Disclosures

Consulting
GenomiCare, Inc. – Member, Scientific Advisory Board
Jiahui Holding Co., Ltd – Lead Clinical Advisor

Speaker’s Bureau
Novartis Pharmaceuticals Corporation

Stock
GenomiCare, Inc.
Agenda

- Personalized Medicine Program at SCI & PSJH
- TAPUR “basket clinical trial”
- Project GENIE
- Data mining projects
- An Evaluation of Wellness in Breast Cancer Survivors
- BEAM: Breast and ovarian cancer risk Education, Assessment and Management
- CARE Fund Breakthrough grant- Proactive Cancer Immunotherapies for Initial and Recurrent Disease
- Future vision for Personalized Medicine
- Challenges

SWEDISH CANCER INSTITUTE
Extraordinary care. Extraordinary caring.
In 1932, Swedish Purchases Million-Volt X-Ray Machine making SCI the first radiation medicine facility west of Mississippi river.
Providence St. Joseph Health Overview

50 hospitals
829 clinics
90 non-acute services
14 supportive housing programs
50k caregivers
38k nurses
20k physicians
2 health plans
1.9m covered lives
$1.6b community benefit

Providence Health & Services
Western Washington, including Swedish Health Services and Pacific Medical Centers

Providence Health & Services
Eastern Washington/Western Montana, including Kadlec Regional Medical Center

Providence Health & Services
Oregon, Providence Health Plan

Providence Health & Services
Southern California (Los Angeles County), including Facey Medical Foundation

St. Joseph Health
Southern California (Orange and San Bernardino counties, the High Desert), including Hoag Health and St. Joseph Heritage Healthcare

St. Joseph Health
West Texas/Eastern New Mexico, including Covenant Health, Covenant Medical Group and FirstCare Health Plans

SWEDISH CANCER INSTITUTE
Extraordinary care. Extraordinary caring.
Personalized Medicine Program at SCI & PSJH
**SCI Mission & Vision**

**SCI Research**
To become the premier cancer clinical research organization in the United States, empowering choice and hope in our patients and their families.

**SCI Mission Statement:** To provide cancer patients the best chance of survival and the highest quality of life while striving to prevent and eliminate cancer through research and innovation.

**SCI Vision Statement:** To be a national and international leader in providing innovative cancer care of the highest quality, that is patient and family centered, and determined by both clinical and biological characteristics of each individual.

**SCI Values**
Collaboration | Compassion | Excellence | Innovation | Mentorship | Respect | Responsibility | Safety | Transparency

**PSJH Strategic Goal 2018-2022**
An integrated scientific wellness, clinical research, and genomics program that is nationally recognized for breakthrough advances.
Swedish Cancer Institute Overview

- Nine multi-disciplinary disease sites
  - Over 200 members of SCI with 88 providers employed
- Comprehensive Supportive Care Services
  - 18 programs
- Approximately 8,000 new cancer patients / year
  - 6082 analytic cases in 2016
- On average, 600 patients accrued into clinical trials annually (including PMRP protocol)
SCI Personalized Medicine "Double Meaning"

- **Clinical practice at the SCI is predicated on a research driven, evidence-based, multi-disciplinary, multi-professional, disease site oriented, patient-centered care model, in the context of Personalized Medicine.** Personalized Medicine in this context focuses on two meanings:

1. **Caring for the whole patient**, to include addressing patient and family socioeconomic, psychological, environmental, and other supportive care needs;

2. **Utilizing molecular (gene, protein, epi-genetic) information** from the patient or their tumor to address cancer risk, prevention, screening, early and accurate diagnosis, treatment of disease, and survivorship.
SCI Personalized Medicine Program

2014 Mar
PMP Panel 1st Edition (68 gene panel)

2014 Sep
Personalized Medicine Research Program (PMRP) Protocol (IRB approved)

2015 Jan
Molecular Tumor Board Launch

2015 Nov
PMP IT Platform (Syapse) Launch

2015 Nov
Personalized Medicine Research Program (PMRP) Protocol (IRB approved)

2015 Nov
PMP IT Platform (Syapse) Launch

2016 Mar
Innovative Therapeutics Unit (Early Phase Clinical Trials Unit) Open
SCI PMRP: Recruitment/Enrollment

• Enrollment
  • 1,275 pts (as of February 20th, 2019); initial focus on solid tumors
• Insurance Status
  • No restrictions
• Cost to Participate in PMRP
  • None (PMP Panel ordered by provider, and billed based on “medical necessity”)
• Language
  • Consent form in English, Vietnamese, Korean, Japanese, Chinese (Mandarin & Cantonese), Russian and Spanish
SCI PMP PANEL: ALTERATIONS BY CATEGORY

PMRP Enrollment: 927 cases
Accelerate speed to patient identification for PM trials

### Patient Cohort Builder

<table>
<thead>
<tr>
<th>Sex</th>
<th>Race</th>
<th>Cancer Type</th>
<th>Histology</th>
<th>Clinical Stage Group</th>
<th>Pathologic Stage Group</th>
<th>Gene Symbol</th>
<th>Biomarker</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>White</td>
<td>Colon, NOS</td>
<td>Adenocarcinoma...</td>
<td>Unknown</td>
<td>IIIA</td>
<td>KRAS</td>
<td></td>
</tr>
<tr>
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<td>Colon, NOS</td>
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<td>IVB</td>
<td>IVB</td>
<td>KRAS</td>
<td></td>
</tr>
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<td>White</td>
<td>Colon, NOS</td>
<td>Adenocarcinoma...</td>
<td>I</td>
<td>I</td>
<td>KRAS</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>White</td>
<td>Colon, NOS</td>
<td>Adenocarcinoma...</td>
<td>Unknown</td>
<td>IIIC</td>
<td>KRAS</td>
<td></td>
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<tr>
<td>Male</td>
<td>White</td>
<td>Colon, NOS</td>
<td>Mucinous adenocarcinoma</td>
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<td>IIC</td>
<td>KRAS</td>
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<td>Colon, NOS</td>
<td>Adenocarcinoma...</td>
<td>I</td>
<td>I</td>
<td>KRAS</td>
<td></td>
</tr>
<tr>
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<td>White</td>
<td>Colon, NOS</td>
<td>Adenocarcinoma...</td>
<td>IVA</td>
<td>IVA</td>
<td>KRAS</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>White</td>
<td>Colon, NOS</td>
<td>Adenocarcinoma...</td>
<td>Unknown</td>
<td>IIA</td>
<td>KRAS</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>White</td>
<td>Colon, NOS</td>
<td>Neoplasm, malig...</td>
<td>Unknown</td>
<td>Unknown</td>
<td>KRAS</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>White</td>
<td>Colon, NOS</td>
<td>Adenocarcinoma...</td>
<td>Unknown</td>
<td>IIB</td>
<td>KRAS</td>
<td></td>
</tr>
</tbody>
</table>

27 patients found
CT Pre-Screening increases patient access to clinical trials while reducing health system staff effort
Gain insight into how your physicians offer precision medicine

Executive Dashboard: Testing Volume
Identify care delivery trends

Executive Dashboard: Testing Statistics

Rolling Year Statistics (August 2017 - July 2018)

<table>
<thead>
<tr>
<th></th>
<th>Total Number of Test Results</th>
<th>Average Actionability Rate*</th>
<th>Average QNS Failure Rate*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2,897</td>
<td>72.70%</td>
<td>29.41%</td>
</tr>
</tbody>
</table>

Rolling Year Trends (August 2017 - July 2018)

Total Number of Test Results by Lab

- 967
- 947
- 599
- 268
- 65
- 31

Actionability Rate*

- Has Actionable Mutation
- No Actionable Mutation

QNS Failure Rate*

- Quantity Sufficient
- Quantity Not Sufficient
Introducing Real-World-Evidence from data sharing network leveraging research-grade data

Swimmer Plot - Stage IV - Non-Small Cell Lung

Patients missing a date of death and date of last contact are excluded from the Swimmer Plot

Measure Names
- Month Death
- Month Last Contact
- Month Mix

Line of Therapy
- 1
- 2
- 3
- 4
- 5
- 6
- 7
- 8
- 9

Months Since Date of Diagnosis
Introducing Real-World-Evidence from data sharing network leveraging research-grade data
SCI Molecular Tumor Board

- Co-chairs
  - Anna Berry, John Pagel, Charles Drescher
- Purpose
  - Multidisciplinary case review focused on clinically relevant gene alterations and associated molecular pathways, with aim of facilitating patient management decisions.
- Conference Structure:
  - Average 3-4 cases including follow-up cases
  - Cases submitted by physicians and selected by Dr. Berry
  - Special Sessions (e.g. Implications for Germline Genetic Testing)
History

- Papillary serous adenocarcinoma of the ovary first presented in 2011, had debulking surgery and adjuvant Taxol and Carboplatin. Recurred in January 2013, abdominal wall, received Letrozole but progressed quickly with a pelvic mass and attempted resection, would have required permanent colostomy. Postoperative radiation therapy in October 2013. Then developed extensive abdominal disease. She was seen at MD Anderson and sequenced by Foundation Medicine. NF2 and CDKN2A/B mutations were found. Mekinist (only 4/wk due to rash) April 2014 to March 2015 with some response, then progression. Avastin, Taxol, Carboplatin June to Nov 2015, then Gemzar to Jan 2016, then Regorafinib (reduced dose due to side effects) until June 2016, then Afinitor to August 2016, then Keytruda. Bowel obstruction in Nov 2016. MATCH lab could not confirm results (NF2 or CDKN2). Back to Regorafinib in Feb 2017.
Recurrent low grade papillary serous carcinoma of ovary (2013 sample, sigmoid nodule).
ABERRATIONS:
- NF2_D154fs*45
- CDKN2A/B loss

*p15^{INK4B} is regulated by CDK4 or CDK6, leading to RB and E2F.
*p14^{ARF} is regulated by MDM2, leading to p53 and p21.
*p16^{INK4A} is regulated by CDK4 or CDK6, leading to RB and E2F.

Sharpless and Sherr, Nature Reviews Cancer, 2015
POSSIBLE THERAPIES:
- Afinitor / Everolimus - mTOR kinase inhibitor, immnosuppressant.
- Torisel / Temsirolimus - mTOR inhibitor.
- Mekinist/Trametinib – MEK inhibitor.
- Tykerb/Lapatinib – EGFR/HER2 inhibitor.
- Defactinib – FAK inhibitor.
- Ibrance/Palbociclib – CDK4/6 inhibitor (TAPUR match).

POSSIBLE CLINICAL TRIALS:
- NCT02943317: Study to Investigate the Safety, Pharmacokinetics, Pharmacodynamics and Preliminary Clinical Activity of Defactinib in Combination With Avelumab in Epithelial Ovarian Cancer (Verastem, TN and others not open yet)
- NCT02546531: Defactinib Combined With Pembrolizumab and Gemcitabine in Patients With Advanced Cancer (Wash U)
- NCT02352844: Everolimus in Patients With Advanced Solid Malignancies With TSC1, TSC2, NF1, NF2, or STK11 Mutations (Wash U)
- NCT02897375: Palbociclib With Cisplatin or Carboplatin in Advanced Solid Tumors (Pfizer, Emory)
Data Assets & Scale
PSJH Cancer Institutes – Current state

26 distinct cancer registry systems

Swedish
Providence WA/MT
Providence OR/CA
Providence AK
Kadlec
PHS Insights

Ent. Data Warehouse

22M+ unique patients

Genome-driven clinical decision support (integrated in Epic)

Syapse

Cancer clinical analytics & outcomes analysis

Operational BI & cost / value analyses

Illustrative patient cohorts in oncology/genomics:
- Historic cancer registry data mart: 810,000+ cases
- Integrated Epic EMR + cancer registry data: 707,000+ cases
- Cancer cases w. “active cancer diagnosis” (baseline clinical EMR data): 303,000+ cases
- Integrated on Syapse platform: 170,000+ cases
- Historic pathology reports (OR Region): 190,000+ cases
- Patients w. NGS cancer profiles: 4,000+ cases & growing

~43,000 net new cancer cases / year across PSJH
## PSJH Cancer Genomics Profiling
### NGS offerings & research alignment

<table>
<thead>
<tr>
<th>Providence Personalized Medicine Panel 170 &amp; 500</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Targeted therapies + Immuno/therapies (I/O)</strong></td>
</tr>
<tr>
<td><strong>170 &amp; 500 Gene panels</strong></td>
</tr>
<tr>
<td><strong>Somatic Only</strong></td>
</tr>
<tr>
<td><strong>MSI and TMB</strong></td>
</tr>
<tr>
<td><strong>Physician Order</strong></td>
</tr>
<tr>
<td><strong>No Research Protocol</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>TriSeq</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Targeted therapies + I/O</strong></td>
</tr>
<tr>
<td><strong>Whole Exome Sequencing + 170 Gene Panel + mRNAseq</strong></td>
</tr>
<tr>
<td><strong>Somatic plus Germline</strong></td>
</tr>
<tr>
<td><strong>MSI &amp; TMB (From Gold Standard Exome)</strong></td>
</tr>
<tr>
<td><strong>Physician Order &amp; Patient Consent</strong></td>
</tr>
<tr>
<td><strong>Research Protocol</strong></td>
</tr>
</tbody>
</table>
Targeted Agent and Profiling Utilization Registry (TAPUR)
Overall Goals of TAPUR

• To learn from the real world practice of prescribing targeted therapies to patients with advanced cancer whose tumor harbors a genomic variant known to be a drug target

• To educate oncologists about implementation of precision medicine in clinical practice
TAPUR Study Primary Objective

- To describe the anti-tumor activity and toxicity of commercially available, targeted anti-cancer drugs prescribed for treatment of patients with advanced solid tumors, B cell NHL or MM with a genomic variant known to be a drug target or to predict sensitivity to a drug.
TAPUR Eligibility

- Patients with advanced solid tumors, B cell NHL and multiple myeloma for whom no standard treatment options exist
- Adequate organ function; PS 0-2
- Results available from a genomic test (FISH, PCR, NGS, WES, IHC for gene expression) performed in a CLIA certified, CAP accredited lab. Labs located or offering services to residents of NY must also have NY State accreditation. Test should be registered with NIH Genetic Test Registry.
# Drugs Available in TAPUR

<table>
<thead>
<tr>
<th>Pharmaceutical Company (Number of Drugs)</th>
<th>Drug(s) Provided for TAPUR Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>AstraZeneca (1)</td>
<td>Olaparib</td>
</tr>
<tr>
<td>Bayer (1)</td>
<td>Regorafenib</td>
</tr>
<tr>
<td>Bristol-Meyers Squibb (3)</td>
<td>Dasatinib, Nivolumab + Ipilimumab</td>
</tr>
<tr>
<td>Eli Lilly (1)</td>
<td>Cetuximab</td>
</tr>
<tr>
<td>Genentech (4)</td>
<td>Trastuzumab + Pertuzumab, Vemurafenib + Cobimetinib</td>
</tr>
<tr>
<td>Merck (1)</td>
<td>Pembrolizumab</td>
</tr>
<tr>
<td>Pfizer (6)</td>
<td>Axitinib, Bosutinib, Crizotinib, Palbociclib, Sunitinib, Temsirolimus</td>
</tr>
</tbody>
</table>
TAPUR Matching Rules

- Specific genomic inclusion and exclusion criteria included for each drug
- Matching at variant level if possible
- Automated rules engine approves/rejects match proposed by treating MD
- If no match proposed or match rejected, treating MD may consult TAPUR MTB
- MTB identifies TAPUR drugs or other options based on tumor genomics
- Thus far, 65% of cases matched by rules engine. Of those sent to MTB, 59% enrolled on a TAPUR study drug
Endpoints

- Primary endpoint: Objective response rate per standard response criteria or SD at 16+ w
- Other endpoints:
  - overall survival
  - progression-free survival
  - time on treatment
  - grade 3-5 AEs per CTCAE
  - SAEs
Statistical Design

- Simon’s two-stage design
- Each tumor type-gene-drug is a “cohort”
- Null Hypothesis: ORR < 15% vs. Alternative Hypothesis: ORR ≥ 35%
- Enroll 10 patients/cohort
  - If 0-1 response, stop
  - If 2 or more responses, enroll additional 18 pts
- Reject null hypothesis if 7 or more responses/28
- 85% power and one-sided Type 1 error rate of 0.10
TAPUR is a Pragmatic Trial

- Broad eligibility criteria
- Physician discretion on genomic testing, drug dosing, dose modifications
- Minimum necessary data collection
- Investigator assessment of response
- Data validation procedures but no auditing/monitoring
- IND exempt per FDA
- However, specific inclusion/exclusion criteria, genomic matching rules and standard response criteria, required evaluations and data submission
Variation in Genomic Targets by Tumor Type N=683(18)
As of Friday, February 23, 2018
23 cohorts have expanded to Stage II. 5 cohorts closed after Stage I.

<table>
<thead>
<tr>
<th>Cohort Status</th>
<th>Treatment</th>
<th>Number of Cohorts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Expanded to Stage II</td>
<td>Cetuximab</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Nivolumab + Ipilimumab</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Olaparib</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Palbociclib</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Pembrolizumab</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Pertuzumab + Trastuzumab</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Sunitinib</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Vemurafenib + Cobimetinib</td>
<td>1</td>
</tr>
<tr>
<td>Permanently Closed</td>
<td>Cetuximab</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Palbociclib</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Sunitinib</td>
<td>1</td>
</tr>
</tbody>
</table>

113 sites in 20 states
TAPUR Study Registration and Enrollment Status
Center: Swedish Cancer Institute
As of: Wednesday, January 23, 2019
Re-enrollments are included (3)

Cumulative plot:
Enrolled of Registered: 60.6%

Registration and Enrollment by Study Month

Participants Registered | Baseline & Cycle 1 Day 1 Visit
Enrolled Patients' Gene + Drug Matches (n = 45)*

* Total number of patient-variant-drug matches is 42 although total enrollment is 45, since three patients received two lines of therapy on trial.
Project GENIE: Genomics Evidence Neoplasia Information Exchange
Goals of Data-Sharing

- Provide clinicians with real-world, aggregated patient data to support clinical treatment decisions.
- Determine treatment outcomes based on molecular fingerprints.
- Research activities:
  - Identify novel response biomarkers
  - Rationalize tumor mutation burden status across NGS platforms
  - Hypothesis generation
Overview

- International pan-cancer registry built through data sharing
  - Driven by openness, transparency, and inclusion

- GOAL: improve clinical decision making
  - Linking clinical genotype to clinical outcomes

- Eight founding participants, now 19
  - North America & Europe
  - Plans for future expansion

- Sponsored research
- Collaborative projects
Participant Geographic Distribution
How the Registry Operates: Baseline Data

19 Sites

Clinical Sequencing

6 mos.

- Data mapped to common ontology and harmonized
- Limited PHI removed
- Data governance, provenance, and versioning in a secure, HIPAA-compliant environment.

Institution-only access 6 months
Consortium-only access 6 months

www.aacr.org/genie/data
Clinical queries are posed based on registry content.

Clinical data required to answer the question are manually abstracted.

Genomic and clinical data linked.

Consortium/sponsor-only access to time of publication.

How the Registry Operates: Detailed Clinical Data
Data Access

- **Terms of Access**
  - DO NOT attempt to identify or contact any patients
  - REQUEST PERMISSION to redistribute the data
  - Give PROPER ATTRIBUTION to the consortium
Publications and Data Usage (08/27/2018)

- **Publications**
  - Landscape paper published in *Cancer Discovery* June 2017
  - Review published in *JCO Clinical Cancer Informatics* Feb. 16, 2018
  - Landscape manuscript cited by 45 articles.

- **Data Usage**
  - 3802 individuals have requested access to the data via cBioPortal.
  - There have been six requests for data redistribution.
Landscape overview of GENIE dataset

Figure 4. Potential clinical actionability. Tumor types are shown by decreasing overall frequency of actionability. Actionability was defined by the union of three knowledge bases: My Cancer Genome (http://mycancergenome.org), OncoKB (http://oncokb.org), and the Personalized Cancer Therapy knowledge base (http://pct.mdanderson.org). For each tumor sample, the highest level of actionability of any variant was considered. Only tumor types with 100 or more samples were included in this analysis.

Summary

- AACR Project GENIE is an international cancer registry containing 48,500+ genomic records and growing.
  - Committed to including new types of sequencing data as the landscape evolves.
- Each record has an associated limited clinical data set.
  - Working to expand the data collected as part of the baseline.
- Currently, more detailed clinical data are curated on individual cohorts in response to specific clinical queries.
- Moving towards collecting a more complete picture of a patient’s journey with cancer yielding clinical, pathologic, radiographic, tumor marker status, and treatment response.
- Taken together, these clinical data allow for the determination of real-world endpoints such as recurrence, DFS, and PFS.
Data Mining Projects
Impact of a personalized medicine research program (PMRP), using targeted tumor profiling and a cloud based clinical trials matching platform, on clinical decision-making.

Thomas D. Brown¹, Paul D. Tittel¹, Philip J. Gold¹, Charles W. Drescher¹, John M. Pagel¹, J. D. Beatty¹, Patra Grevstad¹, Desiree Iriarte¹, Shlece Alexander¹, Madeleine Brindle¹, Xiaoyu Liu¹, Doniell O’connor¹, Mariko Tameishi¹, Danbin Xu², Anna B. Berry³.

Did the NGS Test Results Impact Treatment Planning for the Patient?

Reported for 591 Pts with actionable/applicable GAs; 523 pts evaluable

- Yes in 108 Pts (21%)
- No in 415 Pts (79%)

Conclusions: NGS profiling of tumors with this 68 GA panel has an impact on clinical decision-making in a minority, though substantial number, of pts. Impact on CT participation remains modest. Access to drugs and CT remains an important barrier.
TP53 gain of function (GOF) mutations identified by tumor sequencing performed in the context of a community-based Personalized Medicine Cancer Program.

C. W. Drescher, A. B. Berry, D. J. Beatty, D. Xu, X. Liu, M. Zhang, K. Keith, J. D. Scanlan, J. M. Pagel, P. J. Gold, D. Markowitz, T. L. Benkerson, C. Bonham, M. Tameishi, T. D. Brown. 1Swedish Cancer Institute, Swedish Cancer Institute. 2CellNetix Pathology and Laboratories, Molecular Pathology. 3Swedish Medical Center, The Swedish Center for Research and Innovation. 4Swedish Neuroscience Institute, Ben & Catherine Ivy Center.

EORTC-NCI-AACR Molecular Targets and Cancer Therapeutics Symposium, Nov, 2016.

Table 1: Summary of TP53 sequence results

<table>
<thead>
<tr>
<th></th>
<th>Breast</th>
<th>CNS</th>
<th>Colorectal (CR)</th>
<th>Non-CR GI</th>
<th>NSCLC</th>
<th>Ovary</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>#</td>
<td>%</td>
<td>#</td>
<td>%</td>
<td>#</td>
<td>%</td>
<td>#</td>
</tr>
<tr>
<td>Mt GOF</td>
<td>0</td>
<td>0</td>
<td>12</td>
<td>16</td>
<td>9</td>
<td>11.5</td>
<td>10</td>
</tr>
<tr>
<td>Mt non-GOF</td>
<td>10</td>
<td>16.4</td>
<td>16</td>
<td>21.3</td>
<td>23</td>
<td>29.5</td>
<td>18</td>
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<tr>
<td>VUS</td>
<td>2</td>
<td>3.3</td>
<td>8</td>
<td>10.7</td>
<td>2</td>
<td>3.6</td>
<td>3</td>
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<tr>
<td>Wild-type</td>
<td>49</td>
<td>80.3</td>
<td>39</td>
<td>52</td>
<td>44</td>
<td>56.4</td>
<td>32</td>
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<tr>
<td>Total</td>
<td>61</td>
<td>75</td>
<td>78</td>
<td>63</td>
<td>46</td>
<td>33</td>
<td>112</td>
</tr>
</tbody>
</table>

- Overall 47 pts (10%) of 468 pts were identified as having GOF mutations.
- The frequency of GOF mutations varied by disease site ($X^2 = 37.8, p<0.001$); these results were driven largely by the absence of GOF mutations in patients with breast cancer. GOF mutations in decreasing frequency were: R273C, H or L (n=18), R175H (n=15), R248W or Q (n=13) and P151S (n=1).
- Three of the four R273L occurred in patients with NSCLC, and accounted for 60% of GOF mutations in NSCLC pts.


Data Preparation
- PMRP
- Breast Registry
- Harmonization
- Normalization
- Aggregation
- Manual Abstract From Source Systems (e.g., EMRs)
- Demo
graphics
- Risks
- Diagnosis
- NGS
- Follow-up
- De-Identification

Enumeration
- Variables and Outcomes
- Network Fragments
  - Inputs:
    - Breast cancer stage
    - Clinical/molecular phenotype
    - Metasasis sites
    - Co-morbidities
    - Therapies received
  - Outputs:
    - Progression free survival
    - Treatment response as judged by treating MD
    - Overall survival

Optimization
- Network Models

Simulation
- Ensemble of Models
- Predicted Output
  - Sample
    - Frequency
    - Overall Survival
  - The output of the networks gives a distribution and a confidence interval for the effect of the manipulation, across all models.

Ensemble of Models
- Simulations are run on the ensemble of models found by Optimization. For example, expression of a gene could be reduced to observe an effect on overall survival.

Predicted Output
- Sample
  - Simulation (e.g., predicted scores will generate outputs)
  - Data Lakes 6 Framework

SWEDISH CANCER INSTITUTE
Extraordinary care. Extraordinary caring.
An Evaluation of Wellness in Breast Cancer Survivors
An Evaluation of Biomarkers in Breast Cancer Survivors

Ellis, E; Price N; Rinn K; Kaplan, H; Tameishi, M; Hariharan, R; Fitzgerald, T; Zucker, D; Bunkow, M; Boore, J; Robinson, M; Sanders, K; Crowley, J; Brown, T; Hood, L.

Cancer Diagnosis
- Cancer-Related Cognitive Impairment
- Fatigue
- Stress

Treatment
- Arthralgias
- Weight and body composition changes
- Mucositis/colitis
- Neuropathy
- Depressive symptomatology

Systemic chemotherapy (surgery, hormonal and/or biological agents, and irradiation also allowed)

Evaluation

Dense, Dynamic Data Clouds
- Clinical, genome, gut microbiome, metabolome, blood proteome, immune status, neuro-cognitive measurements, physiological, functional Imaging, ECOG performance status, Quality of Life and outcomes data

Actionable possibilities, quantitative assessment of interventions, discovery possibilities

Scientific Wellness
- Personalized, preventative, and therapeutic, as well as behavioral interventions along with wellness coaching

Extraordinary care. Extraordinary caring.
BEAM: Breast and ovarian cancer risk Education, Assessment and Management
**BEAM**: Breast and ovarian cancer risk Education, Assessment and Management

PI: Charles Drescher, MD; Co-Pis: Thomas Brown, MD, MBA and Christine Lee, MD

**Study:**
A prospective observational cohort study of individuals at high risk for breast and/or ovarian cancer recruited from women referred to Swedish Cancer Institute (SCI) First Hill, SCI-Ballard, SCI-Issaquah and SCI-Edmonds.

**Goals:**
Identify barriers to participation in breast and ovarian cancer risk assessment and management strategies and to understand the educational and support needs of individuals at high risk.

Data generated from this study will be used to develop targeted interventions that can be tested in future research.
Andy Hill CARE (Cancer Research Endowment) Fund

Breakthrough grant:
Proactive Cancer Immunotherapies for Initial and Recurrent Disease
Proactive Cancer Immunotherapies for Initial and Recurrent Disease
Future vision for Personalized Medicine
Future Vision of Personalized Medicine

Targeted Population: Ph. I Candidates/Selected Populations (e.g. refractory disease, CNS, rare malignancies)

High Throughput Screening
Bio-bank

Dense & Dynamic Personal Data Clouds With Advanced Analytics/ Artificial Intelligence (AI)

Biomarker-driven standard of care when appropriate

Molecular Profiling Collaborative (CLIA/CAP/Research)

Next Gen of Clinical Trials Platform

Ph. I - IV

Ph. I /N-of-One
Deep Phenotyping Enables Paradigm Shift in Diagnostics & Therapeutics

Identifying Wellness-Disease Transitions

Challenges
Challenges for Precision Medicine
(In Ascending order)

- Cost and access to genomic testing.
- Cost and access to indicated therapies.
- Lack of actionable gene alterations.
- Education of all stakeholders.
- Patient expectations.
- Complexity of interpretation of data.
- Access to big data solutions.
- Expansion of physicians’ comfort zone.
Challenges to Data Inter-Operability and Sharing

- Diverse informatics platforms, for clinical, research and administrative applications.
- Varying nomenclature for given clinical and scientific data elements.
- Data security and privacy issues, to include HIPPA compliance.
- Data quality, to include arbitrating differences between multiple data sources for the same data elements.
- Evolving technologies and evidence base.
- Continued need for "manual" curation and abstracting of data.
- Cost and reimbursement.
From developing a next generation sequencing panel to help physicians select the most promising therapies for individual patients to embedding a social worker in all disease-specific clinics, this program made personalized medicine a cornerstone of the cancer service line.

Thomas Brown, M.D., M.B.A., Executive Director, Swedish Cancer Institute
In August, 2017, The Academy conducted in-depth telephone interviews with five executives at Providence St. Joseph Health around the process and impact of implementing a precision medicine program in oncology.

Thomas Brown, M.D., M.B.A., Executive Director, Swedish Cancer Institute
Mark Gargett, VP for Digital Integration, Providence St. Joseph Health
Todd Guenzburger, M.D., FACP, Chief Medical Informatics Officer, Providence St. Joseph Health
Paul Tittel, M.H.A., Principal Consultant & Founder, Akesis Solutions LLC; former System Director, Enterprise Amalga & Data Services, Providence Health & Services
Walter J. Urba, M.D., Ph.D., Director of Cancer Research, Providence Health & Services – Oregon

The Health Management Academy (The Academy) is a membership organization exclusively for executives from the country’s Top-100 Health Systems and most innovative healthcare companies.
ABSTRACT Despite rapid advances in molecular diagnostics and targeted therapeutics, the adoption of precision medicine into clinical oncology workflows has been slow. Questions about clinical utility, inconsistent reimbursement for molecular diagnostics, and limited access to targeted therapies are some of the major hurdles that have hampered clinical adoption. Despite these challenges, providers have invested in precision medicine programs in an ongoing search for innovative care models to deliver improved patient outcomes and achieve economic gains. We describe the precision oncology medicine programs implemented by an integrated delivery system, a community care center, and an academic medical center, to demonstrate the approaches and challenges associated with clinical implementation efforts designed to advance this treatment paradigm. Payer policies that include coverage for broad genomic testing panels would support the broader application of precision medicine, deepen research benefits, and bring targeted therapies to more patients with advanced cancer.
ASCO 2018: Spotlight on Innovation in Precision Medicine

- ASCO 2018: Education Session Presentation: "The Informatics of Precision Cancer Medicine", June 1st, 2019
- ASCO 2018 Educational Book: Art and Challenges of Precision Medicine: Interpreting and Integrating Genomic Data Into Clinical Practice
### SCI PMRP TEAM

<table>
<thead>
<tr>
<th>Principal Investigator</th>
<th>Co-Principal Investigator</th>
<th>Co-Principal Investigator</th>
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<th>Technical Expert</th>
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<tr>
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<td>Anna Berry, MD</td>
<td>Charles W Drescher, MD</td>
<td>John Pagel, MD, PhD</td>
<td>Danbin Xu, MD, PhD</td>
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