



**OBBR** Office of Biorepositories  
and Biospecimen Research

## **When Quality Matters Most: Driving Innovative Research and Development Through Emerging Paradigms in Biospecimen Research and Utilization**

**Carolyn C. Compton, M.D., Ph.D.**

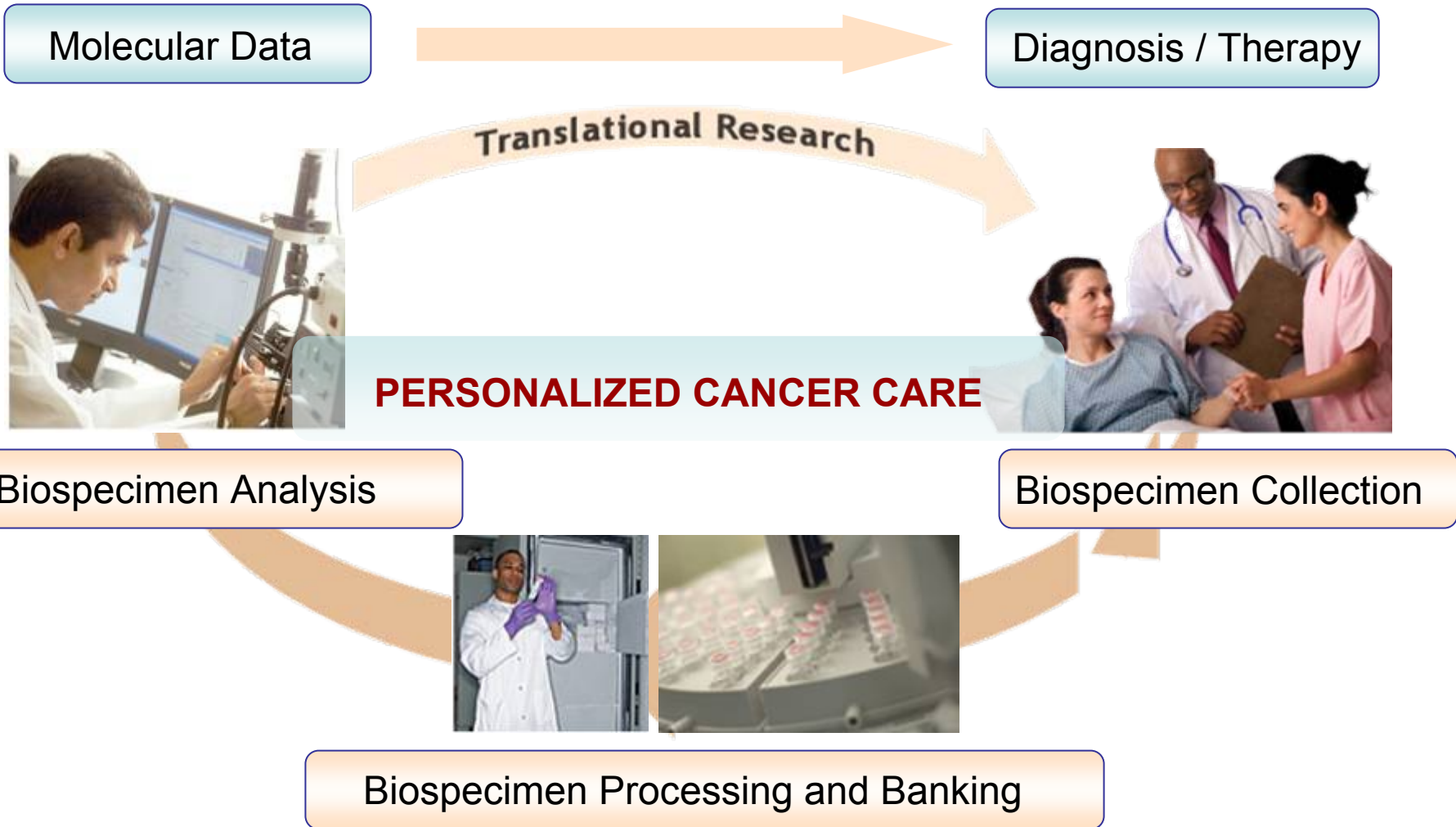
**Director, Office of Biorepositories and Biospecimen Research  
Acting Director, Office of Technology and Industrial Relations  
National Cancer Institute**

**NATIONAL  
CANCER  
INSTITUTE**



# Translational Research Promises to Realize the Vision of Molecular Medicine

**OBBR** Office of Biorepositories and Biospecimen Research





## Biospecimen Resources Pave the Road to Personalized Medicine

OBRR Office of Biorepositories  
and Biospecimen Research

- Biospecimens are the basis of:
  - **Molecular characterization of the disease**
    - Molecular classification
    - Tumor heterogeneity
    - Therapeutic targets
  - **Molecular characterization of the host**
    - Disease susceptibility
    - Adverse Rx outcome risk (pharmacogenomics)



# Molecular Research Using Human Analytes

**OBBR** Office of Biorepositories and Biospecimen Research

**The Cancer Genome Atlas (TCGA)**

**National Community Cancer Centers Program (NCCCP)**

**Genomics**

**Proteomics**

**Metabolomics**

**Clinical Proteomic Technologies Assessment for Cancer (CPTAC)**

**Innovative Molecular Analysis Technologies (IMAT)**

**Alliance for Nanotechnology in Cancer**

**Cancer Genetic Markers of Susceptibility (CGEMS)**

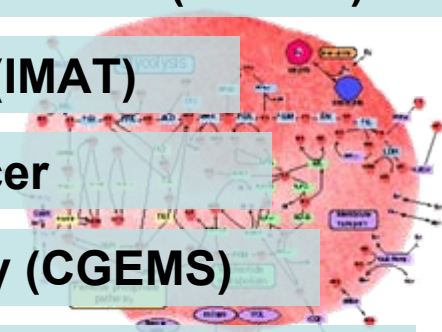
**Clinical trials correlative science**

**Molecular epidemiology programs**

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

**SPORE programs**

**R01 Research**





# Technology Development and Today's Unprecedented Potential for Progress

OBBR Office of Biorepositories and Biospecimen Research

- **Technological change is exponential, not linear**
  - "We won't experience 100 years of progress in the 21<sup>st</sup> century – it will be more like 20,000 years of progress (at today's rate)."
    - Ray Kurzweil, *The Law of Accelerating Returns*
- **Technology accelerates data production → knowledge**
- **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**



## Powerful Tools: Powerful Risks

OBRR Office of Biorepositories  
and Biospecimen Research

- **The technological capacity exists to produce low-quality data from low-quality analytes with unprecedented efficiency**
- **We now have the ability to get the wrong answers with unprecedented speed**
- **Unraveling the massive matrix of misleading data is compromising progress in unprecedented ways**

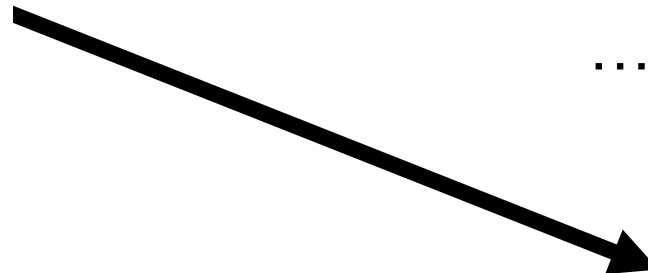


# An Inconvenient Truth.....

Garbage in...



...Garbage out



Diamonds in.....

Courtesy of Gerry Thomas

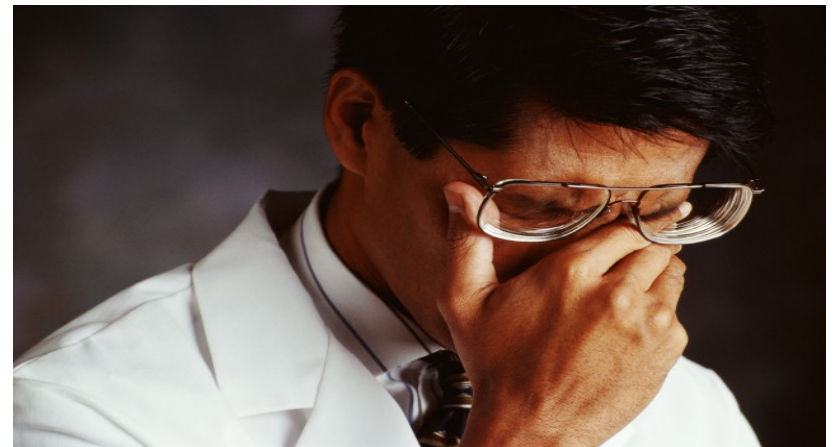




## Molecular Analysis and Human Analytes

OBRR Office of Biorepositories  
and Biospecimen Research

**Challenge for the NCI:** Lack of standardization of human biospecimens and the data associated with them compromises the quality and utility of molecular research dependent on them.







# Addressing the Biospecimen Variation that Compromises Molecular Research

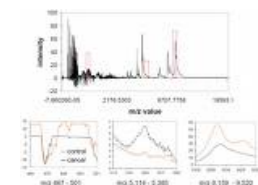
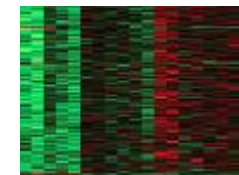
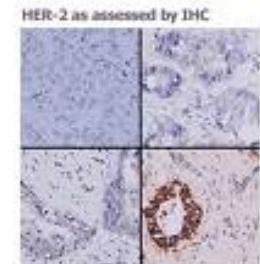
OBBR Office of Biorepositories and Biospecimen Research

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

# Biospecimen Quality Variation Impacts 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**





## **OBBR's Strategic Efforts: Taking Out the Garbage**

**OBBR** Office of Biorepositories  
and Biospecimen Research

- **Optimize and standardize the quality of human specimens for research using a systematic, scientific approach**
- **Remove the barriers to research created by limited availability of high-quality, platform-appropriate human biospecimens**
- **Lay the foundation for tomorrow's standard of care**



## Systematic, Comprehensive Approach to Improving Biospecimen Quality

**OBBR** Office of Biorepositories  
and Biospecimen Research

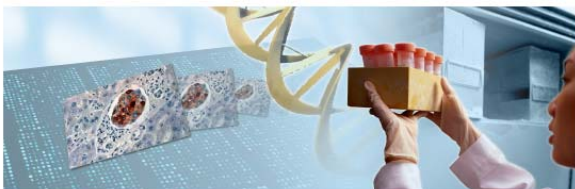
- **Develop state-of-the-science guidance for biobanking**
  - **NCI Best Practices for Biospecimen Resources**
- **Harmonize biobanking practices across NCI/NIH and stakeholder partners**
  - **Intramural: Biorepository Coordinating Committee, Trans-NIH Bioethics Committee, et al.**
  - **Extramural: Group Banking Committee, Translational Research Working Group, NCI Clinical Center, NCI Community Cancer Center Project, SPOREs, et a.**
  - **Coalitions: Interagency Oncology Task Force (FDA,CMS), NCI-FDA-AACR Cancer Biomarkers Collaborative, FNIH Biomarkers Consortium, et al.**



## Systematic, Comprehensive Approach to Improving Biospecimen Quality

OBRR Office of Biorepositories  
and Biospecimen Research

- Facilitate creation of a scientific evidence base for biospecimen procurement, processing, and stabilization
  - Biospecimen Research Database (<http://biospecimens.cancer.gov>)
  - Biospecimen research programs: RFP and BAA
- Partner with accreditation and professional bodies to insure implementation and integration into the medical enterprise
  - College of American Pathologists
  - American College of Surgeons
  - Commission on Cancer



## 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**

<http://biospecimens.cancer.gov>



## The NCI Best Practices Overview

### 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 (caBIG silver)**
- **Establishing reporting mechanisms**
- **Providing administration and management structure**
- **Addressing ethical, legal, and policy issues: informed consent; access; privacy protection; custodianship; intellectual property**
- **Definitions of key terms**



## **OBBR: Building Better Biospecimens**

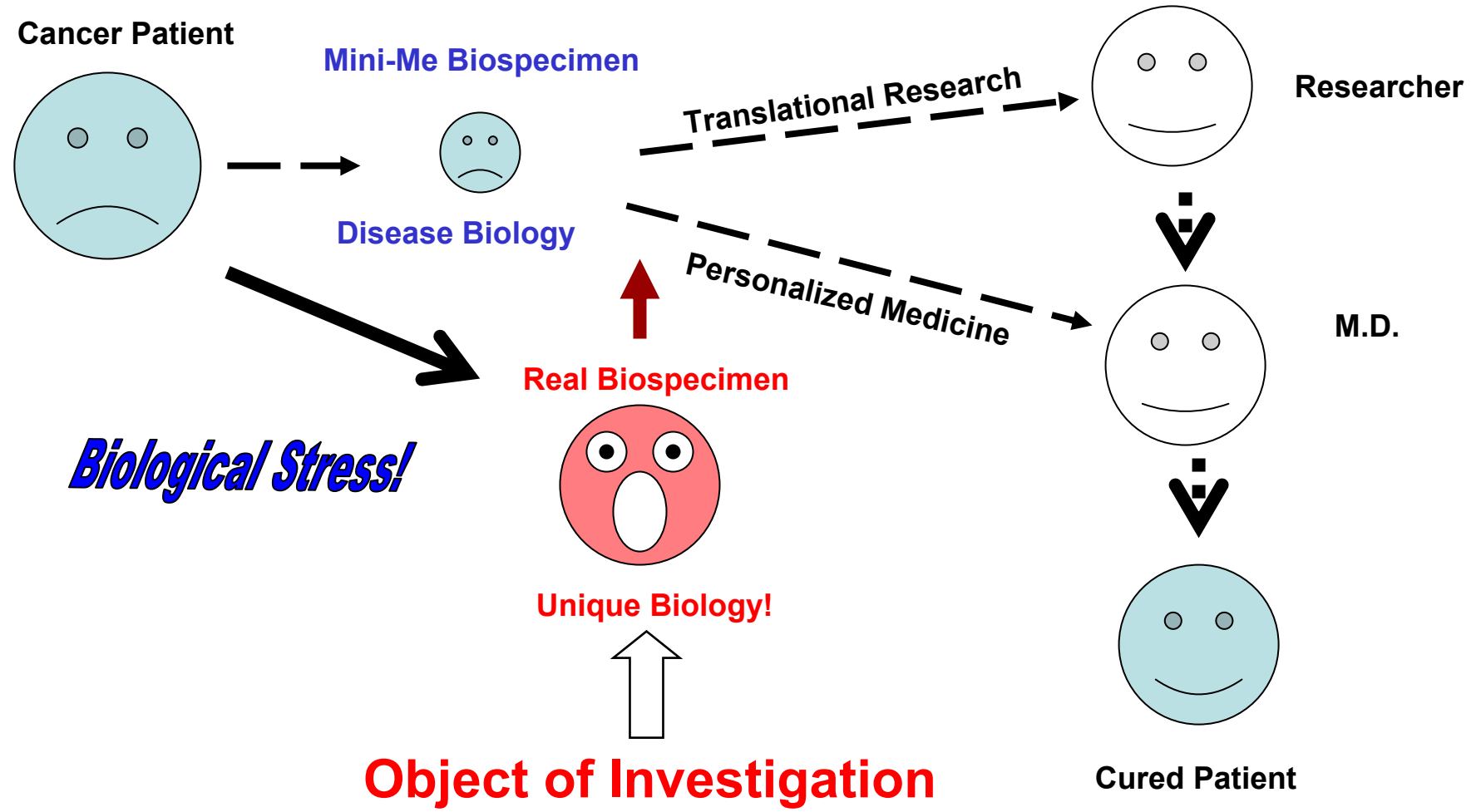
**OBBR** Office of Biorepositories  
and Biospecimen Research

**Developing and implementing  
state-of-the-science, data-driven processes that insure  
the molecular integrity and clinical relevance  
of human biospecimens  
used in cancer research and clinical medicine**





# The Biospecimen as Object of Investigation





# Biospecimen Science

Time 0

No Investment To Date

Specimen is viable and biologically reactive

Molecular composition subject to further alteration/degradation



Patient    Medical/Surgical Procedures    Acquisition    Handling/Processing    Storage    Distribution    Scientific Analysis    Knowledge Base

Pre-acquisition

Post-acquisition

NCI's Biggest Investment



## Variables for Study

### Pre-acquisition variables:

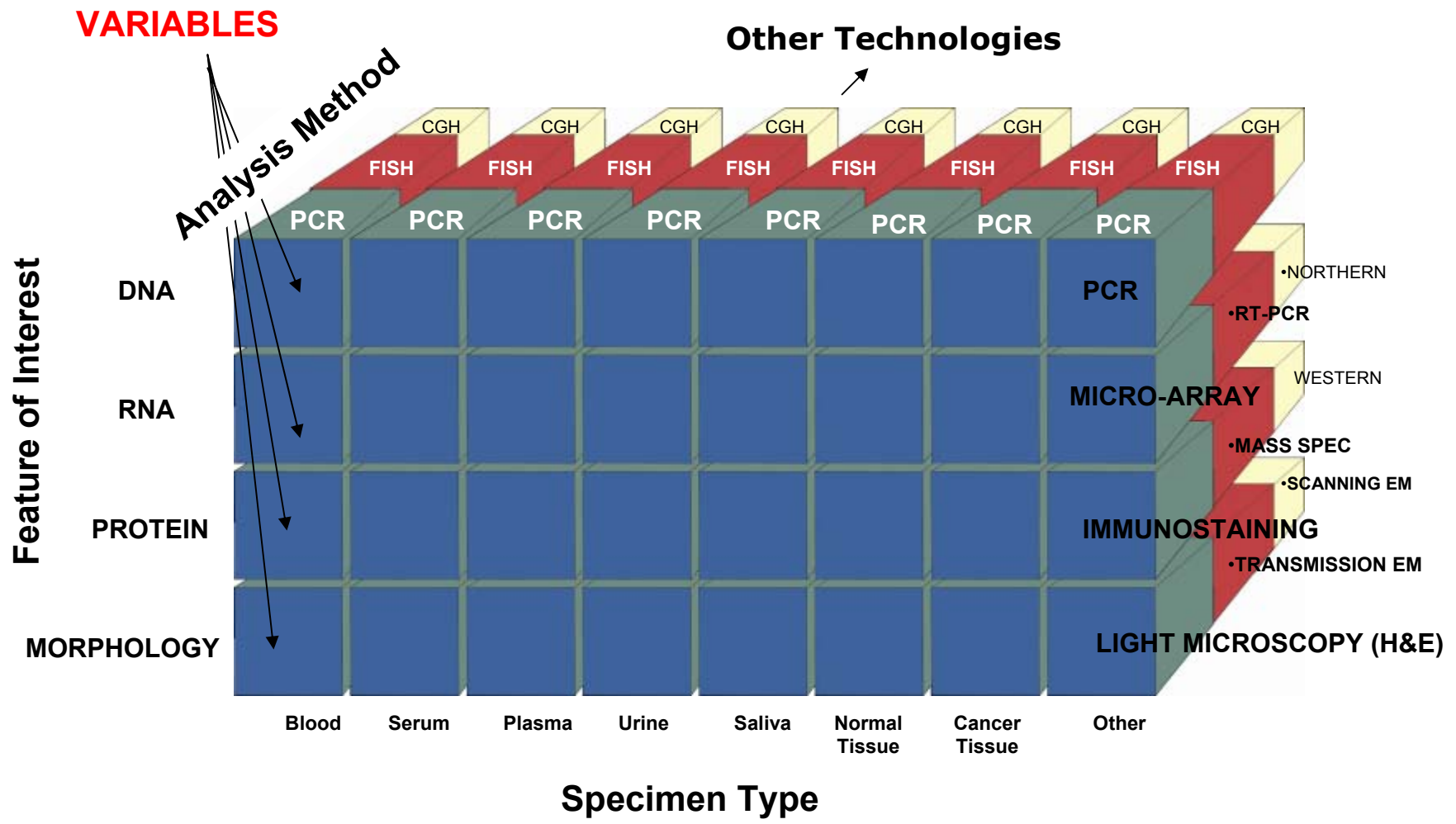
- Antibiotics
- Other drugs
- Type of anesthesia
- Duration of anesthesia
- Arterial clamp time
- Blood pressure variations
- Intra-op blood loss
- Intra-op blood administration
- Intra-op fluid administration
- Pre-existing medical conditions
- Patient gender

### Post-acquisition variables:

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



# The Potential Complexity of the Picture





# The BRN: Supporting Collaborative Research

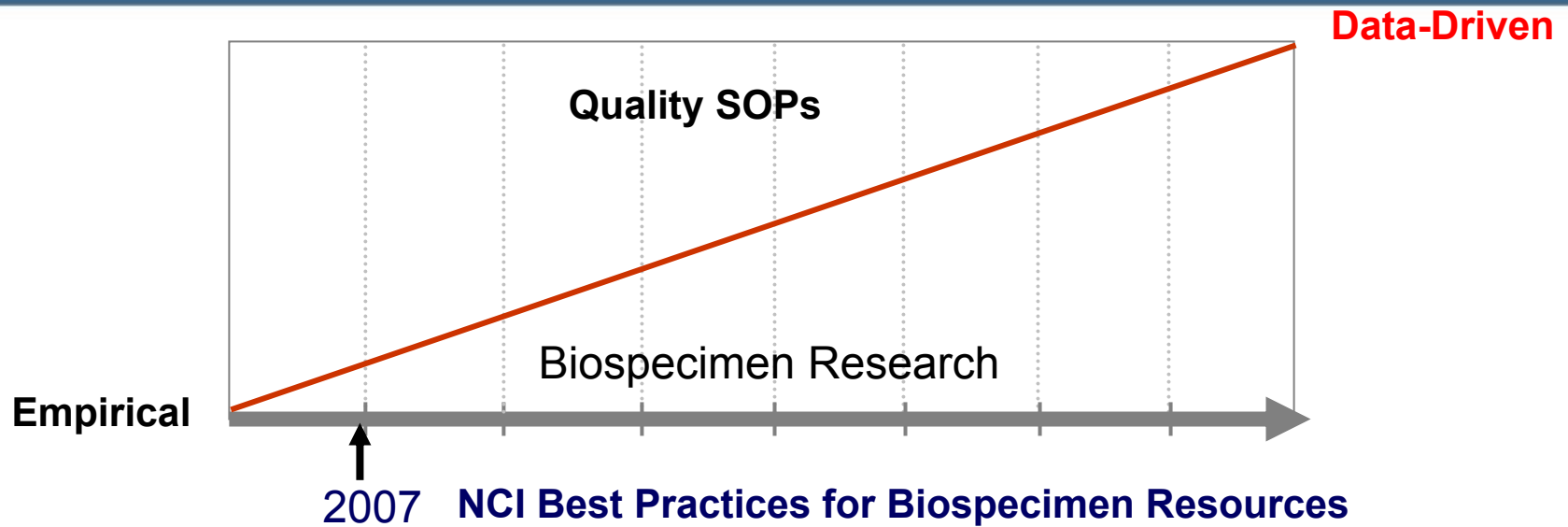
**OBBR** Office of Biorepositories  
and Biospecimen Research

- **Making accessible what we already know:**
  - **The Biospecimen Research Database: A web tool to make existing and emerging biospecimen research data more accessible**
  - **1<sup>st</sup> Annual OBBR Symposium, March 2008: "Advancing Cancer Research through Biospecimen Science"**
  - **2<sup>nd</sup> Annual OBBR Symposium, March 16-18, 2009**
- **Generating new research data on what we don't yet know:**
  - **New Extramural Programs to fill in the ice-cube tray: BAA out now (FedBizOpps); RFP coming soon (mid November)**
  - **Innovative Molecular Assessment Technologies (IMAT) Program – innovative technologic solutions for biospecimens (IMAT Sample Preparation RFA)**
  - **OBBR Intramural Biospecimen Research Laboratory to support biospecimen research for NCI strategic initiatives (TCGA; CPTAC)**



# Pathway to Scientifically Validated Specimen Handling Practices

OBBR Office of Biorepositories and Biospecimen Research



Medical/  
Surgical  
Procedures



Acquisition



Handling/  
Processing



Storage



Distribution

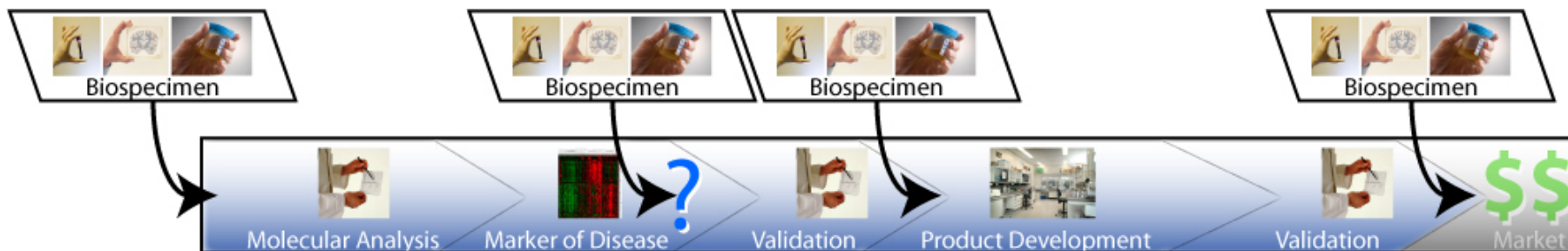


QC/QA



Restocking  
Unused  
Sample

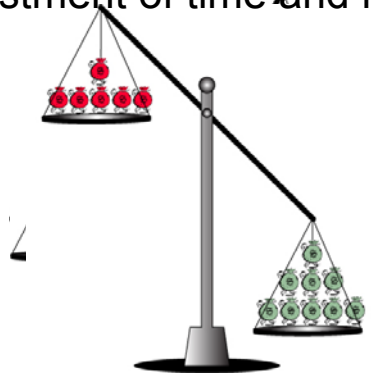
# Developing Cancer Solutions with High-Quality Biospecimens



Any association with specific features—Stage, Grade, Histology, outcome?  
**Yes = COMMERCIAL MILESTONE: MARKET ENTRY?**

- Analysis of Molecular Features
- Identification: Marker of Disease/Disease Feature
- Biomarker Validation  
*Milestone: Confirmation of Disease Biomarker*
- Product Development
  - Diagnostic test (clinical, pathologic)
  - Therapeutic drug
  - Molecular imaging tool
- Product Validation  
*Milestone: Market Entry of Product*

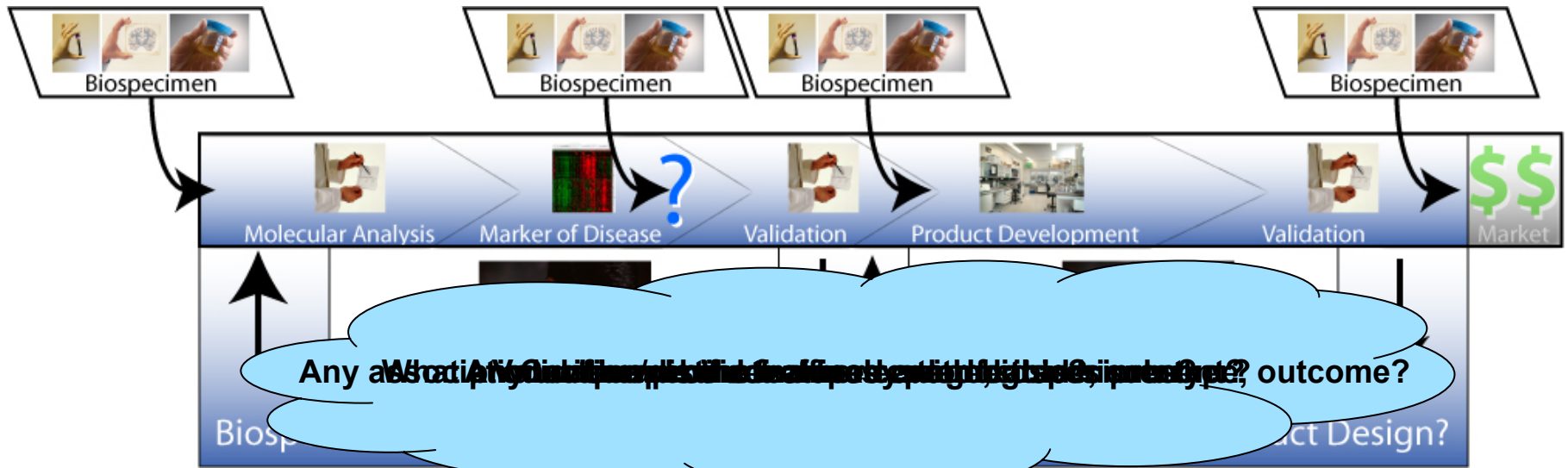
Investment of time and money





# Developing Cancer Solutions with Biospecimens of Unknown Quality

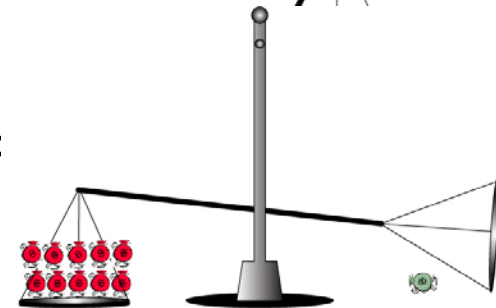
OBBR Office of Biorepositories and Biospecimen Research



- Analysis of Molecular Features
- Identification: Marker of Disease/Disease Feature
- Biomarker Validation
- **Milestone: Confirmation of Disease Biomarker**
- Product Development
  - Diagnostic test (clinical, pathologic)
  - Therapeutic drug
  - Molecular imaging tool
- Product Validation

**CANNOT REPRODUCE ORIGINAL RESULTS**

Investment of time and money







## On the Road to Molecular Medicine.....

OBRR Office of Biorepositories  
and Biospecimen Research

**“If you don’t have time\* to do it right, when will you have time\* to do it over?”**

- [UCLA Basketball Coach, John Wooden](#)

\* money

\* resources

# "Priorities for Personalized Medicine"

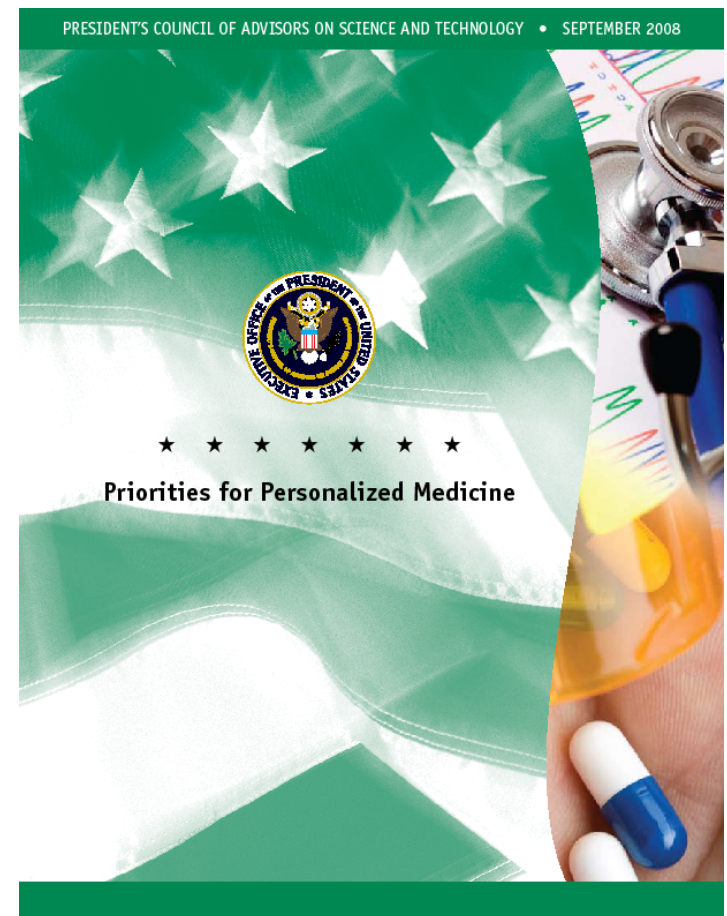
• "The Council believes that the convergence of scientific opportunity and public health need represented by personalized medicine warrants significant public and private sector action to realize the development of a promising class of new medical products."

• Genomics-based molecular diagnostics were determined to have the greatest potential for accelerating progress in personalized medicine; 3 areas of policy development needed:

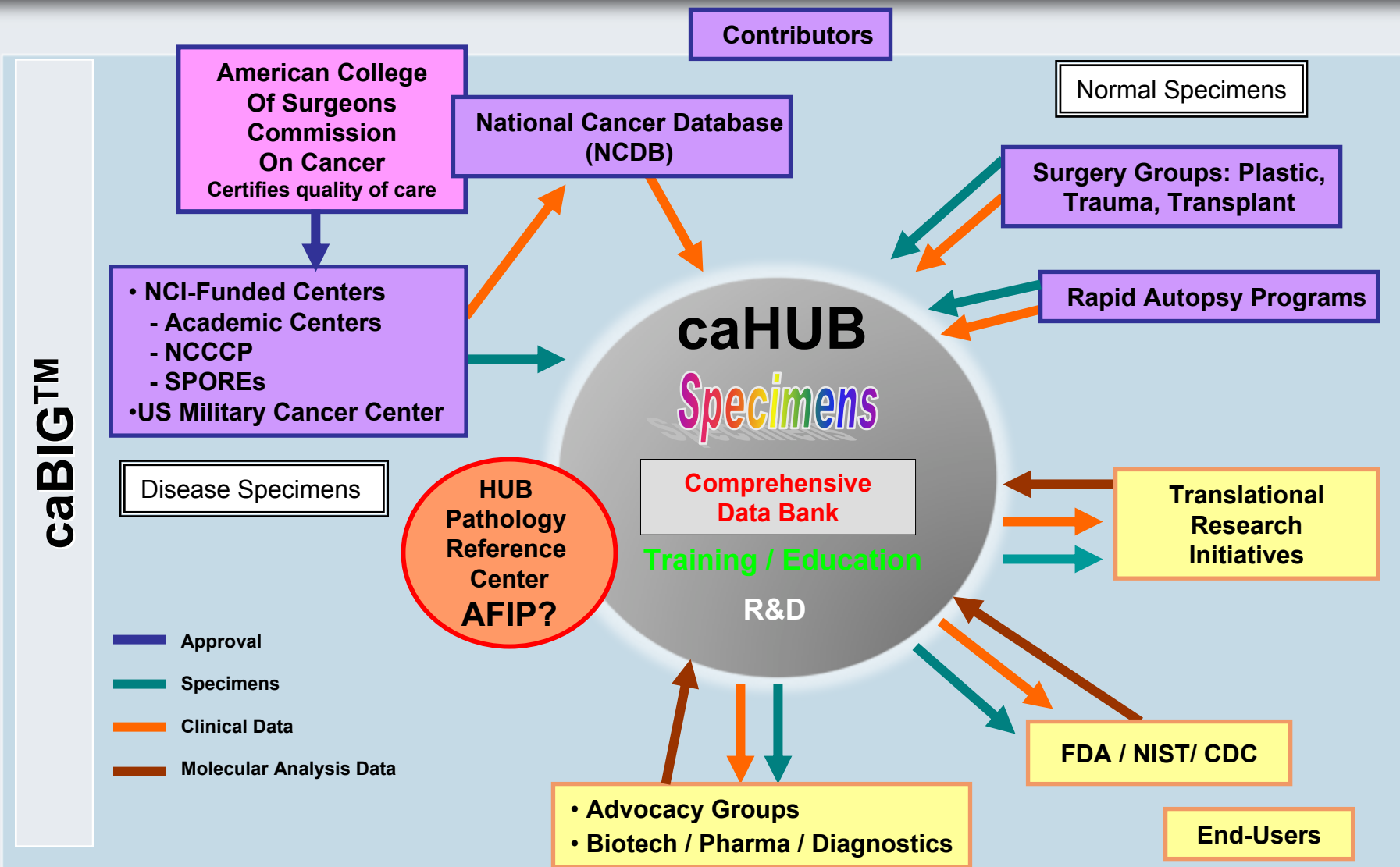
- Technology/tools
- Regulation
- Reimbursement

• **Key Translational Tools, Recommendation 2a:**  
**Create a national network of standardized biospecimen repositories**

- NCI efforts and OBBR guidelines (Best Practices) specifically cited



# caHUB (Cancer Human Bio**bank**)



caHUB: **UNIQUE** • **HIGH QUALITY SPECIMENS** • **HIGH QUALITY DATA** • FROM PTS WHO RECEIVED **HIGH QUALITY CARE**



**OBBR** Office of Biorepositories  
and Biospecimen Research

## **When Quality Matters Most: Driving Innovative Research and Development Through Emerging Paradigms in Biospecimen Research and Utilization**

**Carolyn C. Compton, M.D., Ph.D.**

**Director, Office of Biorepositories and Biospecimen Research  
Acting Director, Office of Technology and Industrial Relations  
National Cancer Institute**

**NATIONAL  
CANCER  
INSTITUTE**