in power**
- **The volume of relevant data is increasing**
- **The complexity of the analysis is escalating**
- **The context of medical application is changing**
  - New targeted therapies
  - Directed uses of old therapies

The Technological Power to Understand the Biologic Complexity of Cancer

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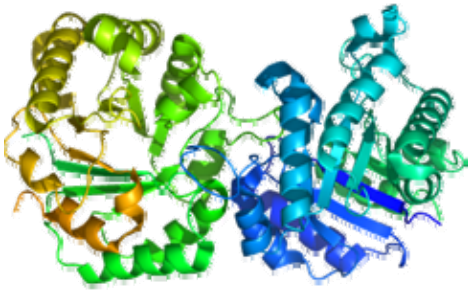
Genomics



Proteomics

Metabolomics

The Technological Power to Understand the Biologic Complexity of Cancer

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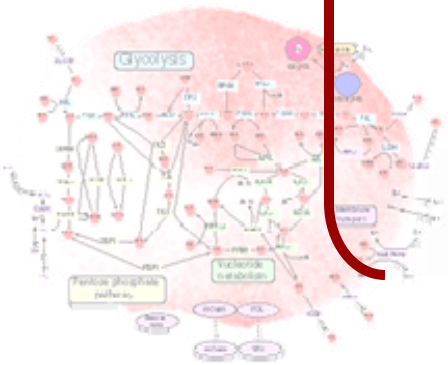
All Depend On High-Quality Biospecimens



Genomics

Proteomics

Metabolomics

The Promise of Molecular Oncology/ Medicine

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Advances in Molecular Technologies and Research

Generic → Personalized

Morphologic diagnosis and phenotypic tumor classification

Generic therapeutic regimens with unpredictable effectiveness

Treatments with unpredictable adverse effects on patients

Molecular characterization of tumor pathways and processes

Targeted therapies tailored to the molecular profile of the disease

Drug regimens planned around host genetics that portend toxicity

Understanding Molecular Biology of Host and Disease

Biospecimens at the Center of the Evolution of Cancer Research

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- In the drive towards personalized molecular medicine, technology is the engine, but biospecimens are the fuel
- It's where the molecules are
  - **Normal specimens: molecular character of the host**
  - **Tumor specimens: molecular character of the disease**
  - **Serum, plasma, urine: circulating or excreted biomarkers, easily accessible**
- However, new technologies have raised the bar dramatically for specimen quality and standardization

The Critical Role of Biospecimen Resources in 21st Century Medicine

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Large quantities of high-quality, clinically annotated biospecimens are urgently needed to:

- Identify targets for detection, diagnosis, treatment, and prevention
- Develop diagnostics that predict drug efficacy
- Validate new therapeutics
- Elucidate molecular mechanisms of neoplasia
- Develop a molecular-based taxonomy of cancer
- Identify biomarkers for susceptibility, screening, recurrence
- Identify biologic variations that determine drug efficacy
- Identify biologic variations leading to drug toxicity

Biospecimen Variation Compromises Quality

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The challenges: All must be met, because all affect quality

- 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

Key Requirements for Biospecimen Resources for Cancer Research

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- Best practice-based, data-driven technical and operational standards to ensure quality and enable reproducible molecular analysis
- High-quality specimen annotation (pathology and clinical data)
- Specimen access through a timely, centralized, peer-review process
- Ethical and privacy compliance through a chain of trust
- State-of-the-art informatics systems to track specimens, associated data (clinical, pathological, and quality control), and patient consents
- Communication and outreach efforts to ensure greatest impact

Key Requirements Found Wanting

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Heterogeneity in practices among NCI-supported biospecimen resources with a resultant lack of:

- **Common procedures, standards, and management principles**
- **Common definitions**
- **Common computerized access to information on specimens**
- **Common approaches to ethical, legal, and policy issues**

A Call To Action

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For NCI's biospecimen resources, the need for standardization and quality management is critical and long overdue.

The Evolution of NCI's Efforts

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2007

- FGGs revised based on public comments and renamed NCI Best Practices for Biospecimen Resources

2006

- First-Generation Guidelines for NCI-Supported Biorepositories (FGGs) published in Federal Register

2005

- First International Summit on Harmonization of biorepositories conducted
- caBIG™ software tools for biorepositories developed

2004

- Analysis of NCI-supported biospecimen resources conducted
- Trans-NCI Biorepository Coordinating Committee formed

2003

- Case Studies of Existing Human Tissue Repositories published
- National Biospecimen Network (NBN) Blueprint published

2002

- Internal and external review process begun
- Biospecimen resources identified as critically important to post-genomics cancer research

NCI Best Practices Development Process

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First-Generation Guidelines (FGGs) for NCI-Supported Biorepositories were reviewed by:

- NIH Office of Science Policy
- DHHS Office for Human Research Protections
- NIH Office of Intramural Research
- NIH Office of Extramural Research
- NIH Office of Technology Transfer
- NIH Office of the General Counsel

FGGs were published in the Federal Register

- Open public comment period, April-July 3, 2006
- Approximately 60 comments received on topics including:
  - biospecimen resource economics
  - informed consent requirements
  - biospecimen resources affected by the FGGs

NCI Best Practices for Biospecimen Resources were published in April 2007

- Consideration and response to public comments
- Reviewed by NIH and DHHS offices listed above
- Reviewed and approved by the NCAB

NCI Best Practices for Biospecimen Resources

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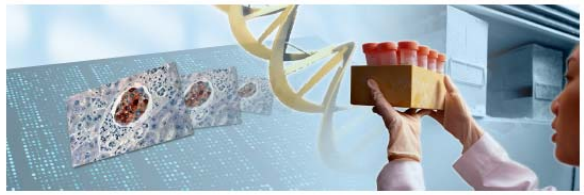

National Cancer Institute
Best Practices for
Biospecimen Resources

June 2007

Prepared by:
National Cancer Institute
National Institutes of Health
U.S. Department of Health and Human Services

Objectives:

- **Unify policies and procedures for NCI-supported biospecimen resources for cancer research**
- **Provide a baseline for operating standards on which to build as the state of the science evolves**

What Is a Biospecimen Resource?

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NCI defines a biospecimen resource as a collection of human specimens and associated data for research purposes, the physical entity where the collection is stored, and all relevant processes and policies.

*Source: NCI Best Practices for Biospecimen Resources

The NCI Best Practices Overview

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The NCI Best Practices include recommendations for:

- Common technical, operational and safety best practices
- Quality assurance and quality control programs
- Implementation of enabling informatics systems
- Establishing reporting mechanisms
- Providing administration and management structure
- Addressing ethical, legal, and policy issues
- Definitions of key terms

NCI Best Practices for Biospecimen Resources

Technical and Operational Guidelines

http://biospecimens.cancer.gov

Technical and Operational Guidelines

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- **Specimen Handling:**
  - Collection
  - Processing
  - Storage
  - Retrieval
  - Dissemination
- **Clinical Data:** Collection and Management
- **Quality Assurance / Quality Control**
- **Biosafety**
- **Biospecimen Resource Informatics:**
  - Data Management
  - Inventory Control
  - Tracking

NCI Best Practices for Biospecimen Resources

Ethical, Legal, and Policy Guidelines

http://biospecimens.cancer.gov

Ethical, Legal, and Policy Guidelines

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- Informed consent
- Access to biospecimens and data
- Privacy protection
- Custodianship
- Intellectual property

Next Steps

The NCI Best Practices: A Living Document

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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 changes in science, law, and policy occur.
- New tools and supplemental guidance in key areas to be added as appendices and/or posted to the OBBR web site:
  - Informatics and caBIG compatibility - available
  - Custodianship – in preparation based on recent symposium
  - QA/QC
  - Economics
  - Biospecimen resource evaluation (self-evaluation)
    - Additional guidance on key elements
  - Biospecimen science and evidence-based SOPs!

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