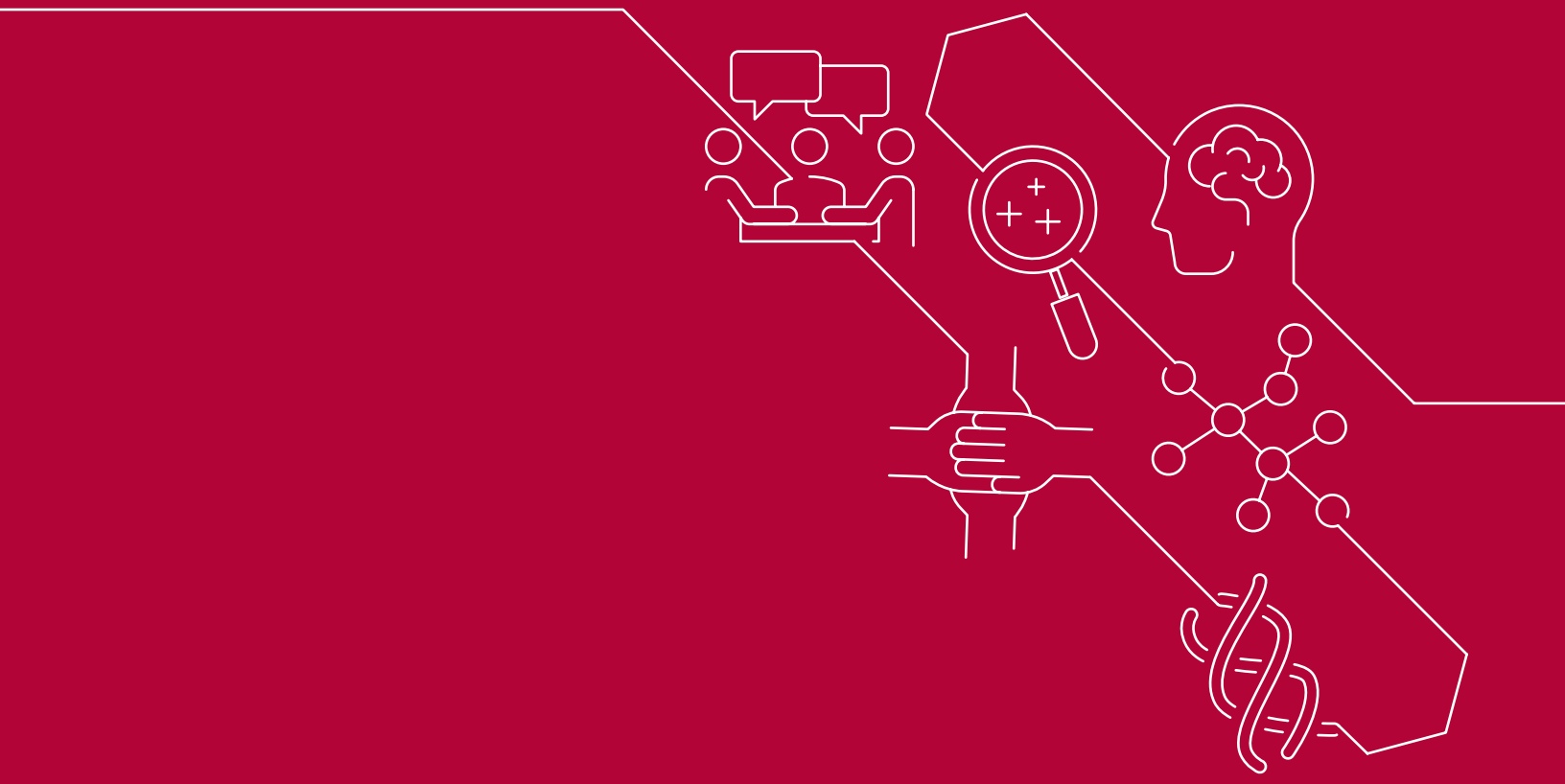
2022

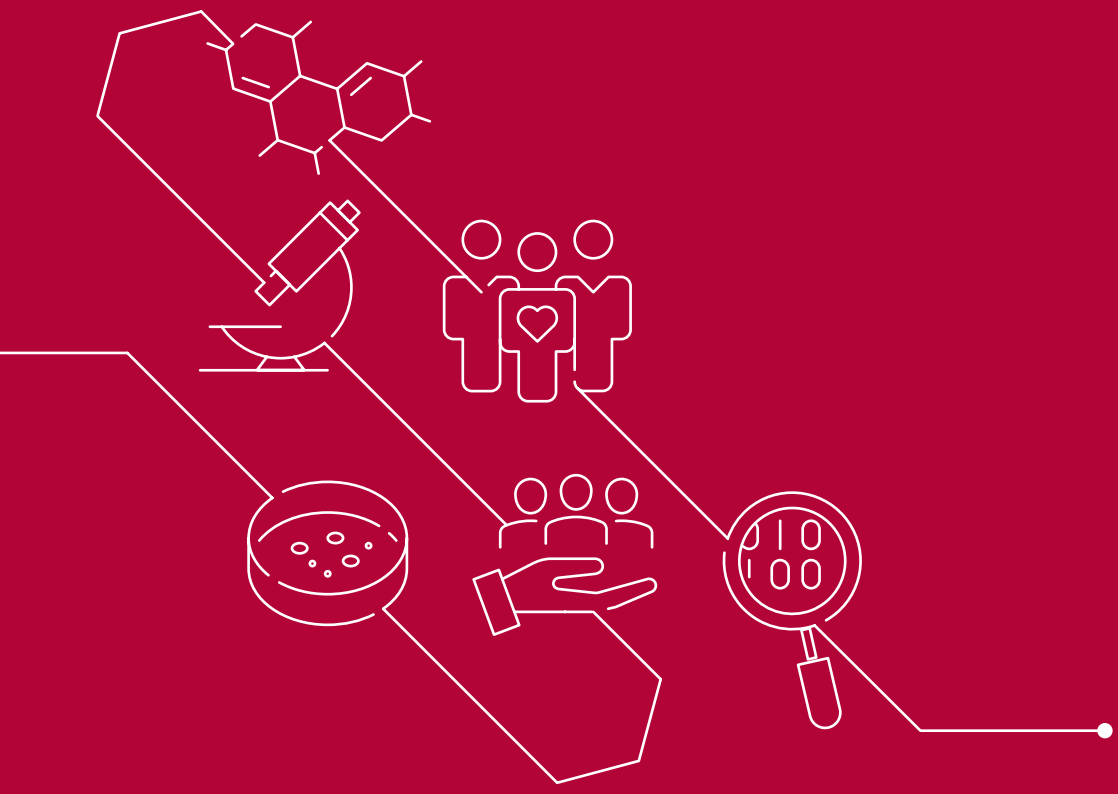
MaineHealth Institute for Research: 2022 Year in Review

MaineHealth Institute for Research



MAINEHEALTH INSTITUTE FOR RESEARCH

2022 YEAR IN REVIEW



MaineHealth

MAINEHEALTH INSTITUTE FOR RESEARCH RESOURCES

For physicians and staff throughout the MaineHealth system, please contact the following staff for information and assistance if you are interested in research projects:

RESEARCH GRANT PROPOSALS:
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NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK
for more information visit:
med.uvm.edu/nne-ctr

Academic Affairs

EDUCATION – INNOVATION – RESEARCH

The division of Academic Affairs leads MaineHealth's medical education, innovation and research efforts to empower the healthcare and scientific workforce of tomorrow, pioneer better ways to care for our patients and communities, and position MaineHealth as a nationally recognized leading academic medical system and biomedical hub.

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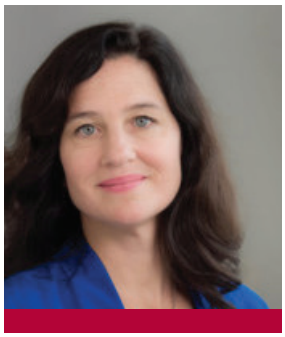
MESSAGE FROM THE DIRECTOR



DEAR COLLEAGUES AND SUPPORTERS,

In the past year we have launched many exciting new initiatives and recruited several new leaders to the Research Institute. One major institutional initiative was transitioning to our new name, MaineHealth Institute for Research and updating our vision and mission. This transition occurred in the spring of 2022 and better communicates what we do: provide services for all in MaineHealth who wish to conduct research, including applying for funding, learning how to do rigorous research, addressing compliance issues and conducting studies.

We have added two new Centers to the institute — the Center for Applied Science and Technology and the Center for Clinical and Translational Science — and changed the name of the Center for Outcomes Research and Evaluation to the Center for Interdisciplinary Population & Health Research (see Centers inset below for details). And we welcomed new leaders: Tammy Myers, CCRP, Kevin Stein, PhD, FAPOS and Adriana Rosato, PhD, who all bring fresh ideas and vision for expanding our research (see New Leaders inset below for details).

CENTERS

CENTER FOR INTERDISCIPLINARY POPULATION & HEALTH RESEARCH (CIPHR)

This research Center changed its name to accurately reflect the research work taking place. CIPHR initiates and evaluates interventions to improve health care quality and safety. CIPHR provides such services as biostatistics, bioinformatics, epidemiology, qualitative research, community-based participatory research and rural health disparities research.

mhir.org/cipher

Director: Kevin Stein, PhD, FAPOS

CENTER FOR APPLIED SCIENCE & TECHNOLOGY (CAST)

This new Center provides the infrastructure that enables the coordinated integration of the research institute's laboratory and clinical/data resources with NorDx clinical instrumentation, data resources and support services. In addition, CAST incorporates emerging technologies and new testing modalities into clinical diagnostics for improved patient care and outcomes.

mhir.org/cast

Directors: Anne Breggia, PhD & Bob Carlson, MD

CENTER FOR CLINICAL & TRANSLATIONAL SCIENCE (CCTS)

This new Center is a multi-disciplinary scientific community linking basic, clinical and translational investigators to collaborate on research across the translational research spectrum. CCTS provides an environment for translational research to flourish by providing research training, education, guidance and mentorship to new translational investigators as well as research support and services such as informatics, team science, data science support and research navigation services.

mhir.org/ccts

Director: Susan Santangelo, ScD

THE CENTER FOR MOLECULAR MEDICINE continues as our premier, nationally-recognized basic science center performing cutting-edge biomedical research to discover the molecular mechanisms of human disease.

mhir.org/cmm *Director: Adriana Rosato, PhD*

Notably this year, the NIH awarded a renewal of our Northern New England Clinical & Translational Research Network in collaboration with the University of Vermont (NNE-CTR, see story on page 10). With resources and support from NNE-CTR and the Center of Biomedical Research Excellence (COBRE) in Acute Care Research and Rural Disparities, we are able to continue to expand our ability to collaboratively engage communities and community members to learn about their priority health issues as well as get feedback and involvement in our research.

These new changes, along with all the incredible research happening at the institute and beyond, inspire me for the future of research at MaineHealth. Please enjoy the work highlighted in our 2022 Year in Review — it is a small snapshot of our staff and the tremendous research they are conducting.

Sincerely,

ELIZABETH A. JACOBS, MD, MPP
Vice President for Research, MaineHealth
Director, MaineHealth Institute for Research

NEW LEADERS

TAMMY MYERS, CCRP
Director, Clinical Trials Office

Ms. Myers is a seasoned academic and industry leader with over 20 years' experience with clinical research program development in HIV/Infectious Disease, Anesthesiology, Orthopedics, Ophthalmology and Oncology. Ms. Myers is adept at multiple aspects of clinical operations (Phase I to IV) including infrastructure development, motivational leadership, support of proprietary platforms, investigator-initiated studies, protocol development and planning and protocol launch. She comes to MaineHealth from The Emmes Company where she was Global Head of Monitoring.

KEVIN STEIN, PHD, FAPO
Director, Center for Interdisciplinary Population & Health Research

Dr. Stein is a behavioral scientist, clinical psychologist and public health executive with more than 25 years of experience in non-profit, health care and higher education sectors. Dr. Stein comes to MaineHealth from the Wellstar Health System in Atlanta, GA, where he served as a clinical health psychologist, coordinated the Psychosocial Oncology Program and provided supportive care to cancer patients treated at the 11 Wellstar Health System hospitals across the state of Georgia.

ADRIANA ROSATO, PHD
Director, Center for Molecular Medicine

Dr. Rosato comes to MaineHealth from the Riverside University Health System and University of California where she served as the Executive Director of Molecular Microbiology and Research. Dr. Rosato is an experienced, nationally and internationally-recognized clinical, basic microbiologist/molecular biologist scientist with special interests in the area of infectious diseases, antimicrobial development and antimicrobial resistance.

NOTABLES

AWARDS

Heather Fairfield Campbell, MS

Heather Fairfield Campbell, Scientific Manager in the Reagan Lab, was awarded a National Cancer Institute Research Specialist Award, also known as a R50. The R50 encourages the development of stable research career opportunities for exceptional scientists who want to pursue research within the context of an existing cancer research program, but not serve as independent investigators. Heather's project is funded for five years and will focus on defining the roles of bone marrow adipocytes (fat cells) and FABP4/5 signaling (fatty acid-binding proteins) in multiple myeloma. Multiple myeloma (MM) is a blood cancer that grows predominantly within the bone marrow. Projects like Ms. Campbell's could lead to a greater understanding of new forms of cancer drug resistance that are driven by fat cell-derived factors.

Alexandra Hinton, MPH

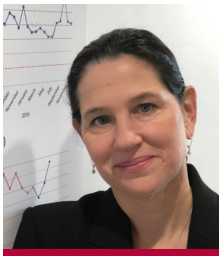
Alexandra Hinton, Research Data Analyst III, was awarded the Statistical Expertise and Network Award from the Cystic Fibrosis Foundation. The purpose of the Cystic Fibrosis Statistical Expertise and Network (CF StatNet) Award is to integrate local statisticians into CF research teams at nearby Therapeutics Development Network sites, like Maine Medical Center (MMC). The three year award will fund collaborative research done by Ms. Hinton and CF clinical investigator, Dr. Jonathan Zuckerman.

Volkhard Lindner, MD, PhD

Volkhard Lindner, MD, PhD, Faculty Scientist, is a Multiple Principal Investigator on an NIH grant awarded to the Medical College of Wisconsin entitled: "Delineating the mechanisms underlying heart valve endothelial repair." Dr. Lindner and his colleagues at Wisconsin, the Jackson Laboratory and Cincinnati Children's Hospital will explore the potential of developing new therapeutic approaches in the treatment of heart valve disease based on promoting intrinsic mechanisms of self-repair.

Matthew Siigel, MD

Matthew Siegel, MD, VP of Medical Affairs for Autism and Developmental Disorders and MHIR Faculty Scientist, was awarded a $2.3 million, 3 year research grant from the Simons Foundation to support Phase IV of his Autism Inpatient Collaborative (the national research network of inpatient autism units, founded by Spring Harbor in 2013). This work is to develop a database and biobank of phenotyping, biosamples and genetic sequencing of over 1700 people with autism, with a particular focus on those severely affected by the disorder, which will then be accessible to investigators worldwide. It is a unique effort, seeking to provide rich data on an understudied group and places MaineHealth as the originator of what will likely be an enduring resource contributing to autism research for years to come.



Elizabeth Jacobs, MD, MPP

Lisbeth Wierda, MPH

Elizabeth Jacobs, MD, MPP, is the Principal Investigator on a two-year, $250,000 award from the Patient-Centered Outcomes Research Institute (PCORI) to build capacity for research dissemination and translation into practice. Dr. Jacobs and co-project lead **Lisbeth Wierda, MPH, Research Program Director,** aim to create a robust, sustainable infrastructure for disseminating evidence from PCOR/CER (patient-centered outcomes research/ comparative effectiveness research) studies to organizations and leaders that can use this evidence to address the needs of patients and communities in rural Maine. The research team will use the funding to address these barriers by building infrastructure through such activities as forming a Research Dissemination Advisory Panel to guide the development and dissemination of materials, creating a publicly-accessible repository of PCOR/CER and hosting learning events. The goal is to reduce rural health disparities by reducing the time to implementation of evidence-based interventions.

IN THE NEWS

Study Finds Another Condition That Vitamin D Pills Do Not Help

The vitamin pills do not prevent bone fractures in most people or protect against many other diseases, adding to questions about medical guidance many now take for granted.

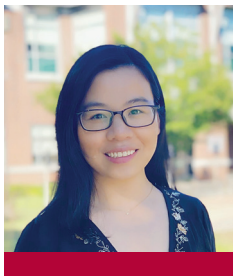
Give this article

Senior Scientist Cliff Rosen, MD, was one of the experts interviewed by the New York Times in July to discuss the current research on vitamin D pills preventing bone fractures. The study of nearly 26,000 people who were assigned to take vitamin D each day found the vitamin had no effect, even among people who had low vitamin D levels or osteoporosis.

National Geographic interviewed **Robert Smith, MD, MPH, infectious disease physician and Director of the Vector-Borne Disease Lab,** for an article in July. Dr. Smith weighed in on why tick-borne diseases have increased in the past 15 years. Some of the reasons include ticks expanding their range due to changing climate which facilitates their spread, while expanding suburbs provide ideal habitat for white-footed mice — their main disease reservoir — and deer, a key host.

NOTABLES CONTINUED...

NEW FACULTY

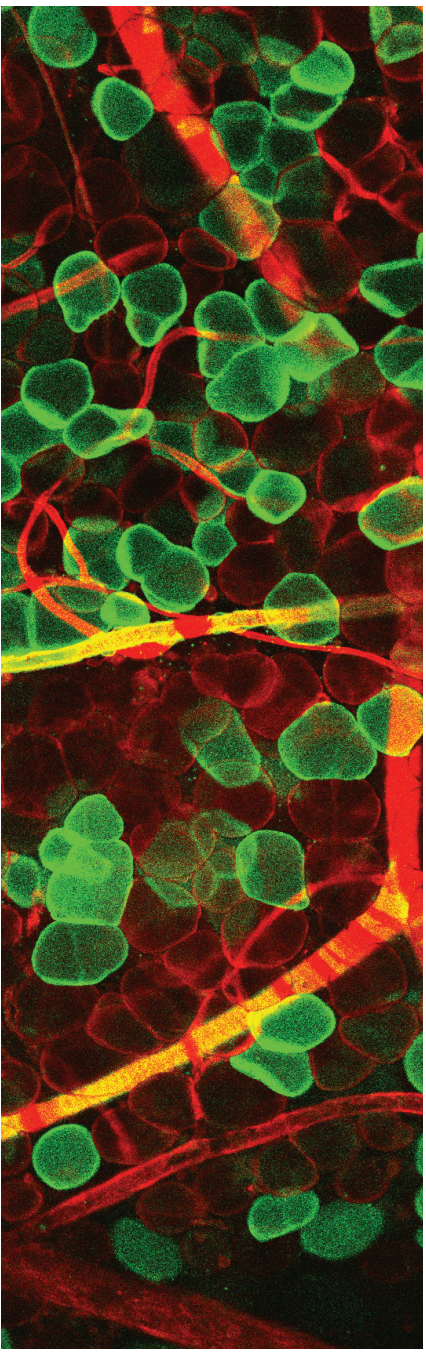


Ziru Li, PhD, joined the Center for Molecular Medicine as a new Faculty Scientist I. Dr. Li did her PhD training at Peking University in Beijing, China and went to the University of Michigan for postdoctoral training. She has led high impact and innovative research in the areas of lipolysis of bone marrow adipocytes, interactions of marrow adipocytes with bone cells, signaling from gastric endocrine cells and effects of bariatric surgery on bone. Dr. Li will be focusing on gut regulation of glucose and lipid metabolism and bone homeostasis.

Roberto Rosato, PhD, has joined the Center for Molecular Medicine as a Faculty Scientist II. Dr. Rosato comes to MaineHealth from the Methodist Hospital System and has a career encompassing more than 20 years of experience and knowledge related to the field of cancer biology and therapeutics, focusing on blood related and solid tumor diseases. Dr. Rosato has been actively involved in all facets of laboratory procedures including modulation of immunotherapeutics and identification of new therapies and mechanisms associated to drug efficacy.

INSTITUTIONAL WORK ON DIVERSITY, EQUITY AND INCLUSION

The MHIR Diversity, Equity and Inclusion Workgroup, formed in 2020, continues to be committed to creating an informed, equitable and inclusive environment for scientific staff and collaborators. Co-chaired by Liz Scharnetzki, PhD (Staff Scientist) and Cole Ferm (Research Program Manager), the group meets monthly to discuss how diversity, equity, inclusion and justice impact the biomedical and health service research questions we ask and the spaces we occupy. In 2022, the workgroup had several national experts join their sessions, including Dr. Myron Beasley, PhD, who spoke about the integral role that food plays in our identity and culture and food stigma and Dr. Tessa Dover, PhD, who spoke about how organizational diversity initiatives may be perceived differently by members of socially advantaged and disadvantaged groups. The workgroup also co-sponsored several interactive workshops, including Strategies for Effective Allyship with Allura Casanova, MS and The History and Contemporary Reality of Black Communities in Maine and Race as a Social Construct in Data and Practice (a two-part series hosted in partnership with Maine Public Health Association, University of Maine Augusta and the New England Public Health Training Center).



ADVANCING PRECISION MEDICINE

The Precision Medicine Council was formed in January 2021 and consists of 13 health care professionals representing a variety of clinical and research areas at MaineHealth. The Council is led by Anne Breggia, PhD, Director of the Center for Applied Science and Technology and is tasked with providing the infrastructure and resources to working groups in five disease areas that were initially identified as having the most potential for advancement of precision medicine initiatives. The working groups, which bring together interdisciplinary teams of physicians and scientists across oncology, cardiology, neurology, pediatrics and benign hematology have initiated and executed many projects focused on improving patient health and outcomes.

2022 HIGHLIGHTS INCLUDE:

- Identifying and partnering with Tempus (Chicago, IL) as a preferred provider for streamlined genetic test ordering and results reporting;
- Instituting a simplified process for lung cancer test ordering;
- Conducting an in depth analysis of molecular testing options for indeterminate thyroid nodules leading to better patient care, significant cost savings and a clinical decision support white paper;
- In collaboration with the Roux Institute, piloting a project designed to launch a nascent digital pathology program at MaineHealth;
- Exploring new software to efficiently match and enroll patients into appropriate clinical trials and recommend appropriate treatment options based on past and present medical history;
- Investigating next generation technology in digital slide imaging for improved diagnostics.

The Precision Medicine Council also welcomed the new Environmental and Lifestyle Factor working group led by Dr. Kevin Stein, Director of the Center for Interdisciplinary Population Health. The Council looks forward to ongoing efforts over the coming year in this vital diagnostic and therapeutic space.

FACTS & FIGURES

2022 LEADERSHIP

EXECUTIVE ADMINISTRATION

Elizabeth Jacobs, MD, MPP
Vice President for Research, MaineHealth
Director, MaineHealth Institute for Research

Kneka Smith, EdD, MPH
Vice President of Operations, Academic Affairs

RESEARCH CENTER LEADERSHIP

Robert Koza, PhD
Interim Director
(September 2021– 2022)

Adriana Rosato, PhD
Director, Center for Molecular Medicine (current)

Kevin Stein, PhD, FAPOS
Director, Center for Interdisciplinary Population & Health Research

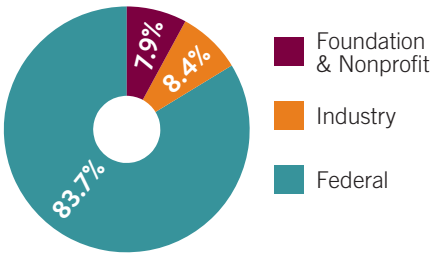
Susan Santangelo, ScD
Director, Center for Clinical and Translational Science

Anne Breggia, PhD
Center for Applied Science and Technology

BY THE NUMBERS

285	Staff Members
$20.6M	Total 2022 Grant Funds
39	New Grants Awarded
250+	Clinical Trial Studies
ONCOLOGY, NEUROLOGY & CARDIOLOGY	Top 3 Clinical Research Areas
275	Scientific Publications
3751+	Biospecimens distributed by the BioBank Tissue Repository, a division of the Center for Applied Science & Technology
12	Core Facilities with State-of-the-Art Equipment
1,000+	COVID positive RNA Samples provided from the Center for Applied Science & Technology in support of NIH N3C Study
129	Learners & Trainees in MHIR's Education & Training Program

2022 SOURCES OF SPONSORED RESEARCH SUPPORT BY SPONSOR TYPE



MaineHealth makes research a priority and also has generously provided support to MHIR's operating budget.
2022 MH Operating Subsidy $10.9 M

2022 INSTITUTE HIGHLIGHTS

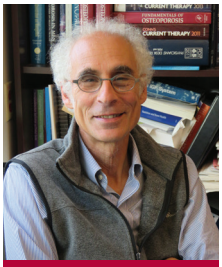
CLINICAL & TRANSLATIONAL RESEARCH

$20 MILLION GRANT FROM NIH SUPPORTS CONTINUED SUCCESS OF NNE-CTR

In August 2022, the NIH announced a five-year, $20 million research grant to the MaineHealth Institute for Research (MHIR) and its partnering institutions, the University of Vermont and the University of Southern Maine, to continue and expand the transformative work of the Northern New England Clinical and Translational Research Network (NNE-CTR) in improving community health through biomedical research in rural New England.

The NNE-CTR was established five years ago to give researchers in rural and underserved communities the tools they need to develop and implement innovative medical treatments for chronic diseases common in Northern New England, such as cancer, heart disease, obesity, diabetes, Alzheimer's disease and substance use disorder. Principal Investigators Cliff Rosen, MD, Associate Director of the Center for Clinical and Translational Science at MHIR and Gary Stein, PhD, Chair of the Department of Biochemistry at the Larner College of Medicine at the University of Vermont, established a set of research cores to support clinical and translational research in Northern New England, with one focus being the engagement of rural providers and practices in research. Some of the pilot projects that researchers developed, such as using telemedicine to quickly identify newborns at rural hospitals who need emergency treatment with therapeutic hypothermia, have now become standards of care in Maine.

Once the COVID-19 pandemic became a threat to health throughout the region, the NNE-CTR also supported the NIH-funded RECOVER study of long COVID, a study of COVID-19 vaccine hesitancy, as well as the National COVID Cohort Collaborative registry that shares clinical data as a part of national COVID research.



Cliff Rosen, MD
Principal Investigator of NNE-CTR

"In just a few years, we are seeing the impact that access to clinical research has on rural communities," Dr. Rosen said. "This new grant will help us build on this success and do more to address health equity and disparities encountered by at-risk populations."

Funding from the new grant will allow the NNE-CTR to invest in professional development for young researchers, new pilot programs to develop innovative disease treatments, community engagement throughout Northern New England and improved data collection and research navigation capabilities. The NNE-CTR also is focused on ensuring that the research reflects Northern New England's diversity in race, gender and socioeconomics.

NORTHERN NEW ENGLAND
CLINICAL & TRANSLATIONAL
RESEARCH NETWORK

For more information on the NNE-CTR:
med.uvm.edu/nne-ctr

RECOVER: RESEARCHING LONG-TERM EFFECTS OF COVID-19

In November 2021, MaineHealth (MH) received approximately $1.5 million from the National Institutes of Health (NIH) for up to four years to participate in a nationwide study of the long-term effects of COVID-19. Researchers from MaineHealth Institute for Research (MHIR) are among those at more than 70 institutions across the country participating in the NIH Researching COVID to Enhance Recovery (RECOVER) Initiative. MH opened RECOVER in December 2021 and this observational study met its initial target of 85 participants across the MH service area in September 2022 (nationwide enrollment goal is 17,000). MH increased its target to 142 and is continuing to enroll participants. The study is particularly interested in participants with a recent (less than 30 days) COVID-19 diagnosis. The MH research team noted high interest in the study from the public and is planning to follow the participants for a maximum of 4 years.

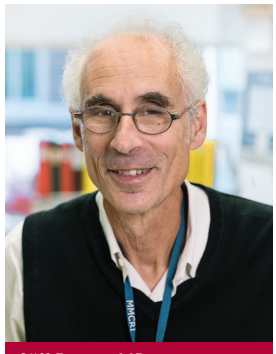
Ivette Emery, PhD

"While it's clear that many patients continue to suffer COVID symptoms for months after recovery, we still don't know why," said Ivette Emery, PhD, translational scientist at MHIR and Co-Investigator for the MH RECOVER site. "This study hopes to answer that question and find some ways to bring relief to those experiencing long COVID."

While the RECOVER study is an observational study, the NIH is in the midst of deploying several treatment studies, as well as additional observational studies that focus on the pathobiology of COVID. MaineHealth is poised to participate in all of these and has begun the planning phase for launching three studies in early 2023.

"I am excited about these upcoming treatment studies," said Cliff Rosen, MD, Senior Faculty Scientist at MHIR and Principal Investigator for the MH RECOVER study. "Together with researchers across the country, we hope to make a significant contribution to the science of how those suffering from Long COVID can get their lives back."

For more information about RECOVER:
recovercovid.org



Cliff Rosen, MD

DATA PLATFORM CONTINUES TO EXPAND COVID RESEARCH ON NATIONAL SCALE

The National COVID Cohort Collaborative (N3C) was created in September 2020 in response to the COVID-19 pandemic. It is a data analytics platform for research on the largest repository of COVID-19 clinical data in the world. Susan L. Santangelo, Director of the Center for Clinical and Translational Science at MHIR, is the Principal Investigator for N3C at MaineHealth (MH). In 2022 MH received additional funding for N3C as well as continuing its participation in an innovative process of linking N3C data with additional datasets, including data on COVID-19 genetic variants. The process, which preserves patient privacy, significantly expands the research potential into exciting new avenues. MH has partnered with NorDx and the Jackson Laboratory in this research analytics work. N3C will ultimately contribute to better management and treatment of COVID-19.

N3C is funded by the National Institutes of Health.

National COVID Cohort Collaborative

For more information:
covid.cd2h.org

RESEARCH TEAM TO STUDY BRINGING REMOTE DIABETES CARE TO RURAL MAINE

In Maine, only 21 endocrinologists are available to serve the 114,000 adults who live with diabetes statewide. As a result, endocrinologists have the capacity to see just 10 percent of the total diabetes population. The vast majority of patients with diabetes therefore receive care through primary care physicians, who would benefit from guidance and advice for supporting and treating patients with devices and on complex treatment regimens.


Irwin Brodsky, MD

Sparked by a connection made by MaineHealth Chief Information Officer, Dr. Dan Nigrin, clinical leaders from Maine Medical Partners Endocrinology & Diabetes Center and MaineHealth Innovation collaborated on a grant to address this need in rural Maine. In December 2021, Kiran Gujral, MD and Irwin Brodsky, MD received a $2.2M from The Leona M. and Harry B. Helmsley Charitable Trust to study how making state-of-the-art diabetes management accessible through virtual platforms impacts the care of people with diabetes who live in rural regions with a scarcity of endocrinology specialists.

Drs. Brodsky and Gujral and their team outlined a novel clinical intervention using DreaMed Diabetes, an AI technology, for optimizing the care of insulin-requiring diabetic patients in rural communities. The grant, which is for 3 years, will be used to create The MaineHealth Virtual Diabetes Clinic (MVDC), a collaborative partnership among subspecialists in endocrinology and diabetes and primary care clinicians that employs state-of-the-art diabetes management technology. The goal of the MVDC is to establish a novel collaborative clinical model for managing insulin therapy in people with diabetes living in rural communities and to study how continuous glucose monitoring technology and an artificial intelligence driven decision tool (DreaMed Advisor®) changes clinically relevant diabetes outcomes.

> There are many studies that show the benefit of continuous glucose monitoring data to support care, but almost all have been done with insulin pump patients and endocrinology specialists. This will be one of the first opportunities to explore potential benefits in primary care, where the vast majority of patients with diabetes receive care.
>
> **– IRWIN BRODSKY, MD**
> *Principal Investigator*

CLINICAL RESEARCH AT PEN BAY MEDICAL CENTER

Research is occurring across the MaineHealth system and one example is at Pen Bay Medical Center's (PBMC) Clinical Research Department, where curiosity and innovative thinking have been an integral part of their success and growth. Caroline Knight, RN, BSN, CCRP, has had a career of 30 years in research at various places across the United States. When she came to PBMC in 2008 there wasn't a coordinated research effort or formal research department. Today she and Stacia Kozidis, MSOTL/R are a team led by Rob Stein, MD, Pen Bay Neurologist and the Medical Director of Clinical Research at PBMC.

Caroline Knight, RN, BSN, CCRP and Dr. Howe with robotic pets.

The breadth of research which has taken place at Pen Bay spans clinical trials in cardiology, oncology, nephrology and neurology, as well as device trials, registries studies and retrospective chart reviews.

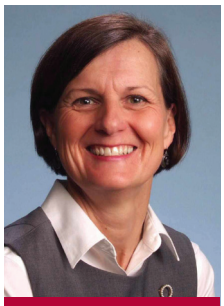
When asked about the model for research at Pen Bay, Ms. Knight responded, "We never say no. When a staff member comes to our department with an idea, we ask how we can help accomplish this." That curiosity helps staff overcome barriers and showcases a unique characteristic of the department. For example, due to the size of PBMC and limited resources, PBMC research coordinators are centralized — not spread out over departments. This has helped to streamline the research process and create greater efficiencies.

A recent pilot study at PBMC demonstrates a distinctive approach to an unmet need. Dr. Barry Howe, PBMC hospitalist, is testing if robotic pets can alleviate delirium in hospitalized patients. Delirium is a temporary state and can cause serious disturbance in mental abilities that results in confused thinking and reduced awareness of surroundings. Dr. Howe had seen success with this technique in a VA hospital where he worked previously. The study goal is to determine if the pet can reduce the time patients are sedated, length of stay and time needed for a person to supervise the patient. If this pilot is successful, the results will be used to apply for additional funding to broaden the study to include other locations.

According to Dr. Stein, "There's a broad spectrum of research at Pen Bay and throughout MaineHealth — it's exciting to see the growth in research throughout the MaineHealth system as we work to improve the health of the people of Maine and beyond."

CANCER TRIALS OPEN NEW DOORS FOR TREATMENT

ADDRESSING BARRIERS FOR RURAL COMMUNITIES TO PARTICIPATE IN CANCER MOONSHOT BIOBANK & PRECISION ONCOLOGY TRIALS


Susan Miesfeldt, MD


Neil Korsen, MD

Susan Miesfeldt, MD is the lead investigator on a study looking at the barriers to rural and socioeconomically disadvantaged cancer patients participating in Cancer Moonshot Biobank (CMB) and related precision oncology clinical trials. Dr. Miesfeldt and co-investigator Neil Korsen, MD, have completed the first phase of this research which gathered information from cancer patients living in rural Maine, oncologists and clinical trial support staff. The information is being used to improve access to patient education and outreach materials, strengthen relationships with community outreach groups for distribution of recruitment materials and engage and assist clinicians and support staff to encourage patient enrollment in CMB and related research.

In June 2022, these researchers received additional funding for phase two work aimed at examining the barriers that immigrant and refugee cancer patients face to participating in biobanking and related precision oncology trials. Both phases of work are dedicated to recruiting cancer patients from diverse racial, cultural, ethnic and socioeconomic groups, which will help promote diversity, equity and inclusion throughout the MaineHealth Cancer Care Network and nationally.

This work is funded through the MaineHealth Cancer Care Network as a supplemental grant from the National Cancer Institute (NCI) Community Oncology Research Program and falls under the National Institutes of Health NCI Moonshot Biobank research program*.

*WHAT IS CANCER MOONSHOT BIOBANK?

The Cancer Moonshot Biobank (CMB) was started by the NCI to help researchers better understand and treat cancer. CMB seeks to collect longitudinal blood and tissue samples throughout a patient's treatment path from 1,000 oncology research participants over five years. The samples are highly annotated with clinical data over a patient's course of treatment and importantly, samples are submitted to national research laboratories to explore both resistance and sensitivity mechanisms. The NCI is focused on obtaining a diverse set of biosamples representative of the U.S. population, not only diversity across gender, race and ethnicity but also among socioeconomically disadvantaged populations living in rural communities. Anne Breggia, PhD, Director of the Center for Applied Science and Technology, is the MaineHealth Site Principal Investigator. In Maine, the program consists of a network of seven hospitals serving a large, mainly rural population throughout the state as well as portions of New Hampshire, including several hard-to-reach island communities.

For more information:

moonshotbiobank.cancer.gov

NCI CANCER MOONSHOT
A program of the National Cancer Institute of the National Institutes of Health

DID YOU KNOW?

- MaineHealth is the nation's 3rd top enroller to Cancer Moonshot Biobank
- MaineHealth Cancer Care Network has 11 sites; visit **mainehealth.org/cancer** to see a map of network locations.
- The MaineHealth NCI Community Oncology Research Program (NCORP) is one of only two NCORPs across the country with 4 investigators participating on NCI Steering Committees (SCs) and Task Forces (TFs):

  Christine Lu-Emerson, MD
  NCI Brain Tumor SC

  Leslie Bradford, MD
  Ovarian Cancer TF

  Sharon Siegel, MD
  Clinical Imaging SC

  Vatche Tchekmedyian, MD
  Med, Metastatic & Recurrent Head & Neck Cancer SC

- MaineHealth NCORP Leadership:

  Scot Remick, MD
  Contact Principal Investigator

  Leslie Bradford, MD
  Principal Investigator

  Peter Rubin, MD
  Principal Investigator

For more information on how you might be able to participate in a clinical trial, visit: **mainehealth.org/cancer**

> Nearly 90% of cancer care in our nation is provided in community and rural settings. Thanks to the NCI Community Oncology Research Program, MaineHealth continues to develop and provide cancer care and education for Maine's rural communities.
>
> — SCOT REMICK, MD

LOOKING FOR CANCER INDICATORS IN BLOOD TESTS


Leslie Bradford, MD

Using blood tests to detect cancer early may seem like an impossibility, but research in this area is on the rise due to support from the National Cancer Institute. One such example soon to begin in early 2023 at MaineHealth is the Alliance Multicancer Early Detection (MCED) Biobank Study. Dr. Leslie Bradford, Principal Investigator and her team will work with MaineHealth Cancer Care Network and MaineHealth Primary Care Physicians to recruit patients with cancer, healthy individuals without cancer and individuals with a high suspicion for cancer.

Cancer is still the leading cause of death in the state of Maine and remains the second leading cause of death worldwide. While dramatic advances have been made in cancer care, there are still no screening tests available for the majority of life threatening cancers. Most screening tests involve procedures that can be uncomfortable or invasive, such as a pelvic exam for a PAP test to screen for cervical cancer or a colonoscopy to screen for colon cancer. The Alliance MCED Biobank Study will contribute to a greater understanding of how to detect multiple types of cancer through far less invasive blood tests. This study presents an exciting opportunity to develop testing that may reduce cancer mortality, reduce treatment costs for our patients and improve the effectiveness of cancer screening.

IMPROVING PATIENT OUTCOMES AFTER CARDIAC ARREST BY RECRUITING THE IMMUNE SYSTEM

In January 2021, MaineHealth Institute for Research (MHIR) was awarded a five-year, $12.8 million Centers of Biomedical Research Excellence (COBRE) grant by the National Institute of General Medical Sciences of the National Institutes of Health. The funding is being used to help support acute care clinical research and reduce rural health disparities in acute care settings.

Some of the basic science research team (L-R): Lacey Knudsen, BS, Joanne DeKay, MS, Mary Sorcher, MS, Dr. Seder, Dr. Ryzhov and Dr. Tsibulnikov.

The COBRE in Acute Care Research is developing a statewide research and care network in Maine that addresses health barriers associated with limited resources, expertise and access in rural areas. It includes four clinical studies and two pilot studies. One of the studies underway investigates how the types and activity of white blood cells that patients have in their bloodstream after resuscitation from cardiac arrest (CPR) may impact their recovery.

David Seder, MD, Chief of Critical Care Services at Maine Medical Center and Sergey Ryzhov, MD, PhD, Faculty Scientist at MHIR, are leading this project, which began enrolling patients in the spring of 2021. This research team comprised of physician-scientists at Maine Medical Center and basic/translational scientists at MHIR, has a rich history of collaboration on the role of inflammation after cardiac arrest.

"Cardiac arrest is followed by post-cardiac arrest syndrome, which is characterized by systemic inflammation in the blood and may cause death by neurological injury, circulatory collapse, or multi-organ system failure," said Dr. Seder. The researchers are analyzing the activity of different kinds of white blood cells that may protect against excessive inflammation and prevent multi-organ system failure. Dr. Seder went on to say, "The ultimate goal of our work is to develop individualized treatment for each patient that offers more specific benefits and fewer risks than a "one-size-fits-all" traditional approach. We believe this approach will improve outcomes in patients with cardiac arrest."

In the fall of 2022, the study had approximately 63% of participants enrolled. To date, data indicate that regulating white blood cell response after cardiac arrest might provide new therapeutic opportunities.

"Each year more than 600,000 Americans suffer cardiac arrest and despite improved cardiopulmonary resuscitation (CPR), post-resuscitation therapy and cardiovascular support care, overall outcomes remain poor," said Dr. Ryzhov. "We hope that long-term this research will contribute to developing new therapies and better care for patients recovering after cardiac arrest."

IMPROVING CARE FOR ADOLESCENTS WITH MENTAL HEALTH CHALLENGES

Dr. Woodberry (second from right) and her research team.

The COBRE in Acute Care Research & Rural Disparities awards two pilot projects per year*. Dr. Kristen Woodberry was awarded a pilot project in January 2022. She is collecting stories from adolescents and young adults with psychotic symptoms about what helped or hindered their finding effective help. The study is particularly interested in whether specific attitudes (e.g., importance of self-sufficiency, mental health stigma), mental health literacy, the availability and training of local providers, or other factors differ for rural versus non-rural youth and families. The research team is collaborating with a University of Maine researcher to collect similar data in Northern Maine. The project is also exploring what young people with psychotic experiences might want or find helpful in talking to others with similar experiences, particularly when they are first making sense of these experiences. Dr. Woodberry and her team want to use this information to adapt proven early intervention programming like Maine Health's PIER and Resilience programs for Maine's rural communities and to reach young people earlier when these supports are most powerful. The project is still seeking people 14-40 with psychotic experiences who have not received care at PIER or Resilience, as well as seeking input from their parents or caregivers.

***WHAT IS A PILOT PROJECT?**

A pilot project is a smaller study that can be performed in a limited time frame (usually within 1 year) and may be designed to establish feasibility, experimental models, protocols, samples, or procedures for a larger study. Our Northern New England Clinical & Translation Research Network, two Centers of Biomedical Research Excellence (COBREs) and institutional cardiovascular center programs all provide pilot project funding to researchers to get a new idea off of the ground. Pilot project funding may lead to revisions or improvements in the plan of a larger research study, data for a larger grant application and abstracts/publications.

POPULATION & HEALTH SERVICES RESEARCH

COMMUNITY RESEARCH PARTNERSHIP TRANSLATES SCIENCE INTO MESSAGES TO MOBILIZE A COMMUNITY

As the need for more community involvement in research grows, it can be daunting for clinicians and researchers to visualize what that looks like in practice. Funded by the Northern New England Clinical and Translational Research network (NNE-CTR), Resilience Matters to ME, is a community-research collaboration that is focused on helping build resilience and a healthy community in the Oxford Hills area of Western Maine. This project team is comprised of Western Maine community members, Healthy Oxford Hills (a community coalition affiliated with Stephens Memorial Hospital) and staff from the MaineHealth Institute for Research's Center for Interdisciplinary Population & Health Research. This community-research collaboration team worked together to translate complex health information into messages about Adverse Childhood Experiences or ACEs.

ACEs refers to common types of adversity that children experience in their home and lived environment that can significantly increase risk for a host of poor health outcomes. Community members chose ACEs as their focus due to its far-reaching implications for individual well-being and health. If left untreated, ACEs can trigger complex biological reactions predisposing a person to numerous health conditions including cancer, heart disease, diabetes and poor mental health. Brendan Schauffler of Healthy Oxford Hills and Co-Facilitator on the project shared, "Childhood adversity is very common, not only in our community, but around the country. In Oxford County, 25% of high school students report having 4 or more ACEs."

hard things happen

But these things do not define us.

connecting helps us rebuild

One positive relationship can make a difference.

Resilience Matters to ME is working to ensure all community members, no matter what age, know about the effects of ACEs and the many resources available to help everyone build resilience and a healthier community. "This group has been working together now for two years. This fall the work has come to fruition through a community campaign spreading impactful, targeted messages designed to raise awareness about ACEs and offer actions people can take to prevent and reduce their impact," said Lisbeth Wierda, Research Program Director and Co-Facilitator of this project.

This project demonstrates the essential role that the community voice plays in translating research to wider audiences in a way that promotes action across many sectors of the community, including healthcare professionals, schools, workplaces, community news/media and more.

Though the messaging campaign just started, the team hopes this is only the beginning of businesses and community being inspired to work together to raise awareness, connect those in need with resources and normalize this issue.

For more information see the website created for the project: **resiliencematterstome.org**

OXFORD HILLS PROGRAM LAUNCHES TO ADDRESS OBESITY IN CHILDREN & ADOLESCENTS

"Bright Bodies," an evidence-based pediatric weight management intervention, is the focus of a multi-center study led by Dr. Mona Sharifi at Yale University and funded by the National Heart Lung and Blood Institute. Dr. Abby Fleisch, a pediatric endocrinologist at Maine Medical Center and faculty scientist at MaineHealth Institute for Research, is the Site Principal Investigator of the study at MaineHealth and Dr. Victoria Rogers, Senior Director of the Maine Medical Center Let's Go obesity prevention program, is a Co-Project Lead.

Photos include Bright Bodies staff and participants

Maine is one of three implementation sites for Bright Bodies, which just launched in the Oxford Hills region in October 2022. Prior to launch, the research study team spent the last two years evaluating historical dissemination sites of Bright Bodies, optimizing the Bright Bodies package materials and refining dissemination of the program at three sites (Maine, Alabama and California) serving populations with racial and ethnic, rural-urban and geographic diversity.

"It is gratifying to see the launch of a new program with an amazing staff in the Oxford Hills community. We are most looking forward to watching participants progress through the program and establish a network for support," said Dr. Fleisch. A key resource to the program coming together was the Northern New England Clinical and Translational Research Network, which provided community connections for staff and location.

The program, located at Stephens Memorial Hospital, is a high-intensity, family-based intervention for childhood obesity where children and their families meet twice per week for 3-6 months and engage in nutrition, behavior modification and exercise classes. The Bright Bodies team at Stephen's Memorial is comprised of Alyson Byard, Social Worker and Program Coordinator, Amelia Baker, Nutritionist and Guy Pollino, Exercise Specialist. "I have been impressed with our Bright Bodies team. They have been so supportive of the families," said Dr. Rogers. "Several parents have commented that it's a relief to talk to people who know what they're going through."

Over the next two years, the research team will evaluate participant progress and analyze BMI data in hopes to see improvement in weight goals and wellbeing.

Patients can be referred by their primary care doctor. *Learn more about the Bright Bodies weight management program at:* **brightbodies.org**

BASIC RESEARCH: DISCOVERIES IN THE LAB

RESEARCH REDEFINES METABOLIC DISEASE WITH DISCOVERY OF MAJOR SUBTYPES OF OBESITY


Joe Nadeau, PhD

Drs. Joseph Nadeau (MHIR Faculty Scientist) and Andrew Pospisilik (Van Andel Institute, Grand Rapids, MI), who co-lead the PERMUTE (Probabilistic & Epigenetic Regulatory Mechanisms for Unexplained Trait Emergence) Working Group, recently reported research that redefines metabolic disease with discovery of major subtypes of obesity and related conditions. Published in the journal Nature Metabolism in September 2022, the findings offer a more nuanced understanding of obesity than current definitions and may one day inform more targeted ways to precisely diagnose and treat metabolic disease. Drs. Nadeau and Pospisilik are co-Investigators on a $9.6M NIH Transformative Research Award that supports this pioneering research.

According to the Harvard School of Public Health, nearly 40% of American adults aged 20 and over are obese and 71.6% are overweight. Despite these alarmingly high percentages, we still do not have a basis for diagnosing and treating individuals based on their unique inherited and acquired disease risk.

Utilizing a combination of mouse models and data from twins, the research team discovered novel kinds of metabolic subtypes that influence individual body types, two of which are associated with leanness and two to obesity. Perhaps the most remarkable feature of their discovery is the role of chance — non-genetic non-environmental factors — in disease risk.

"Approximately 50% of the variation in risk for disease is linked to genetic and environmental influences. That means as much as 50% of risk comes from something else," said Dr. Nadeau. This phenomenon, which the authors call unexplained phenotypic variation (UPV), offers both a research challenge to scientists and untapped possibilities to manage metabolic disease for clinicians.

Their research indicates that the roots of UPV may lie in epigenetics — how cells control gene activity during development without changing the DNA sequence. Epigenetics is the reason individuals with the same genetics, such as twins, usually show slightly different traits, for instance eye color and hair color and even disease risk. The PERMUTE study shows how chance can change epigenetic features, leading to these subtypes even among genetically identical individuals in similar environments. The unexpectedly powerful role of chance highlights the need to consider epigenetics together with genes and environment as drivers of metabolic conditions.

Drs. Nadeau and Pospisilik are hopeful that the team's findings will guide development of future precision medicine strategies that may be used in doctors' offices to better understand individual patients' health and inform their personalized care.

RESEARCHING CAUSES OF CARDIOVASCULAR DISEASE

Dr. Liaw (first row third from left) and members of her lab.

Lucy Liaw PhD, Faculty Scientist, was awarded her R01* renewal from the National Heart, Lung and Blood Institute at the NIH. This renewal will continue the work she began in 2018 to study perivascular adipose tissue, which surrounds major blood vessels in the body. This adipose tissue contributes to the cellular neighborhood of the circulatory system and changes during obesity and metabolic disease. This project includes collaborations between basic scientists and vascular surgeons to understand differences in the adipose tissue (or connective tissue consisting mainly of fat cells) in patients with varying levels of cardiovascular disease. In this project, the focus is on patient populations in generally good health versus those with cardiometabolic or vascular disease.

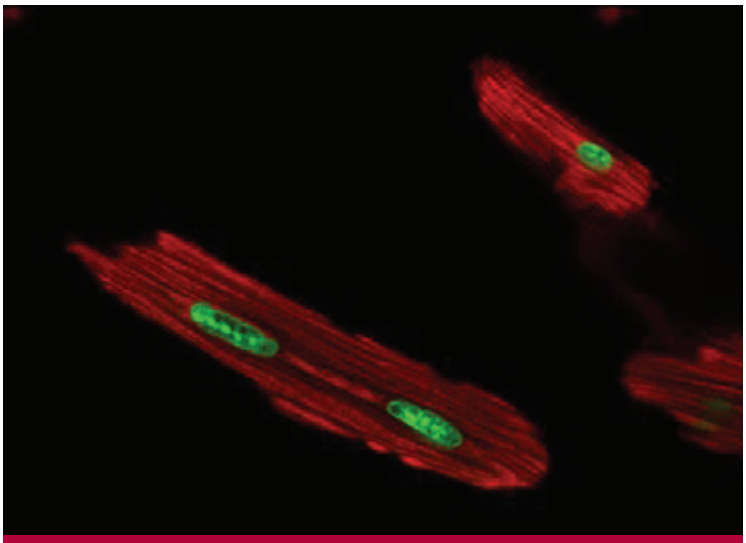
***WHAT IS AN R01?**

The NIH R01 is the "gold standard" of investigator-initiated research grants awarded by the National Institutes of Health. It is generally a four-five year grant in the range of $250,000-$500,000 direct costs per year that addresses a biomedical question that can involve basic, translational or clinical research.

"Obesity and metabolic disease are risk factors for cardiovascular diseases and their increasing prevalence has led to increased rates of vascular disease. I am hopeful these studies will broaden understanding of how adipose drives disease or can be protective to vascular health," said Dr. Liaw.

Research studies like this will help scientists and physicians to understand what causes cardiovascular disease, ultimately leading to improved prevention and treatments for patients.

NEW THERAPEUTIC TARGETS IN CARDIOVASCULAR MEDICINE FOR PATIENTS WITH DIABETES



Cardiac myocytes

The Myocardial Biology and Heart Failure (MBHF) Research Lab, led by Douglas B. Sawyer, MD, PhD and Sergey Ryzhov, MD, PhD, conducts basic and translational research focused on mechanisms by which the heart maintains cardiac function and recovers after injury. In May 2022, the MBHF Lab published research results in the journal Cellular Signalling from an IRB-approved protocol in which patients scheduled for coronary artery bypass grafting surgery at Maine Medical Center were recruited to undergo myocardial biopsy and venipuncture for the collection of cardiac and immune cells. Using novel techniques to analyze different types of cardiac cells from these samples and with parallel studies in a comparable human cell line, the research team detected and measured the amount, location and status of cardioprotective ErbB receptors (a family of protein receptors involved in intracellular signaling).

In patients with diabetes mellitus and cells cultured in high glucose, the number of ErbB2 receptors located on the surface of the cell and the amount of signaling generated by those receptors were decreased, while there was no observed decrease in the total number of ErbB2 receptors. Inhibition of ADAM10, a protein that cuts ErbB2 receptors from the cell surface, prevented the effects of high glucose. This research provides insight into a new potential therapeutic target for the prevention of microvascular complications in patients with diabetes

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SUMMER UNDERGRADUATE RESEARCH PROGRAM BENEFACTORS

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NEXT GENERATION

PARTNERSHIP WITH UNIVERSITY OF MAINE FOSTERS LEARNING AND CAREERS IN BIOSCIENCE

One of the driving principles at MaineHealth Institute for Research is to mentor and help train the next generation of investigators, physicians, nurses and other health professionals. Partnerships are at the heart of our work to provide opportunities for students to experience biomedical research first hand. For more than ten years, MHIR has collaborated with the University of Southern Maine (USM) to offer internships to undergraduates interested in STEMM Careers. The connection began when Dr. David Champlin, Associate Professor of Biology at USM, sought placements for two of his students in MHIR Labs. Dr. Lucy Liaw, MHIR Director of Research Education & Training Programs, welcomed the chance to provide hands-on experience for students in Center for Molecular Medicine labs. Over the next few years, student interest in MHIR internships increased. The USM students' level of academic preparedness, along with support from USM advisor Champlin, resulted in positive experiences for the MHIR labs hosting students and the strength of the program has grown year to year.

IAN GANS, PhD

Ian Gans was in one of the first intern cohorts, starting in the fall of 2012. Ian went on to pursue a PhD at the University of Maine Graduate School of Biomedical Sciences and Engineering and in 2022 he returned to MHIR as a Postdoctoral Research Fellow in the laboratory of Dr. Calvin Vary. Dr. Gans says of his early experiences at MHIR, "My fascination with biology really started in high school, but I came to research kind of late after working other jobs I sort of hated. My internship at MHIR opened my eyes to a world of amazing research that I could actually take part in. I gained valuable lab experiences and confidence in my ability to contribute, as well as a foot in the door that set me on a rewarding career path. Now I have a three year old daughter who thinks macrophages are cool, so maybe she's getting that early start."

MHIR now hosts ten to twelve students each academic year, some of whom go on to participate in the MHIR Summer Undergraduate Research Program. Dr. Champlin was able to secure funding through the Maine Economic Improvement Fund to provide students with a stipend, which allows students the freedom to intern without the pressure to take on additional part-time jobs. From Dr. Champlin's perspective the partnership has been highly impactful for his students. He saw a need for his students to have real world experience and exposure to a professional environment. The connection with MHIR has offered his students just that opportunity: "There are two critical pieces to our success. One is a set of wonderfully diverse, talented, hardworking interns. The other is mentors working between two institutions to provide career development support before, during and after the internship. The success of the program is both fascinating yet also sensible. It's about hard work, guidance, enthusiasm," said Dr. Champlin.

DAWOOD JIMALE, BS

Dawood Jimale, now a Technical Manufacturing Chemist at Abbott Laboratories in Scarborough Maine and a student in the Roux Institute's Master's in Biotechnology Program, participated in the internship program in 2020. "This internship helped me understand and get a feeling for what I would like to do after graduation. I got the chance to work around talented people and learn from their experiences. The valuable skills I gained during my internship helped me to get my first job as a QC Analyst at Lonza Biologics."

NEXT GENERATION CONTINUED...

To date, more than 125 USM students have participated in internships with 28 different MHIR research mentors. From available alumni data, 56% of students ended up in a research career/field, 28% pursued a healthcare or medical career and 9% went into a data analytics or IT related field. Beyond the statistics there are many stories of students for whom a USM-MHIR Internship was the key that opened doors to their current careers. USM students have been hired into research positions at MHIR, joined prestigious medical and graduate school programs and gone on to join Maine and New Hampshire's flourishing bioscience community.

MARY SORCHER, MSc

Mary Weatherbee Sorcher recently rejoined the MHIR Myocardial Biology & Heart Failure (MBHF) Research Lab led by physician-scientist Dr. Douglas Sawyer, who is also MaineHealth's Chief Academic Officer. Mary says the internship at MHIR in 2017 was critical to helping her define her future career steps, including her pursuit of a Master's Degree in Molecular Neuroscience. "My internship at MHIR was formative for my career in science. My mentors kindled my curiosity, taught me bench and critical-thinking skills for high-quality research and cheered me on. The lab's translational collaborations with Maine Medical Center inspired my graduate education pursuits. I'm thrilled to be back working with this amazing group of people." Leaders like Dr. Sawyer highly value the opportunity to host undergraduate interns in their labs.

Looking to the future, Dr. Champlin and Dr. Liaw see opportunities for further connections between MHIR and USM departments, providing internship opportunities for students interested in data science and bioinformatics, public health and applied science. "Our program welcomes diverse students and we have a strong track record of training the future workforce in Maine and New England. Working with our academic partners creates synergy in experiential learning," said Dr. Liaw.

SAMANTHA WHITE, BS

Samantha White, a 2017 intern, eventually became the Lab Coordinator for The Quality Control Collaboratory (QC2) at the University of Southern Maine which works in partnership with the Maine Brewers' Guild to provide laboratory analysis and testing for the craft beverage industry. The internship at MHIR was impactful. "As an intern at MHIR, I benefited from the expertise of my mentors and the larger MHIR community of scientists and professionals. The skills I developed at the bench and as a researcher at MHIR propelled my career in science and allowed me to take a leadership position at the Quality Control Collaboratory at USM after graduating. I cannot imagine having the confidence and experience needed to do my job without the training I received during my internship and am so grateful for the opportunity MHIR, MEIF and USM afforded me."

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