Partnering with patients to accelerate discoveries in cancer research

Michael Dunphy, MS
mCODE Community of Practice
August 28, 2020
Patient-partnered research is changing the future of cancer

Watch Film
The Scientific Need in Cancer Research

- **Ultimate goal:** To understand what drives cancer so that we eventually can interpret every patient’s cancer genome, identify the optimal treatments, and anticipate and preempt resistance before it arises.

- There’s been a lot of progress, but we still have much work to do.

- What will it take to get there? Detailed molecular and genomic characterization of thousands of tumor and germline samples along with clinical, pathologic, and radiologic data.
Challenges to Studying Patient Tumor Samples

Only 5% of U.S. cancer patients are enrolled in clinical trials

85% of U.S. cancer patients are treated in community settings

Most tumor samples have not been readily available for study

Technology, social media, and cultural changes now provide a new opportunity to engage cancer patients and directly partner with them in this research
Objective: To generate a publicly available database of clinical, genomic, molecular, and patient reported data in cancer to accelerate discoveries and the development of new treatment strategies.
The Metastatic Breast Cancer Project

Help transform our understanding of metastatic breast cancer.

If you have metastatic breast cancer, join a nationwide movement of patients, doctors, and scientists by sharing your tumor and/or blood samples, your medical information, and your voice. Together, we can speed the development of future therapies.
MBCProject: Patients Enrolled, Consented, and Saliva Received

- Registered
- Consented
- Saliva Received

Associated Press Article and Video

ASCO 2016

Facebook post by a metastatic breast cancer patient/advocate

Facebook and Twitter posts by patients/advocates

SABCS 2015

Launch With Advocacy Partners

- 1670 medical records received
- 586 tumors from 425 patients
- 401 tumor/saliva pairs w WES
- 993 blood samples w ULP-WGS
- >1700 institutions represented
Patient-Partnered Research

“I want to live and watch my children grow up, but if I can’t, then I want to leave a legacy and a cure.”
—Houston, TX

“As someone who does not live near a research center and therefore cannot easily participate in trials, I finally feel like I can contribute.”
—Lake Tahoe, CA

“Amazing how happy that little box makes you feel! I felt like a 2 year old. Let me help! I feel a sense of pride and belonging because of this.”
—Minneapolis, MN

“Giving us HOPE for the future and if not for some of us, for our families.”
—Scottsdale, AZ
Enable cancer patients anywhere to share their information and samples with researchers everywhere.
Count Me In Team
Current Projects

- Metastatic Breast Cancer Project
- Angiosarcoma Project
- Metastatic Prostate Cancer Project
- Esophageal & Stomach Cancer Project
- Brain Cancer Project
- Osteosarcoma Project
<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Patients registered</td>
<td>5,817</td>
<td>526</td>
<td>978</td>
<td>264</td>
<td>167</td>
<td>128</td>
<td>7,880</td>
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<tr>
<td>Consent signed</td>
<td>3,245</td>
<td>423</td>
<td>718</td>
<td>191</td>
<td>105</td>
<td>100</td>
<td>4,782</td>
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<tr>
<td>Patient Reported data collected</td>
<td>3,245</td>
<td>416</td>
<td>718</td>
<td>191</td>
<td>105</td>
<td>87</td>
<td>4,762</td>
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<tr>
<td>Med records received (patients)</td>
<td>1,359</td>
<td>276</td>
<td>496</td>
<td>108</td>
<td>46</td>
<td>3</td>
<td>2,288</td>
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<tr>
<td>Saliva sample received</td>
<td>2,019</td>
<td>240</td>
<td>513</td>
<td>113</td>
<td>67</td>
<td>-</td>
<td>2,952</td>
</tr>
<tr>
<td>Blood sample received</td>
<td>1,110</td>
<td>96</td>
<td>403</td>
<td>68</td>
<td>1</td>
<td>-</td>
<td>1,678</td>
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<tr>
<td>Tissue received (samples/patients)</td>
<td>586/425</td>
<td>212/141</td>
<td>186/184</td>
<td>76/52</td>
<td>7/7</td>
<td>-</td>
<td>1,067/809</td>
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<tr>
<td>Whole exome (WES) from germline</td>
<td>399</td>
<td>242</td>
<td>77</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>718</td>
</tr>
<tr>
<td>WES from tumor sample</td>
<td>344</td>
<td>137</td>
<td>51</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>532</td>
</tr>
<tr>
<td>RNA-seq from tumor sample</td>
<td>279</td>
<td>27</td>
<td>8</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>314</td>
</tr>
<tr>
<td>ULP-WGS from cfDNA</td>
<td>993</td>
<td>96</td>
<td>301</td>
<td>68</td>
<td>-</td>
<td>-</td>
<td>1,458</td>
</tr>
<tr>
<td>WES from circulating tumor DNA</td>
<td>143</td>
<td>18</td>
<td>47</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>208</td>
</tr>
</tbody>
</table>
Data Sharing and Use by External Researchers

- WES, RNA-seq, germline, and clinical data from MBCp, ASCp, and MPCp are publicly available

- Significant increase in data inquiries and downloads over the past few months

- More than 30 peer-reviewed papers using the data have been published; multiple others are in preparation / under review
The Angiosarcoma Project: enabling genomic and clinical discoveries in a rare cancer through patient-partnered research

CMI Data Generation Process

Patient clicks “Count Me In” → Patient completes survey → Patient signs consent form → Patient signs medical release form → Patient provides saliva and/or blood sample → Patient’s steps: Study team’s steps:

Processes that can scale with demand

- Updates and insights are provided to patient
- Medical records are requested and received
- Saliva and/or blood kits are mailed to patient
- Tissue samples are identified in medical records
- Tissue samples are requested and received
- Tissue, blood, saliva samples are sequenced

Data is linked, de-identified, and shared

Patient-reported data is cleaned and standardized → Medical records are abstracted → Sequencing data is analyzed
CMI Data Generation Process

1. Patient clicks "Count Me In"
2. Patient completes survey
3. Patient signs consent form
4. Patient signs medical release form
5. Patient provides saliva and/or blood sample
6. Medical records are requested and received
7. Saliva and/or blood kits are mailed to patient
8. Tissue samples are identified in medical records
9. Tissue samples are requested and received
10. Tissue, blood, saliva samples are sequenced
11. Sequencing data is analyzed
12. Data is linked, de-identified, and shared
13. Patient-reported data is cleaned and standardized
14. Medical records are abstracted
15. Updates and insights are provided to patient

Patient’s steps:
Study team’s steps:
Current State

Dedicated team of Clinical Research Coordinators:

- Review each patient’s Medical Release Form
- Contact each hospital’s medical records department
- Electronically fax a request for records
- Log and track medical record PDFs received by electronic fax

75% of hospitals have an EMR, and yet 75% of medical communication is via fax\textsuperscript{1}

\textsuperscript{1}: Vox "The Fax of Life"
Clinically Annotated Genomic Data
# Clinically Annotated Genomic Data

<table>
<thead>
<tr>
<th>Category</th>
<th>EHR</th>
<th>PRD</th>
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</thead>
<tbody>
<tr>
<td>Demographics</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Disease Characteristics</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Pathology / Receptors</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Treatments / Dates</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Responses to Treatments</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Risk Factors</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Family History</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Tumor Genetics</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Germline Genetics</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

The diagram on the right illustrates the distribution of various therapies, including:

- Palbociclib
- Fulvestrant
- Capecitabine
- Olaparib
- Nivolumab

The x-axis represents the number of patients, while the y-axis likely indicates the cumulative number of patients receiving the respective therapies.
ADDENDUM Breast Pathology Report

RESULTS

1: Diagnosis

**Right Breast**: 0.0: Poorly differentiated invasive ductal carcinoma (tubule formation 3/3, nuclear pleomorphism 3/3, mitotic rate 2/3), measuring 1.9 cm in maximal length in this material.

**Gross Description**: The specimen is received in formalin labeled with the patient’s name and "Right Breast 1.00". The specimen consists of multiple light tan to yellow tan soft tissue fragments measuring 2.1 x 1.2 x 0.3 cm in aggregate. The entire specimen is submitted in 1 cassette(s) labeled "1A". Specimen radiograph is attached / performed.

**Ischemic time**: hrs: min; fixation time: hrs: min; /Test

**Comments**

**PREDICTIVE/PROGNOSTIC MARKERS**

The invasive carcinoma demonstrates:
- Estrogen receptor (ER): NEGATIVE, 0% nuclear staining;
- Progesterone receptor (PgR): NEGATIVE, 0% nuclear staining;
- HER-2 neu score: NEGATIVE (0 staining);

Case reviewed in departmental conference. The results were verbally communicated to the requesting physician.

*PD-L1 SP142 (Tecnetiq™) assay to aid in the evaluation of patient eligibility for anti-PDL1 cancer immunotherapy treatment is available at CBLPath and may be performed upon request.

ER clone (SP1) ultrawiew DAB detection; computer assisted quantitative IHC.
PR clone (1E2) ultrawiew DAB detection; computer assisted quantitative IHC.
Ventana Pathway HER2 neu/4B5 ultrawiew DAB detection.

Negative and positive (internal if applicable) controls show appropriate results. This evaluation is performed according to guidelines issued by CAP/ASCO.
Pathology Abstraction Questions

- When was the sample collected?
- Where in the body was the biopsy taken?
- Was the biopsy taken from the left or right side?
- What is the biopsy type?
- Is there evidence of ductal carcinoma in situ (DCIS)?
- Is there evidence of lobular carcinoma in situ (LCIS)?
- What is the tumor grade?
- What is the histology of the tumor?
- What is the estrogen receptor (ER) status?
- What is the estrogen receptor (ER) percentage?
- What is the progesterone receptor (PR) status?
- What is the progesterone receptor (PR) percentage?
- What is the overall HER2 status?
- What were the results of the HER2 fluorescence in situ hybridization (FISH) assay?
- What were the results of the HER2 immunohistochemistry (IHC) assay?
- What is the HER2 ratio?
- What is the HER2 copy number?
- What is the CEP17 copy number?
- What is the Ki67 copy number?
ALBERT fine-tuned on 43 patients

**ROC curve** (AUC = 0.92)

- **Sensitivity**
  - Value (logodds < 20): 87.1%
  - Value (logodds < 10): 72.7%
- **Specificity**
  - 81.6%
  - 90.5%
- **Precision**
  - 53.1%
  - 66.3%
- **Accuracy**
  - 82.6%
  - 86.8%
Changing Landscape

HIPAA

- Patients have the right to obtain their medical records

21st Century Cures Act

- Defined data elements as US Core Data for Interoperability (USCDI)
- Adopted Fast Healthcare Interoperability Resources (FHIR V4) as an API standard
- Reduces information blocking: clinical notes must be available via API

*Patients have the right to their data, and now a common framework to enable that*
Changing Landscape

- Defining a standard in the USCDI is a good first step
- Version 1 still leaves a majority of the full clinical story as unstructured text in notes
- FHIR and USCDI will continue to evolve to meet additional use cases such as oncology-specific data elements
Piloting Electronic Medical Record Acquisition

- **Patient Data Manager (PDM) Pilot**
  - 15 Patient Pilot study
  - Patients will use MITRE’s PDM app to obtain medical records via API and share with CMI
  - Gap analysis between PDM data, manually abstracted data, and mCODE data standard will identify NLP opportunities

- **Natural Language Processing Collaboration**
  - Leveraging pilot data and reference databases, we will explore data curation tool development to optimize manual abstraction
  - Areas include: medical record summarization, document classification, identifying regions of interest
Patient Data Manager

Simple to share

Interesting to work with

Images: MITRE
Piloting Electronic Medical Record Acquisition

CMI – mCODE Data Flow

Providers w/ structured data
- EHRs
- LIS
- Other clinical apps

Reference Labs
- LIS

3rd party apps
- TBD

Providers w/ unstructured data
- EHRs
- LIS
- Other clinical apps

future

mCODE

Apple Health Record

DSTU2 Interface
STU3-Interface
R4 Interface (new)

future

Count-Me-In

Structured / Semi-structured data translation

mCODE Record (FHIR R4)

Trials Matching / Other mCODE Apps

PDF, text, etc.

CMI Data Store

Abstraction / Curation

iPhone
### Structural Maps – Creation of CancerPatient

- **Mapping of element names and data types**

#### Profiles
- **profile_id (PK):** 100
- **user_id:** 123
- **first_name:** John
- **last_name:** Doe
- **gender:** M
  
- **Resource**
  - **profile_id (FK):** 100
  - **user_id (FK):** 123
  - **resource_type:** Observation
  - **resource:** (AHR FHIR JSON)

#### Abstract (Schema TBD)
- **study_id:** 200
- **variable_name**
- **var_description**
- **value**
- **user_id (TBD):** 123

**CancerPatient Conversion Logic**

<table>
<thead>
<tr>
<th>CMI element</th>
<th>mCODE Resource Path</th>
</tr>
</thead>
<tbody>
<tr>
<td>Profiles: user_id</td>
<td>CancerPatient::Patient.identifier.id</td>
</tr>
<tr>
<td>Profiles: first_name</td>
<td>CancerPatient::Patient.name[0].given</td>
</tr>
<tr>
<td>Profiles: last_name</td>
<td>CancerPatient::Patient.name[0].family</td>
</tr>
<tr>
<td>Profiles:gender</td>
<td>CancerPatient::Patient.gender</td>
</tr>
</tbody>
</table>

**mCODE conversion module**

- CancerPatient + Provenance
- mCODE Record (FHIR R4)

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*Slide: May Terry*
Acknowledgements

- ALL patients participating
- Nikhil Wagle
- Corrie Painter
- Elana Anastasio
- Colleen Nguyen
- Mary McGillicuddy
- Rachel Stoddard
- Sara Balch
- Taylor Cusher
- Beena Thomas
- Alyssa Damon
- Shahrayz Shah
- Rafael Ramos
- Tania Hernandez
- Netsanet Tsegai
- Lauren Sterlin
- Fergie Ulysse
- Imani Boykin
- Brett Tomson
- Shawn Johnson
- Jamie Holloway
- Jim Palma
- Samantha Sullivan
- Andrew Zimmer
- Esme Baker
- Simone Maiwald
- Rich Nordin
- Erin Gwozdz
- Jen Lapan
- Pegah Taheri
- Jordan Doucette
- Sarah Winnicki
- Parker Chastain
- Taylor Cusher
- Roeshana Moore-Evans
- Lauren Ryan
- Max Krevalin
- Dewey Kim
- Jorge Buendia
- Esha Jain
- Sara Semonian
- Miguel Iizarbe
- Eli Van Allen
- Kristen Zarrelli
- Tania Simoncelli
- Jesse Boehm
- Deb Dillon
- Jon Bistline
- Jared Cosulich
- Playground
- Carol Lowenstein
- Kristen Anderka
- Samira Bahl
- Alicia Wong
- Katie Larkin
- Sam Pollock
- Emily Moore
- Niall Lennon
- Sheila Fisher
- Carrie Cibulskis
- Stacey Gabriel
- Viktor Adalsteinsson
- Gavin Ha
- Greg Gyudish
- Sarah Reed
- Sam Freeman
- Nelly Oliver
- Karla Helvie
- Kate Mulherin
- Levi Garraway
- Bina Venkataaraman
- Bang Wong
- David Siedzik
- Scott Sutherland
- Lee McGuire
- Scott Sassone
- Emily Lipscomb
- Andrea Saltzman
- Stacey Donneley
- Jenny Rood
- Jenn Chen
- Justine Levin-Allerhand
- Elizabeth Frank
- Eric Winer
- Eric Lander
- Todd Golub

MITRE:
- Salim Semy
- May Terry
- Rob Dingwell
- Zach Lister
- Dan Potter
- Lauren Levine

The Count Me In Team
Acknowledgements