2023 YEAR IN REVIEW
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DEAR FRIENDS,

It is an honor to share with you some of the remarkable research achievements and ongoing activities from our MaineHealth community in 2023. We sometimes describe our Research Institute as "small but mighty". Certainly when one visits 81 Research Drive, that description can seem accurate. But consider the footprint of our research community. We have clinical trials ongoing across nearly every department and region. We have grown research training in multiple disciplines in collaboration with a growing number of academic partners, impacting the career development of many across MaineHealth. Our collaborations cross institutional, national, and international boundaries. There is no question that research is accelerating the pace of MaineHealth’s journey achieving our vision, and helping to transform Maine into a vibrant biomedical research ecosystem. Building our research programs in collaboration with our community was a clear priority for our former VP for Research, Dr. Elizabeth Jacobs, and we are grateful for her contributions to the work of community engagement over her three years of leadership.

Thank you for taking the time to read through this report, which highlights just a fraction of the great work supported by MHIR in 2023. At the risk of misleading folks into thinking I have favorites (I don’t — I love all the great work!), our team (Rosen, Ryzhov, Emery) is part of a NIH funded national effort to understand ‘long COVID’, shining a light on how a dysregulated immune system might prolong symptoms, and present a novel target for therapeutic intervention (see page 10). This is one example of the increasing collaborations across the clinical/basic spectrum. Another is the work of Damien Carter, MD and Igor Prudovsky, PhD, supported by the Department of Defense, examining new mechanisms to improve tissue repair after burn injury (see page 16). An additional notable grant award that is bringing together diverse teams of investigators to solve big problems is the $12.9M from the National Institutes of Health renewing our Center of Biomedical Research Excellence (COBRE) in Metabolic Networks grant led by Lucy Liaw, PhD (see page 15 for details).

We are on a journey. Somewhere along this journey, we will all recognize that MaineHealth is a learning health system, a great place to get care, as well as a great place to live, learn, grow and lead. Thank you for your interest in our research programs, and for supporting the curiosity and engagement so critical to our success on this journey.

Sincerely,

DOUG SAWYER, MD, PHD
Chief Academic Affairs Officer
Interim Vice President of Research

MESSAGE FROM THE DIRECTOR

WATCH OUR NEWEST VIDEO TO LEARN MORE ABOUT OUR RESEARCH
CNN interviewed Robert Smith, MD, Director of the Vector Borne Disease Lab and infectious disease physician, in June for an article on tick season and the rise of tick-borne diseases.

NNE-CTR FUNDS PILOT PROJECT AT UNE TO DEVELOP CHRONIC PAIN REGISTRY FOR MAINE

This year investigators from the University of New England (UNE) and MaineHealth received grant support from the Northern New England Clinical and Translational Research Network (NNE-CTR) to establish a comprehensive, statewide chronic pain registry, aimed at advancing epidemiological research and ultimately enhancing health care practices in pain management throughout the state of Maine. Dr. Ling Cao, professor in the Department of Biomedical Sciences within UNE’s College of Osteopathic Medicine, is spearheading the pilot project.

Research shows about 30% of Mainers are living with chronic pain. By working together to identify the prevalence of chronic pain throughout the state, investigators from UNE and MaineHealth aim to foster greater research and treatment options for patients suffering from this debilitating condition. The collaborative effort will draw on the unique expertise of both institutions to create a robust database that will serve as a tool for epidemiological studies and clinical research.

Robert Koza, PhD, Faculty Scientist was appointed as a standing member of the National Institutes of Health Diabetes and Digestive and Kidney Diseases grant review study section committee for Fellowships in Diabetes Endocrinology & Metabolic Diseases.

Katherine Motyl, PhD, Faculty Scientist was appointed as a standing member of the National Institutes of Health Skeletal Biology and Developmental Disease grant review study section committee.

Cliff Rosen, MD, Senior Scientist, was awarded membership into the Association of American Physicians (AAP). The AAP is a society of America’s leading physician-scientists who are elected based on their enduring, impactful contributions to improve health.

NEW FACULTY

Cara Frankenfeld, PhD, joined MHIR’s Center for Interdisciplinary Population & Health Research (CIPHR) in August 2023. Dr. Frankenfeld comes to MHIR from the University of Puget Sound where she was an Associate Professor of Epidemiology and Biostatistics and served as the Program Director for the inaugural Public Health Program. Dr. Frankenfeld leads the CIPHR analyst team and also serves as a technical expert and resource with regards to epidemiology, biostatistics, data analytics, research methods and study design. Her expertise is in research design and analysis of complex data, such as microbiome, metabolome, diet, and spatial factors.
AWARDS

In the awards list below we showcase the recipients of new research grants awarded in the past year. These awards signify not only a commitment to advancing knowledge but also a celebration of the diverse and impactful projects that have garnered support. Join us in recognizing the recipients of this year’s research grants.

KEY:
AHA: American Heart Association
PCORI: Patient Centered Outcomes Research Institute
NNE-CTR: Northern New England Clinical and Translational Research Network
NIH: National Institutes of Health

Damien Carter, MD
Physician Investigator
Stimulating Skin Regeneration after Burn Injury
MDI Biological Laboratory/NIH

Eben Estell, PhD
Staff Scientist in the Rosen Lab
Career Development Award: The Role of Irisin in Initiating Resorption during the Skeletal Response to Exercise
NIH

Maxwell Afari, MD
Physician Investigator
Clinical Fellow Research Education Program
AHA

Eben Estell, PhD
Staff Scientist in the Rosen Lab
Career Development Award: The Role of Irisin in Initiating Resorption during the Skeletal Response to Exercise
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Maxwell Afari, MD
Physician Investigator
Clinical Fellow Research Education Program
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James Bonhoff, MD
Physician Investigator
Tufts CTSI Career Development Award: Pediatric Asthma Specialty Care
NIH

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Improve Access & Health Equity for Children with Type 1 Diabetes
Montana Pediatrics/Leona M. & Harry B. Helmsley Charitable Trust

Carolyn Chlebek, PhD
Postdoctoral Fellow in the Rosen Lab
Determination of bone quality following weight loss in obese preclinical models
Stryken/ORS (Orthopaedic Research Society)
Women’s Research Fellowship

Lisbeth Balligan, MPH
Research Program Director
Building Capacity to Disseminate Patient Centered Outcome Research Evidence
PCORI

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Research Program Director
Building Capacity to Disseminate Patient Centered Outcome Research Evidence
PCORI

Emily Carter, MD
Physician Investigator
Hospital Elder Life Program vs. Family-Augmented HELP for Prevention of Delirium
Marcus Institute for Aging Research at Hebrew Rehabilitation Center/PCORI

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AWARDS

Robert Smith, MD
Physician Investigator

Environmental Vector Surveillance
Maine Center for Disease Control and Prevention

Elizabeth Turner, MD
Physician Investigator

Effects of Tranexamic Acid on Traumatic Brain Injury
New England Surgical Society

David Seder, MD, PhD
Principal Investigator

Matt Lynes, PhD
Faculty Scientist

Acute Care COBRE Team
Science Supplement: Brown Adipose Tissue as a Potential Therapeutic Target in the Post-Resuscitation Period
NIH

Jonathan Zuckerman, MD
Physician Investigator

Elevating Remote Cystic Fibrosis Care
University of North Carolina at Chapel Hill/Cystic Fibrosis Foundation

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Facts & Figures

2023 Leadership

Executive Administration
Doug Sawyer, MD, PhD
Chief Academic Affairs Officer, and Interim VP of Research

Elizabeth Jacobs, MD, MPP
Vice President of Research, MaineHealth
Director, MaineHealth Institute for Research (September 2020 – September 2023)

Kneka Smith, EdD, MPH
Vice President, Academic Affairs

Research Center Leadership
Anne Breggia, PhD
Director, Center for Applied Science and Technology

Adriana Rosato, PhD
Director, Center for Molecular Medicine

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

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

By the Numbers

261 Staff Members

$25.6M Total 2023 Grant Funds

29 New Grants Awarded

250 Clinical Trial Studies

Oncoogy, Neurology, & Cardiology Top 3 Clinical Research Areas

159 Scientific Publications

1499 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

139 Learners & Trainees in MHIR’s Education & Training Program

1 Patent Issued for Methods, Compositions, and Kits for Producing Beige Adipocytes and Treating Metabolic Disorders; Aaron Brown, PhD, Faculty Scientist

2023 Sources of Sponsored Research Support by Sponsor Type

78% Federal

13% Industry

9% Foundation & Nonprofit

MaineHealth makes research a priority and also has generously provided support to MHIR’s operating budget. 2023 MH Operating Subsidy $12.1 M
The impact of clinical trial participation on patients cannot be understated. Trial participants can develop strong, special relationships with the study investigators and clinical research coordinators. MaineHealth clinical research staff go above and beyond to engage patients to provide a further understanding of what they will experience on a trial, how it will impact them directly, and how it provides hope for future patients.

One such example was demonstrated through patient gratitude this year. Jen Dalton, RN, Clinical Research Nurse Coordinator, received a unique gift from a patient who was getting cancer treatment during a clinical trial for five and a half months. To mark her journey and show her appreciation for her care experience, the participant created a piece of pottery in her studio in Jen's honor. The patient described the pottery as a replica of a shaman to represent healing powers, with roots in Easter Island where her trial treatment originated. This heartwarming story highlights the research team's patient-centered focus and tremendous impact on patients' engagement in their care experience.

The MaineHealth Clinical Trials Office has demonstrated success in multiple types of clinical trials across the disease continuum in 2023. Such projects have included interventional and observational trials aimed at prevention, screening and early detection, treatment, care delivery, and quality of life of a range of diseases and medical conditions. A few examples of these types of trials are highlighted below.

**Rare Disease: Therapy for Patients with Homocystinuria**

_Wendy Smith, MD, Principal Investigator_
_Clinical Research Coordinator: Julia Taylor_

Only a couple of patients in Maine have this rare genetic condition. Homocystinuria (HCU) is a rare but potentially serious inherited condition where the body has trouble breaking down certain amino acids. This causes a harmful build-up of substances in the blood and urine. This trial has been life changing for the participant MaineHealth enrolled in the trial. The Clinical Trials Office has completed participation in phase 2 (testing effectiveness and safety) and is awaiting the release of the phase 3 study (confirming effectiveness and comparing to other treatments).
ScreenState/Prevention: Evaluation of the Bexa™ Breast Examination

Christina Cinelli, MD, Principal Investigator
Clinical Research Coordinator: Jaqueline Lapointe, RN

In just a few months the study team enrolled 325 patients to this trial. The trial is testing a new device (Bexa) that aims to add specificity and improved diagnostic ability for breast cancer detection. The trial is expected to be completed by the end of 2023.

LEARN MORE ABOUT THE TRIAL

Care Delivery, Adverse Event Prevention: Mepitel Film for the Reduction of Radiation Dermatitis in Breast Cancer Patients

Matthew Cheney, MD, Principal Investigator
Clinical Research Coordinators: Jennifer Soda, RN, Robin Donovan

Mepitel film (MF), is an adhesive silicone dressing. This trial is focusing on addressing a common complaint of breast cancer patients receiving radiation, which is radiation dermatitis (a burn that is a common side effect of receiving radiation). The trial’s focus is to test if MF reduces radiation dermatitis in breast cancer patients undergoing post-mastectomy radiation therapy. The MaineHealth team leads the country in enrollments, more than doubling the enrollments of the next closest site.

LEARN MORE ABOUT THE TRIAL

COVID RESEARCH CONTINUES WITH PROMIS

In the spring of 2023 MaineHealth Institute for Research (MHIR) was awarded $802,753 by the National Institutes of Health (NIH) to explore a theorized cause of Long COVID. The Pathobiology in RECOVER (Researching COVID to Enhance Recovery) of Metabolic and Immune Systems (PROMIS) study will examine whether the virus that causes COVID remains hidden in the fat tissue of patients with Long COVID, stressing their immune systems to the point of potential failure.

The study is part of the nationwide RECOVER Initiative that seeks to understand, prevent and find treatments for Long COVID. MaineHealth has been a RECOVER study site since November 2021 and completed successful enrollment earlier this year.

“Part of the challenge with treating Long COVID is that we still don’t know what causes it,” said Cliff Rosen, MD, Senior Scientist at MHIR and the study’s Principal Investigator. “If we can prove that the virus persists in the fat tissue of patients with Long COVID, we can start targeting treatments that impact that part of the body.”

Dr. Rosen and MHIR colleagues and co-Principal Investigators Ivette Emery, PhD, and Sergey Ryzhov, MD, PhD, are working with colleagues at the University of Kentucky and Pennington Biomedical Research Center at Louisiana State University to examine the blood of 60 current RECOVER study participants in Maine, Kentucky and Louisiana. Researchers are testing for the virus as well as certain proteins that the virus may be activating, causing Long COVID symptoms.

continued next page...
MHIR is analyzing fat tissue biopsies from participants in collaboration with investigators at Brigham and Women’s Hospital, and the University of Oregon. Together, scientists will determine if tissue samples carry the virus, and whether they are creating substances that can lead the immune system to cause fatigue, brain fog, and other Long COVID symptoms. The study is expected to take one year.

“We know people with Type 2 diabetes and obesity are at higher risk for Long COVID,” Dr. Ryzhov said. “This study may bring us closer to understanding the biology behind why that is, and may be a first step towards preventing Long COVID, too.”

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. Successful collaborative research was highlighted from colleagues across the country studying COVID on behalf of the National COVID Cohort Collaborative (N3C) Consortium. This published work reviews community factors impacting risk for breakthrough infections among fully vaccinated persons by rurality. MaineHealth Institute for Research collaborators include: Kimberly Murray, MPP; Susan Santangelo, ScD; and Cliff Rosen, MD.

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According to the Centers for Disease Control and Prevention, vaccine development can often take 10-15 years. There is one disease in particular that has a 20 year history of vaccine development with a few false starts: Lyme disease.

MaineHealth is a part of this long-awaited clinical trial which is occurring at Pen Bay Medical Center (PMBC). Pfizer Pharmaceutical is the sponsor of the trial which is underway in Europe and the US. Lyme disease is a common illness caused by bacteria found in deer ticks. If left untreated, Lyme disease can progress to cause severe, sometimes permanent symptoms. Currently, there are no approved vaccines available for humans to prevent Lyme disease.

PBMC is the only MaineHealth hospital and one of only two sites in Maine participating in the study, which is evaluating if a Lyme vaccine is safe and effective for preventing Lyme disease in people who have been exposed through tick bites. The research team includes Dr. Robert Stein, PMBC neurologist and Medical Director of Clinical Research at PMBC, who is the Principal Investigator, Dr. Robert Smith, infectious disease physician and Director of the Vector-borne Disease Lab at MHIR, who is an affiliated investigator and Caroline Knight, RN, BSN, CCRP, who is the Clinical Research Nurse Coordinator for the study.

In the trial, 50% of participants receive the Lyme vaccine while 50% will receive a placebo. The investigational vaccine mechanism works by pre-emptively blocking a surface protein of the bacteria in the feeding tick during the time it takes to infect someone after the bite. Blocking the surface protein inhibits the bacterium’s ability to leave the tick and infect humans. The study will take place over approximately two years, during which time participants will receive a total of four immunizations and five blood draws over the course of seven visits.

Study participants are healthy adults aged 18 and older who had not been diagnosed with Lyme disease in the three months prior to enrollment. All enrolled participants live, work, or recreate in areas prone to ticks.

If the vaccine is effective, the next step is going through the Federal Drug Administrative (FDA) process for approval. “It’s really exciting to see commercial interest in getting a Lyme vaccine after such a long time,” said Dr. Stein. “Our next challenge will be deciding the criteria for who will benefit most from the vaccine if approved. Thankfully antibiotic treatment is effective for treating Lyme disease, but a vaccine would preempt the infection from the start.”
POPULATION & HEALTH SERVICES RESEARCH

DR. ABBY FLEISCH EXPANDS PFAS RESEARCH IN MAINE AND BEYOND

Abby Fleisch, MD, MPH, a pediatric endocrinologist at Maine Medical Center and faculty scientist in the Center for Interdisciplinary Population & Health Research, has been researching the health effects of per- and polyfluoroalkyl substances or PFAS across the lifespan. She is immersed in PFAS research which is evident by the fact that she received not one, but three National Institutes of Health (NIH) grants in 2023 to advance this work.

PFAS Background

PFAS have been around since the 1940s, but only in recent years have they gained attention in the news both nationally and in Maine due to their potentially harmful health effects. PFAS are synthetic chemicals added to clothing, furniture, and carpets to make the items non-stick and stain-repellant. PFAS or “forever chemicals” don’t naturally break down, so they stay in our bodies for years and in the environment for decades, contaminating water and food.

PFAS in Central Maine

One of Dr. Fleisch’s NIH grants is well underway and occurring in central Maine. Dr. Fleisch and Dr. Rachel Criswell from Redington-Fairview General Hospital, were awarded a two-year NIH exploratory grant to look at exposure pathways and mental health impact of PFAS-contaminated biosolids (treated sewage sludge that meets the EPA pollutant and pathogen requirements for land application and surface disposal). Drs. Fleisch and Criswell are working with a central Maine community that has been impacted by PFAS. Enrollment began in September with town halls that included enrolling participants, and collecting data and blood draws. In addition, the research team has established a community advisory board which has helped with study material development such as the study questionnaire. The board will continue to advise the study team and will meet quarterly throughout the study.

This work will help establish a cohort (a group of participants followed over a period of time) with PFAS exposure from biosolids, evaluate potential exposure pathways, and characterize associations with anxiety and people's views on health risks and feelings of being stigmatized about PFAS exposure.

“We hope that our study will help to guide other communities affected by biosolids across the US,” said Dr. Fleisch. “We want to help these communities by generating exposure mitigation advice and interventions to build resilience.”

PFAS and Long-term Health Effects

Dr. Fleisch’s other NIH awards are just getting started. She is a Principal Investigator along with Dr. Emily Oken of Harvard Pilgrim Health Care on a five-year grant from NIH’s National Institute of Environmental Health Sciences. This study will investigate the impact of PFAS on musculoskeletal health and cardiovascular disease among older adults in the Diabetes Prevention Program Outcomes Study. The study will also examine the potential for lifestyle behaviors such as diet and physical activity to mitigate these health impacts. Notably there is little data currently on PFAS and cardiovascular disease — this work will be integral to adding to the current body of knowledge and guiding health advisories moving forward.

In her third grant this year, Dr. Fleisch is a Co-Investigator on a National Institute of Arthritis and Musculoskeletal and Skin Diseases research grant led by Dr. Jeffrey Driban at the University of Massachusetts. The overarching goal of the grant is to examine the extent to which PFAS exposure is associated with the development of osteoarthritis. Dr. Fleisch will specifically advise/assist the principal investigator and study team on study design, data analysis planning, and manuscript preparation in relation to the PFAS exposures.

“I am looking forward to conducting these studies,” Dr. Fleisch said. “I hope our findings will help to inform health advisories as well as exposure reduction and health guidance for people who have been exposed.”

PFAS and Reduced Breastfeeding Duration

Lisa Rokoff, PhD, Staff Scientist in the Center for Interdisciplinary Population & Health Research, published research this year in the journal Science of the Total Environment that explores PFAS, chemicals used in several consumer products, in pregnancy and breastfeeding. Dr. Rokoff and her colleagues, including Dr. Fleisch, found that women with higher blood concentrations of specific PFAS were more likely to terminate breastfeeding earlier. This work corroborates prior studies in animals suggesting that PFAS may adversely impact the ability to produce human milk and thus successfully breastfeed, which is important to promote the health of both infant and mother. More research is needed, and it is hoped that this foundational work will guide the clinical care of people exposed to PFAS and inform PFAS-related health policies.

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The average time it takes to bring research into clinical practice is 17 years. Implementation may take even longer in rural settings where health care organizations and providers lack ready access to academic resources and timely, relevant evidence on which to consider new ways of providing health care or on which to base their routine treatment and care decisions. These delays contribute to rural and other health disparities in Maine. Elizabeth Jacobs, MD, MPP, formerly an investigator with the MaineHealth Institute for Research (MHIR), initiated this two-year research capacity-building project that will be looking at the processes to help close this gap. Following her departure, the study continues under the leadership of Lisbeth Balligan, MPH, MHIR Research Program Director.

This project, funded by the Patient-Centered Outcomes Research Institute (PCORI), began in early 2023 and is building capacity for research dissemination and its translation into practice. PCORI is a nationally recognized funder that is unique in its prioritization of the stakeholder voice and expertise throughout a research project.

More Equitable Access to the Latest Research

Ms. Balligan, along with their team and stakeholder collaborators, aims to create a robust sustainable infrastructure for disseminating evidence from patient-centered outcomes research/comparative effectiveness research (PCOR/CER) studies to organizations and leaders that can use this evidence to address the needs of patients and communities in rural Maine.

The initial focus of the project is dissemination of research that investigates how to improve the delivery of behavioral health and opioid use disorder treatment, both important priorities of Maine communities.

The research team has created a Research Dissemination Advisory Panel, made up of a cross-section of healthcare administrators and medical professionals throughout Maine. The panel gives guidance on the study content and the process of developing and distributing scientific evidence that is most relevant to rural Mainers. This includes:

- Guiding the development and dissemination of easy-to-read and understand one-page research summaries
- Creating a publicly-accessible repository of PCOR/CER studies
- Learning events

The majority of the planning work, or phase one of the study, began in early 2023. Phase two will be about building infrastructure to disseminate the findings and could take approximately two to three years.

“I am excited about the upcoming community feedback sessions later this year. I’m also eager to witness the sharing of information across Maine and our stakeholders, which will help create a stronger and lasting framework with active community involvement.” said Ms. Balligan.

Having an established infrastructure and standardized way to make research and the findings accessible and understandable to health care leaders and providers will help decrease rural health disparities across Maine. By reducing the time to implementation of evidence-based interventions, we can improve patient care and health outcomes.
BASIC RESEARCH: DISCOVERIES IN THE LAB

$12.9M FROM NIH EXPANDS CENTER FOR METABOLIC HEALTH

Major grant news for the research institute in 2023 was the National Institutes of Health (NIH) awarding MaineHealth a five-year, $12.9 million renewal of its Center of Biomedical Research Excellence (COBRE) in Metabolic Networks grant. The funding will advance research infrastructure for the study of metabolic diseases, including obesity, diabetes, osteoporosis and lipid and energy imbalances.

This grant renewal will allow MaineHealth Institute for Research (MHIR) to build upon the success of this COBRE, which was established through a five-year, $11 million NIH grant in 2017. In the first five years of the COBRE, MHIR researchers studied how metabolically active tissues, including fat, bone and the brain, use energy and control overall metabolism in the body, and how this is altered during disease.

In these next five years, researchers will study the impact different kinds of fat tissue may have on diabetes, how bariatric surgery to treat metabolic disease affects bone health, the effects of night shift work on gestational diabetes during pregnancy and beyond, and stigma in diabetes care. As these researchers obtain independent grants, new opportunities will become available to support additional investigators who study metabolic diseases that are prevalent in Maine and across the country.

“Our goal is to make new discoveries that can serve the health and medical needs of our communities while continuing to recruit and support the research careers of junior investigators,” said Lucy Liaw, PhD, faculty scientist at MHIR and the principal investigator for this grant. “We do that by providing a strong advisory and mentorship network for our researchers and high-quality shared scientific resources. This foundation launches the career of faculty researchers, who create opportunities for our workforce and train the next generation of researchers.”

Four investigators who began their careers with funding through the COBRE now lead their own grant-funded research: Aaron Brown PhD, Katie Motyl PhD, Michaela Reagan PhD — all at MHIR — and Christine Lary, PhD, a research associate professor at the Roux Institute at Northeastern University and adjunct faculty scientist at MHIR.

Aaron Brown, PhD:
“Thanks to our COBRE program, I was able to access a wide range of valuable resources that proved essential to my professional development as a researcher. These resources included state-of-the-art equipment, funding for research projects, and access to highly experienced mentors who provided guidance and support as I worked to establish myself as an independent investigator.”

Kate Motyl, PhD:
“Being a project leader on the COBRE helped me to develop lifelong collaborations with outstanding scientists and taught me the value of team science. Working together as a group, the COBRE team accomplished much more than we could have if we were all working independently.”

Michaela Reagan, PhD:
“I am so grateful to Cliff Rosen and Lucy Liaw for initiating and leading the M-COBRE, which allowed me to move from Massachusetts to Maine, meet new collaborators, learn about new scientific fields, and develop my dream job as an independent faculty member researching cancer and bone diseases.”

Christine Lary, PhD:
“I really enjoyed being a COBRE project leader. I got connected with Doug Kiel as a mentor and he continues to be my mentor to this day. I learned how to use the Framingham Heart Study to address important mechanistic questions in fellow project leader Katie Motyl’s work on beta blockers in bone. I have collaborated with other COBRE project leaders including Aaron Brown with miRNA work on my R01 and with Michaela Reagan and Anyonya Guntur with bioinformatics help of their projects. I received so much mentoring and support in my R01 application. Overall, I really learned the nuts and bolts of being an independent scientist and learned a ton of science along the way.”

The grant renewal will continue to develop the careers of young scientists. The program also brings state-of-the-art molecular, cellular, and physiological technologies to research communities at MaineHealth and across the state.
BASIC RESEARCH: DISCOVERIES IN THE LAB

Team Science
Matthew Lynes, PhD, Faculty Scientist and Dave Seder, MD, MMC Critical Care Physician, received a Team Science Award from MHIR’s Acute Care COBRE. With this funding the research team will focus on the activity of brown adipose tissue as a potential therapeutic target in the post-resuscitation period and assess effects on glucose homeostasis and inflammation. Dr. Lynes is also one of the Project Leads on the Metabolic COBRE (see page 15). By combining expertise in the areas of post-resuscitation cardiac arrest care (Dr. Seder) and brown adipose tissue biology (Lynes Lab) the team will take a team science approach to define patient subpopulations that benefit from therapeutic hypothermia after cardiac arrest and identify a novel tissue target to mitigate post arrest alterations to glycemia, ultimately improving patient outcomes.

SHEDDING BLUE LIGHT ON ADDRESSING THERAPIES FOR OBESITY-RELATED DISORDERS
Adipose tissue, often referred to as body fat, plays a pivotal role in our health. Unlike excess white adipose tissue, which is strongly associated with the development of obesity, type 2 diabetes, and negative cardiovascular outcomes, brown adipose tissue is positively linked to improved health and reduced risk of cardiometabolic diseases. Faculty Scientist, Aaron Brown, PhD, and his dedicated team at the MaineHealth Institute for Research are diligently working to unravel the secrets of activating brown adipose tissue to enhance calorie expenditure and explore its therapeutic potential for weight reduction. While there are drugs currently under study to activate brown fat, many of them come with unfortunate side effects that are difficult to reverse and may even heighten the risk of cardiometabolic diseases, which is precisely the opposite of their intended effect. However, Dr. Brown’s lab has achieved significant breakthroughs through the application of optogenetics, a cutting-edge technique that leverages the power of light to precisely manipulate specific cellular processes. They successfully engineered brown fat cells to be responsive to light by incorporating a light-inducible gene from a soil-dwelling bacterium. This innovative approach allowed them to delve into the potential of light-based activation for brown fat cells. Their groundbreaking research revealed that stimulation of these photosensitive brown fat cells with blue light resulted in a remarkable 400% increase in the burning of calorie-rich fuel substrates, such as sugars and fats. This exciting work was published in the journal iScience this year.

By shedding light on the mechanisms through which brown fat cells enhance energy expenditure via optogenetic activation, Dr. Brown’s work opens doors to the development of potential therapies aimed at reversing obesity-related disorders. While these experimental approaches are not yet ready for use in humans, the hope for effective obesity therapies shines brighter than ever.

UNDERSTANDING THE EFFECTS OF TRANEXAMIC ACID IN BURN CARE
Damien Carter, MD, Burn, Trauma & Critical Care Surgeon at Maine Medical Center and Igor Prudovsky, PhD, DSc, Faculty Scientist at MaineHealth Institute for Research, were awarded a Department of Defense grant in 2020. This grant funding was to study tranexamic acid (TXA) and its ability to reduce tissue edema and prevent burn wound conversion. Burn wound conversion occurs when shallow second-degree burns “transform or convert” to deeper wounds. The study came to a close this year with Drs. Carter and Prudovsky finding that TXA is effective in reducing burn wound conversion and suppressing lung edema after burns. The research team also learned that TXA suppressed the expression of inflammatory cytokines in lungs and heart and invasion of inflammatory cells into lungs. This exciting work could benefit both military and civilian burn patients in austere environments.
The ROUX Institute’s Future of Healthcare Founders Residency program, in partnership with Northern Light Health, MaineHealth and the Maine Venture Fund, provides mentorship, financial support and clinical and technical expertise to innovative companies in health care with the aim of improving patient care in Maine.

Radiolife, founded by Sergio Ribeiro, MBA, is one of 10 companies in the Future of Healthcare Founders Residency program’s first cohort. Radiolife has developed the Cube Scan instrument which can detect the presence of viruses, bacteria and potentially cancer cells in saliva, blood and other body fluids in less than 20 seconds. The technology is based on the unique radio wave signatures of particles combined with artificial intelligence (AI) analysis and has the potential to quickly make a diagnosis of which respiratory infection a patient may have (RSV, Flu or COVID). Currently, independent testing for each of these viruses must be done to make an accurate diagnosis which may take over 24 hours to determine, resulting in delays to appropriate treatments. In preliminary testing of 1,347 swab samples from patients with respiratory infections, the accuracy of the Cube Scan was 98.07% when compared to the standard PCR method of testing for COVID-19.

Anne Breggia, PhD and Robert Carlson, MD, co-Directors of the Center for Applied Science and Technology (CAST), will work with the Radiolife team to provide technical expertise and the samples needed to validate this new testing technology and move it forward into the practice of medicine throughout Maine.

“It is exciting to be a part of the process to advance technology which could better help discerning flu-like diseases and serve as a point of care testing for many infectious diseases. Providing physicians with rapid test results will expedite initiation of appropriate therapies which could be a game changer for patient care,” said Dr. Breggia. She went on to say, “This could be especially impactful in treating infants and older patients that are immune compromised and where the treatment window is critical.”

The project is in the early stages of study design and proof of concept testing in a variety of biofluids. This will be followed by comprehensive assay validation testing by CAST and submission of this data by Radiolife to the Federal Drug Administration for approval.

Another initiative this year from the Center for Applied Science and Technology (CAST) is a project that aims to develop algorithms for the diagnosis of prostate cancer by incorporating artificial intelligence (AI) and digital pathology.

Prostate cancer is the second most common cancer worldwide and the second leading cause of cancer in men, accounting for over 1,000,000 diagnoses and 350,000 deaths each year. It is estimated that 1 in 6 American men will be affected by this disease in their lifetime. Rapid diagnosis is essential to expedited treatment but this is challenged by an increased volume of prostate cancer cases coupled with a decline in the number of pathologists needed to make a diagnosis.

Anne Breggia, PhD and Bob Carlson, MD, co-Directors of CAST, are collaborating with Bilal Ahmad, MD, Spectrum Pathology, and Saeed Amal, PhD, Associate Professor of the ROUX Institute, to create a platform for the rapid diagnosis of prostate cancer based on algorithms developed using AI and machine learning tools applied to digital images of prostate cancer tissue that are representative of various stages of prostate cancer. The 5-year project will scan over 2,000 slides of tissue from patients with benign to metastatic disease. Once developed, the platform will decrease the time to diagnosis and initiation of therapy thereby improving patient care, especially in the rural setting, and will address the problem of a rising number of prostate cancer cases combined with a declining number of pathologists.

“Using AI and machine learning tools to analyze whole slide images can help us improve the way we diagnose prostate cancer, potentially making it easier to detect the disease in its early stages and ultimately improving patient outcomes,” said Dr. Carlson.
MaineHealth’s physician scientists are collaborating with artificial intelligence (AI) experts from Northeastern University’s Roux Institute to create better ways of using data from routine health care to enhance disease prediction, diagnosis and treatment. One such project that started this year was HEA(RT), or Healthcare Enabled by AI in Real Time. Maine Medical Center, a part of MaineHealth, houses one of the state’s only cardiothoracic intensive care units, where patients recover from heart, lung, and other types of chest surgery. Monitoring devices already collect health data on these patients, such as vital signs, oxygen levels, and electronic medical records. The research team from MaineHealth includes Robert Kramer, MD, Director of Research, Division of Cardiothoracic Surgery, and Doug Sawyer, MD, PhD, MaineHealth’s Chief Academic Officer and Interim VP of Research. They have teamed up with the Roux Institute’s Rai Winslow, Director of Life Science and Medical Research and Melanie Tory, Director of Data Visualization Research. The team is developing a cardiac solution that is using cardiac monitoring data and AI to predict when a patient may suffer an unexpected event, and allow the care team to intervene to prevent it. This technology holds a lot of promise for improving outcomes across the continuum of care and might be applied to other clinical situations as the work develops.

Over the coming year real patient data will be analyzed in a new way, allowing the team to understand early markers of clinical events or deterioration. Over the next several years the team envisions developing ways to bring that information back to the healthcare team in a way that enables timely interventions.

“We are excited to be on the cusp of changing the way information gathered in the course of a person’s care is managed, and we envision a future where the health care team is functioning at a higher level, providing safer, and more predictably reliable care,” said Dr. Sawyer.
UNDERGRADUATES:

Traci Francis, an undergraduate from Vassar worked with Drs. Liz Scharmetzki and Kevin Stein in the Center for Interdisciplinary and Population Health Research. Her research, A scoping review of lung cancer-related policy in Maine was selected for a poster presentation at the Maine Public Health Association annual conference.

Tara Mullen, a Bowdoin senior, successfully defended her senior thesis based on her work with the research team of Dr. Kristen Woodberry. The title of her thesis was Examining the predictive value of anxiety, depression, and suicidal ideation screening in determining psychosis risk.

MEDICAL STUDENTS:

Siddhant Sharma, medical student at University of New England College of Osteopathic Medicine, won the UNE Fall Research Forum Basic Science Research award for his work with Dr. Ziru Li, Bile Acids Partially Mediate the Bone Reduction and Marrow Adiposity Loss Caused by Vertical Sleeve Gastrectomy in Mice.

Nichole Moore, a Tufts Maine Track medical student working with Dr. Kinna Thakrar, gave an oral presentation at a national addiction medicine conference and also first authored an invited article for a special collection on infectious disease/substance use issues entitled, Health care professional perspectives on discharging hospitalized patients.

GRADUATE STUDENTS:

Madeleine Nowak, University of Maine PhD student in the Koza Lab, received the poster award for Biomedical Sciences at the University of Maine Student Symposium in April for her poster entitled Hepatic Signaling Effects on Adipose Tissue Mest and Fat Mass Expansion, and also won a BioME Seed Grant for Adipose Gene Expression May Be Regulated by Circulating Hepatokines.

Marissa McGilvrey, graduate student in the Liaw Lab, received an American Heart Association predoctoral fellowship for Methionine restriction and perivascular adipose tissue biology. This fellowship award for $65,000 supports Marissa’s PhD thesis dissertation research and Dr. Lucy Liaw is her mentor.
RESEARCH TRAINING & EDUCATION

RESEARCH FELLOWS:

Rebecca Mountain, PhD, was awarded a K01 Mentored Research Scientist Development Award from the National Institutes of Health. Her research will study the impact of social isolation on bone metabolism. This competitive 5-year award allowed her to complete her postdoctoral training and move into a Staff Scientist role under the continued mentorship of Dr. Katherine Motyl.

Eben Estell, PhD, was awarded a K01 Mentored Research Scientist Career Development Award from the National Institutes of Health. Eben’s research studies the signaling pathways by which irisin, a signaling factor released from muscle during exercise, affects key cells within bone to guide adaptation of the tissue. This competitive 5-year award allowed him to complete his postdoctoral training and move into a Staff Scientist role under the continued mentorship of Dr. Cliff Rosen.

MENTORS:

Clifford Rosen, MD, won the 2023 MaineHealth Institute for Research Faculty Mentor of the Year award. This award is intended to recognize a faculty member or supervisor who has provided exemplary scholarly or professional mentorship.

Lucy Liaw, PhD, and Kinna Thakarar, DO, MPH, are multiple Principal Investigators on a newly awarded T35 grant, entitled Enhancing research training for Maine Track / Tufts medical students from the National Heart, Lung, and Blood Institute at NIH. T35 grants are institutional training grants that support short-term training of predoctoral students interested in careers in biomedical, behavioral, or clinical research. The five year grant will provide funding for 10 students each summer (50 total) to engage in rigorous, full-time summer research training experiences.

Sergey Tsibulnikov, PhD, research fellow working with Drs. Sergey Ryzhov and Doug Sawyer in the Myocardial Biology and Heart Failure Lab, presented with colleagues at several science education outreach events, including Maine Bioscience Day, the Maine Science Festival, and the STEMM Festival at the Owl’s Head Transportation Museum.
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MaineHealth Institute for Research is already one of the most innovative research organizations in the nation.

With your help, we can achieve even more.

By donating to research, you help bring the latest scientific discoveries to the bedside and improve the quality of care patients receive. Today’s groundbreaking study could be tomorrow’s life-saving treatment. Your gift will help support research that furthers our understanding of disease processes, which enables us to develop better diagnostics and treatment.

Areas of opportunity for support of MaineHealth Institute for Research’s laboratory-based or clinical research projects include: Cardiovascular Disease, Cancer, Metabolic Disease, Molecular Biology and Genetics, Clinical Trials, Population Health Research, Psychiatric Research, and Vector-Borne Diseases.

Our efforts go beyond research, as well: by supporting our summer student scholarships, you will help us educate and cultivate the next generation of researchers, and ensure that the quest for knowledge and insight continues for years to come.

If you’re interested in supporting the work of MaineHealth Institute for Research, please contact the Philanthropy Department at 207-662-2669.

**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:

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