Role of the Cancer Registry and Tumor Bio-Repository in Improving Patient Outcomes

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Cancer: GAPS in KNOWLEDGE

- Better Screening
- Molecular classification of tumors
- Better understanding of prognosis
- Mechanisms (treatable) of metastasis
- Mechanisms of therapy resistance
- Biomarkers of radiotherapy response
- Markers of toxicity
We need better lab tests!
Product Cycle of Biomarker

- Discovery
- Technical Validation
- Clinical Validation
- Clinical Implementation
- Assay Improvement

Research Labs
Hospital Labs
Product Cycle of Biomarker

Discovery

Technical Validation

Clinical Validation

Clinical Implementation

Assay Improvement

Research Labs

Hospital Labs

Biomarker “black hole”
Product Cycle of Biomarker

- Discovery
- Technical Validation
- Clinical Validation
- Clinical Implementation
- Assay Improvement
- Hospital Labs
- Research Labs

TOTAL CANCER CARE CASES
CANCER BIOMARKERS

Prognosis

Who needs extra treatment?

Prediction

What Treatment?

Toxicity

Who should avoid Treatment?
Level of Evidence

- **Level 1**
  - prospective, high power, specifically addressing utility of marker in question
  - meta analysis of several small studies
- **Level 2**
  - Clinical Trial companion study in which marker is also evaluated
- **Level 3**
  - performed on assembly of cases taken for other reasons
Components of a Biobank

• Purpose of Bank
• Patients / Controls
• Ethics
• Type of Specimens
• Preprocessing
• Storage
• Retrieval
• Data Annotation
• Distribution
• Quality Control
Governance and Management

- Director medical and scientific
- Executive Committee
- Tissue Distribution Committee
- Staff
Purpose of Bank

• ? Specific Hypothesis
• Types of samples – Blood, tissue, hair, nails, urine
• Special processing (plasma, serum, living cells)
• Specimen Tracking and labeling
• How to store
  – Liquid nitrogen
  – Mechanical freezer
  – other
Patients / Subjects

• How to identify – do you need controls?
• How to obtain informed consent
• Privacy concerns
• Are patients infectious?
• Access to Medical Records
• Data storage
• Withdrawal of consent
Preoperative and Operative Variables

Patient factors
Blood pressure
Sepsis
Nutritional status
Toxic exposures
Hormone effects
Tumor effects
Medication
Anesthesia
Type of operation
Treatments
Radiation

Uterus: Room temperature stability timecourse

Relative mean intensity (percent of time zero)

Time post excision (minutes)

Lance Liotta
Ethics

- Informed consent
- Coercion
- Harm to patient
- Loss of Privacy
- Withdrawal of consent
- What assays will be done (Genetics)
- Involvement of Industry, 3rd parties
- Cost recovery (specimens cannot be sold)
- Re-contact in the future
- What happens to specimens if bank closes
Specimens

- Standard operating procedures
- Type of specimen? Extra / Diagnostic (FFPE)
- Who will collect/? Risk of collection
- Preanalytical Variation
- Verification of specimen
- Preprocessing and fractionation
- Avoid freeze Thaw
- Label and tracking
- Type of freezing
Storage

- Types of freezers
- Stability of Specimen over time
- Secure Access
- 24 hr monitoring on-call
- Maintenance and supplies
- Back-up
- Power
- Capital replacement plan
- Contract it out?
Specimen Distribution

- Who decides
- Specimens reserved
- For profit company use
- MTA / IP / ethics
- Cost recovery
- Specimen derivatives (DNA, RNA, Proteins etc)
- Update inventory
- Restocking
- Assay Results
Annotated Information

- What clinical data to collect
- Who will collect and curate data
- Access to medical records
- Accuracy / Audits
- Storage of data / data bases
- Access to data
- Data analysis
- ? Clinical update
- ? Entry of assay results
Multiple variables can affect the molecular integrity of the biospecimen

Variables (examples):
- Antibiotics
- Other drugs
- Type of anesthesia
- Duration of anesthesia
- Arterial clamp time

Variables (examples):
- Time at room temperature
- Temperature of room
- Type of fixative
- Time in fixative
- Rate of freezing
- Size of aliquots

Pre-acquisition

Post-acquisition
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Variations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Venipuncture (Needle gauge, details of blood collection set)</td>
<td>Needle gauge and priming volumes differed</td>
</tr>
<tr>
<td>Phlebotomy (tourniquet technique, patient position, tube order, blood source, volume collected)</td>
<td>Patient position varied from seated to lying down, variable tube orders, variable venipuncture sites</td>
</tr>
<tr>
<td>Collection device</td>
<td>Different types of tubes</td>
</tr>
<tr>
<td>Blood derivative and processing (anticoagulant type, processing time and protocols)</td>
<td>Different anticoagulants, different temperatures, different centrifugation temperatures and speeds</td>
</tr>
<tr>
<td>Amount of elapsed time between collection and storage</td>
<td>Variations between institutions</td>
</tr>
<tr>
<td>Storage (temperature, elapsed time for storage, storage duration, storage material, shipping temperature)</td>
<td>Different elapsed times before storage, different storage temperatures</td>
</tr>
</tbody>
</table>
Potential Effects of Biospecimen Variables

- **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
Total Cancer Care: A Personalized Approach to a Patient’s Health Journey

**Survivorship**
- Behavioral Research
- Psychosocial & Palliative Care
- Family Needs
- Health Outcomes

**Relapsed Disease**
- Recurrence Therapy
- Drug Discovery
- Adaptive Trial Design

**Treatment**
- Primary Therapy
  - Multimodality
  - Target Based
- Post Therapy
  - Surveillance
  - Clinical Trials Matching

**Prognosis**
- Molecular Oncology
- Biomarker Analysis

**Populations at Risk**
- Risk Factors
- Genetics
- Early Detection
- Health Disparities

**Intervention**
- Prevention
- Lifestyle/Nutrition
- Education

**Diagnosis**
- Genomics/Proteomics
- Imaging Modalities
- Nanotechnology

**Behavioral Research**

**Psychosocial & Palliative Care**

**Family Needs**

**Health Outcomes**

**Recurrence Therapy**

**Drug Discovery**

**Adaptive Trial Design**

**Prevention**

**Lifestyle/Nutrition**

**Education**

The Necessary Components

- Clinically annotated bio-repository for tumor and normal specimens
- Partnership among researchers, clinicians, regulators, policy makers, and patients to design an integrated information network system
Implementing Personalized Medicine in a Cancer Center

David A. Frenstermacher, PhD,* Robert M. Wensham, MD, MS, FASCO, FACP,* Dana E. Hallion, PhD,* and William S. Dalton, PhD, MD*

Abstract: In 2006, the Moffitt Cancer Center started a cooperative agreement with the University of Florida Cancer Center for the Moffitt-University of Florida Cancer Supportive Care Center. This effort has led to the creation of a new integrated cancer care delivery system that focuses on delivering personalized medicine. The goal of this system is to provide patients with the best possible care, while minimizing the side effects of treatment. The system includes a comprehensive program of supportive care services, including psychological, social, and spiritual support, as well as access to the latest research and clinical trials. The success of this program is due to the collaboration between the two institutions and the commitment of the staff to providing the best possible care to patients.

Keywords: supportive care, integrative medicine, patient outcomes

Cancer is the second leading cause of death in the United States, affecting 1 in 2 men and 1 in 3 women in their lifetimes, with an estimated 1.6 million new cases and more than 570,000 deaths annually based on the 2011 statistics. The total cost of cancer care in the United States has increased to $229 billion from treatment, morbidity, and mortality. The increasing cost of cancer care in the United States has increased by 7% each year since 2000, and the overall cost of cancer care in the United States has increased by 15% since 2000, with an estimated $229 billion in 2011. The rising cost of cancer care in the United States is due to the increasing number of patients, the increasing cost of treatments, and the increasing cost of supportive care. The cost of cancer care in the United States is expected to increase by 10% each year until 2020, with an estimated $339 billion in 2020. The rising cost of cancer care in the United States is due to the increasing number of patients, the increasing cost of treatments, and the increasing cost of supportive care. The rising cost of cancer care in the United States is due to the increasing number of patients, the increasing cost of treatments, and the increasing cost of supportive care.
The Approach for Cancer

The Total Cancer Care Protocol

- Can we follow you throughout your lifetime?
- Can we study your tumor using molecular technology?
- Can we recontact you?
Partners in the Fight Against Cancer
Total Cancer Care™ Consortium

Expansion of consortium sites will encourage information exchange
M2Gen Offices, Bio-repository 100,000 sq ft in Tampa, FL
- **Four unit capacity** of 2.4 Million samples
- **Stores** samples in a -80°C environment
- **Handles** samples in a -20°C environment
- **Retrieves** samples using NEXUS proprietary ‘Cool Transition’ technology
- **Flexibility** to accommodate a wide variety of samples, vessels and labware
- **Automated** 24/7 monitoring system in place
- **Automated Inventory** functionality provides real-time inventory tracking of stored biospecimens
Total Cancer Care Protocol To-Date

As of 3/06/2012

18 Consortium Sites (including MCC)
85,775 Consented Patients
   MCC (60%)
   Sites (40%)
32,257 Tumors Collected
   MCC (35%)
   Sites (65%)
16,226 Gene Expression Profiles
   (TCC Consented since inception)

Data Generated from Specimens

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>CEL Files (Gene Expression Data)</td>
<td>16,226 files</td>
</tr>
<tr>
<td>Targeted Exome Sequencing</td>
<td>4,016 samples</td>
</tr>
<tr>
<td>Whole Exome Sequencing (Ovary, Lung, Kidney)</td>
<td>535 samples</td>
</tr>
<tr>
<td>Whole Genome Sequencing (Melanoma)</td>
<td>13 samples with normal pairs</td>
</tr>
<tr>
<td>SNP/CNV (Lung, Breast Colon)</td>
<td>559 samples</td>
</tr>
</tbody>
</table>
"We need to be true to patients by insisting on collecting data and conducting clinical trials, as Moffitt is doing."

Roy Beveridge, MD
Chief Medical Officer, US Oncology Network (McKesson)
Houston, Texas
Major Milestones – Patents Issued

- **Patent #1** Issued January 10, 2012: Computer Systems & Methods for Selecting Subjects for Clinical Trials
- **Patent #2** Issued March 6, 2012: The Consortium as a Value Network for Receiving Patient Data, Tracking & Distribution
- **Patent #3** Issued March 13, 2012: A System for Selecting Treatment based on Clinical Data, Molecular Profiles & Evidence-Based Data

The TCC Patent Portfolio consists of 3 issued patents and 3 pending patent applications.
An integrated information platform that creates real-time relationships and associations from disparate data sources needed to create new knowledge for improved patient treatments, outcomes and prevention.
Four Portals to Total Cancer Care™

- **Researcher View**
  - Cohort Identification
  - Molecular Profiling
  - Biomarker Discovery
  - Comparative Effectiveness

- **Patient View**
  - Personal Health Record
  - Longitudinal Follow-up
  - Personalized Search

- **Administrators View**
  - Operational Dashboards
  - Quality & Safety Reporting
  - Meaningful Use

- **Clinician View**
  - Decision Support
  - Clinical Pathways
  - Clinical Trial Matching
  - Access for Affiliate Network

Next Generation Health and Research Informatics Platform
Power of the TCC Database

- Integration of molecular, clinical, biospecimen and patient self-report data
  - Gene expression data, Exome sequencing data, SNP/CNV data for new diagnostics, prognostic response and new drug discovery

- Ability to match patients to clinical trials
  - Right treatment for the right patient using molecular markers for patient selection

- Development of “Secondary Use” of Data, including Comparative Effectiveness Research and Pharmacovigilance
  - What works best for whom based on evidence by following patients throughout their lifetime
  - Clinical Decision Tool for Diagnostics & Therapy
The Vision: New Approaches to Early Phase Clinical Trials
Clinical Trials of the Future

Clinical Trial Challenges
- Trial activation too slow
- Trial accrual too slow
- Patients do not want to leave home
- 80% of cancer care delivered locally
- Trials are searching for patients

Moffitt/M2Gen Solution
- Develop a consortium network for trials
- Obtain molecular data from patient tumors
- Maintain clinical data on patients
- Use database to match drugs with patients
- Faster and smaller trials

Faster trials  Fewer Patients  Biomarker Driven
Granular Searchability

Newly Diagnosed Metastatic/Locally-Advanced Patients

One Tumor Type: 344
- 275
- 220
- 209
- 167
- 134
- 107
- 42
- 30

Selected Assumptions Reducing Sample Size
- Starting sample size
- Availability of biopsy (-20%)
- Adequacy of biopsy (-20%)
- Assay failure (-5%)
- Death/Morbid/Toxicity (-20%)
- Temporal readiness (-20%)
- Performance status (-20%)
- Prevalence of Mutation (-60%)
- Pt/MD Choice of Rx (-30%)

Diminishing # of Eligible Patients

Trial-Ready
Part of the Solution

“The Moffitt Cancer Center in Tampa, Florida, for example, runs a Total Cancer Care programme that unites 18 hospitals, compiling medical history, tissue samples and genetic information about each patient’s tumour. Samples are all stored for future analysis, and patients can consent to doctors contacting them about trials.”

“.....Moffitt is paving the way towards a new era of customizing treatment based upon individual characteristics.”

Edward Abrahams, Personalized Medicine Coalition President

“We think Moffitt demonstrates how all health care facilities will operate in the future.”

Wayne A. Rosenkrans, Jr., Distinguished Fellow, MIT Center for Biomedical Innovation and Chairman of the Personalized Medicine Coalition Board of Directors

PMC Personalized Medicine Coalition

- Dr. William Dalton received the 2010 Leadership in Personalized Medicine Award
- “Under Dr. Dalton’s leadership, Moffitt is paving the way towards a new era of customizing treatments based upon individual characteristics.”
Rapid Learning Information System for Cancer Care & Research

- Improved: Treatments, Affordability, Accessibility

- Outcomes Data

- Enabler: Data Warehouse, Data Integration and RIE

- Cancer Patient to Cancer Diagnosis & Treatment to Treatment Data Images, Molecular Profiles

- Biomarker Discovery, Clinical Trials, Target Discovery, CER/Outcomes

- Basic Science, Clinical/Translational Science, Population Science

- TOTALCANCERCARE™
Designing a New Research & Healthcare Network Model

- Offices & Clinics
- Hospitals & Healthcare Networks
- Insurers
- Research Information Exchanges
- Researchers Centers & Networks
- Personal Health Records
- Genomic Data & Annotation Services
- Patients

OCR FOCUS
Outcomes of New Cancer Therapies: Enhancing the Process and Creating Meaningful Value
Robust Cancer Patient Database

- Database is a robust, scalable dataset of oncology patients across multiple indications
- Database links TCC patient, clinical and molecular data and enables granular, customized and efficient searches
  - Incorporates secondary data derived from the database – clinical trial results, third-party research, etc.
- Standardized data format across the platform facilitates integration of data from outside sources
- “Hub and spoke” model provides standardized data quality and easy access to information
Special Collections

- Metastases
- Tumors “on” treatment
- Sequential samples
- Circulating tumor cells
- Stem cell isolates
- Primary cultures
- xenografts
Summary

- Biospecimens hold the clue to future treatment improvement
- Every laboratory is a potential biobank