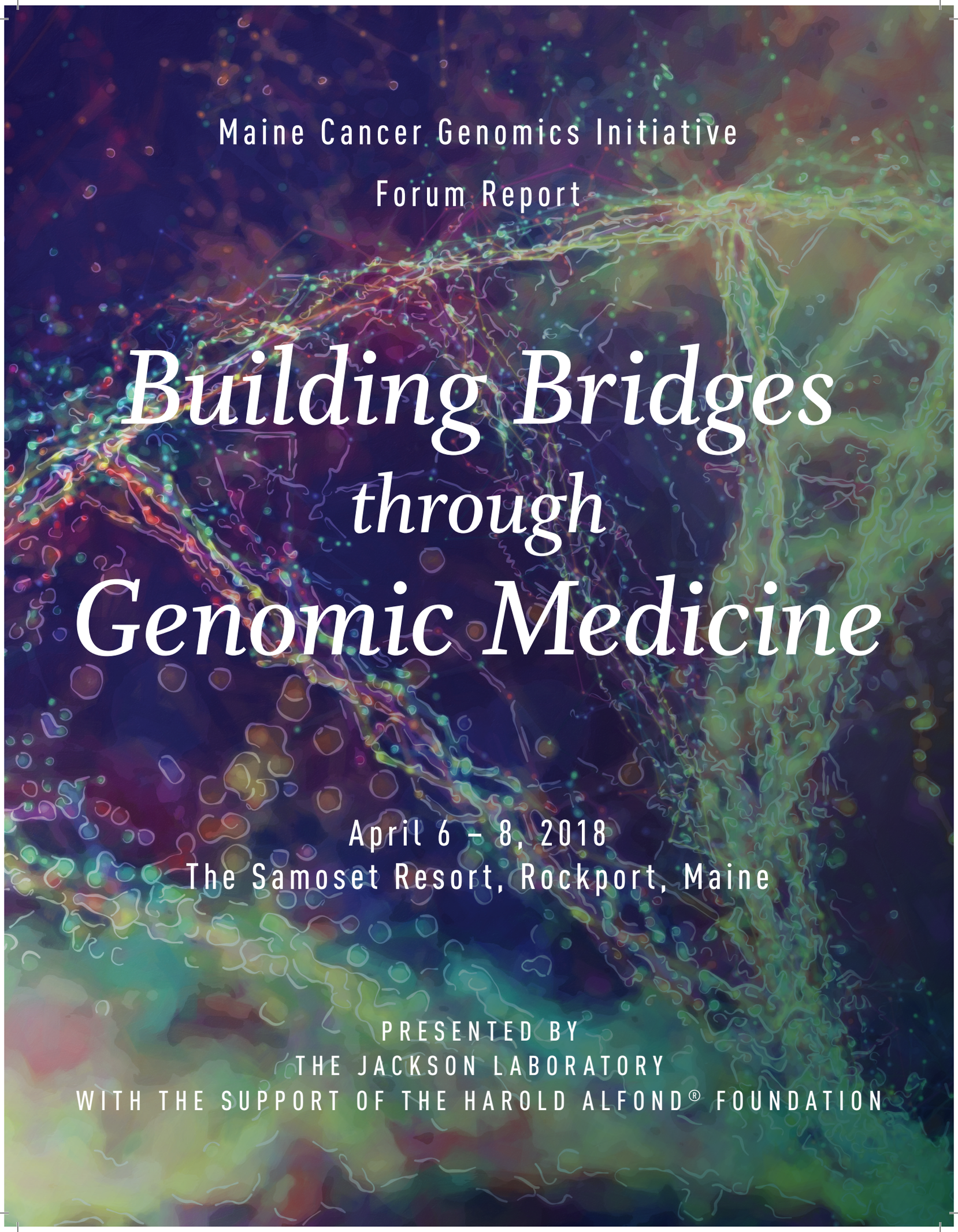


Maine Cancer Genomics Initiative

Forum Report

Building Bridges through Genomic Medicine

April 6 – 8, 2018

The Samoset Resort, Rockport, Maine

PRESENTED BY

THE JACKSON LABORATORY

WITH THE SUPPORT OF THE HAROLD ALFOND® FOUNDATION

Building Bridges Through Genomic Medicine

Executive Summary

A late-season snowstorm greeted attendees arriving for the 2nd annual Maine Cancer Genomics Initiative (MCGI) Forum, held April 6 – 8, 2018, at The Samoset Resort. The snow provided an unexpected meteorological parallel to the first forum, held the previous February, but inside the meeting rooms almost everything had changed. Following its founding in June 2016 with support from the Harold Alfond® Foundation, MCGI has progressed from a mostly abstract goal to a robust, first-of-its-kind program bringing the latest cancer research to community clinical oncology settings. In less than two years, it has changed cancer care in healthcare systems and oncology practices throughout Maine.

The forum brought together cancer specialists, genetic counselors, researchers, administrators and Senior Aging Committee Staffer, Sarah Khasaniwah, from the office of Senator Susan Collins. The group gathered to hear presentations and discuss a variety of topics, including new discoveries in cancer research, the implementation and integration of genomics in the clinic, the need for patient and physician education, and future directions in both diagnosis and targeted treatments. With more than 150 patients enrolled, nearly every Maine oncology practice participating, and close to 20 genomic tumor boards completed, clinic-based patient impact is increasing statewide. MCGI is just getting started; the future promises significant improved patient access to rapidly evolving cancer genomic technologies. The effort will serve as a model and provide data for similar community-based programs nationwide.

Genomics research

Jeffrey Chuang, Ph.D., Associate Professor, The Jackson Laboratory

Clinical progress begins with basic research discoveries and Chuang provided an overview of his work to derive clinically useful knowledge from the vast amounts of cancer research data now available. Chuang is a computational biologist who combines diverse data types, including tumor genomics, gene expression profiles and mutation rates, to investigate cancer traits such as the evolution of tumors, the changes that occur during metastasis and the interplay between the tumor and surrounding cells and tissues. He also uses his findings to model outcomes for various cancer subtypes and noted that a particular challenge for such work is the lack of consistent and accurate clinical outcome data. Better access to such patient data will provide enhanced understanding of how a given variable affects cancer progression and mortality rates.

Another component of Chuang's research program is working with patient derived xenograft (PDX) mouse model data. PDX mice, which are implanted with tumor tissue taken directly from patients, provide an important preclinical testing resource for cancer therapies. At a time when many targeted cancer therapeutics are being developed for clinical trials, pharmaceutical companies are struggling to recruit enough patients with the particular cancer attributes or mutation profiles required. PDX mice can help by providing an effective experimental platform to improve and accelerate therapy testing. Chuang is working to establish standardized pipelines for PDX data and analysis to be shared with the research community.

Edison Liu, M.D., President & CEO, The Jackson Laboratory

In addition to his administrative duties, Liu runs a research laboratory investigating cancer genomics, with a focus on triple-negative breast cancer (TNBC). TNBC provides oncologists with relatively few treatment options, as it doesn't respond to hormonal and/or targeted therapies effective for other breast cancer subtypes. Understanding the distinct genomic hallmarks of TNBC would provide new therapeutic targets, with the potential to yield more effective treatment strategies. Liu presented his lab's research into a genomic disruption called the tandem duplicator phenotype (TDP) implicated in TNBC and other difficult-to-treat cancers, including ovarian cancer.

TDP results from dysfunctions in DNA replication, leading to a segment of DNA being duplicated and inserted into the genome. The implications are complex, but TDP can contribute to cancer when an oncogene is duplicated and expressed twice and when a tumor suppressor gene is disrupted and rendered non-functional by the insertion of the duplicated segment. Development of TDP is caused by deficiencies in BRCA1 specifically, which is hypothesized to contribute to the DNA replication problems. Liu's lab has further determined that TDP-positive cancers are particularly vulnerable to cisplatin and other platinum-based therapies, indicating a more targeted frontline therapy for cancers with this genomic signature.


MCGI
Housekeeping
•Please sit at the table color that corresponds to the color dot on your name-tag
•If you do not know which table to sit at – ask a staff member!

Clinical genomics

Andrew Hertler, M.D., FACP, Chief Medical Officer, New Century Health

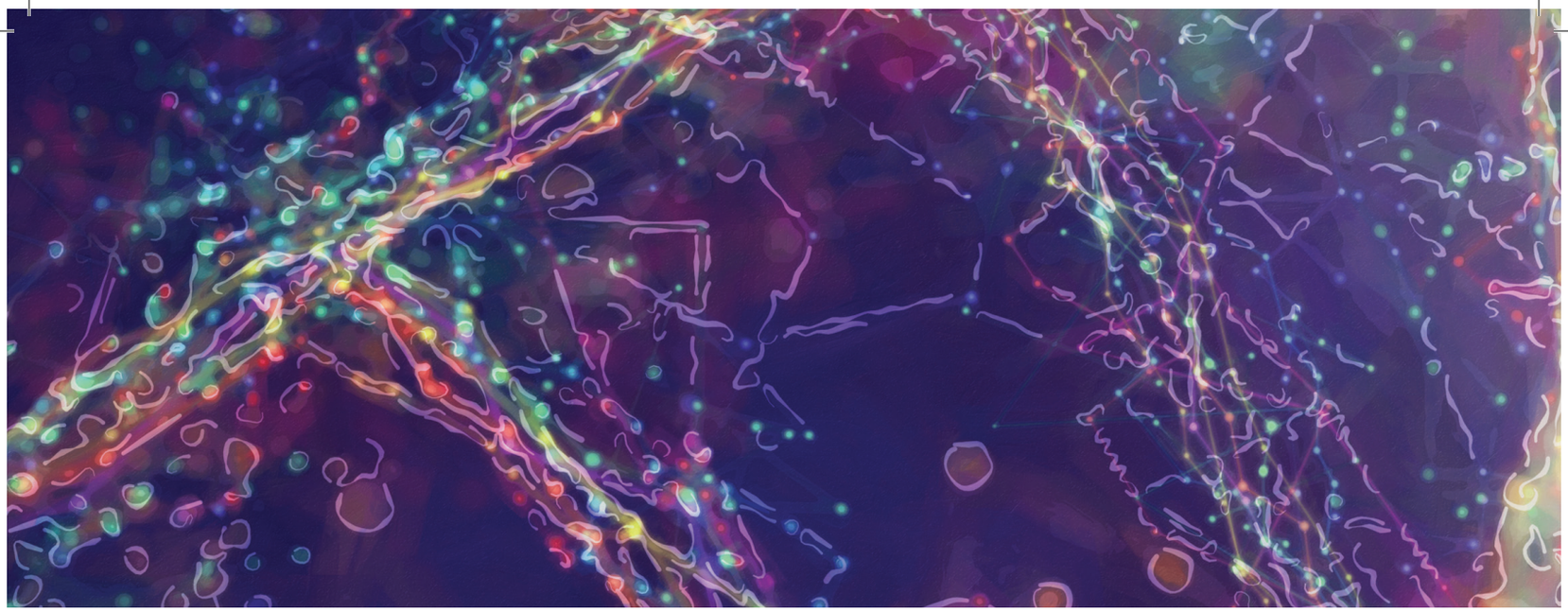
Genomics research results are clinically useful only when they yield improved diagnostics and therapies, and more precise ways of implementing them. Hertler noted in his talk on clinical pathways that integrating genomics into clinical care can be quite challenging. Using the latest data and incorporating input from practicing physicians and outside experts, Hertler and New Century Health (NCH) develop pathways to drive standardization of care based on the best available evidence for a particular patient population. NCH's current effort is to develop clinical pathways in oncology that are able to rapidly incorporate advances in genomics and precision medicine.

The pathways developed by NCH yield recommendations based on scores related to therapy efficacy and severity of side effects. The strength of the existing evidence and therapy costs are also considered. Once implemented, the pathways act as a resource to provide physicians with easy-to-interpret care options for their patients. Hertler said that the advent of precision medicine and targeted therapies has greatly increased medical complexity, particularly in oncology, which has increased the importance of pathways to help guide clinical decisions. Traditional International Classification of Diseases (ICD) guidelines used to largely drive therapy selection, but with the advent of accessible sequencing and biomarker discovery, individual patient data now plays an important role. The potential benefits are significant, but only if the complexities and costs are properly managed.

Lincoln Nadauld, Executive Director, Precision Genomics, Intermountain Healthcare

Precision oncology, incorporating tumor DNA sequencing and molecular analysis to guide therapy decisions, is already well established at Intermountain Healthcare. Nadauld presented how Intermountain, a not-for-profit system based in Utah with 22 hospitals, more than 1,600 physicians and advanced practice clinicians at about 180 clinics, has developed and implemented precision oncology workflows over the past several years. The data show that these workflows lead to improved patient outcomes and even decreased overall costs at Intermountain. The insights gained and process improvements made — including rapid analysis and regular tumor board consultations — are helping to guide MCGI efforts across Maine healthcare systems now.

Moving forward, Nadauld's vision is to go beyond precision medicine as it is currently implemented to focus more on prevention, wellness and the significant reduction of healthcare costs. Intermountain is beginning to mine its own biorepository, which contains 4.5 million archival samples accumulated since 1975, to match sample molecular profiles, therapy administered and patient outcomes over a much larger cohort. Related to this, Intermountain seeks to offer pharmacogenomics testing, inherited risk allele testing, and genome services for a wide range of customers. Indeed, its lofty ultimate goal is to become the most genetically advanced healthcare system in the world.



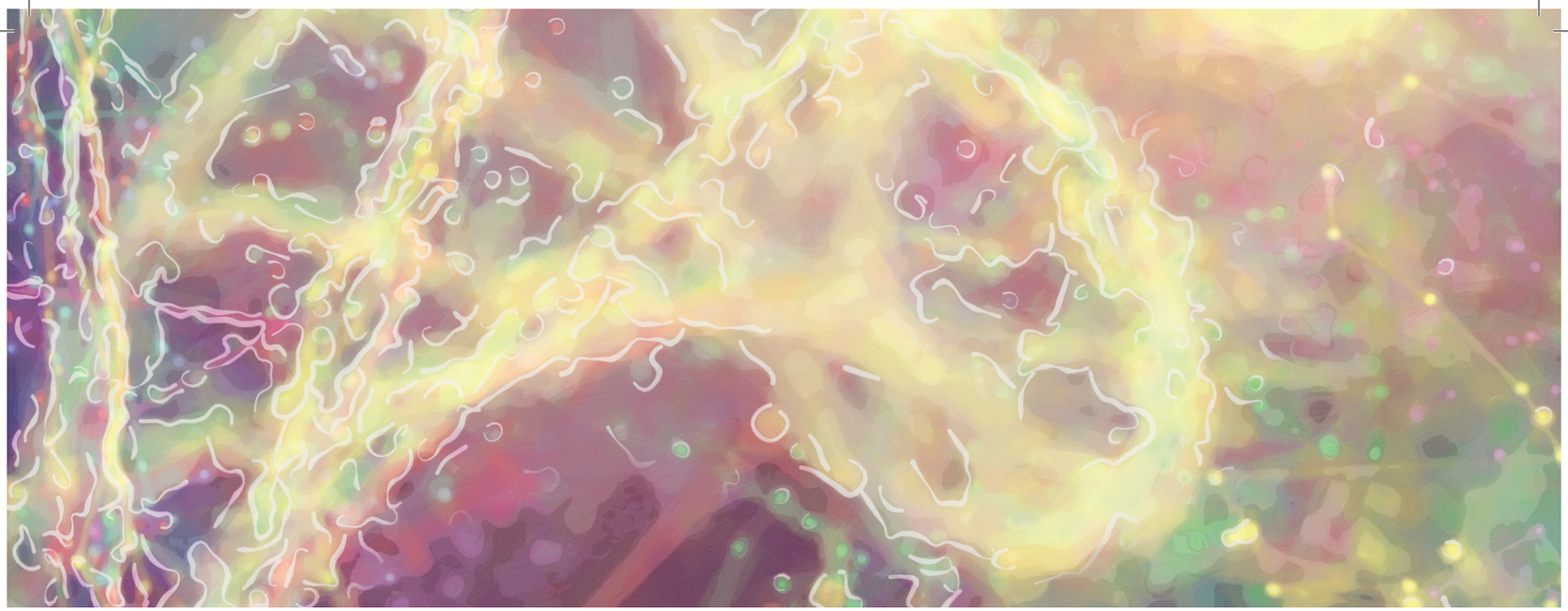
Genomics in practice

Educational breakout session: Communicating with Patients about Cancer Somatic Testing

Genomic testing is a powerful new tool for understanding the molecular drivers and vulnerabilities of tumor cells, but also a complex and unfamiliar technology for most patients. A critical challenge for physicians who order cancer somatic testing is to introduce and explain this new technology to patients in an understandable way. Therefore, a vital part of MCGI is to provide the education necessary to effectively implement all components of precision oncology, including communicating with patients about cancer somatic testing.

This participatory breakout session sought to build confidence for clinicians who are utilizing this new technology within their practices through MCGI. The majority of the session was devoted to role play exercises with professional Standardized Patients, who are specially trained to behave as actual patients would in a clinical setting. Small groups of forum participants engaged in guided discussion of the goals and challenges of communicating about genomic tumor testing. Several participants were paired with a Standardized Patient, and reenacted a physician-patient discussion introducing genomic tumor testing. Participants then engaged in a guided reflection about what they observed, and brainstormed useful communication strategies and practices. Dr. Christian Thomas from New England Cancer Specialists (NECS) capped off the session with a role play involving two Standardized Patients in front of the other attendees.

The goal of the session was to provide clinicians participating in the MCGI with practical feedback and tools they can use with their patients when discussing cancer somatic testing. No one can teach everything about genomic tumor testing within the time frame of a doctor's visit, but effective communication about its nature, value and limitations is imperative for patients to make informed decisions about whether or not to undergo testing.



Implementation breakout session: Implementing Cancer Somatic Testing in Community Oncology Practice

A better title for the forum's final session might have been "What is MCGI Doing Right, What Can Be Improved and Where Do We Go from Here?" The purpose of this session was to explore key stakeholders' perspectives regarding MCGI protocol implementation. Attendees included oncologists, pathologists, genetic counselors, study coordinators and practice administrators at MCGI enrollment sites. Breakout sessions were facilitated by MCGI team members, and participants were encouraged to provide candid feedback from their experiences at their respective organizations. Participants divided into groups to discuss the patient, provider, and organizational perspectives, tumor boards, and future directions. Breakout groups then reported back their discussions, including their "burning questions" that were addressed at the end of the session by a panel of experts. The goals of this session were to provide attendees an opportunity to inform the future direction of MCGI, and to engage stakeholders in a collective discussion about MCGI and genomic tumor profiling in Maine.

The good news is that MCGI is off to a strong start and, even with the rapid growth over the past year, participants are looking for further expansion of testing as well as educational and patient support resources. The tumor boards in particular were unanimously lauded as effective and valuable. Participant suggestions included working more with hospital and healthcare system executives — something that's in the works now that oncologists have been engaged — and developing a Maine base for clinical trial information and enrollment. Also, a key issue moving forward is sustainability, so building future capacity for MCGI is likely to require new funding sources. With the valuable participation of nearly every oncology practice in the state, MCGI has developed a powerful and unique program to improve cancer care throughout Maine. And as cancer research accelerates and new discoveries continue their translation to the clinic, its impact and recognition promises to continue to grow.

About the Maine Cancer Genomics Initiative

The mission of the Maine Cancer Genomics Initiative (MCGI) is to enable widespread access to clinical cancer genomic tests for the Maine oncology community and to increase the understanding of cancer genomics by Maine oncology clinicians.

MCGI is enabled through generous financial support from The Harold Alfond® Foundation and leverages the strengths of key medical and bioscience research institutions in Maine to create an alliance focused on precision cancer diagnostics and treatment.

About The Jackson Laboratory

The Jackson Laboratory (www.jax.org) is an independent, nonprofit biomedical research institution with more than 2,000 employees. Headquartered in Bar Harbor, Maine, it has a National Cancer Institute-designated Cancer Center, a facility in Sacramento, Calif., and a genomic medicine institute in Farmington, Conn. Its mission is to discover precise genomic solutions for disease and empower the global biomedical community in the shared quest to improve human health.

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The Jackson Laboratory

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