The Cancer HUman Biobank (caHUB)

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The NCI Addresses the Challenge

Consensus of the Broad Scientific Community:
The lack of high-quality, clinically annotated human specimens has become the limiting factor for translational cancer research.

The NCI Moves Stepwise Towards Solutions:
• Standards
  • The *NCI’s Best Practices for Biospecimen Resources*
• Science
  • The Biospecimen Research Network
  • The Biospecimen Research Database
  • The Innovative Molecular Analysis Technologies
• Specimens and Service
  • The Cancer Human Biobank
Understanding the Problem:
The Siloed National Biobanking Landscape

• Collection, procession, storage procedures differ
• Degree and type of data annotation varies
• Scope and type of patient consent differs
• Access policies are lacking or unknown to potential users
• Materials transfer agreement conditions differ
• Supporting IT structures differ in capacity and functionality

→ WIDE VARIATION IN QUALITY OF SPECIMENS AND DATA
Key principles for a national biobank:

- **Standardized** procedures for biospecimen collection and distribution
- **Standardized** data sets and data vocabulary
- **Integrated** information technology system to support all functions
- **Harmonized** approached to ethical and legal issues
  - Standardized consent, MTAs
- **Transparent** governance and business models
  - Transparent access policies
- **Large** well-designed, standardized specimen sets
The Cancer Human Biobank vision:

- unique, centralized, non-profit public resource
- source of adequate and continuous supplies of human biospecimens and associated data of measurable, high quality acquired within an ethical framework
- source of high-quality biobanking services for the community
Issues for caHUB During the Past Year

- Verification of the need for caHUB
- Development planning
- Fundamental details
  - Who will provide the specimens
  - Who will use the specimens
  - How data will be collected and handled
  - How the specimens will be used (scientific purposes)
- Business plans and timelines
- Funding: $60M ARRA funds allotted to caHUB in 2009
The Need for caHUB

- The need for caHUB has been clearly enunciated from all sources:
  - Survey of 5,000 NCI investigators
  - Market research using focus group sessions with academia, industry, regulator decision-makers
    - Office of Management and Budget-approved
    - Performed by NCI Office of Communication and Education with Strat@com
  - Interviews with commercial tissue providers and industry users (economics considerations study by Booz Allen Hamilton)
  - caHUB Users Workshop
  - Mining of request data from the NCI Tissue Locator: last 7 years
  - Direct input to OBRR from potential users: CTEP, NCI Patient Characterization Center (PCC), numerous biomarkers programs
Key Findings:
- Biospecimens come chiefly from local sources; little sharing occurs
- Both the quality and quantity of available biospecimens are unsatisfactory
- Research findings are questioned because of specimen quality
- Research scope is limited by biospecimen availability

Benefits of a National Biobank:
- Inspire confidence in quality of specimens
- Ensure ethical collection standards

Development Challenges:
- IP constraints
- Infrastructure

Barriers to Contribute:
- IP constraints

Strong support for a national biobank concept from all stakeholders
There is clear and universal need for a National, Standardized, Human Biospecimen Resource (NSHBR)

For all audiences, the level of consistency and standardization that could be offered is the most important benefit

An NSHBR has the opportunity to define standard operating procedures (SOPs) for the field/industry

In fact, stakeholders are counting on it
In high demand and short supply:

- **Benchmark samples**: biospecimens collected through standardized collection, handling, storage, processing and distribution procedures, with strict quality control and associated metrics
  - Comparable standard-of-care samples to test “generalizability” of new products
- **Cases with multiple aliquots**: Confirmation of prior studies or the opportunity to contribute information to prior studies based on new technologies
- **Statistically valid numbers of biospecimen sets**
- **Fully defined “patient case sets”**
  - Tumor
  - Adjacent normal tissue
  - Tumor periphery (invasive border)
  - Pre- and post operative blood samples
  - Urine
  - **Rich clinical data and outcome information for patient**
- **Non-surgical samples**: normal tissues; metastases; premalignant disease
caHUB: Centralized Model

- High quality specimens
- High quality data
- From patients receiving high quality care

- Tumor specimens and data from patients in COC-approved institutions
- Normal specimens and data from rapid autopsy and OPO programs

caHUB
High Quality Specimens
High Quality Data
From patients who receive high quality care

Centralized Resource: Cost and Quality Control Efficiencies
The caHUB Comprehensive Data Resource: The Heart of the HUB

- Provide user access to caHUB
- Ensure patient privacy and confidentiality
- Allow submission of data on patients and specimens
- Integrate patient, specimen and analysis data from multiple sources
- Perform QA/QC on all data
- Allow researchers to query specimen inventory based on data types
- Allow requesting of specimens
- Allow requesting, analysis, and download of datasets
The caHUB Business Model: A Commodities and Services Model

**COMMODITIES: Cost Recovery**

Distribution of specimens and data  
Increasing value of aliquots over time with increasing data richness: Time-dependent maturity

**SERVICES: Revenue Generation**  
Build on existing infrastructure and improve return on investment: Not time-dependent

- **Biobanking services to other initiatives**  
  - Other NCI/NIH  
  - Rare diseases  
  - Advocacy  
- **Education and training**  
  - Pathology and laboratory functions  
  - Operating room functions  
  - IT and data management  
  - Biostatistical and analytic methods

- **Consulting services**  
  - Biobanking methods and best practices  
- **Biobanking support service to industry**  
  - Assay development  
  - Clinical trials

- **Laboratory space and services**  
  - Research incubator functions  
  - Longer term in-house research contracts
caHUB Business Model

Commodities and Service-Based Model

caHUB Platinum Specimen Catalog

- Genotyping
- Protein Microarrays
- DNA Expression Profiling
- Sequencing
- Molecular Derivative Isolation
- Proteomics Analysis

Sample Orders
Data Orders
Customized Processing Services
Managed Collections “Front Door” Concept
Center of Excellence Training

GTEx
PCC
CTEP (clinical trials)
TCGA
Advocacy

Pathology Review
Quality Assurance
Laboratory Best Practices
SOP Training
Research Services

NIH NCI caHUB Economic Study
Continuous Process Improvement

- caHUB will establish policies and procedures that will ensure its continued responsiveness to the changing needs of the research and product development communities
  - Goals for performance metrics and success factors
  - Routine assessment of performance against metrics
  - Customer Satisfaction Program
  - Ongoing market analysis to be responsive to trends in translational research and advances in biomedical technology
  - Transparent mechanism for receiving and responding to public input
caHUB, A Transformative Initiative

More Efficient Research
- Reduction in re-experimentation due to higher quality samples
- Avoided cost of incremental labor from PIs and lab technicians, researchers
- Avoided cost of replacing failed samples because of higher sample quality
- Avoided time delays and labor costs for recontact and reconsent of patients for new studies

More Efficient Use of Resources
- User leverage of caHUB’s systems infrastructure, reducing the need to purchase and maintain requisite infrastructure
- User leverage of caHUB goods and services, decreasing labor costs to process samples in order to meet research requirements

Ensured Implementation of Best Practices
- Increased comparability (quality and uniformity) of specimen and data sets
- Ensured compliance reducing implementation and monitoring costs

Stronger Clinical Correlation
- Increased quality and uniformity of data for more accurate modeling
- Avoided re-collection of data, saving time and cost
caHUB, A Transformative Initiative

More Efficient Product Development and Regulatory Approval

- Higher quality analytes, advancing biomarker research
- Higher quality specimens, helping reduce clinical trials timeframes and costs
- FDA recognition of “platinum” status specimens, leading to more rapid approvals for new drugs and diagnostics

More Efficient Technology Development and Clinical Implementation

- Standardized samples allowing direct performance comparisons
- Benchmark biospecimens allowing calibration, performance monitoring and operator proficiency testing

Added Clinical Value: Improved Standards of Care

- Increased speed of transition from research standards to standards of care
- More rapid implementation and standardization of diagnostic assays in clinical laboratories
caHUB, A Transformative Initiative

- Increase in lives saved
- Improvements in quality of life
- Positive impact on personal economics
- Savings to healthcare systems
- Positive impact on national economics (GDP, tax revenues)
Team OBBR and FOBBRs

- Jim Vaught
- Helen Moore
- Nicole Lockhart
- Sherry Sawyer
- Kim Myers
- Mark Lim
- Joyce Rogers
- Jim Robb
- Joanne Demchok
- Richard Aragon
- Priyanga Tuovinen
- Benjamin Fombonne
- Ian Fore /caBIG
- Kenyon Erickson /caBIG
- Andrew Breychak /caBIG

SAIC Frederick Colleagues
- Mark Cosentino
- Mariana Gonzales del Riego
- Steve Buia

caHUB Planning Participants
- Elaine Gunter
- Deborah Collyar
- Neil Mucci
- Peter Fielding
- Ann Ashby
- Todd Carolin
- Dean Keser
- Don Jin
- More than 200 contributors
Silos: Biospecimen and Biospecimen Data Variation Thwarts Innovation in Medical Science

Scientific Progress?

Cannot reproduce original data
Biospecimen/Data Standardization Advances
Innovation in Medical Science

Scientific Progress
Developing Biomarkers with Biospecimens of Unknown Quality

- 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

**Pre-analytical artifact?**
**Incorrect identification?**
**Incorrect characterization?**
**Poor product design?**

**Investment of time and money**

- CANNOT REPRODUCE ORIGINAL RESULTS

**STOP**

- DO NOT ENTER
### Accrual and Inventory Maturation

<table>
<thead>
<tr>
<th>Fiscal Year</th>
<th>Number of Tumor Cases</th>
<th>Number of Normal Cases</th>
<th>Total Number of Cases per Fiscal Year</th>
<th>Total Case Accrual</th>
<th>Total Aliquots per year</th>
<th>Total Aliquot Accrual</th>
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<tr>
<td>2011</td>
<td>1,000</td>
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<td>918,300</td>
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<tr>
<td><strong>Total</strong></td>
<td><strong>26,000</strong></td>
<td><strong>11,500</strong></td>
<td><strong>37,500</strong></td>
<td><strong>37,500</strong></td>
<td><strong>918,300</strong></td>
<td><strong>918,300</strong></td>
</tr>
</tbody>
</table>

30% Optimal Case Collection = 3 Optimal Tumor Modules (6 FF/6 SC/12 SF/6 UF/3 CC) + 3 Optimal Normal Modules (6 FF/12 SF/6 UF)

40% Average Case Collection = 1 Optimal Tumor Module (2 FF/2 SC/8 SF/2 UF/1 CC) + 2 Optimal Normal Modules (4 FF/8 SF/4 UF)

30% “Worst” Case Collection = 1 Minimal Tumor Module (1 FF/1 SC/1 SF) + 2 Minimal Normal Modules (2 FF/2 SF/2 UF)
Life After Regulatory Approval: Biospecimens Throughout a Product’s Lifespan

Diagnostic Tests / Laboratory Assays

Standardized Benchmark Biospecimens

Define standards
- Test execution
- Tolerance for variation
- Test performance

Daily execution
- Quality Assessment
- Quality Control
- Calibration

- Decreased false negatives and false positives
- Improved Standard of Care
“There is an opportunity for the NIH to be the ‘Statue of Liberty’ in creating a vision for how to collect, annotate, store and distribute samples in a standardized way.”

- Steve Gutman, FDA
3 Fundamental Factors That Drive Pricing

- **Fit for Purpose – Relationship to Pricing**
  - The research application and scientific question being addressed
  - Specifics of the collection protocol
  - Specific project needs (e.g. normal, diseased, tissue origin, specimen type, etc.)

- **Sample Quality and Specificity – Relationship to Pricing**
  - Quality and specificity price drivers:
    - Specimen rarity and size requirements
    - Extent of customized processing requested
    - Clinical parameters (e.g. treatments, etc.), and pathology parameters (e.g. tumor subtype, positive tissue markers) requested

- **Data Richness – Relationship to Pricing**
  - Outcomes data are in high demand
  - Comprehensive data sets may double sample price
  - Customized data increases the sample price
Importance of a National Biospecimen Resource
Cited on Many Levels

- Genomics and Personalized Medicine Act of 2007
- Dept. of Health and Human Services, Personalized Health Care Report, Sept. 2007
- President’s Council of Advisors on Science and Technology: Priorities for Personalized Medicine, Sept. 2008
- President’s Cancer Panel Report, Maximizing Our Nation’s Investment in Cancer, Sept. 2008
- Kennedy-Hutchison Cancer Bill (ALERT Bill: “War on Cancer, Part II”), 2009
- The NCI Bypass Budget for FY2010
Folks at the National Cancer Institute (NCI) are heading up an effort to establish the U.S.’s first national biobank — a safe house for tissue samples, tumor cells, DNA and, yes, even blood — that would be used for research into new treatments for diseases. By fall, the group hopes to have mapped out a plan for a national biobank; the recent stimulus showered on the government by the Obama Administration might even accelerate that timetable.

Time Magazine March 23, 2009
Time Magazine November 25, 2009