The Importance of High-Quality Biospecimens to the Research Enterprise: The Road to Molecular Medicine

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Cancer: Our #1 Health Problem

- 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
- $190 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

Beating cancer
The new frontier of molecular medicine

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 had been fought but 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 a few drugs are now available, and that a few forms of the disease, particularly in children, have been treated more aggressively. But the original success has been due to the hope that a drug might save a person with cancer at some point in his life; has actually been seen more often.

The past three decades of effort have seen more disappointments than advances. The most deadly forms of cancer have been studied at length. The battle against cancer is at a turning point. Some of recent advances, it is becoming possible to imagine a time in the not-too-distant future when new medical treatments will be able to cure the disease, transforming it from a potent killer into something akin to a chronic illness. The war against cancer no longer carries a certain death in the heart of the diagnosed with it may not be far away from us all.

Researchers have uncovered much of the basic molecular biology of cancer, and by the optimism of knowledge that the Human Genome Project has provided over the past ten years, they have come to understand much more clearly than before the term "cancer" properly refers not to a single disease, but rather to a whole set of diseases that have in common only the fact that they are caused by cells that do not know when to stop dividing. Not understanding has now reached the point where it can be turned into therapy. The next few years should see a wave of treatments that will add up to a big change in the way that cancer is viewed and dealt with by society.
Evolution of Molecular Oncology

Advances in Molecular Technologies and Research

The Past Century

- Established symptomatic disease
- Morphologic diagnosis and phenotypic tumor classification
- Generic therapeutic regimens
- Treatments have unpredictable adverse effects on patients

21st Century

- Early detection and prevention
- Molecular characterization of tumor pathways and processes
- Targeted therapies
- Drug therapy based on host genetics that define response

Understanding Specific Biology of Host and Disease
Translational Research Promises to Realize the Vision of Personalized Medicine

Molecular Data → Biospecimen Analysis → Biospecimen Processing and Banking → Biospecimen Collection → Diagnosis / Therapy

PERSONALIZED CANCER CARE

Office of Biorepositories and Biospecimen Research
The Road to Personalized Medicine

In the world of personalized medicine, the biospecimen is the center of the universe

- **Molecular characterization of the host**
  - Disease susceptibility
  - Treatment efficacy (e.g., pharmacogenomics)

- **Molecular characterization of the disease**
  - Molecular classification of tumor
  - Characterization of tumor heterogeneity/therapeutic targets
Molecular Research Using Human Analytes

The Cancer Genome Atlas

National Community Cancer Centers Program

Clinical Proteomic Technologies Assessment for Cancer

Innovative Molecular Analysis Technologies

Alliance for Nanotechnology in Cancer

Cancer Genetic Markers of Susceptibility

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

- 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*

- 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

- We now have the technological capacity to produce low-quality data from low-quality analytes with unprecedented efficiency.
- We can now get the wrong answers with unprecedented speed.
- Unraveling the massive matrix of misleading data may compromise progress in unprecedented ways.
- “The faster you go, the behinder you get.”
The First Rule of Science

GARBAGE IN  →  GARBAGE OUT
• Optimize and standardize the quality of human specimens for the research that will drive the development of personalized cancer medicine

• Remove the barriers to cancer research represented by the 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

- Develop state-of-the-science guidance for biobanking
  - NCI Best Practices for Biospecimen Resources
- Harmonize of biobanking practices across the NCI/NIH enterprise
- Partner with accreditation and professional bodies to insure implementation and integration into the medical enterprise
- Facilitate the creation of a scientific evidence base for biospecimen procurement, processing, and stabilization that will enable the translational research leading to personalized cancer medicine
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.
What is Biospecimen Science?

Understanding the Impact of Pre-analytical Variables on the Biological State/Molecular Composition Biospecimens

**Time 0**

Specimen is **viable** and biologically reactive

Molecular composition subject to further alteration/degradation

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**Pre-acquisition**

**Post-acquisition**

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

What is Biospecimen Science?
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

**Feature of Interest**
- DNA
- RNA
- PROTEIN
- MORPHOLOGY

**VARIABLES**
- Analysis Method
- Other Technologies

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

**Technologies**
- PCR
- FISH
- MICRO-ARRAY
- RT-PCR
- NORTHERN
- CGH
- IMMUNOSTAINING
- RT-PCR
- MASS SPEC
- TRANSMISSION EM
- LIGHT MICROSCOPY (H&E)
- WESTERN
The Biospecimen as Object of Investigation

- Patient
  - Cancer
  - Disease Biology?
  - Real Biospecimen
    - Unique Biology!
    - Object of Investigation
    - Cured Patient

- Mini-Me Biospecimen
  - Translational Research
  - Personalized Medicine

- Researcher
  - M.D.
Changing the World....

- We are here to discuss, launch, and legitimize a new domain of scientific investigation
  - Why it is critical
  - Why it is crucial to start now: what is at stake
  - Who’s affected: the stakeholder’s speak
  - How to begin and how to move forward
  - How to integrate this science into the fabric of medical practice
Time for Change

• “If you do what you've always done, you'll get what you've always gotten.”
  - Anthony Robbins

• What we’ve got is no longer good enough to meet the needs of science, medicine, and technology - to serve patients

• Must enable the change that will change the world
  • Remove the single most significant obstacle to progress in translational research (and ultimately personalized medicine)
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