THE 2024 MAINE CANCER GENOMICS INITIATIVE FORUM

PORTLAND SHERATON AT SABLE OAKS
SOUTH PORTLAND, MAINE
APRIL 12 - 13, 2024

2024 MCGI FORUM

*presented by The Jackson Laboratory
Leading the search for tomorrow's cures

Day 1: Friday
April 12th, 2024

Scan or click to participate in Q+A

8:00 am to 10:00 am
CONTINENTAL BREAKFAST

9:00 am
REGISTRATION OPEN

10:00 am to 11:30 am — pre-registration required
CRC PRE-CONFERENCE WORKSHOP:
UNDERSTANDING GENOMIC TEST RESULTS FOR CLINICAL RESEARCH STAFF *
Lindsey Kelley, MPH, M.S., CGC | The Jackson Laboratory
Kate Reed, MPH, Sc.M., CGC | The Jackson Laboratory

Welcome

12:00 pm to 12:10 pm
OPENING REMARKS
Jens Rueter, M.D. | The Jackson Laboratory

12:10 pm to 12:30 pm
PATIENT ADVOCACY KEYNOTE:
SURVIVAL OF THE STRATEGIC INCLUDES PATIENT EMPOWERMENT
Terri Conneran, B.Sc. | KRAS Kickers

Session 1: Patient Advocacy
Bárbara Segarra-Vásquez, D.H.Sc. | University of Puerto Rico

12:30 pm to 12:50 pm
PATIENT ADVOCACY GROUPS CAN BE
YOUR PARTNER ON PRECISION MEDICINE
Nikki Martin, M.A. | LUNGevity Foundation

12:50 pm to 1:10 pm
MULTI-DISCIPLINARY RESEARCH IN LI-FRAUMENI SYNDROME:
SPANNING THE SPECTRUM FROM ETIOLOGY TO PREVENTION
Payal Khincha, MBBS, MSHS | National Cancer Institute, NIH

1:10 pm to 1:30 pm
PANEL DISCUSSION: PATIENT ADVOCACY

1:30 pm to 2:00 pm
BREAK

Session 2: New Approaches to Genomic Care
Sarah Sinclair, D.O. | Northern Light Health

2:00 pm to 2:20 pm
DON'T BE DRAMATIC, IT'S ONLY SOMATIC:
BUILDING A SOMATIC TO GERMLINE TESTING PROTOCOL IN ONCOLOGY
Dana Farengo-Clark, M.S., CGC | University of Pennsylvania

2:20 pm to 2:40 pm
CANCER EARLY DETECTION AND MONITORING VIA CFDNA AND CTDNA
Cristian Tomasetti, Ph.D. | City of Hope & TGen

2:40 pm to 3:00 pm
EHRs - PROMISES, PITFALLS, AND
OPPORTUNITIES FOR PRECISION ONCOLOGY CARE AND RESEARCH
Peter Gabriel, M.D., MSE | Penn Medicine

3:00 pm to 3:20 pm
PANEL DISCUSSION: NEW APPROACHES TO GENOMIC CARE

3:20 pm to 3:40 pm
BREAK

*Not all presentations and activities are available to virtual attendees

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Session 3: Emerging Research
Ed Liu, M.D. | The Jackson Laboratory

3:40 pm to 4:00 pm

DISSECTING TUMOR-MICROENVIRONMENT INTERACTIONS AND THEIR ROLE IN THE EVOLUTION OF GLIOBLASTOMA

Frederick Varn, Ph.D. | The Jackson Laboratory

4:00 pm to 4:20 pm

MOLECULAR SUBTYPES OF TRIPLE-NEGATIVE BREAST CANCER AS PREDICTORS OF RESPONSE TO PLATINUM-BASED CHEMOTHERAPY

Francesca Menghi, Ph.D. | The Jackson Laboratory

4:20 pm to 4:40 pm

PANEL DISCUSSION: EMERGING RESEARCH

4:45 pm to 5:30 pm

POSTER HALL

5:30 pm to 7:30 pm

DINNER & RECEPTION

5:45 pm

Keynote Address
PRECISION CANCER MEDICINE: THE FUTURE IS HERE*

Razelle Kurzrock, M.D. | Medical College of Wisconsin

Day 2: Saturday
April 13th, 2024

Scan or click to participate in Q+A

7:00 am to 8:30 am

CONTINENTAL BREAKFAST

Session 4: New Approaches
Leah Graham, Ph.D. | The Jackson Laboratory

8:30 am to 8:50 am

IMMUNOTHERAPY ACROSS CANCER TYPES— EFFECTIVENESS AND ADDRESSING CHALLENGING SITUATIONS

Douglas Johnson, M.D. | Vanderbilt University Medical Center

8:50 am to 9:10 am

SCALING PRECISION ONCOLOGY - IN OR OUT OF REACH?

Benedikt Westphalen, M.D. | CCC Munich

9:10 am to 9:30 am

PANEL DISCUSSION: NEW APPROACHES

9:30 am to 10:30 am

BREAK & HOTEL CHECK-OUT

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Day 2: Saturday

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Session 5: Genomics Across the Continuum from Diagnosis to Treatment

Richard Schilsky, M.D. | University of Chicago

10:30 am to 10:50 am

GLIOMAS AND FAMILIAL RISK- THE GLIOGENE STUDY

Melissa Bondy, Ph.D. | Stanford University

10:50 AM TO 11:10 AM

NOVEL STRATEGIES FOR IMMUNE INTERCEPTION OF CANCERS IN LYNCH SYNDROME

Jason Willis, M.D., Ph.D. | The University of Texas MD Anderson Cancer Center

11:10 AM TO 11:30 AM

THE RATIONALE AND CHALLENGES OF DUAL MAPK PLUS IMMUNOTHERAPY

Ryan Sullivan, M.D. | Mass General Cancer Center

11:30 AM TO 11:50 AM

PANEL DISCUSSION: CLINICAL TRIALS

11:50 AM TO 1:00 PM

LUNCH

Claiming continuing education credits?

Don't forget to complete the post-event evaluation.

Session 6: Genomic Tumor Boards

Johannes Fischer, M.D., MBA | The Jackson Laboratory

Lindsey Kelley, M.P.H., M.S., CGC | The Jackson Laboratory

1:00 PM TO 2:00 PM

GTB PANEL: RESISTANCE MECHANISMS

Kathlene Gravelin, M.S., CGC | Northern Light Health

Todd Knepper, Pharm.D. | Moffitt Cancer Center

Jill Kolesar, Pharm.D. | University of Kentucky

2:00 PM TO 3:00 PM

GTB PANEL: IMPORTANCE OF CLINICAL TRIALS

Kathlene Gravelin, M.S., CGC | Northern Light Health

Richard Schilsky, M.D. | University of Chicago

Christine Walko, Pharm.D. | Moffitt Cancer Center

Session 7: Genomic Medicine in Cancer: The Big Picture

Jens Rueter, M.D. | The Jackson Laboratory

3:00 pm to 3:20 pm

PRECISION ONCOLOGY: MOLECULAR MEDICINE IN PRACTICE

David Thomas, FRACP, Ph.D. | University of New South Wales

3:20 pm to 3:40 pm

PANEL DISCUSSION: GENOMIC MEDICINE IN CANCER: THE BIG PICTURE

*Not all presentations and activities are available to virtual attendees

AMA Designation Statement

The Maine Medical Education Trust designates this enduring activity for a maximum of 10.0 AMA PRA Category 1 Credit(s)™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

Joint Providership Statement

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the Maine Medical Education Trust and The Jackson Laboratory. The Maine Medical Education Trust is accredited by the Maine Medical Association Committee on Continuing Medical Education and Accreditation to provide continuing medical education for physicians.

The National Society of Genetic Counselors (NSGC) has authorized The Jackson Laboratory to offer up to 0.983 CEUs or 9.83 Category 1 contact hours for the activity 2024 MCGI Annual Forum. The American Board of Genetic Counseling (ABGC) will accept CEUs earned at this program for the purposes of genetic counselor recertification.

This nursing continuing professional development activity was approved by the Northeast Multistate Division Education Unit, an accredited approver by the American Nurses Credentialing Center's Commission on Accreditation.

Presented by The Jackson Laboratory
with the support of The Harold Alfond Foundation

MCGI Forum - 2024

The 2024 Maine Cancer Genomics Initiative (MCGI) Forum may have changed venues, but it did not see a change in its weather fortunes. Torrential rains and wind blanketed Portland, hampering the travel plans of some attendees and speakers. Nonetheless, the virtual component worked seamlessly, and a large in-person contingent was still able to gather to discuss past progress, current status, and future plans for MCGI and other precision oncology programs. In his opening remarks, Medical Director Jens Rueter, M.D., noted that MCGI was originally designed as an observational study, and the Forums were an integral part of the study. Indeed, the first Forums dealt in large part with on the need to educate physicians, nurses, other healthcare professionals, and patients about genetic testing, targeted therapies, and potential patient benefits.

Now, in 2024, precision oncology and genome-matched therapies are much more familiar concepts, but there remains a need to expand and improve access to targeted therapies, including those in clinical trials, for patients. Rueter noted that MCGI is making a real difference in both oncology practice and patient outcomes in Maine, and its success has become a model for those seeking to bring precision oncology to community and rural healthcare settings within the U.S. and around the world. But care delivery is always about and for the patients, and it was therefore fitting that the first session of the Forum focused on patient perspectives and the need to engage and include patients in the precision oncology process and care decisions. Other sessions covered new ways to deliver genomic care, emerging research progress, keys to therapy decision making by genomic tumor boards, expanding precision oncology around the world, and more.

Session 1: Patient advocacy
Moderator: Barbara Segarra-Vasquez, D.H.Sc., University of Puerto Rico

Keynote: Terri Conneran, B.Sc., KRAS Kickers
Survival of the strategic includes patient empowerment
Speakers: Nikki Martin, M.A., LUNGevity Foundation
Patient advocacy groups can be your partner on precision medicine
Payal Khincha, MBBS, MSHS, National Cancer Institute
Multi-disciplinary research in Li-Fraumeni syndrome: Spanning the spectrum from etiology to prevention

It seems obvious that the patient is the focal point of all cancer care, but the advent of precision oncology has too often left patients behind. As Terri Conneran noted in her keynote speech to open the Forum, she received genomic testing upon being diagnosed with cancer, but no report from that testing, which had identified a KRAS mutation as a driver of her cancer. Her experience has led her to patient advocacy, emphasizing the importance of patient engagement and education to improve decision making and, ultimately, outcomes. Nikki Martin documented how providers can be reluctant to discuss test results with patients because of their perception of poor patient understanding, so her work with the LUNGevity Foundation focuses on patient education and the use of accessible terminology. Like Conneran, her goal is to reduce confusion and facilitate patient participation in cancer care. Payal Khincha's work at the NIH provides a specific case study, as she partners with patients and families affected by Li-Fraumeni syndrome (LFS), which confers very high lifetime cancer risks. The emotional toll of LFS and the frequent screening required is high, so improving patient wellbeing needs to go beyond physical/clinical care to also address the biobehavioral costs.

Session 2: New approaches to genomic care
Moderator: Sarah Sinclair, D.O., Northern Light Health

Speakers: Dana Farengo-Clark, M.S., CGC, University of Pennsylvania
Don't be dramatic, it's only somatic: Building a somatic to germline testing protocol in oncology
Cristian Tomasetti, Ph.D., City of Hope, TGen
Cancer early detection and monitoring via cfDNA and ctDNA
Peter Gabriel, M.D., MSE, Penn Medicine
EHRs—promises and pitfalls and opportunities for precision oncology care and research

At the same time that effective delivery of precision oncology improves patient care, it stresses healthcare processes and infrastructure. It requires new data formats, coordinated support, additional clinical interpretation and decision making, and more. Dana Farengo-Clark focused on the latter, as somatic tumor testing can indicate the need for subsequent germline testing, but the path from a tumor diagnosis that informs treatment to clinical genetics that informs familial risk is unclear. Penn has developed a clinical dashboard, PreAct, that automates as much of the somatic-to-germline pipeline as possible. Cristian Tomasetti explored the implications of liquid biopsies. Given that less than half of diagnosed cancers are detected by screening, blood-based detection has the potential to greatly improve early detection, though it remains a significant challenge. The monitoring space has progressed rapidly, however, and is guiding therapy with the need for fewer invasive biopsies. Peter Gabriel, also of Penn, revisited the digital space, discussing the current status of EHRs, in which every benefit seems to have a flip side, complicating their potential for assisting with precision oncology. He presented the PennChart Genomics Initiative, intended to make it easier within their Epic system to find data and support clinical decision support across a large cancer center.

Session 3: Emerging research
Moderator: Edison Liu, M.D., The Jackson Laboratory

Speakers: Frederick Varn, Ph.D., The Jackson Laboratory
Dissecting tumor-microenvironment interactions and their role in the evolution of glioblastoma
Francesca Menghi, Ph.D., The Jackson Laboratory
Molecular subtypes of triple-negative breast cancer as predictors of response to platinum-based chemotherapy

Better cancer care delivery depends on a better understanding of cancer's complexity and resistance mechanisms, which can only be provided through basic research. Two Jackson Laboratory researchers presented their latest investigations into two difficult-to-treat cancers, glioblastoma and triple-negative breast cancer. Frederick Varn studies the effects of front-line treatments on the evolution of glioblastoma, a brain cancer known for its high rate of recurrence and lethality. There have been no improvements to the regimen of surgery, radiation and chemotherapy used to treat glioblastoma, but Varn's research shows that it can lead to genetic changes that make certain subtypes more proliferative and aggressive upon recurrence. New therapeutic strategies must therefore restrict the cells' ability to change and adapt and target specific remaining cell states. Francesca Menghi researches why different patients respond differently to platinum-based treatments for homologous recombination deficient triple negative breast cancers. Her studies have

shown the importance of BRCA1 mutation state versus methylation in the initial tumor and the effect it can have on treatment response and the development of therapy resistance.

Keynote address: Razelle Kurzrock, M.D., Medical College of Wisconsin
Precision cancer medicine: The future is here

During her dinnertime keynote address, Razell Kurzrock noted that the light microscope, invented in 1590, is still the tool of choice for diagnosing many cancers. We now have many molecular tests available to improve diagnostics, led by genome sequencing, which Kurzrock argued should be applied universally and early in cancer care to guide care before cancer heterogeneity emerges. Clinical trials are also due for design, as smaller, genetic mutation- or defect-based clinical trials will speed the development of new targeted therapies. And for metastatic cancers, which are highly individual to each patients, an N-of-1 clinical trial design, using multi-omic interrogation and personalized combination therapies, provides a new paradigm for developing more effective treatment strategies. Kurzrock's current work is focused on proving the value of these approaches and implementing them in the clinic.

Session 4: New approaches
Moderator: Leah Graham, Ph.D., The Jackson Laboratory

Speakers: Douglas Johnson, M.D., Vanderbilt University Medical Center
Immunotherapy across cancer types—effectiveness and addressing challenging situations
Benedikt Westphalen, M.D., CCC Munich
Scaling precision oncology—in or out of reach?

In the Forum's second session on new approaches, the speakers touched upon different aspects of the road to progress. Douglas Johnson focused on immunotherapies, the use of which is being refined after the initial burst of eye-catching success but also, at times, frustratingly low response rates. Anti-PD-1/PD-L1 therapies alone have now been approved for use in about 20 different cancers, but it remains difficult to distinguish potential responders from non-responders up front. One distinguishing feature that may be used to help tailor immunotherapies is mismatch repair proficient versus deficient cancers, as mismatch repair deficient tumors "look" much more different to the immune system compared with normal tissues. Benedikt Westphalen looked at precision oncology from a wider scope, with a focus on optimizing delivery of genome-matched care. He cited a scenario in which, out of 400 patients with a targetable mutation, only 120 actually receive a matched drug and less than a quarter of those actually respond. The situation needs to improve, and fulfilling the promise of precision oncology depends on wide and equal patient access to diagnostic technology and therapeutics. Employing an integrated care approach that doesn't divide diagnostic testing from treatment planning and execution will help.

Session 5: Genomics across the continuum from diagnosis to treatment
Moderator: Jens Rueter, M.D., The Jackson Laboratory

Speakers: Melissa Bondy, Ph.D., Stanford University
Gliomas and familial risk—the Gliogene study
Jason Willis, M.D., Ph.D., The University of Texas MD Anderson Cancer Center
Novel strategies for immune interception of cancers in Lynch syndrome

Ryan Sullivan, M.D., Mass General Cancer Center
The rationale and challenges of dual MAPK plus immunotherapy

Speakers addressed the importance of specific genomic attributes and how they can affect care for various cancers. Melissa Bondy returned to glioma, noting that while radiation exposure is the best-known risk factor, a genetic predisposition has been found in about 5% of families. A large international consortium is studying the genes implicated in "familial" glioma development and, while a lot of work remains, the research has identified two genes in particular—POT1 and HERC2—that may be involved with gliomagenesis. Jason Willis discussed Lynch syndrome (LS), caused by autosomal dominant germline mutations in mismatch repair (MMR) pathway genes. Given that patients with Lynch syndrome have an extremely high risk for colorectal and other cancers, preventative measures are of particular importance. Research has identified shared neoantigens that represent compelling targets for vaccine development that works at the pre-cancerous stage for immune interception and prevention of LS-related cancers. Ryan Sullivan presented on how to combine immunotherapies with BRAF targeted therapies in BRAF-mutant melanoma. The work is ongoing, but finding the right synergy between MAPK targeting and PD1/PDL1 checkpoint blockade may provide a key. There is the need to reduce side effects and long-term benefits were inconsistent, but everyone had tumor regression up front, so further trials hold promise.

Session 6: Genomic tumor boards: Resistance mechanisms
Moderator: Johannes Fischer, M.D., MBA, The Jackson Laboratory

Panelists: Kathlene Gravelin,M.S., CGDC, Northern Light Health
Todd Knepper, Pharm.D., Moffitt Cancer Center
Jill Kolesar, Pharm.D., University of Kentucky

To shed light on the types of data received by genomic tumor boards and the decision pathways they must navigate, two specific cases of recurrent cancers were presented and discussed, as well as input received from the Forum audience. The cases highlighted treatment resistance mechanisms, whether primary (mediated by factors present before therapy) or acquired (developed after receiving therapy). The cases presented and discussed involved an older male treated for colon cancer with a p53 mutation who acquired resistance and a middle-aged female treated for non-small cell lung cancer with an ALK fusion, for which there are targeted therapies but that frequently lead to treatment resistant metastases.

Session 7: Genomic medicine in cancer: The big picture
Moderator: Jens Rueter, M.D., The Jackson Laboratory

Speaker: David Thomas, FRACP, Ph.D., University of South Wales, Omico
Precision oncology: Molecular medicine in practice

Discussion:
Panelists: Barbara Segarra-Vasquez
Ryan Sullivan
Razelle Kurzrock
Benedikt Westphalen

The final session of the Forum provided a truly international look at the current state of precision oncology delivery, as well as the challenges that remain. Jens Rueter began by proposing MCGI as a paradigm for the future, providing comprehensive biomarker testing for all patients, leading to genomic tumor board review and a structured therapy decision tree. David Thomas presented his work in providing precision oncology care throughout Australia, beginning with a regional program to deliver molecular programming in 2011 to nationalizing the program in 2019 by establishing Omico as an independent, not-for-profit organization, to today's goal of establishing Australia globally as a premier hub for cancer research and precision oncology practice through a modernized national healthcare system. Of particular importance is attracting clinical trials, build capacity and train the workforce for clinical trial delivery, and integrate precision oncology into routine care models throughout the continent, including rural areas.

During the closing panel discussion, each of the panelists provided their closing thoughts and future goals.

Barbara Segarra-Vasquez: As patients traverse their oncology journey, they don't have enough time to learn everything they have to learn, so they should be partners with their healthcare providers through the journey. The situation is improving, as patient advocates are now invited to many cancer meetings, but that's a new development. Oncologists and other caregivers have to be realistic when talking with patients, but patients want quality of life to be part of their equation, so it's important to have that as a consideration when establishing priorities and making care decisions.

Ryan Sullivan: It's important to provide broader access to clinical trials. The ability to get novel, promising agents out to communities not connected with large academic medical centers is a critical piece of infrastructure that's still missing. The initial trial stages are difficult to roll out too far, as they can be very intense, with the need to constantly monitor for toxicity and side effects, but later stages assessing efficacy can access other populations and be spread farther to community sites that have the proper support.

Razelle Kurzrock: The N of 1 therapy strategy fits well within the context of all of the precision oncology components discussed at the forum: genomic tumor boards, platform trials, etc. In the future, every patient with cancer needs tumor sequencing as a standard of care, and the treatment strategy has to be individualized, with customized drug combinations. The system also needs to move to treat earlier disease, beginning treatment at the time of diagnosis before the tumors have had the ability to evolve.

Benedikt Westphalen: Precision oncology has a bright future, with all the pieces of the puzzle in hand. The Forum has covered a lot of those pieces—KRAS changing from undruggable to targetable, the development of public-private partnerships in Australia, the N of 1 paradigm discussed by Dr. Kurzrock, and more. Now we have to take the pieces and build the proper care infrastructure within each area to deliver the best care possible with available technology. The Forum shows us that it's doable if people work together to overcome the obstacles.