



Maine Medical Center
Research Institute

2019 Year in Review

MAINE MEDICAL CENTER RESEARCH INSTITUTE

mmcri.org

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Cover photo from Heather Fairfield Campbell, Research Associate in the Reagan Lab. This image shows stem cells differentiating into fat cells, which are marked using a blue stain for the nucleus, a green stain for cell filaments, and a red stain for the fat droplets inside the cells. By growing and studying differentiation outside the body like this, we can better understand how bone marrow stem cells and fat cells contribute to diseases such as cancer, inflammation, or obesity in the bone marrow.

Back cover image from Robert Koza, PhD, Faculty Scientist. This image represents adipose tissue from a mouse model that allows for cell type-specific fluorescent labeling (red) of a nuclear envelope protein. Blue and green fluorescence indicate chromatin and lipid droplets.

Dear Friends



What a year for research at Maine Medical Center Research Institute, Maine Medical Center (MMC), MaineHealth (MH), and the state of Maine! Much of this we owe to Don St. Germain, MD, our Director and Vice President of Research from 2009 until he retired in April 2019. Don's commitment to development of clinical research infrastructure was perfectly in tune with the unification of MH, enabling successful funding to a number of individual investigators as well as programs that highlight this year's successes.

The growth of clinical trials across MH has been remarkable in 2019. Under the leadership of Dr. Bob Kramer, MMC is now a part of the National Heart, Lung, and Blood Institute (NHLBI) supported Cardiothoracic Surgical Trials Network. Dr. Scot Remick led the expansion of the MH Cancer Care Network now supported by the National Cancer Institute Community Oncology Research Program. Drs. Forrest Sheppard and Joseph Rappold have put together a clinical trial that will benefit both military and civilian trauma patients funded by the Department of Defense. In the words of Bill Caron, President of MH, these research programs are 'game-changers' for MH, providing valuable clinical trials to our community.

Research training continues to develop at MMCRI with the receipt of our first institutional training grant (T32) in collaboration with the University of Maine (Orono) to support training of doctoral students. Dr. Lucy Liaw has worked closely with her co-leaders of the program at UMaine to develop a rich undergraduate training program over the past decade, with graduates of our program advancing to faculty as well as industry positions, and all of it helping to develop the biomedical research community in Maine.

An emerging theme at MMCRI is the study of metabolism. This is in part due to the established research programs of endocrinology-focused faculty including Drs. Arturo Hernandez, Cliff Rosen, and Rob Koza. In addition, we welcome Dr. Joseph Nadeau to this group (see page 6) who joined MMCRI in October. The Center of Biomedical Research Excellence in Metabolism, led by Dr. Liaw, as well as Dr. Abby Fleisch's program in environmental epidemiology, are also contributing to this research and aiding the development of a program of distinction in this area.

The work at MMCRI is truly science with and for our community. In the coming months, we will complete our recruitment of a new VP of Research, and embark on a combined medical education and research strategic planning process for MH. Stay tuned – there is more to come in 2020!

Sincerely,

Douglas Sawyer, MD, PhD
Chief Academic Officer, Maine Medical Center
Interim Director, Maine Medical Center Research Institute

In 2017 MMCRI received \$20M from the National Institutes of Health to establish a Northern New England Clinical & Translational Research Network (NNE-CTR). Maine Medical Center and the University of Vermont are the lead organizations. Other partners include the University of Southern Maine and the Dartmouth CO-OP Primary Care Practice-Based Research Network. NNE-CTR's Mission: Enhance the health of people in northern New England (ME, NH, VT), by fostering and coordinating clinical, translational and educational research activities.



2019 NOTABLES

NNE-CTR participants from Maine, Vermont & New Hampshire



426

60% women

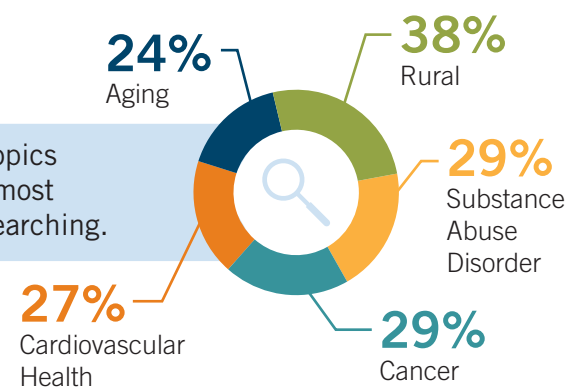
More than one half of registrants are women

Pilot Projects

28 pilot program letters of intent submitted

6 pilot projects awarded

Top 5 research topics participants are most interested in researching.



MMCRI At A Glance

2019 Leadership

Executive Administration

Douglas Sawyer, MD, PhD
Chief Academic Officer, MMC
& Interim Director, MMCRI

Rick McAllister, MEd
Senior Director,
Research Administration

Research Center Leadership

Thomas Gridley, PhD
Director, Center for
Molecular Medicine

Paul Han, MD, MA, MPH
Director, Center for Outcomes
Research & Evaluation

Clifford Rosen, MD
Director, Center for Clinical &
Translational Research

Susan Santangelo, ScD
Director, Center for
Psychiatric Research

2019 Fast Facts

230 Staff Members

\$25M Total 2018 Grant Funds

35 New Grants Awarded

200+ Clinical Trial Studies

Oncology, Cardiology, and Neurology

Top 3 Clinical Research Areas

252 Scientific Publications

Core Facilities with state-of-the-art equipment and BioBank Tissue Repository which distributed over 3,700 biospecimens

12

Learners & Trainees in MMCRI's Education & Training Program

69

11 Patents filed

11

Active companies launched:
Cryptomedix – Dr. Peter Brooks
Soft Robotics Angiography – Dr. Robert Ecker
New Paradigm Therapeutics – Dr. Cliff Rosen

3

2019 Sources of Research Support by Sponsor Type

10.5%: Industry

20.0%: Foundation & Nonprofit

69.5%: Federal

MaineHealth makes research a priority and also has generously provided support to MMCRI's operating budget. 2019 MH Operating Subsidy \$9.3M

NIH Fund Collaborative National Research Networks

In 2019 MMCRI became a part of several national clinical trial research networks sponsored by the National Institutes of Health (NIH). These awards give researchers an opportunity to collaborate with colleagues and research organizations across the country on large clinical trials as well as to broaden our research and increase innovation at MMCRI.



RESEARCH AREA: **CANCER**

NETWORK: National Cancer Institute Community Oncology Research Program (NCORP)

PRINCIPAL INVESTIGATOR: Scott Remick, MD

The MaineHealth Cancer Care Network will implement a new cancer research program that aims to reach more Mainers in their own cities and towns, ensuring they have access to the best possible patient care. For more details, see article on page 11.



RESEARCH AREA: **CARDIOTHORACIC SURGERY**

NETWORK: Cardiothoracic Surgical Trials Network (CSTN)
National Heart, Lung, and Blood Institute

PRINCIPAL INVESTIGATOR: Robert Kramer, MD

In partnership with the Dartmouth-Hitchcock Medical Center, MaineHealth will join a national network to increase cardiac surgery clinical trials in rural areas. For more details, see article on page 29.



RESEARCH AREA: **EMERGENCY CARE**

NETWORK: Strategies to Innovate Emergency Care Clinical Trials Network (SIREN)
National Institute of Neurological Disorders and Stroke

PRINCIPAL INVESTIGATOR: Michael Baumann, MD

Maine Medical Center emergency care physicians and researchers will conduct clinical trials to study what treatments work best for patients with emergency conditions or injuries.



RESEARCH AREA: **LUNG INJURIES AND SEPSIS**

NETWORK: Prevention & Early Treatment of Acute Lung Injury (PETAL)
National Heart, Lung, and Blood Institute

PRINCIPAL INVESTIGATOR: Richard Riker, MD

Maine Medical Center is a part of this national clinical research consortium to conduct clinical trials that address the prevention and treatment of acute lung injury.

National Institute on Aging

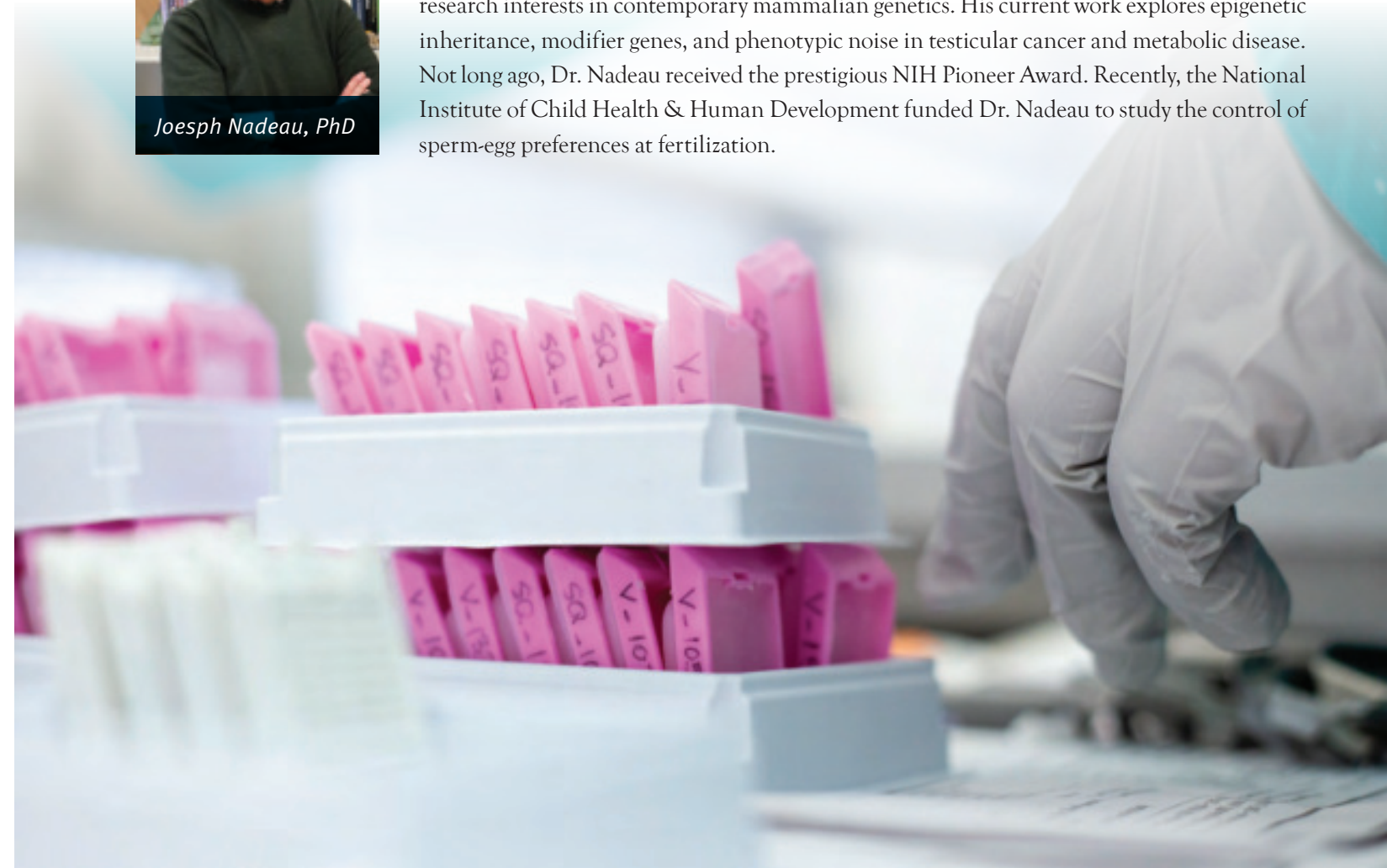
The National Institute on Aging (NIA) sponsored a Director's Regional Meeting on November 7, 2019 at the University of Southern Maine, hosted by the Northern New England Clinical & Translational Research Network (NNE-CTR). This was a successful one-day meeting on research and training for individuals new to research on aging as well as those underrepresented in aging research. Dr. Cliff Rosen, Director, Center for Clinical & Translational Research at MMCRI and Co-Principal Investigator of the NNE-CTR, is part of an international team of researchers who put together a position statement, published in the journal *Science*, that lays out a new healthcare framework to help aging populations stay healthier for longer.



Joseph Nadeau, PhD

New Principal Investigator Joins MMCRI

Dr. Joe Nadeau joined Maine Medical Center Research Institute as a Senior Faculty Scientist in the Center for Molecular Medicine. Dr. Nadeau came from the Pacific Northwest Research Institute. He is an internationally known human and mouse geneticist with wide-ranging research interests in contemporary mammalian genetics. His current work explores epigenetic inheritance, modifier genes, and phenotypic noise in testicular cancer and metabolic disease. Not long ago, Dr. Nadeau received the prestigious NIH Pioneer Award. Recently, the National Institute of Child Health & Human Development funded Dr. Nadeau to study the control of sperm-egg preferences at fertilization.

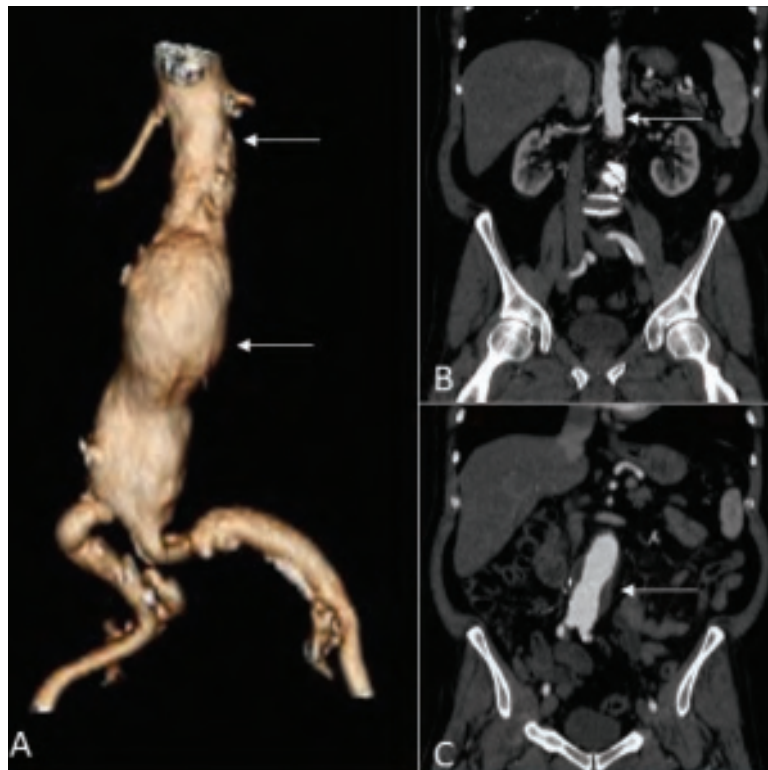


PILOT PROJECTS: A CATALYST FOR RESEARCH

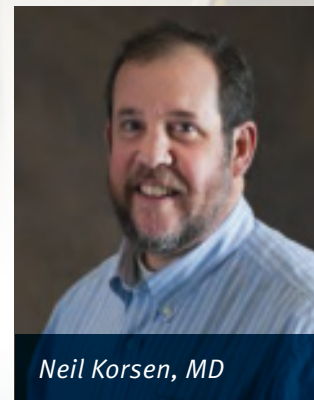
Sometimes a research study requires initial experiments prior to launching the full study. A pilot project is a smaller study that can usually be performed in a limited time frame (within 1 year), and may be designed to establish feasibility, experimental models, protocols, samples, or procedures for a larger study. Our Northern New England Clinical & Translation Research Network, Center of Biomedical Research Excellence (COBRE) in Metabolic Networks, and institutional cardiovascular center programs all provide pilot project funding to researchers to get a new idea off 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 or publications. See below for examples of two recent and promising pilot projects.

Pilot Project: A closer look at cardiovascular disease

Dr. Kimberly Malka was recruited to Maine Medical Center as part of the Vascular Surgery group, and also spends some of her time developing a translational research program at Maine Medical Center Research Institute. She received a pilot project from the COBRE in Metabolic Networks to study cardiovascular diseases that require open abdominal surgeries, including abdominal aortic aneurysms. Dr. Malka’s study will allow for the procurement of vascular and surrounding adipose tissue from patients with cardiovascular disease that require vascular surgery. These tissues will be studied at the molecular and cellular level in the lab to identify new target pathways that may distinguish diseased from healthy tissue. The outcomes of this study are expected to increase our understanding of the progression of diseases such as aneurysms, and suggest new targets for medical management of disease.



3D reconstruction and CT images of an Abdominal Aortic Aneurysm. A. 3D reconstruction based on a CT scan of a patient with an abdominal aortic aneurysm. Top arrow points to normal aorta below the renal arteries while the bottom arrow points to the aneurysm. B. Coronal view of a CT scan from the same patient with the segment of normal aorta below the renals in view (arrow). C. Coronal view of a CT scan from the same patient with the segment of aneurysmal aorta in view (arrow).



Neil Korsen, MD

Pilot Project: Helping at-risk seniors maintain functional independence

Because the populations of Vermont, New Hampshire, and Maine are among the oldest in the nation, we need to provide services for seniors who are at risk of losing their independence, particularly in rural areas. Michael LaMantia (University of Vermont), Neil Korsen (MMCRI), and Meaghan Kennedy, Project Manager (Dartmouth University) have been awarded a pilot project from the NNE-CTR, entitled, “Feasibility of a Community Health Workers (CHW) Intervention for Functional Decline in Rural Older Adults.” This project trains CHWs to deliver interventions for rural older adults who have early signs of memory loss, depression, and difficulty with mobility.

MILESTONE

MMCRI celebrated its 20th Anniversary of the ground breaking at 81 Research Drive in October 2019.

Areas of Research

CANCER

NEUROSCIENCE & ADDICTION

CARDIOVASCULAR DISEASE

OBESITY & METABOLIC DISEASE

PUBLIC HEALTH

IMPROVEMENTS IN CLINICAL CARE

CANCER

CENTER FOR MOLECULAR MEDICINE

Michaela Reagan, PhD

Understanding Multiple Myeloma

Obesity is linked to many cancers, including multiple myeloma, a cancer that forms in a type of white blood cell termed the plasma cell. However, the bridge between obesity and myeloma is not well understood. In spring of the 2019, Dr. Michaela Reagan received an American Cancer Society Research Scholar Grant to investigate the question “how do bone marrow fat cells support myeloma tumor cells?”. The study’s long-term goals are to understand molecules from fat cells and related mechanisms that drive multiple myeloma growth. This research could lead to paradigm-shifting concepts to guide the development of new anti-myeloma therapies. Dr. Reagan spoke about her research and also led a MMCRI team at the American Cancer Society (ACS) Making Strides of Greater Portland 5K Walk in October.



Dr. Reagan (far right) pictured with part of her research team at the ACS walk in October.

Pradeep Sathyanarayana, PhD

Discovery of a Novel Protein in Neutrophil Biology: Implications During Fighting Infections & Chemotherapy

Dr. Pradeep Sathyanarayana is the Principal Investigator for a recently awarded grant from The National Institutes of Health’s National Heart, Lung, and Blood Institute. The funding will be used to better understand the function and role of the CD34 family of proteins, which are known to mark the blood forming stem cells in hematopoiesis, or the formation of blood cells. This research addresses the balance between effective immunity and inflammation, especially during times of stress, disease, infection or treatments such as chemotherapy or ionizing radiation, when the immune system can be compromised.

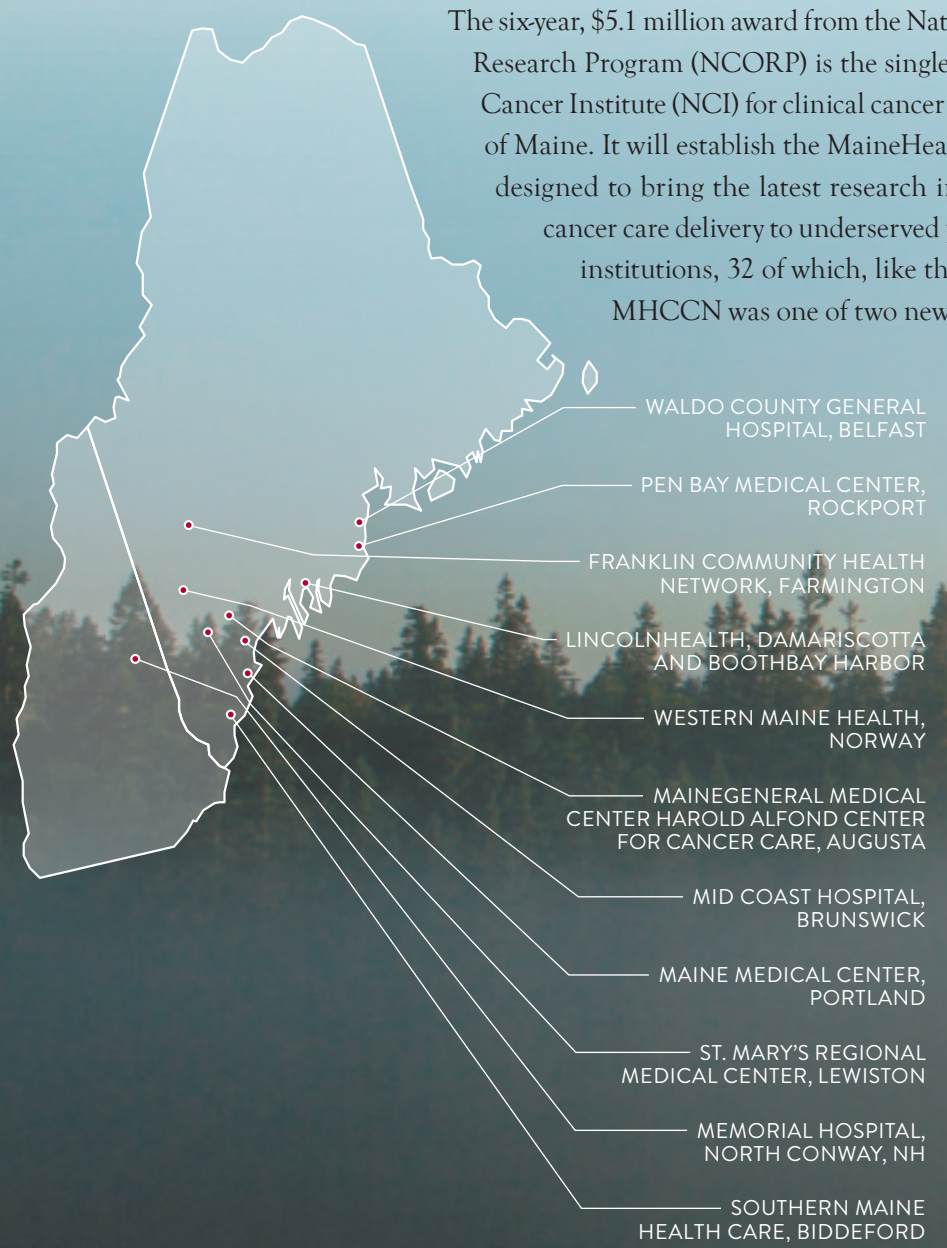


Research Team (L to R): Aldona Karaczyn (Staff Scientist), Dr. Pradeep Sathyanarayana (Principal Investigator) and Dr. Cal Vary (Co-Investigator)

MAINEHEALTH CANCER CARE NETWORK RECEIVES \$5.1M GRANT FROM NATIONAL CANCER INSTITUTE

Cancer patients across Maine and Carroll County, New Hampshire will now have access to far more advanced clinical trials in their home communities, thanks to a major federal research grant awarded to MaineHealth and which includes the participation of the entire MaineHealth Cancer Care Network (MHCCN). This network, which includes 11 MaineHealth partner hospitals and organizations, offers a robust research arm in partnership with Maine Medical Center Research Institute.

The six-year, \$5.1 million award from the National Cancer Institute Community Oncology Research Program (NCORP) is the single largest grant ever extended by the National Cancer Institute (NCI) for clinical cancer research and cancer clinical trials in the state of Maine. It will establish the MaineHealth Cancer Care Network Lifespan Program, designed to bring the latest research in cancer prevention, cancer treatment and cancer care delivery to underserved populations. NCORP is funding a total of 46 institutions, 32 of which, like the MHCCN, are community-based sites. The MHCCN was one of two new sites to join this prestigious NCI network.



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



The MHCCN Lifespan Program will be the only oncology program in Northern New England to enroll patients in NCI clinical trials at every stage of the cancer continuum, from prevention to survivorship, and from pediatric to adult. Some of the studies will focus on cancer control and prevention, with a goal of reducing the incidence, risk and mortality rates for cancer and improving quality of life for survivors. Others will aim to improve the way cancer care is delivered.



We believe patients should have access to advanced care close to home — wherever they live. This grant is a transformational award that will bring a wide variety of clinical trials to our rural communities.

— Dr. Scot Remick
Chief of Oncology
Maine Medical Center

NCORP was developed out of a recognition that both patients and scientific research benefit when cancer clinical trials are offered to people where they live, not just at major institutions in large urban areas.

“Patients often feel that in order to get state-of-the-art care and to enroll in clinical trials, they need to travel to a major metropolitan area,” said Scot Remick, MD, Maine Medical Center’s Chief of Oncology and one of the three principal investigators of the Lifespan Program. “We believe patients should have access to advanced care close to home — wherever they live. This grant is a transformational award that will bring a wide variety of clinical trials to our rural communities.” In addition to Dr. Remick, Christopher Darus, MD and Peter Rubin, MD, will serve as the study’s second and third principal investigators.

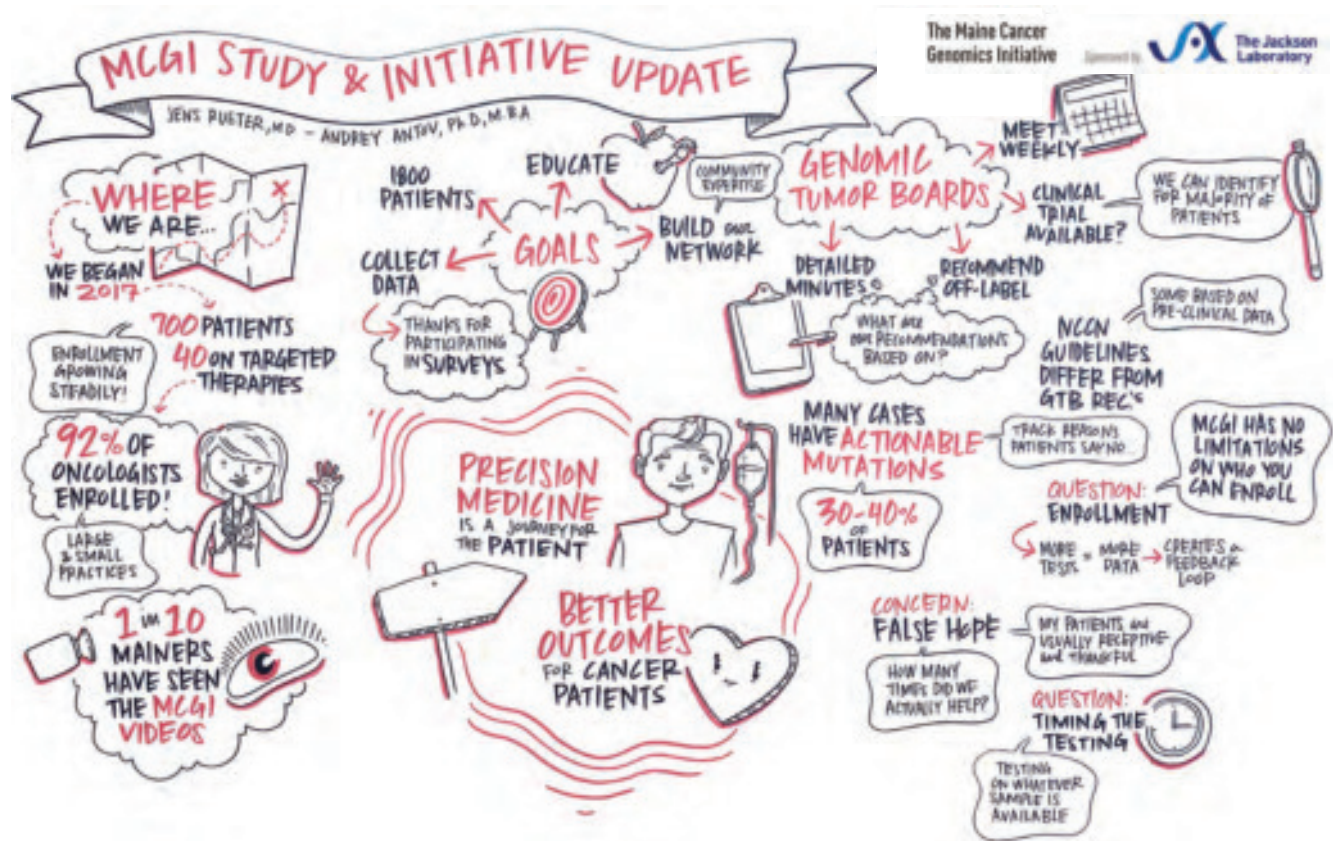


A program of the National Cancer Institute of the National Institutes of Health

While numerous studies suggest cancer patients in rural settings have higher mortality rates than those in urban areas, a 2018 study published in the Journal of the American Medical Association found that cancer patients in rural and urban settings had similar outcomes when they had uniform access to a clinical trial. MaineHealth’s network of clinical trials and other research activities specifically target health conditions present in the populations its hospitals and practices care for, allowing patients to receive trials that are medically appropriate in their own community. According to the Centers for Disease Control and Prevention, Maine has the eighth highest cancer mortality rate in the nation. The state also has the third highest rate of pediatric cancer. Patients currently have access to clinical trials through the MHCCN at Maine Medical Center, Maine General Medical Center, Southern Maine Health Care, Stephens Memorial Hospital, Waldo County General Hospital and Pen Bay Medical Center. St. Mary’s Regional Medical Center and Mid Coast Hospital are expected to begin enrolling cancer patients through the MHCCN in early 2020. The Lifespan Program will help extend the reach of clinical trials to Franklin Memorial Hospital, Lincoln Health and Memorial Hospital in North Conway, NH as well as increase the number of clinical trials available to patients at other locations within the MHCCN. The number of clinical trials available to oncology patients in the MHCCN is expected to nearly triple during the life of this grant.

CENTER FOR OUTCOMES RESEARCH AND EVALUATION

Maine Cancer Genomics Initiative: Progress on Precision Medicine for Cancer Treatment Testing



“Capturing the Forum through artistic note taking” The forum is a yearly learning opportunity for all clinicians and affiliates participating in the MCGI initiative to come together, share lessons learned and learn about new developments.

Maine has among the highest cancer incidence and mortality rates in the US, with approximately 9000 new cancer cases diagnosed each year. Genomic tumor testing (GTT) is a new technology that promises to revolutionize cancer treatment by enabling therapy to be targeted to particular genomic variations in tumors. However, little is known about the appropriate strategies for implementing GTT in clinical practice, or the effects of this new technology on clinical outcomes and patient care.

To address these knowledge gaps, MMCRI’s Center for Outcomes Research & Evaluation (CORE) researchers, led by Dr. Paul Han, are partnering with the Jackson Laboratory (JAX)

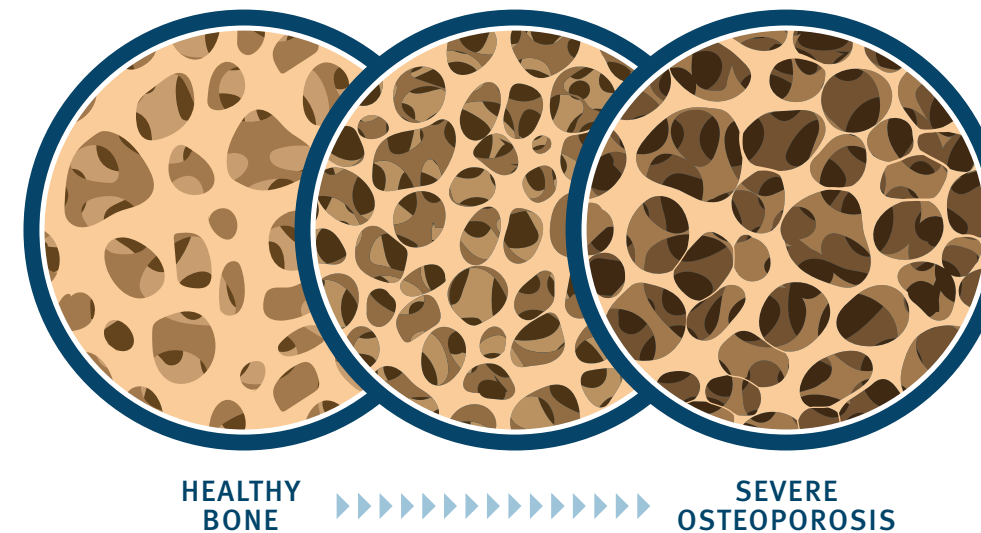
on a 5-year statewide project: the Maine Cancer Genomics Initiative (MCGI). Led by Drs. Jens Reuter & Andrey Antov at JAX, and supported by the Harold Alford Foundation, the MCGI is a unique collaboration engaging oncologists across Maine. CORE leads the outcomes evaluation component of the MCGI, which is utilizing a mixed-methods approach to assess participating oncologists’ and patients’ experiences with GTT. The work is identifying key needs and barriers to the effective implementation of GTT in clinical practice, including physician and patient education. The initiative aims to recruit a total of 1800 patients, and will generate a wealth of important data that will help researchers understand and improve the implementation of GTT in oncology care.

CENTER FOR OUTCOMES RESEARCH AND EVALUATION

Christine Lary, PhD

A Look at Pharmacogenomics – Beta Blockers & Bone Density

Pharmacogenomics analyzes how the genetic makeup of an individual affects a patient’s response to drugs. Dr. Christine Lary is leading the charge in a pharmacogenomic study to further investigate the impact of beta blockers on bone mineral density. This project is funded through the Centers of Biomedical Research Excellence (COBRE) in Mesenchymal and Neural Regulation of Metabolic Networks. It involves close collaboration with Dr. Douglas Kiel at Hebrew SeniorLife and Harvard Medical School and collaborators at Brown University, and the University of Graz in Austria.



Osteoporosis is a debilitating and costly bone condition that causes fractures in 33% of women and 20% of men over the age of 50, resulting in more than 2 million fractures per year in the US with annual hospital costs exceeding \$28 billion. Recent studies show that beta blocker use may improve bone mineral density (BMD) and decrease risk of fracture. Beta blockers are drugs currently used to control heart rhythm, treat angina, and reduce high blood pressure. This project used the Framingham Osteoporosis Study to measure the association between beta blocker use and bone mineral density of the hip and spine and to characterize molecular mechanisms involved through analysis of microRNA (ribonucleic acid – RNA is a type of nucleic acid) and gene expression data from the whole blood of participants. The researchers have found that certain microRNAs correlate with beta blocker use and increased BMD and have also shown that these biomarkers correlate significantly with reduced fracture risk in a prospective hip fracture group of elderly nursing home residents from Austria. “I hope to validate these findings in an upcoming clinical trial of beta blocker use for bone mineral density protection in post-menopausal women as well as to investigate the mechanism further in cell culture and animal models,” said Dr. Lary. This work will increase our understanding of treatment pathways for osteoporosis which will ultimately help improve outcomes for patients with osteoporosis.

CENTER FOR PSYCHIATRIC RESEARCH

Kristen Woodberry, MSW, PhD

Understanding the Emergence of Serious Mental Health Challenges in Adolescents and Young Adults

Adolescence and early adulthood, a period of relatively good physical health, is the peak period of onset for serious disorders of mental health. Dr. Kristen Woodberry's research team has been engaged in two projects over the course of the past year related to the onset of major mental illness in this age group. The Daily Life Study, an Exploratory/ Developmental Research Grant funded by the National Institute of Mental Health (NIMH), is funding the collection of data on the daily experiences of young people ages 15-25 through a smartphone app. The young people report on thoughts, emotions, and aspects of social context multiple times a day for three weeks. The aim of the study is to explore whether day-to-day fluctuations

in thoughts and mood might help to predict mental health challenges over time. The questions that are being explored include: could fluctuations help predict the onset of a major depressive or manic episode, an exacerbation of psychotic symptoms, or an increase in suicide risk? There is no strong evidence that early intervention programs such as MMC's Portland Identification and Early Referral (PIER) program (mmcri.org/pierprogram) can improve outcomes for young people experiencing a first episode of psychosis if they are detected early enough. Thus identifying predictors and indicators of emerging mental illness has become a high public health priority.=

Dr. Woodberry is also involved in a second project, the Screening for Early Emerging Mental Illness (SEE-ME) study, currently being conducted in the Adolescent Medicine Clinic at Boston Children's Hospital. This project is exploring the potential to improve early detection within primary and integrated medicine settings. For this study, adolescents and young adults ages 14-21 answer a series of questions on an iPad while waiting for their clinic appointments. Researchers are hoping to learn more about how common some of the early warning signs of mental illness are in adolescents and young adults. These initial data will be leveraged to pursue funding for a large population study to better understand how to distinguish true warning signs from benign experiences during this important period and within general healthcare settings. Visit psychosisscreening.org to learn more about the early warning signs of psychotic illnesses and see the new tools Dr. Woodberry's team created to support primary care and integrated behavioral health specialists recognize and respond to young people in time to get them the right help.

The Maine Medical Center Research Institute Team L to R: Zach Harris, Anna Cloutier, Katherine Elacqua, Tan Twigg, Kate Powers, and Dr. Kristen Woodberry



Matt Siegel, MD

New Possibilities in Behavior Prediction for Parents of Children with Autism

A collaborative group of researchers, led by Dr. Matthew Siegel, Faculty Scientist at MMCRI and VP of Medical Affairs for Development Disorders at Maine Behavioral Healthcare, is examining the link between physiologic arousal and aggressive behavior in youth with autism. This work encompasses a multi-center \$3.1 million study funded by the Simons Foundation of New York, NY and the Nancy Lurie Marks Family Foundation of Wellesley, MA. In the first study year, the group established reliability of data collection across sites and completed data collection with over 40 youth with autism in inpatient psychiatric units. In June, Dr. Siegel and his team published an article in the leading autism journal, *Autism Research*, demonstrating that with data from their first 20 participants, they were able to predict the onset of aggressive behavior 60 seconds in the future, using physiologic data collected by a wearable bio-sensor that is much like a Fitbit, with accuracy approaching 80%.



Dr. Siegel working with a patient

“In the coming year we aim to collect physiologic and behavioral data from another 100 participants, and use that data to refine our prediction algorithm to increase accuracy and lead time for an aggressive event,” said Dr. Siegel. Once satisfied with the performance of the algorithm, they will move into the final phase of the study, which is a randomized trial testing the effect on staff behavior and their response to impending aggression when they receive a predictive warning. “This is a very exciting step, where we begin to try to address and prevent serious problem behaviors before they occur, opening a whole new window for intervention in autism,” indicated Dr. Siegel.

This research study is being performed through the Autism & Developmental Disorders Inpatient Research Collaborative (ADDIRC), a research network of specialized child psychiatric hospital units that serve children and adolescents with autism and other developmental disorders. The ADDIRC was founded in 2013 by Dr. Siegel and is coordinated by MMCRI/Maine Behavioral Healthcare.



This is a very exciting step, where we begin to try to address and prevent serious problem behaviors before they occur, opening a whole new window for intervention in autism.

— Dr. Matthew Siegel
Faculty Scientist, MMCRI

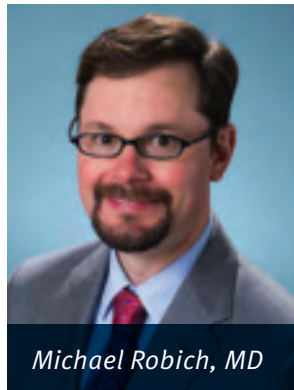
VP of Medical Affairs for Development Disorders, MBH

CENTER FOR CLINICAL & TRANSLATIONAL RESEARCH

Michael Robich, MD

Can Resveratrol Help Patients with Diabetes & Heart Disease?

There are 29 million patients with diabetes and about 5 million patients with heart failure in the United States. Diabetes prevents efficient metabolism of fuel, causes inflammation and vascular disease that blocks normal blood flow, and inhibits the function of the heart after injury. These changes make diabetics more susceptible to heart attacks and heart failure



Thanks to the American Heart Association's effort to lead the fight against these diseases, Dr. Michael Robich, a Maine Medical Center (MMC) Cardiac Surgeon, received a Mentored Clinical & Population Research Award from the AHA with Dr. Doug Sawyer serving as the mentor. Begun in 2017, this project is a unique collaboration among cardiologists, cardiac surgeons, and basic scientists. During this time physicians have been safely collecting tissue from the hearts of patients undergoing heart surgery. They have collected and assessed the function of endothelial cells, a measure of vascular health, and can measure the level of endothelial injury. In addition they have studied the make-up of caveolae, structures on the cell membrane, that are important for cell signaling and are negatively impacted by diabetes. "This research will allow for a greater understanding of how diabetes impacts metabolism in the heart," said Dr. Michael Robich.

In 2019 the second phase of the study began, which included enrolling patients to examine how resveratrol changes the metabolic profile of the heart. Resveratrol is a plant compound found in grapes, red wine, some berries and peanuts. In previous studies it has been shown that resveratrol can improve heart metabolism and function in pigs with diabetes and chronic lack of blood flow to the heart.

Understanding how the heart is impacted by diabetes and reversing the negative effects could lead to decreased rates of heart failure and death in diabetic patients as well as offer new treatment options.



Our understanding of how the heart heals itself is just beginning. This project will provide a unique platform to study any supplement or drug and the effect on the heart. This is a very common approach used in cancer surgery, but has not been utilized to learn about the heart.

— Dr. Michael Robich
Cardiac Surgeon
Maine Medical Center

Sergey Ryzhov, MD, PhD and David Seder, MD Basic & Clinical Researchers at MMC Work Together to Investigate the Role of Inflammation after Cardiac Arrest

Each year more than 500,000 Americans suffer cardiac arrest, and despite improved cardiopulmonary resuscitation (CPR), post-resuscitation therapy, and cardiovascular support care, overall outcomes remain poor. Post-cardiac arrest syndrome (PCAS) is defined as a condition after resuscitation following a massive injury to all organs, most notably (but not limited to), the brain. PCAS is characterized by development of systemic inflammatory response, which contributes to additional brain tissue damage. This inflammation-associated tissue damage may be an important target for therapies.

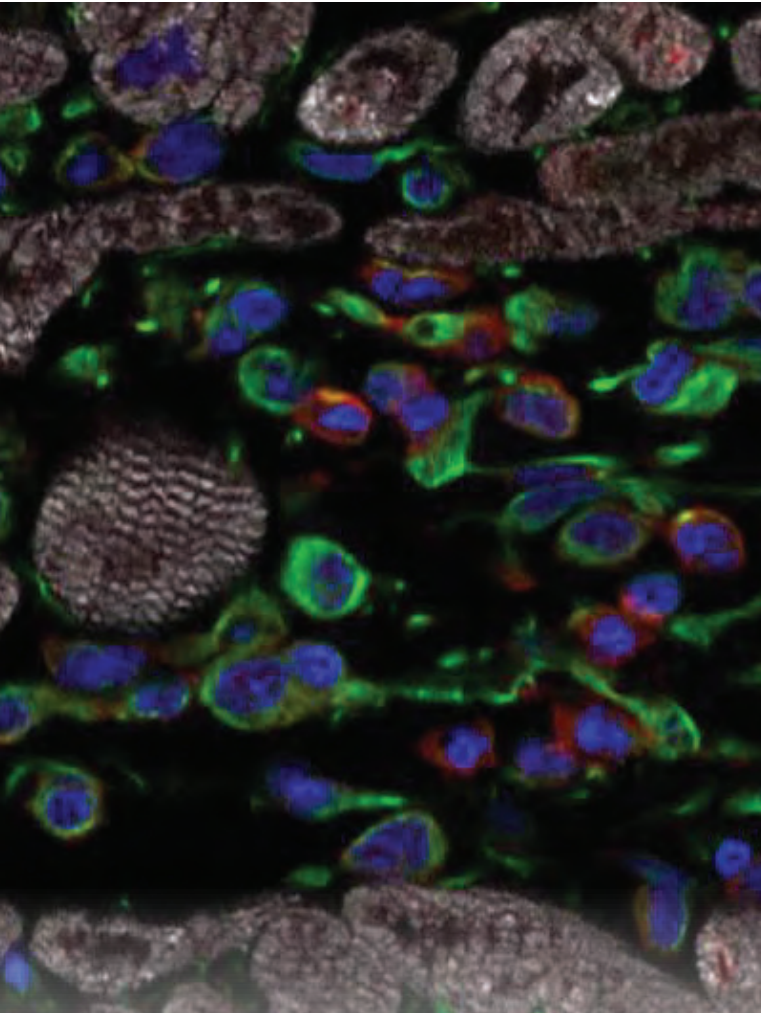
In 2015, a collaboration between physician-scientists from MMC's neurocritical care unit (led by Dr. David Seder) and basic scientists from MMCRI (Drs. Sergey Ryzhov & Ilka Pinz) began to investigate the role of inflammation after cardiac arrest. Later in that year, this collaboration was funded by the Cardiovascular Research Institute pilot grant program and resulted in fostering an approach to better understand and potentially solve clinical problems identified in the patient-care setting using high-quality basic science research.

This group has been examining the diversity of the inflammatory response in patients with cardiac arrest which results in differences in patient outcomes. The work also includes identifying protective pathways that would allow immunotherapeutic approaches to improve post-cardiac arrest care. Immunotherapeutic approaches or immunotherapy is the treatment of disease by activating or suppressing the immune system.

In 2019 the investigators published their findings in the Journal of American Heart Association. They identified the new, previously unrecognized role of adaptive immunity (T and B cells, or lymphocytes) in the protection against massive injury after cardiac arrest. In addition, they found that lymphocytes contribute to generation of the potent anti-inflammatory molecule adenosine. The capability of lymphocytes to produce adenosine correlates with better survival after cardiac arrest.

This exciting work increases the potential of developing new therapies and better care for patients with cardiovascular disease.

CENTER FOR MOLECULAR MEDICINE



Neuregulin-1 signaling promotes healing of injured cardiac tissue. The image demonstrates a high expression of the receptor for Neuregulin-1 (red) on cardiac progenitors (green) in a sample obtained during coronary artery bypass grafting surgery.

Doug Sawyer MD, PhD and Calvin Vary, PhD **The National Institutes of Health Awards \$1.9M to Study Cardiac Cell Therapy**

Maine Medical Center Chief Academic Officer, Doug Sawyer, MD, PhD, and MMCRI Faculty Scientist Calvin Vary, PhD are the Principal Investigators on a \$1.9 million grant from the National Heart, Lung and Blood Institute (NHLBI) to study how certain adult stem cells might be used to reverse heart failure when injected into the heart. The pre-clinical study may someday lead to new strategies to treat heart failure.

Drs. Sawyer and Vary are joined by two colleagues at MMCRI, Ilka Pinz, PhD and Sergey Ryzhov, MD, PhD. The research team is looking into whether certain kinds of heart cells might be more effective than others in regenerating heart tissue when injected into a failing heart. The award also will allow them to study whether these cells can be manipulated into healing a heart more effectively and whether stem cells from other parts of the body may be just as effective at healing as those coming from the heart. The stem cells have all been collected from MMC patients who have consented to a small biopsy of heart tissue at the time of cardiac surgery.

“Cell therapy is a promising area of science that may one day reduce the number of patients who need current advanced therapies such as heart transplant and mechanical pumps,” Sawyer said. “Studies like this help us understand what may make some stem cells better at repairing an injured heart than others.”

Lucy Liaw, PhD **How Anti-Aging Diets Impact Vascular Health**

Obesity is a risk factor for the accelerated development of cardiovascular disease, and a steady increase in obesity, particularly in youth, has made this condition a major public health problem. Dr. Lucy Liaw is taking a closer look at diets and cardiovascular disease thanks to her recent Transformational Project Award from the American Heart Association. The major problem the Liaw Lab will address is why obesity and fat expansion lead to greater occurrence or severity of vascular disease. This research will study how anti-aging diets impact fat surrounding blood vessels and vascular health. Long-term results from studies like Dr. Liaw’s could lead to potential therapies to increase health and reverse the effects of cardiovascular disease.



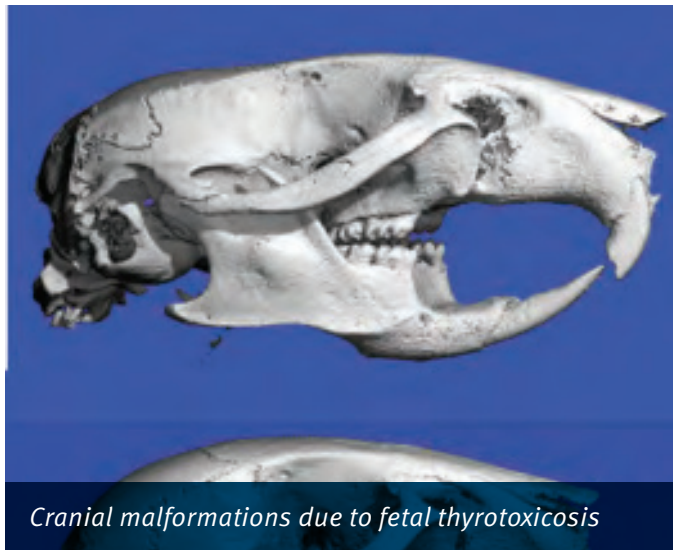
Lucy Liaw, PhD

CENTER FOR MOLECULAR MEDICINE

Arturo Hernandez, PhD

Investigating the Connection between Thyroid Hormone and Congenital Defects

The Hernandez Laboratory was awarded a two-year National Institutes of Health exploratory grant entitled “Congenital abnormalities resulting from fetal thyrotoxicosis”. The award started in March 2019 and was funded by the National Institute of Dental and Craniofacial Research (NIDCR). The project will examine craniofacial, encephalic and heart defects in a genetically modified mouse model that exhibits an excess of thyroid hormone (thyrotoxicosis)



Cranial malformations due to fetal thyrotoxicosis

during fetal life. Many of the defects analyzed, including cleft palate, hydrocephalus, facial malformations, Chiari malformations (a condition in which brain tissue extends into the spinal canal), heart defects and others, do not have a clear origin in humans. The research aims to show that an excess of thyroid hormones in utero (which may occur in humans due to maternal thyroid disease or exposure to endocrine disruptive chemicals) may contribute to such abnormalities. This may lead to studies in humans to evaluate the association between those defects and fetal thyrotoxicosis, and raise awareness about the importance of pro-actively monitoring thyroid parameters before and during pregnancy to prevent congenital defects.

Robert Koza, PhD

How Modifications on DNA Affect Obesity

Drs. Rob Koza and Igor Prudovsky, Faculty Scientists at MMCRI, are the principal investigator and co-investigator on a \$1.3 million award from the NIH’s National Institute of Diabetes and Digestive and Kidney Diseases to study how changes in the expression of a certain gene affect obesity. The hope is that studies of this gene, known as mesoderm specific transcript (MEST), could someday lead to new strategies for the treatment of obesity and type 2 diabetes. Dr. Koza and his team have been studying the epigenetic regulation of MEST. Epigenetic processes can determine whether genes are expressed, or “turned on.” Dr. Koza’s previous studies indicate that animals are less likely to become obese on a high-fat diet when MEST is not expressed or expressed at low levels. What scientists have yet to determine is the function of MEST in the body and the precise epigenetic processes that regulate its expression. This study aims to answer those questions.

“Identifying the molecular pathways by which MEST facilitates the expansion of fat mass and regulates blood glucose could be the first step towards a new way to help treat obesity,” Dr. Koza said. “Years from now, these studies may also define new early interventions doctors could take to help patients prevent the development of obesity and type 2 diabetes.”



Robert Koza, PhD

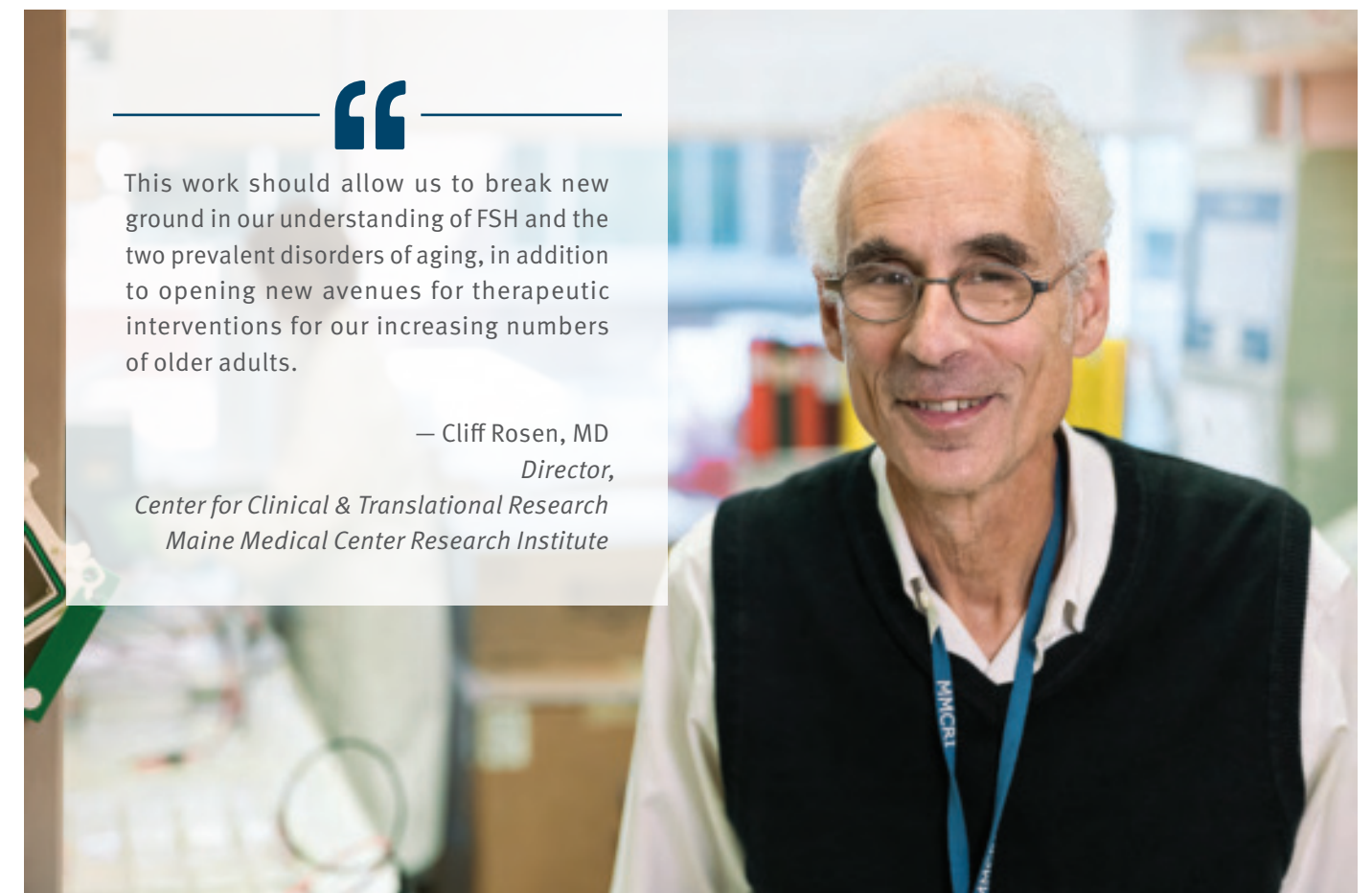
Metabolic diseases like obesity and diabetes are a focus of researchers at MMCRI because of their prevalence in Maine. In 2016, the Centers for Disease Control and Prevention listed Maine as having a diabetes rate of 8.5 percent and obesity rate of 30 percent, the highest in New England.

CENTER FOR CLINICAL & TRANSLATIONAL RESEARCH

Cliff Rosen, MD, Participates in Multi-Center Study that will Focus on Role of Hormones in Obesity & Osteoporosis

Obesity and osteoporosis are global public health hazards that commonly affect older individuals and often co-exist in postmenopausal women. In February the NIH’s National Institute on Aging awarded \$12.5M for a collaborative project among several institutions to study obesity and osteoporosis. The lead Principal Investigator for this multi-center research study is Dr. Mone Zaidi at Icahn School of Medicine at Mount Sinai. Among the other collaborators are: Maine Medical Center Research Institute (MMCRI), University of Texas Southwestern Medical Center and the University of California at San Francisco.

Dr. Cliff Rosen, Director, Center for Clinical & Translational Research and Faculty Scientist at MMCRI, is one of the study’s Principal Investigators and will lead the work at MMCRI. This study was born from a longstanding collaboration between Drs. Zaidi and Rosen, the results of which were published in the journal *Nature*, in 2017. They identified follicle-stimulating hormone (FSH) as a unique target to prevent both obesity and osteoporosis. This current study will take a closer look at FSH as a potential therapeutic target for treatment of both diseases.



This work should allow us to break new ground in our understanding of FSH and the two prevalent disorders of aging, in addition to opening new avenues for therapeutic interventions for our increasing numbers of older adults.

— Cliff Rosen, MD
Director,
Center for Clinical & Translational Research
Maine Medical Center Research Institute

CENTER FOR OUTCOMES RESEARCH AND EVALUATION

Dr. Abby Fleisch, MD, MPH to Study Impact of Household Chemicals

In spring 2019, the NIH’s National Institute of Environmental Health Sciences awarded Maine Medical Center \$2.2 million to study whether certain chemicals that are commonly found in household items may be contributing to obesity in teenagers, and potentially making those teens more susceptible to osteoporosis later in life.

The study will test for PFAS in samples of the teens’ blood and for phthalates in their urine. Researchers also will measure body fat and bone density using a special kind of X-ray machine. Each child filled out a food questionnaire that will help the research team investigate how much of the PFAS and phthalate exposure has come from diet and how much has come from the environment.

The study looks at the impact of perfluoroalkyl and polyfluoroalkyl substances (PFAS) and phthalates on about 500 teenagers who have been enrolled since birth in Project Viva, a longitudinal research study of mothers and children in Eastern Massachusetts. PFAS are synthetic chemicals added to clothing, furniture and carpets to make the items non-stick and stain repellent. Phthalates are added to personal care products such as shampoos and lotions to retain scents. They are also used to improve flexibility in plastics. Studies in animals suggest that these classes of chemicals may disrupt common biological pathways to increase the risk of both high body fat and low bone mineral density.



Dr. Fleisch testified to the U.S. Congress regarding her research on the role of PFAS exposure on cardiometabolic and bone health. Her testimony will be part of a Congressional educational briefing on this topic.

“Adolescence is an important time when our bodies build up both bone and fat,” said principal investigator Abby Fleisch, MD, MPH, a Pediatric Endocrinologist at MMC and Faculty Scientist at the Maine Medical Center Research Institute. “Few human studies have looked at how these chemicals in our environment could be impacting our fat accumulation and the health of our bones.”

Dr. Fleisch received the National Institute of Environmental Health Sciences’ Outstanding New Environmental Scientist (ONES) award to conduct the study. The ONES program was formed to cultivate future leaders in environmental health and support innovative research projects. We expect that this research could lead to ways to curb obesity and osteoporosis later in life.

Research and Outreach Help Improve Outcomes for Lung Cancer Patients

The Maine Lung Cancer Coalition (MLCC) is a 4-year statewide, multi-institution, multi-disciplinary initiative, begun in August 2016, with goals to improve evidence-based lung cancer prevention, early detection, stakeholder engagement and education, and research and data analytics to gain a better understanding of lung cancer determinants, disparities, and outcomes. MMCRI is the lead institution for the Coalition, which is led by Dr. Paul Han (Principal Investigator), Dr. Neil Korsen (Co-PI), and Leo Waterston (Project Director). The MLCC is funded by grants from the Bristol-Myers Squibb Foundation, Maine Cancer Foundation and Anthem Blue Cross & Blue Shield, and in-kind support is provided by the Maine Economic Improvement Fund via the University of Southern Maine. The MLCC brings together diverse stakeholders across the state to work together to reduce suffering and death from lung cancer, with a special focus on vulnerable rural populations with limited access to health care.

In 2019, the MLCC provided key educational and public health information to lawmakers and policy-makers about the health impacts of radon and the need for lung cancer screening. This educational effort was helpful in advancing public health policy. In August 2019, two important laws were enacted that will improve the health of Maine citizens. First, “An Act to Require Public Schools to Periodically Test for Radon” recommends radon testing for all occupied public school buildings every five years and stipulates that all new schools will use radon resistant construction materials. Second, “An Act to Provide Lung Cancer Counseling and Screening for MaineCare Recipients” will require MaineCare (the state’s Medicaid program) to provide coverage for eligible individuals for their shared-decision making physician visit and for low dose CT scan screening, using evidence-based guidelines.

In September, MLCC, in association with its partner Quality Counts, a Qualidigm Company, initiated a Project ECHO™ program to help increase lung cancer screening in Maine. The program connects Maine community hospitals with new or emerging lung cancer screening programs to well-established programs in the state. Project ECHO’s model of web-enabled, case-based virtual learning sessions promotes mentorship, collaborative learning, and the sharing of best practices around lung cancer screening.



Leo Waterston, MLCC Project Director and Susan Leeds, CORE Research Coordinator at the Hall of Flags at the State House in Augusta.



For more information about the MLCC, visit: mainelungcancercoalition.org

CENTER FOR OUTCOMES RESEARCH AND EVALUATION

Colorectal Cancer Screening & Shared Decision Making

Drs. Kathleen Fairfield and Paul Han are currently partnering on a five-year project, PRIMED: Promoting Informed Decisions about Cancer Screening in Older Adults. Led by researchers at Massachusetts General Hospital and funded by a grant from the Patient-Centered Outcomes Research Institute (PCORI), the study aims to enroll adult patients aged 76-85 and their physicians to compare strategies for supporting clinicians in conducting shared decision-making (SDM) conversations with these patients about colorectal cancer screening (CRC). SDM is a process during which patients and clinicians make decisions about care plans together, based on the best available scientific evidence and patients' individual values and preferences.

There is uncertainty about the value of CRC screening in elderly patients, and decisions need to be individualized and shared. The PRIMED study is testing clinician-focused methods of promoting SDM conversations about CRC screening in this population. Across Maine and Massachusetts, investigators aim to recruit 50 clinicians to take part in the study and 500 patients receiving care from these clinicians. In August, the PRIMED study completed its first year, with the CORE team successfully enrolling and training their target number of clinicians. CORE anticipates that patient recruitment and screening will commence in December 2019.



NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK



Rural Core Team (L to R): Project Manager, Lisbeth Wierda, MPH, Dr. Neil Korsen, and Research Navigator, Kerri Barton, MPH.

Community Engagement Key to Health Research in Rural Communities

The Northern New England Clinical and Translational Research Network (NNE-CTR) was established in July 2017 to enhance the health of people in Maine, New Hampshire and Vermont by fostering and coordinating clinical, translational and educational research activities. The Rural Health Research and Delivery Core of the NNE-CTR ensures these activities reach rural parts of our state. Current partnerships include three rural communities: Western Maine Health in Norway, Pen Bay Medical Center in Rockport, and Waldo County General Hospital in Belfast. Projects focus on opioid use disorder, adverse childhood experiences, hepatitis C, and chronic disease.

The Rural Core of the NNE-CTR, led by Dr. Neil Korsen, Kerri Barton, and Lisbeth Wierda, has utilized a community-engaged research approach to work with community residents and clinicians in the Norway area to develop a community-driven research project. The Rural Core also sponsored a training in 2019 on Boot Camp Translation (BCT), an evidence-based method of engaging communities to translate medical information into actionable, locally-relevant materials and messages. Thirteen participants representing MaineHealth, Dartmouth, Healthy Oxford Hills, Preble Street, and the Coastal Healthcare Alliance Community Health and Wellness Department attended this training. The Rural Core is now working to obtain funding to conduct more BCT efforts and to evaluate their impact.



For more information on the NNE-CTR and the Rural Health Research Delivery Core, visit: nne-ctr.net

VECTOR-BORNE DISEASE LABORATORY

Risk of Tick-borne Illness Linked to Climate, Deer

The Vector-borne Disease Lab began its research in 1989 under the direction of co-PIs Peter Rand, MD, and Robert Smith, MD MPH, to study the invasion of the blacklegged (deer) tick (*Ixodes scapularis*) into Maine. Lyme disease, anaplasmosis, babesiosis, relapsing fever, and deer tick virus are pathogens transmitted to humans through the bite of an infected deer tick. From 1989-2013, Vector-borne Disease Lab staff collected a unique dataset on tick abundance. Susan Elias joined the lab in 2000, and recently completed a PhD program—partially funded by the National Science Foundation at the University of Maine. Elias used the lab’s long-term tick dataset to assess the multiple drivers of range expansion of the deer tick. “People ask me if we would still have our deer tick problem without climate change,” said Elias. “And my answer is yes, but climate change is adding to the challenge.” Elias found that increasing tick

abundance in Maine was correlated with warmer winters, earlier accumulation of growing-degree days, increasing summer humidity, and higher white-tailed deer abundance. The research shows Maine residents can mitigate the effect of climate change by managing the landscape for better health. “I tell property owners and townspeople: if you can only do two things to reduce ticks in the environment, keep your deer numbers down to a healthy level and remove invasive Japanese barberry, which harbors deer ticks.” The Maine Climate Council was launched on September 19, 2019, charged with bringing new jobs, cleaner air, and a stronger economy through a science-based commitment to reduce greenhouse gas emissions 80% by 2050. Elias was asked to serve on the Council’s Science and Technical Subcommittee. According to Elias: “It’s time to translate the science into sound health policy.”

Invasive Japanese barberry — habitat of deer ticks

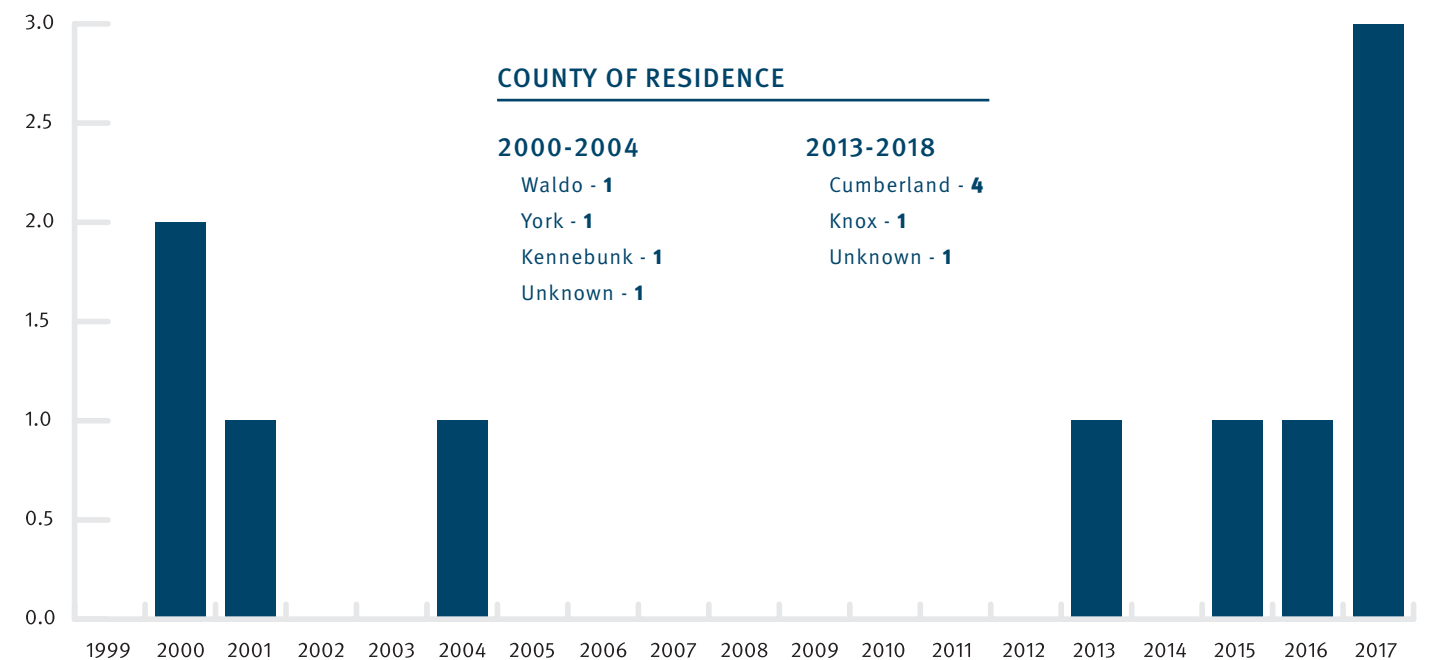
Further Research Increases Understanding of Powassan Virus in Maine

Powassan virus (POWV) is a tick-borne illness that is found primarily in the upper mid-western and northeastern regions of the United States, as well as parts of Canada. It can cause a serious viral infection of the brain and the tissues surrounding it, called encephalitis, which leaves half its victims with permanent neurological damage. Although still considered rare, the number of reported cases of Powassan encephalitis has risen dramatically over the past 10 years.

A grant from the Maine Outdoor Heritage Fund, has allowed the Vector-borne Disease Laboratory at MMCRI to study the geographic distribution, rate of infection, and genetic characterization of POWV in the deer tick, which up until now was not well documented in Maine. Rebecca Robich, Staff Scientist, is leading this effort and currently the lab has collected data from five different health areas in Maine. The results were published in 2019 in the American Journal of Tropical Medicine and Hygiene. This work has prompted additional research on the possibility that POWV might exist in small microhabitats in nature consisting of just the right mixture of environmental factors for the virus to propagate. The lab is currently investigating whether or not habitat type plays a role in POWV transmission. Five different habitat types are currently being examined: shrub, open field, edge (where open field meets forest), forest with sparse, native shrub, and forest with invasive species in the understory such as Japanese barberry.

It is important to note that, currently only a small percentage of deer ticks in Maine carry POWV, and serious cases of this disease remain very rare. The lab’s work will help better understand Powassan virus transmission and disease risk in our region and could lead to better control measures in the future for this serious virus.

HUMAN POWASSAN VIRUS CASES IN MAINE



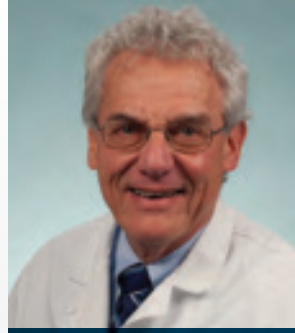
Source: Maine Center for Disease Control and Prevention

IMPROVEMENTS IN CLINICAL CARE

Collaborative Network to Improve Access to Cardiac Clinical Trials in Rural Areas

Dr. Robert Kramer, MD, Director of Cardiac Surgery Research & Quality Improvement at Maine Medical Center (MMC) and Dr. Alexander Iribarne, MD, MS, cardiac surgeon and Director of Cardiac Surgery Research at Dartmouth-Hitchcock Medical Center (DHMC) are principal investigators on a \$3.9 million grant from the NIH's National Heart, Lung, and Blood Institute. This grant was awarded in the spring and will establish a collaborative network to increase access to cardiac surgery clinical trials among rural populations.

DHMC and MMC are now linked Clinical Research Centers that support the NIH Cardiothoracic Surgical Trials Network (CTSN). CTSN was established in 2007 to create an infrastructure for conducting major clinical trials in cardiac surgery. The grant will have a significant impact on rural cardiac surgery patients in Maine and New Hampshire, states with the oldest populations in the nation, according to the most recent U.S. Census data. Maine is also the state with the highest percentage of its population living in rural or non-metropolitan areas. People residing in rural areas of northern New England often have higher-than-average rates of cardiovascular disease. This high cardiovascular disease burden, coupled with challenges in access to care, often contribute to a shorter life expectancy for patients in rural areas compared with those in metropolitan areas.



Robert Kramer, MD

“The evidence-based medicine of today is the research of yesterday,” Dr. Kramer said. “This grant allows us to tap into a network of clinical trials that is being performed across the country, and will improve high-quality care for our rural populations.”

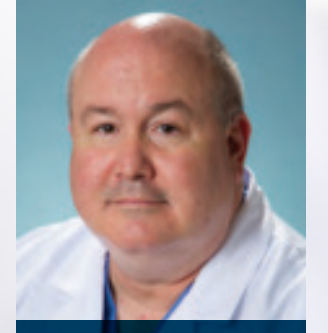
The grant also provides funding to train the next generation of cardiovascular clinical researchers in late-stage translational research, through a Clinical and Implementation Research Skills Program (CIRSP). The CIRSP program will provide junior faculty and fellows from DHMC and MMC with comprehensive didactic training and mentored research, and will also provide funding for the education and training of national scholars drawn from populations traditionally underrepresented in clinical research.

“The CIRSP program will be a valuable resource for young surgeons from MMC and DHMC who wish to engage in clinical research,” said Doug Sawyer, MD, co-investigator on the grant and MMC’s Chief Academic Officer. “As doctors, we always want to move towards providing the most up-to-date treatments for our patients, and building our research capabilities is an important way to do that.”

\$1.5M Department of Defense Contract Focuses on Helping Trauma Patients



Forest Sheppard, MD



Joseph Rappold, MD

This summer Drs. Forest Sheppard and Joseph Rappold received a Department of Defense contract to develop a non-blood based, logistically simple solution to resuscitate critically injured and bleeding patients in both military and civilian settings. Given that hemorrhage is the leading cause of preventable death in trauma and traumatic induced hemorrhage is responsible for over 90% of potentially survivable deaths due to traumatic injury in both settings, this research could have great long-term benefits. The study will use FDA-approved therapeutics in combination as a new non-blood resuscitation therapy, facilitating quick clinical and optimally reduced blood product use. This exciting work will benefit both military and civilian trauma patients in austere and rural settings where blood and blood products are limited or not available and optimally improve trauma outcomes and survival.

IMPROVEMENTS IN CLINICAL CARE

CREST II Trial: Hope for Patients at Risk for Stroke

Dr. Robert Ecker, is leading a neurosurgery and vascular surgery team at Maine Medical Center (MMC) that is participating in the National Institutes of Health sponsored multi-center international trial called CREST II. The CREST II study compares three different methods of stroke prevention, to find the safest and most effective treatment for people who have narrowing of their carotid artery (a major blood vessel in the neck) with no symptoms. The stroke prevention methods include intensive medical management alone compared to intensive medical management in combination with a procedure to reopen the carotid artery (revascularization) for treatment of plaque buildup. The two procedures available in this trial are carotid endarterectomy (removal of plaque inside the artery) and carotid stenting (inserting a stent inside the carotid artery to increase blood flow). All study participants receive intensive medical management to help control their risk factors for stroke.

The surgeons participating at MMC have been selected by the study investigators for their extensive clinical experience. Patients once screened as appropriate for enrollment are randomized to best medical management alone or to carotid intervention. MMC is the tenth enrolling site nationally. As a companion study, MMC is participating in CREST H which is looking at patients with decreased blood flow to the brain prior to carotid intervention (endarterectomy or stenting) to see if they have improved cognitive function after treatment. Both studies hope to reduce risk and improve treatment for patients with narrowing in their carotid arteries.

Robert Ecker, MD

New Cystic Fibrosis Therapy Heralded as Groundbreaking

Cystic Fibrosis (CF) is the most common fatal genetic disease in the US. Maine Medical Center's CF program, overseen by Ana Cairns, DO (children) and Jonathan Zuckerman, MD (adults), is very active in conducting research to improve treatment. Since 2008, the Maine CF program has participated in the Cystic Fibrosis Foundation's Therapeutics Development Network (TDN), which provides key support throughout the U.S. to improve treatment of this disease; the foundation funds clinical trial development at 92 centers nationally with demonstrated expertise in clinical research.

There are exciting developments underway in the treatment of CF. Our Maine site was part of the trial that brought the latest, groundbreaking therapy known as "the triple combo," elexacaftor/tezacaftor/ivacaftor (Trikafta™) to market in 2019, a highly promising treatment. Elexacaftor and

tezacaftor are modulators designed to fix the defective CF transmembrane protein (CFTR) so that it can move to the proper place on the cell surface. Ivacaftor then helps facilitate the opening of the chloride channel to allow

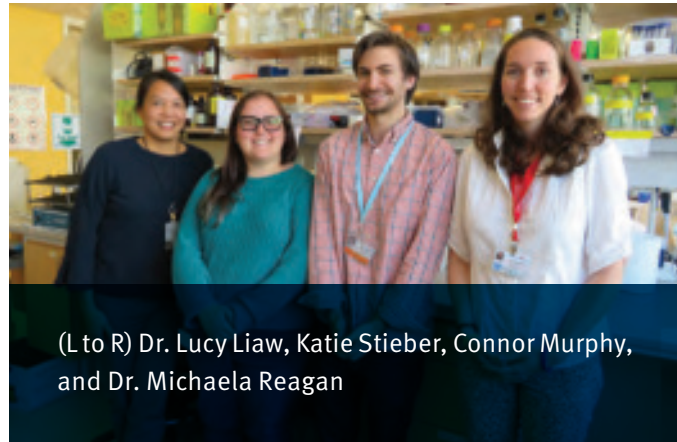
chloride and sodium (salt) to move in and out of the cell. This combo corrects the malfunctioning protein made by the CFTR gene. This triple combo has been approved for 90% of the CF population over age 12. Taken as a pill twice daily, this therapy will reduce mortality from CF by improving lung function and quality of life and reducing pulmonary exacerbations. Additionally, a study of Trikafta™ in children with CF ages 6-11 years old is currently underway. The CF Foundation recently unveiled a \$500 million initiative aimed at developing treatments for the 10% of patients not eligible for a CFTR modulator and to continue their quest for a cure for this disease. The Maine site will be involved in this new initiative as it moves forward.



Dr. Ana Cairns, Pediatric Pulmonologist, and Principal Investigator for the Trikafta trial

FOSTERING FUTURE SCIENTISTS

Institutional Research Training Grant Awarded



(L to R) Dr. Lucy Liaw, Katie Stieber, Connor Murphy, and Dr. Michaela Reagan

Dr. Lucy Liaw, Faculty Scientist and Director of Research Training Programs at MMCRI is a Principal Investigator for a new five-year, \$1.07 million dollar Institutional Training grant (T32) awarded by the National Institutes of Health to the University of Maine Graduate School of Biomedical Science and Engineering (GSBSE). The grant will support the training of GSBSE PhD students in biomedical science and engineering. Maine Medical Center Research Institute is one of six institutions throughout the state where GSBSE students perform mentored thesis research, making discoveries that help physicians and researchers better understand human disease. MMCRI faculty members will be participating as mentors in this program, which will fund



Our training program focuses on transdisciplinary research, which bridges different fields and perspectives to advance knowledge in the biosciences.

— Lucy Liaw, PhD
MMCRI Faculty Scientist and
Director of Education & Training

6 pre-doctoral fellows annually. The program started in July 2019, and to date two graduate students at Maine Medical Center received a competitive T32 slot: Connor Murphy is being mentored by Dr. Michaela Reagan and Katie Stieber is mentored by Dr. Lucy Liaw.

STEM Goes Red

In December 2019 MMCRI hosted the second annual STEM Goes Red program, sponsored by the American Heart Association. Fifty young women from local high schools including South Portland High School, Deering High School, and Portland High School came to MMCRI to learn about careers in Science, Technology, Engineering, and Math (STEM). The goal is to close the gender gap in STEM fields and to inspire students to become advocates for women’s heart and brain health – and to perhaps pursue careers in research and cardiology.

Students heard from women in STEM careers, including research scientists at MMCRI, a VP of Information Technology at UNUM, and a Manager of Diagnostics Services at Maine Medical Partners MaineHealth Cardiology. Presenters spoke about their career paths, obstacles they overcame, and why they love their STEM field.



Dr. Lucy Liaw addresses students at STEM Goes Red event.

“I would consider pursuing STEM studies because I found most of the medical topics exciting. There needs to be more awareness about women’s heart health and how we can all take care of our hearts,” said Angelina DeAza of Deering High School.

MMCRI & University of Southern Maine Team Up to Provide Research-Intensive Master’s Program

After a long and successful partnership providing internship opportunities at MMCRI for University of Southern Maine (USM) undergraduate biology students, the two institutions have teamed up to offer a new Research-Intensive Master’s program at USM and MMCRI. Students participating



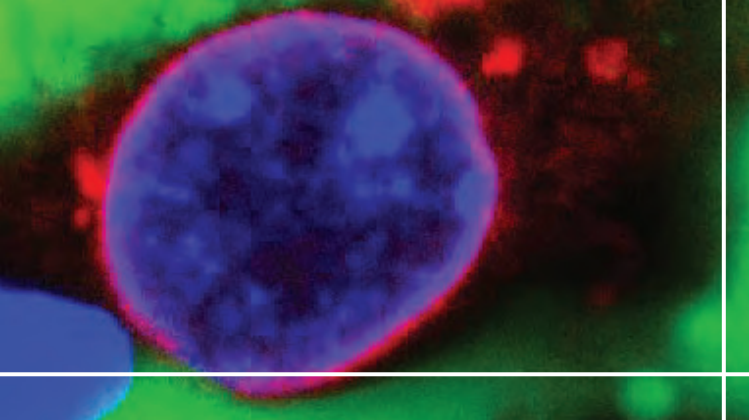
Mariah Farrell of the Reagan Lab and Bethany Fortier of the Liaw Lab

in the program will complete course work through USM and will conduct Master’s thesis research at MMCRI, under the mentorship of faculty scientists. Two MMCRI staff members, who at one time participated in USM undergraduate internships at MMCRI, are now in the Master’s Program. Bethany Fortier, a member of the Liaw Lab, says “I was thrilled to have the opportunity to work toward my Master’s degree in a framework that allowed me to continue the relevant, translational research I had started

Education & Training Fast Facts

- 12 PhD students
- 3 Master’s students
- 8 Research fellows
- 33 Academic interns, over
- 13 Labs & research areas
- 28 Summer student research program participants (6 MMC/Tufts University Maine Track students, 22 undergraduates)
- 4 International scholars
- 5 Maine Medical Center students & residents

during my internship. The contributions and strengths of both institutions blend so well to deepen my knowledge and expand my skills. I could not ask for a better fit in a graduate program.” Mariah Farrell of the Reagan Lab also welcomed the opportunity to participate in the new program, “During my intern year, the Reagan Lab supported my inquisitive nature and independence which sparked my decision to have a career in research. Building off my intern year, the Master’s program will allow me to continue to gain research experience while growing as a scientist.” MMCRI and USM look forward to growing this innovative new program.



Support Our Research

MMCRI Research Resources

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

RESEARCH GRANT PROPOSALS:

Michele Locker
Senior Grants Administrator
lockem@mmc.org or 207-396-8144

RESEARCH CONTRACTS:

Colleen O'Neill
Contracts Officer
coneill@mmc.org or 207-396-8058

COMPLIANCE & INSTITUTIONAL REVIEW BOARD:

Elizabeth Campbell
Director of the Office of Research Compliance
ekcampbell@mmc.org or 207-661-4472

CLINICAL TRIALS:

Krista Garrison
Director of Clinical Trials
garrik@mmc.org or 207-396-8074

RESEARCH NAVIGATION:

Wendy Craig
Research Navigator
navigation@mmc.org or 207-662-6438

NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK:

For information visit: nne-ctr.net

MMCRI is already one of the most innovative research organizations in the nation.

With your help, we can achieve even more.

By donating to MMCRI, 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 MMCRI's laboratory-based or clinical research projects include: Cardiovascular Disease, Cancer, Bone and Mineral Disease, Molecular Biology and Genetics, Clinical Trials, Psychiatric Research, and Vector-Borne Diseases.

Our efforts go beyond research, as well: by supporting our summer 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 Maine Medical Center Research Institute, please contact Kristen Crean of the Philanthropy Department at 207-662-3895 or by email at kcrean@mmc.org.



81 Research Drive · Scarborough, ME 04074

☎ 207-396-8100

mmcri.org