TOTAL CANCER CARE:
CREATING PARTNERSHIPS TO ADDRESS PATIENT NEEDS

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Moffitt Cancer Center

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MOFFITT CANCER CENTER

- Third largest cancer center by patient volume in the United States-located in Tampa, Florida
- NCI-designated Comprehensive Cancer Centers
- Consistently ranked among the nation’s best hospitals by U.S. News & World Report
- 4,500 Staff - 299 Faculty
- 17,000 New Patients per Year
- 206 beds
- More than $70 million in active grant support
- $1 billion+ Economic Impact in local community

...To contribute to the prevention and cure of cancer....
How do we develop an integrated network information system that is obviously necessary to deal with the overwhelming amount of information being generated in basic, translational and clinical, research needed to support personalized medicine (aka, molecular medicine, precision medicine)?
SOLUTION ELEMENTS FOR PERSONALIZED MEDICINE AS A SOLUTION FOR IMPROVED HEALTHCARE
DALTON ET AL, CLIN CANCER RES; 16 (24) DECEMBER 15, 2010, PG 5987

• Addresses healthcare as a **public issue** and seeks to improve **access, affordability and quality of care** by developing an information system to assist in making clinical decisions based on outcomes and comparative effectiveness.

• Integrates **new technologies** into the standard of care in an **evidence-based** fashion to identify populations at risk, personalize treatment and improve individual outcomes.

• Provides an approach to identify the **best treatment for individual patients** based on clinical and biological characteristics of a patient and their disease.

• Creates a **network of health care providers, patients, and researchers** who contribute and share information from individual patients to ultimately improve care of all patients by learning from the experience of others.
DESIGNING A RESEARCH & HEALTHCARE INFORMATION EXCHANGE

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
Vision of Total Cancer Care

- Identify the needs of the patient & their families
- Develop an evidence-based approach to meet those needs
- Develop markers to predict need so they can be prevented
The Total Cancer Care™ Protocol

- May we follow you throughout your lifetime?
- May we study your tumor using molecular technology?
- May we re-contact you?
Moffitt, headquartered in Tampa, Florida, is a not-for-profit institution founded in 1986

- Awarded Comprehensive Cancer Center status by the NCI
- Moffitt has partnered with 17 additional consortium sites nationwide to enroll patients in Total Cancer Care

Moffitt + Consortium Sites

Key Aspects of TCC Patient Consent

- Can we follow you throughout your lifetime?
- Can we study your tumor with molecular technology?
- Can we recontact you?

- ~200 patients each week are consented to TCC for life
- More than 90,000 patients consented, 33,000 tumors collected, 16,000 tumors profiled and 4,000 tumors sequenced

M2Gen

- Started in 2006 to develop commercial opportunities related to Total Cancer Care
- Manages consortium network operations related to TCC, including consent and tissue collection
- Receives clinical data on patients
- Obtains molecular data from patient tumors
- Matches treatments to patients using molecular and clinical data
THE MOFFITT TOTAL CANCER CARE EXPERIENCE: PERSONALIZED MEDICINE IN CANCER

The Cancer Journal, November/December 2011

Implementing personalized medicine in a cancer center.
Fenstermacher DA, Wenham RM, Rollison DE, Dalton WS.
Department of Biomedical Informatics, H. Lee Moffitt Cancer Center & Research Institute, Tampa, FL, USA. dfenster@moffitt.org

Abstract
In 2006, the Moffitt Cancer Center partnered with patients, community clinicians, industry, academia, and 17 hospitals in the United States to begin a personalized cancer care initiative called Total Cancer Care. Total Cancer Care was designed to collect tumor specimens and clinical data throughout a patient’s lifetime, with the goal of finding “the right treatment, for the right patient, at the right time.” Because Total Cancer Care is a partnership with the patient and involves collection of clinical data and tumor specimens for research purposes, a formal protocol and patient consent process was developed, and an information technology platform was constructed to provide a robust “warehouse” for clinical and molecular profiling data. To date, more than 76,000 cancer patients from Moffitt and consortium medical centers have been enrolled in the protocol. The Total Cancer Care initiative has developed many of the capabilities and resources that are building the foundation of personalized medicine.
TOTAL CANCER CARE TO DATE

18 Consortium Sites (including MCC)

94,522 Consented Patients
MCC (62%)
Sites (38%)

33,980 Tumors Collected
MCC (38%)
Sites (62%)

16,226 Gene Expression Profiles (TCC Consented since inception)

Data Generated from Specimens

<table>
<thead>
<tr>
<th>Method</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, Colon)</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>
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</tbody>
</table>
BENEFITS OF THE TCC OPT-IN APPROACH

- Patients become active partners in a life-long study of their disease
- Enables the ongoing ability to match patients to clinical trials and re-contact patients when there is a therapy that may be of benefit to them
- Allows for ongoing collection of clinical, outcomes and self-reported data from patients and their health providers
- Creates ability for a Phase IV trial and accelerated drug approval
THE HEALTH & RESEARCH INFORMATICS PLATFORM
TOTAL CANCER CARE DATABASE: THE NEXT GENERATION HEALTH & RESEARCH INFORMATICS PLATFORM (HRI)

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

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

- **Administrators View**
  - Operational Dashboards (i.e. new pt report)
  - Quality & Safety Reporting
  - Health outcomes & cost of care analysis

- **Clinician View**
  - Point-of-care decision support (personalized medicine)
  - Clinical Pathways
  - Clinical Trial Matching
  - Access for Affiliate Network
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.
GOALS FOR THE HRI PLATFORM

 Establish a flexible data integration, management and analysis platform to address patient-specific outcomes research.

 Provide the ability to query the large volume of data currently collected as part of the Total Cancer Care study.

 Create an information architecture that supports research through a central data “hub”.

 Advance Moffitt’s ability to repurpose this data for research needs by linking key domains of data including
  • Clinical
  • Molecular
  • Biospecimen
  • Epidemiological and health outcomes data

 At point of care, provide clinicians and patients with all available treatment options based on phenotypic and genotypic characteristics and their comparative effectiveness for personalized decision-making.
Some representative examples of business level data domains:

- Demographics
- Cancer Stage
- Diagnosis
- Treatment
- Drugs
- Labs

Integrated Data Warehouse

Patient Cohort Examples:

- Newly Diagnosed, Primary Pancreatic, having CEL File.
- Primary Breast Cancer, Survival Time >30 months, Disease Stage 1-4, Diagnosed with Type 2 Diabetes, currently on Metaformin.
- Female with myelodysplastic syndrome, currently taking vidaza as 1st course chemotherapy, initially diagnosed in 2007-2008.
1. Extract source data
2. Load data to Staging/Landing Zone
3. Data Profiling & Cleansing, and then load data into HDM Interface Tables
4. Load data from HDM interfaces to HDM, further cleansing and other data services
5. Other Data Services
### Data Dictionary Navigation

<table>
<thead>
<tr>
<th>Data Element Name</th>
<th>Definition</th>
<th>Alias</th>
<th>Data Element Derivation</th>
<th>Comments</th>
<th>Internal Data Source</th>
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</thead>
<tbody>
<tr>
<td>Age Began Smoking in Years</td>
<td>Age began regularly smoking cigarettes expressed in number of years since birth.</td>
<td>No</td>
<td></td>
<td>How old were you when you started smoking cigarettes regularly?</td>
<td>Galvanon</td>
</tr>
<tr>
<td></td>
<td>The date of completion of the questionnaire needs to be taken into consideration for the most recent version and response to the survey question.</td>
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<td></td>
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<tr>
<td>Cigarette Average Daily Use Count</td>
<td>Average number of cigarettes smoked per day.</td>
<td>No</td>
<td></td>
<td>How many cigarettes do/did you smoke per day?</td>
<td>Galvanon</td>
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<td>Cigarettes per day - EPQ V3</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>How many cigarettes on average do/did you smoke per day?</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cigarettes per day</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>The date of completion of the questionnaire</td>
<td></td>
</tr>
</tbody>
</table>
The HRI Platform allows for data queries across multiple source systems, enabling real-time identification of patient cohorts for clinical trials.

- Demographics/other non-clinical info:
  - Gender
  - Race
  - Ethnicity
  - Age at dx
  - Vital Status
- Primary Site of Diagnosis, Histology, Stage at Diagnosis
- Basic traits for each treatment type:
  - Chemo, radiation, surgery, hormonal therapy, immunotherapy, transplant, other
- Biobanking:
  - Tumor tissue available for research
  - CEL file available
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

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**Patient data available – drill down capabilities to 5 levels of detailed data elements.**

**Tissue specimen data available – drill down capabilities to 5 levels of detailed data elements.**
**Mutation Catalogue Viewer**

**BGI Sample**
- WES
- WGS
- TCG
- Pipeline

**KRAS**
- Name
- Function
- KRAS and Cancer
- Location in Sequence
- Mutation Type

**Mutation Analysis**
- Sample Count by Type
- Select Gene
- List All Genes

**User Management**
- List Users
- List Roles
- List Permissions

**Introduction**

The purpose of this web application is to analyze KRAS mutation frequency across all tissue types for Next Generation Sequence (NGS) data from BGI.

The data for this application is generated by a pipeline for NGS.

**NGS Pipeline**

Initial reading data (Short Read) is first align to one another, and then align to a reference genome by using BWA alignment.

GATK is used to further process the sam/bam file from BWA and the final result is SVN/Indel calling represent by VCF files.

Annovar is used to annotate SNVs, insertion, and deletions to generate information about mutated genes, proteins, etc.

Click [here](#) to see the pipeline.

**KRAS**

For the BGI TCG data, there are about 70 different types of KRAS mutations. This application list all these mutations, although some mutation almost happen in almost every samples.

For example, mutation R161R (Arginine) is a silent mutation, and it happen in 3999 samples out of the 4000 samples! We list this Kind of mutation here just for completeness.

**KRAS Mutation Analysis**

Out of the 68 KRAS mutations, you can select one or multiple mutations and the application will give you a report for the frequency across all the tissue types for the selected mutation or mutations. A bar chart is also used to show the frequency of the mutations.

Please note that the frequency report and chart include all tissue types, even that only have a very small count. The frequency for such tissues maybe not accurate.

**Technology**

This web-based application is running on Tomcat web server and using Java as the programming language. We use jQuery - a jQuery plugin - for generating the bar chart, and it’s a pure client side technology using Javascript.
Select Gene ➔ List of all mutations across all samples ➔ Select Mutation

Filter by: Mutation Type, Exon, dbSNP id ...
Mutation Catalogue Viewer – Frequency Overview

**Mutation Frequency (DDR2) at Sites:**

[M4411, T692N]

<table>
<thead>
<tr>
<th>Tissue</th>
<th>Protein</th>
<th>Sample with Mutation</th>
<th>Total Sample</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BONE MARROW</td>
<td>M4411</td>
<td>1</td>
<td>117</td>
<td>0.6547</td>
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<tr>
<td>BONE MARROW</td>
<td>T692N</td>
<td>2</td>
<td>117</td>
<td>1.7084</td>
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<td>BRAIN</td>
<td>M4411</td>
<td>12</td>
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<td>T692N</td>
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<td>155</td>
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<td>399</td>
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<td>399</td>
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<td>LARGE BOWEL</td>
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<td>LUNG</td>
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<td>LYMPH NODES</td>
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<td>195</td>
<td>10.78923</td>
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</tbody>
</table>

**Frequency of Selected mutations**  Filter List  Select Tissue

Filter by: Tissue, Sample Size, Frequency ...
**Benefits of Enterprise Data:**
- Sharing data across the organization, many groups can share valuable resources
- Centralized data management and resources adds value to enterprise data by improving data quality and documentation

**Benefits of Spoke Data Mart:**
- Flexibility for spokes to create custom perspectives
- Inclusion of external data with cleansed enterprise (hub) data
- Leverages enterprise resources for department specific spoke data requirements
- Spokes should report back data analysis to the hub with a standard data model to create a catalog of analysis and share best practices

**Critical infrastructure to emerging publication and archiving needs.**
More on “SPOKES”

“Spokes” will link existing subject-specific databases to information in the Hub and provide the end users with a seamless front-end for querying;

- Disease-specific spokes used for:
  - Clinic operations
  - Outcomes research (with regulatory approvals)
- Administrative spokes used for:
  - Strategic planning/Decision support
  - Quality indicator dashboards
  - M2GEN operations
Total Cancer Care Committee Structure

Total Cancer Care Steering Committee

Establishes policy for TCC resources & sets strategic goals.

TCC Faculty Advisory Committee

Provide advice & input to TCC Steering Committee on issues that impact faculty use of TCC resources.

Protocol Operations Subcommittee

Oversees operational & regulatory aspects of TCC Protocol at Moffitt & Consortium

Data & Tissue Management & Release Subcommittee

Oversees policies & processes for release of data & TCC acquired tissue for research

Data Acquisition Subcommittee

Oversees strategies for clinical and research data acquisition and integration

Information Technology Subcommittee

Oversees strategy & selection of technology solutions to support TCC

As of March 19, 2013
The TCC Database represents a truly unique and powerful resource that allows for the creation of associations and rapid learning.

Integration of patient’s clinical data, tissue and molecular data provides:

- Ability to discover new biomarkers and drug targets
- Enhanced ability to match patient to right treatment or clinical trial
- Superior data set for clinical decision-making
- Improved ability to track and understand patient treatments, outcomes and costs
The TCC Database represents an invaluable resource for research scientists, and has been utilized in several high-impact publications to-date.
The Patient Portal Page “My TCC”

Welcome, PATIENTPORTALONLY XTEST | About Moffitt | Sign Out of My Moffitt

Patient Portal > Home

Upcoming Appointments

Date | Location | What to Expect | Change/Cancel
--- | --- | --- | ---
Tue, Apr 24, 2012 9:00 AM EST | GI Clinic Khalidoun Aimhanna MD | Patient Instructions Questionnaire | Please contact your clinic to make schedule changes
Mon, Apr 30, 2012 1:00 AM EST* | Women’s - Gyn Sachin M Apte MD | Patient Instructions | Please contact your clinic to make schedule Changes

* Please note that procedural days and times may be subject to change. If your procedure time changes, you will be contacted by one of our staff members to provide you with updated instructions and information.

Support Services

New Patient Resources
New Patient Orientation
Patient and Family Orientation
Infusion Center Orientation
Radiation Oncology Orientation Video
Patient Education

Moffitt News
Breast cancer survivors improve health with RENEW

Helpful Links
American Cancer Society
Cancer.gov
**TOTAL CANCER CARE + PATHWAYS**

- Data Collection
  - Real time
  - Efficiency
  - Standardization

- Clinical Pathways

- Treatment Variation
  - Standardized Measures
  - Comparative Effectiveness Research

- Information "Push"
  - Clinical Decision Support
  - Patient Portal
  - Translation and Implementation
Designing a New Research & Healthcare Network Model

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

HRIE OPTIONS

Regional Hub 1

Regional Hub 2

HRIE

Trial Matching

Biomarker Discovery

Secondary Data Use
RAPID LEARNING INFORMATION SYSTEM FOR CANCER CARE & RESEARCH

Cancer Patient

Improved:
- Treatments
- Affordability
- Accessibility

Outcomes Data

Biomarker Discovery

Clinical Trials

Target Discovery

Basic Science

Clinical/Translational Science

Population Science

CER/Outcomes
THANK YOU!