2019

2018 Year in Review - Maine Medical Center Research Institute

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Maine Medical Center
Research Institute

2018 Year in Review

MAINE MEDICAL CENTER RESEARCH INSTITUTE

mmcri.org

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Cover photo from Dr. Michaela Reagan's Lab. 3D Silk Scaffold Confocal Image using stains for human white adipose (fat) tissue taken from liposuction samples, on silk scaffolds. Green stains are cell filaments, red stains are lipids, and purple/blue is autofluorescence of scaffold.

Back cover from Josh Boucher PhD, Staff Scientist Liaw Lab. Human retinal endothelial cells (cells that form the linings of blood vessels) were coated to fibrin beads and allowed to form sprouting blood vessels through the process of angiogenesis over 7 days.

Dear Friends

I am delighted to inform you of some of the activities and accomplishments of the research community at Maine Medical Center in 2018. Coming on the heels of several years of increased funding from NIH and other agencies, 2018 has been one of dedicated engagement by our investigators and scientific staff in their laboratories and in our communities to implement their exciting research projects.

A few examples include the clinical trial of early tracheostomy in patients who have suffered severe stroke now being conducted in our intensive care units under the leadership of David Seder, the maturation of several projects conducted by our junior investigators on the Center of Biomedical Research Excellence Award directed by Lucy Liaw, and the implementation of the Northern New England Clinical and Translational Research Network led by Cliff Rosen in collaboration with colleagues at the University of Vermont School of Medicine and the University of Southern Maine (*graphic, p. 3*).

Community engagement forms the basis of and is integral to many programs recently implemented, as typified by the Maine Lung Cancer Coalition and the Maine Cancer Genomics initiative based in our Center for Outcomes Research and Evaluation and led by Paul Han. It is also the hallmark of several research programs in our Center for Psychiatric Research, where Matt Siegel and his team are using biosensor technology to improve the care of autistic individuals, and where Kristen Woodberry is enhancing the engagement of family in the care of patients with early psychosis disorders. Another example highlighted herein is the dedicated work of Alexa Craig to develop a state-wide video communication system to optimize the assessment and care of newborns with brain injuries incurred during birth.

Expanding community engagement has also been the focus of our education and training programs. Grants received in 2017 from the American Heart Association and the Maine Community Foundation are now supporting the expansion of our summer internship program and high school education program in order to reach students from underserved communities in rural Maine.

I am immensely proud and appreciative of the outstanding work of these programs. This focus on engagement and community is helping us chart a course for how we can best support colleagues across MaineHealth in our newly unified health system. I hope you enjoy taking a closer look at the research and the individuals conducting this tremendous work.

Sincerely,

Don St. Germain, MD
 Director & Vice President of Research
 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.

2018 NOTABLES

Additional funding supplement was received to study the impact of opioid prescribing laws.

Prescription drug and opioid overdose has risen sharply over the last decade and is considered one of our most pressing public health issues.

MMCRI At A Glance

2018 Leadership

Executive Administration

Donald St. Germain, MD
Director & VP Research

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*

Susan Santangelo, ScD
*Director, Center for
Psychiatric Research*

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

2018 Fast Facts

203

Staff Members

18M

Total 2018 Grant Funds

38

New Grants Awarded

200+

Clinical Trial Studies

Oncology, Cardiology, and Neurology

Top 3 Clinical Research Areas

264

Scientific Publications

12

Core Facilities with State of the Art Equipment and BioBank Tissue Repository which distributed over 3000 biospecimens

73

Learners & Trainees in MMCRI's Education & Training Program

"Compositions and methods for treating inflammation and fibrosis",
Dr. Peter Brooks, Dr. Leif Oxburgh, and Jennifer Caron, Research Associate, Brooks Lab.

2018 Issued Patent

2018 Sources of Research Support by Sponsor Type

12.0%: Industry

20.6%: Foundation & Nonprofit

67.5%: Federal

Areas of Research

CANCER

CENTER FOR MOLECULAR MEDICINE — LEIF OXBURGH DVM, PHD

Kidney Cancer

The Oxburgh laboratory is helping to fill the knowledge gap in the field of kidney cancer thanks to the Department of Defense Kidney Research Program award the lab received in September 2018. Their work focuses on modeling the effects of stroma on clear cell renal cell carcinoma, which is the most common kidney cancer. Stroma is the connective, functionally supportive framework of a biological tissue. The lab will develop a system to study the interactions between cancer cells and the normal cells that surround them. The

project will analyze the effect of the cellular environment within the kidney on the aggressiveness of tumors. In order to understand this better, researchers will combine tumor cells with normal cells from kidney cancer patients and tumors of differing aggressiveness. A promising practical result of this work will be a means to model tumors from individual cancer patients. This may be an important tool in personalized medicine as it has the potential to enable testing of anti-cancer drug activities at the level of the individual patient.

CANCER

NEUROSCIENCE & ADDICTION

CARDIOVASCULAR & METABOLIC DISEASE

PUBLIC HEALTH

IMPROVEMENTS IN CLINICAL CARE

INTERNATIONAL TIES

FOSTERING FUTURE SCIENTISTS

CANCER

CENTER FOR OUTCOMES RESEARCH & EVALUATION

Maine Cancer Genomics Initiative

The Center for Outcomes Research and Evaluation (CORE) is in the second year of a five-year initiative to lead the outcomes evaluation component of the Maine Cancer Genomics Initiative (MCGI). Supported by the Harold Alfond Foundation, the MCGI is a unique collaboration between research and clinical institutions. CORE Principal Investigator Dr. Paul Han and Drs. Jens Reuter & Andrey Antov from the MCGI team at Jackson Laboratory, have partnered to study the implementation of tumor genomic testing and downstream outcomes that will inform the implementation of precision medicine in oncology. This work will also develop a sustainable research-healthcare system partnership model.

The MCGI is on its way to reaching the goal of providing tumor genomic testing to 1,800 Mainers. Analyses will look at provider and patient surveys and qualitative interviews. The data provide information on oncologists' use, confidence, attitudes, and perceived barriers to implementing genomic tumor testing, as well as patients' beliefs and attitudes towards the role tumor genomic tumor testing plays in their health care journey. Together, these data play a vital role in helping us understand how to implement tumor genomic testing in community oncology settings, and shedding light on physician and patient knowledge, attitudes and beliefs towards this new technology.

MAINE HEALTH CANCER CARE NETWORK EXPANDING

Research Connections: MaineHealth Cancer Care Network

Cancer is the most common cause of death across our communities, and hundreds of caregivers from across the MaineHealth system have come together to focus their efforts on prevention and treatment. The MaineHealth Cancer Care Network (MHCCN) was launched in 2014 to provide comprehensive coordinated cancer care to patients across Maine. This network, which includes 11 MaineHealth partner hospitals and organizations, offers a robust research arm, in partnership with Maine Medical Center Research Institute and the Jackson Laboratory Cancer Center in Bar Harbor. The network, supported by a grant from The Harold Alfond Foundation, not only provides treatment, but prevention and education initiatives as well.

In 2018 the MHCCN nearly doubled its number of enrolling trials, expanded its National Cancer Institute Network Group, continued to build Maine Medical Center based trails in specialty areas, increased its research staff by sixty percent, and established an Oncology Protocol Review Committee.

For more information about MHCCN visit: mainehealth.org/cancer

NEUROSCIENCE & ADDICTION

CENTER FOR MOLECULAR MEDICINE — ARTURO HERNANDEZ, PHD

Neuroendocrinology & Metabolism

The Hernandez laboratory successfully competed for a 5-year renewal of their NIH research grant entitled “Transgenerational Epigenetic Programming of the Thyroid axis”, funded by the National Institute of Diabetes, Digestive and Kidney Diseases. The project aims to delineate how abnormal exposure to thyroid hormones during development influences the endocrine function and metabolic programming in future generations via inherited but non-genetic mechanisms. This research can shed light on why some individuals are more likely to be susceptible to obesity and metabolic disease, based on differences in their hormonal systems.

CENTER FOR PSYCHIATRIC RESEARCH — MATT SIEGEL, MD

Research Funding for Novel Biosensors will Help Parents of Children with Autism

In October 2018, the Simons Foundation of New York, NY and the Nancy Lurie Marks Family Foundation of Wellesley, MA awarded Maine Medical Center Research Institute (MMCRI) and Maine Behavioral Healthcare (MBH) a \$3.1 million grant to study the use of wearable biosensors to provide real-time warnings of impending aggression in children with autism. Dr. Matthew Siegel, a Faculty Scientist at MMCRI and VP of Medical Affairs for Development Disorders at MBH is the Principal Investigator for the project.

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/MBH.

Imagine the possibilities for prevention and a family's quality of life if we can accurately predict that one of these behaviors will likely happen in the next 2 minutes. Suddenly, we are able to know when things are not going well, provide coping strategies, and increase safety. ...Put simply, this is a potentially transformative approach to serious problem behaviors in autism.

— Dr. Matthew Siegel
Faculty Scientist, MMCRI
VP of Medical Affairs for Development Disorders, MBH

The goal is that these watch-like devices will enable clinicians and caregivers to predict challenging behaviors in children with autism and create a new opportunity to intervene and prevent problems before they occur. Current approaches to behavioral problems in autism have primarily focused on what happens after the behavior occurs. This three-year clinical study will investigate whether physiology signals such as heart rate and sweating can indicate the probability of an impending aggressive episode, and allow people in the environment to receive a warning.

Dr. Siegel wearing a biosensor

NEUROSCIENCE & ADDICTION

CENTER FOR PSYCHIATRIC RESEARCH — KRISTEN WOODBERRY, MSW, PHD

Understanding Early Psychosis in Youth

Seventy-five percent of adult mental illnesses emerge by age 24, with the majority appearing between ages 15 and 24. Given increasing evidence for the benefits of early intervention, identifying predictors and indicators of emerging mental illness is a high public health priority. In 2018, The National Institute of Mental Health (NIMH) awarded an Exploratory/Developmental Research Grant to new Faculty Scientist Kristen Woodberry, MSW, PhD to collect dynamic data in adolescents and young adults at risk for or in the early stages of severe mental illness. The project aims to better understand the interaction of emerging symptoms and social context over time.

Using a smartphone app, the Daily Life Study is collecting 6 mood and symptom reports a day for 21 days in 60 Boston and Portland area youth ages 15-25. By comparing the daily reports of those with and without psychotic symptoms, Dr. Woodberry hopes to identify whether youth with psychotic symptoms experience greater mood variability than their non-psychotic peers, and whether mood variability predicts

psychotic symptoms or thoughts of self-harm. This project is a preliminary step in a line of research examining the interaction of mood and psychosis and identifying patterns or sequences that can predict critical events such as suicide attempts during the early course of major mental illness. Early course symptom dynamics are also expected to inform our understanding of illness progression and help develop novel interventions to interrupt pathological sequences and improve functional outcomes.

This project is one arm of a broader effort to build on Maine Medical Center's leadership role in Early Intervention in Psychosis, initiated through the nationally-recognized Portland Identification and Early Referral (PIER) program, pioneered by Dr. William McFarland. Dr Woodberry is working closely with PIER Clinical Director, Sarah Lynch, Drs. Doug Robbins and Susan Santangelo, and Maine Health leadership to build a regional Center of Excellence focused on early psychosis research, training, and coordinated specialty care.

Woodberry Research Team (L to R):
Kate Powers, Research Assistant, Dr. Woodberry, and Anna Cloutier, Research Nurse Coordinator

NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK RECEIVES ADDITIONAL FUNDING IN 2018

Supporting Public Health Initiative to Fight the Opioid Crisis in rural New England

In 2016, Maine and Vermont responded to the opioid crisis with legislation regarding opioid prescribing guidelines and requirements for prescription drug monitoring programs. The goal was to reduce access to opioids and make it more difficult for patients to obtain prescriptions from multiple providers. Through supplemental NIH funding received in 2018 by the Northern New England Clinical and Translational Research Network (NNE-CTR), Maine Medical Center Research Institute (MMCRI) and its partnering institution, the University of Vermont (UVM), are now studying the impact that stricter opioid prescribing laws have had on population health in northern New England.

Dr. Kathleen Fairfield of MMCRI and the Department of Medicine at Maine Medical Center and Drs. Valerie Harder and Timothy Plante of UVM, will analyze whether that legislation has successfully led to a decrease in opioid-related overdoses, hospitalizations and other medical events and whether there were unintended consequences, such as patients suffering from substance use disorders turning to the illegal use of heroin instead. The team also will analyze whether outcomes are different for various patient demographics, such as whether they live in a rural or urban area.

Dr. Kathleen Fairfield

While this grant provides additional funds for the NNE-CTR to focus on a specific issue of the opioid crisis on our community, the Network continues to fund pilot projects that focus on the other aspects of the opioid crisis, highlighted on the next page.

This research provides us the opportunity to study the impact of state laws regarding opioid prescribing while engaging with a wide variety of community members in real time. We hope this work will help inform clinical care of patients, community-based interventions, future policy changes and additional research.

— Dr. Kathleen Fairfield
MMCRI's Lead Investigator on the NNE-CTR's Opioid Grant

NEUROSCIENCE & ADDICTION

Dr. Katherine Motyl

NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK — REDUCING OPIOID ABUSE**Katherine Motyl, PhD: Direct and indirect mechanisms of opioid-induced bone loss**

Opioid prescription can be extremely addictive and is associated with substantial morbidity and mortality. Receipt of prescription opioids is associated with a 3 to 4-fold increase in fracture risk. This is concerning because opioids are often prescribed for fractures and metastatic cancer. Though opioids are associated with an increased risk of bone fracture, the mechanisms of this risk are unclear. Dr. Katherine Motyl was awarded a pilot project in 2018 through the Northern New England Clinical & Translational Research Network (NNE-CTR) to study direct and indirect mechanisms of opioid -induced bone loss. Dr. Motyl will test if bone loss from opioids is due to elevated sympathetic nervous system output to bone, as well as test to see if opioids impact bone directly through interactions with osteoclasts (a large bone cell that absorbs bone tissue during growth and healing). This work will fine tune treatment and prevention strategies for patients who are prescribed opioids.

Kinna Thakrar, DO, MPH: Rural Harm Reduction Access and Regional Trends (Rural HeART)

Dr. Thakrar's NNE-CTR pilot project grant seeks to examine access to harm reduction services among people who inject drugs and are hospitalized with infectious complications. With increasing incidence of hepatitis B, hepatitis C, and ineffective endocarditis in Maine over recent years, there are particular concerns about high-risk persons who inject drugs in rural areas being able to access harm reduction services such as syringe site programs, which have been shown to effectively reduce the transmission of infections, deliver overdose prevention and education, increase vaccinations, and facilitate referrals for medication for addiction treatment.

Although the infectious complications of injection drug use (IDU) are serious and costly, relatively little attention has been paid to characterizing the epidemiology of IDU-associated infectious complications or utilization of harm reduction services. Results of this study will help inform future interventions to improve access to harm reduction services in Maine and potentially other areas of northern New England.

For more information about the NNE-CTR visit: nne-ctr.net

CARDIOVASCULAR & METABOLIC DISEASE

CENTER FOR MOLECULAR MEDICINE — LUCY LIAW, PHD

Investigating the Causes of Cardiovascular disease

Why is obesity a risk factor for cardiovascular disease? This is one of the questions being addressed in a project in the Liaw laboratory that was funded by the National Heart, Lung, and Blood Institute at the NIH in July 2018. The study focuses on perivascular adipose tissue, which surrounds major blood vessels in the body. This adipose tissue contributes to the cellular neighborhood of the circulatory system, and changes during obesity and metabolic disease. This project includes collaborations between basic scientists and vascular surgeons to understand differences in this adipose tissue in patients with varying levels of cardiovascular disease. Studies will address the interesting scientific questions of how the adipose tissue surrounding vessels can influence or protect from disease. Because cardiovascular disease and obesity are two of the most prevalent health issues, this research will have significant impact for a majority of the country’s population. The goal is to understand what causes cardiovascular disease so that it can be prevented or treated more effectively.

Progenitor cells surrounding blood vessels can be collected from patients with cardiovascular disease and studied in the lab for their ability to become adipocytes, or fat cells. Image shows human progenitor cells grown as three dimensional aggregates and programmed to become adipocytes. The resulting “adipospheres” show green staining of lipids, red staining of perilipin1, a lipid droplet-associated protein, and blue stained nuclei. This adiposphere model allows us to better mimic human fat tissue in the research lab.

CENTER FOR MOLECULAR MEDICINE – ILKA PINZ, PHD AND DOUG SAWYER, MD, PHD

Nutrition’s Impact on Cardiovascular Disease

Diet plays an important part in our overall health and in disease prevention. However there is little research on the impact of specific diets in patients with type 2 diabetes mellitus (T2DM) and with ischemic heart disease (the term given to heart problems caused by narrowed heart arteries). Patients with T2DM and ischemic heart disease have substantially higher chances to develop certain illnesses than those without T2DM, and more frequently develop heart failure. Strategies to improve glycemic control with insulin or drugs taken orally have not impacted cardiovascular

(NRG) signaling in cardiac muscle cells. Insulin and NRG signaling are important not only for the metabolism of sugar, but also for survival signals in a stressed heart. Drs. Ilka Pinz and Douglas Sawyer received a pilot project award from MMCRI’s Center of Biomedical Excellence in Metabolic Networks in late 2018 to study nutrition’s impact on type 2 diabetic patients with heart disease. They will test how short-term Mediterranean diet consumption changes the fat composition of cardiac muscle cells and thus protects insulin and NRG signaling in humans. This work will increase

disease and mortality outcomes in T2DM patients with known heart disease. Our research in mice and humans has shown that a western style diet with a high amount of saturated fat impairs not only insulin but also neuregulin

our understanding of the molecular pathology that dietary choices influence and will help to develop new treatments for type 2 diabetic patients with heart disease.

CARDIOVASCULAR & METABOLIC DISEASE

NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK

Teresa May, DO: Opioid and Non-opioid Related Cardiac Arrest Outcomes in Northern New England

Cardiac arrest is the third leading cause of death in North America, with great variation in survival rates in different regions of the U.S. These differences may be due to factors related to the patients, emergency medical services, or hospitals. Dr. May was awarded a pilot project in 2018 through the Northern New England Clinical & Translational Research Network to study these factors across the states of Maine, New Hampshire and Vermont. Other factors that may influence patient outcomes are whether the cardiac arrest is related to opioid use, and whether the patient suffering the arrest lives in a rural or more populated region. Dr. May will study variations in the provision of health services and patient outcomes for both opioid related and non-opioid related cardiac arrest, broken down by geographic region throughout Maine, New Hampshire and Vermont. Dr. May's work will help define the geographic barriers to cardiac arrest care throughout Northern New England, and should help impact care for cardiac arrest patients in the current opioid epidemic, affording the opportunity to improve clinical outcomes in the region in both opioid related and non-opioid related cardiac arrest.

For more information about the NNE-CTR visit: nne-ctr.net

Research in Metabolic Disease

Publication in scientific journals is a key way that scientists share their results with the scientific community. MMCRI investigators had 264 publications in 2018. Two of those reported exciting breakthroughs in major scientific publications and are highlighted below.

Cliff Rosen, MD, Director of the Center for Clinical & Translational Research, in collaboration with scientists at the Dana-Farber Cancer Institute and other organizations, has discovered that irisin, a hormone released by muscles during exercise, directly acts on key regulatory cells that control the breakdown and formation of bone, raising the prospect of new treatments for bone-thinning disorders like osteoporosis. This research was published in December 2018 in the journal *Cell*.

Aaron Brown, PhD, reported in the journal *Cell Reports* (December 2018) that an anti-diabetic fat generated in the lab could be used to help develop new drugs and treatments for diabetic and obese patients. For example, long-term, this fat could be transplanted into patients to burn calories or secrete anti-diabetic molecules that alleviate the disease. Researchers in Dr. Brown's lab plan to first test the anti-diabetic fat by transplanting it in mouse models of obesity and diabetes prior to human studies. The work was funded in large part through MMCRI's COBRE award entitled "Mesenchymal and Neural Regulation of Metabolic Networks."

Dr. Cliff Rosen

PUBLIC HEALTH

VECTOR-BORNE DISEASE LABORATORY

A Surge in Anaplasmosis

Cases of anaplasmosis, a tick borne infection that is particularly severe in the elderly, dramatically increased in Maine over the past 5 years (Figure 1). With the assistance of a private donation, the Vector-borne Disease Laboratory team launched a project to determine if risk of infection varies geographically in Maine by testing ticks collected from northern and southern tiers of the state. In addition, parallel research investigated patterns of disease diagnosis and the frequency of hospitalization, in order to gain a better understanding of the causes of the observed increase in cases. The goal is that this knowledge will lead to more focused public health approaches to the prevention of anaplasmosis.

Earlier Diagnosis of Lyme Disease

Dr. Robert Smith and Research Associate Susan Elias began a collaboration with the company MicroB Plex on a National Institutes of Health funded project in 2018 to examine the effectiveness of a diagnostic test to aid in the detection of early Lyme disease in patients in southern Maine. This project will expand in 2019 to involve three geographic areas in Maine: Greater Portland, with Maine Medical Center Research Institute as coordinator; Mid-coast Maine with a study center at Pen Bay Medical Center; and southern Maine at Southern Maine Health Care. A clinical site associated with Johns Hopkins Medical Center in Baltimore is also a partner. This novel approach to diagnosis may lead to earlier confirmation of Lyme disease, as well as the possibility of distinguishing past from current infection. The linkage of several different clinical sites in Maine for studies of tick borne disease is a promising prototype for future diagnostic and treatment trials.

A Focus on Disease Carrying Mosquitos

With support from a Maine Centers for Disease Control grant, Research Assistant Margret Welch and vector ecologist Charles Lubelczyk established an insectary in cooperation with the University of Southern Maine in Gorham to test the development of pesticide resistance in native species of mosquitoes that are of medical or veterinary importance. Testing for pesticide susceptibility will include vector mosquitoes from across geographic regions in Maine. This movement of a new mosquito species capable of transmitting disease in Maine, coupled with the recognition of the mosquito-transmitted virus (Jamestown Canyon virus), is of great concern, and the lab's mosquito surveillance program, guided by Lubelczyk and Field Biologist Libby Henderson, is integrating this study with other studies on the effectiveness of chemical controls and public and veterinary risks of mosquito-borne disease.

Chuck Lubelczyk, Vector Ecologist for MMCRI, completing field work.

PUBLIC HEALTH

CENTER FOR OUTCOMES RESEARCH & EVALUATION

Maine Lung Cancer Coalition: a statewide collaboration

The Maine Lung Cancer Coalition (MLCC) is a 4-year statewide, multi-institution, multi-disciplinary initiative begun in August 2016, with funding from the Bristol Myers Squibb Foundation, with the goals of improving lung cancer prevention, early detection, stakeholder education, and research and data analytics for 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 Kersen (Co-PI), and Leo Waterston (Project Director). The MLCC brings together diverse stakeholders across Maine 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.

The MLCC, through its partner the MaineHealth Center for Tobacco Independence, received a grant for \$30,000 in 2018 from Anthem Blue Cross and Blue Shield Foundation

to integrate evidence-based smoking cessation treatment into lung cancer screening. The project targets older, heavy smokers residing in rural Maine who are at high lung cancer risk and have been referred for lung cancer screening with low-dose CAT or CT scan (LDCT).

Other highlights in 2018 include launching pilot projects to generate evidence on ways of improving access to lung cancer prevention and screening services to populations in Maine. These projects include studies of the geographic burden of lung cancer and utilization of lung cancer screening and treatment services; community members' perceptions and attitudes regarding lung cancer risk and prevention; use of telemedicine to conduct shared decision making consultations for lung cancer screening; and a statewide survey of primary care physicians' knowledge and attitudes regarding lung cancer screening.

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

NORTHERN NEW ENGLAND CLINICAL & TRANSLATIONAL RESEARCH NETWORK

Improving Health in Rural Communities across New England

Over 60 percent of Maine's population lives in a rural area and Maine is the 2nd most rural state in the nation (based on population density). The Northern New England Clinical and Translational Research Network (NNE-CTR) was established in July 2017 to enhance the health of people in northern New England (ME, NH, VT) by fostering and coordinating clinical, translational and educational research activities.

One key goal of the NNE-CTR is to bring clinical and translational research opportunities to rural communities in Maine. Dr. Neil Kersen is leading this effort in Maine through the Rural Health Research and Delivery Core, which has begun to build partnerships with rural clinicians and practices to increase their participation in clinical trials. Dr. Kersen has also worked with rural clinicians to help them develop their own research ideas, providing technical assistance as needed.

The Rural Core is working closely with two rural communities in Maine: Western Maine Health in the Oxford County area and Pen Bay Medical Center on the Maine coast in Rockport. To connect the community with

clinicians and researchers in the Oxford County Area, the Rural Core sponsored a community symposium: Building Partnerships for Rural Health Research in June 2018. The event was attended by 40 participants including researchers, clinicians and community members. The Rural Core is now working with a subset of symposium participants to develop a research project targeting individuals impacted by Adverse Childhood Experiences.

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

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

IMPROVEMENTS IN CLINICAL CARE

The Cystic Fibrosis Foundation Awards MMC \$1.1M for Multi-Center Study

In July of 2018, the Cystic Fibrosis Foundation awarded Maine Medical Center \$1.1M for a multi-center study investigating complications associated with use of midline and peripherally inserted central venous catheters (PICCs) in Cystic Fibrosis (CF) patients. Cystic Fibrosis is a progressive, genetic disease that causes lung infections which often require repeated courses of intravenous antibiotics through PICCs or midline catheters. A range of adverse events such as clots, infection and permanent distortion of blood vessels can arise from use of these catheters. Identifying risk factors for these complications should help healthcare providers prevent injury and improve overall outcomes in this vulnerable population. Dr. Jonathan Zuckerman, Maine Medical Center and Dr. Alex Gifford, Dartmouth-Hitchcock Medical Center, are the lead Principal Investigators for the project. “To date, no multicenter study has carefully investigated these complications in a large, diverse group of adult and pediatric CF patients. We are excited to leverage the resources and talents available through Maine Medical Center Research Institute to coordinate such a large effort,” said Dr. Zuckerman. The study will include 10 sites across the United States and span 3 years.

A peripherally inserted central venous catheters (PICC) Close Up

For more information on this study, visit: picccf.org

Dr. David Seder, MD: Stroke Study Continues to Make Progress

SETPOINT2 is an international, multi-site clinical trial to improve outcomes for patients who have suffered a severe stroke by assessing the best timing of tracheostomies. Heading this study is Dr. David Seder, the U.S. Principal Investigator (Maine Medical Center), along with Dr. Julian Bösel, the German Principal Investigator (Kassel University Hospital). SETPOINT2 stands for **S**troke-Related **E**arly **T**racheostomy vs **P**rolonged **O**rotracheal **I**ntubation in **N**eurocritical Care **T**rial2.

Dr. David Seder

The study is entering its third year, and 2018 marked considerable growth with patient enrollment and new site activations. The SETPOINT2 findings could benefit patients because the timing of a tracheostomy may affect the amount of sedating medications that is required, and could affect brain recovery and the body’s ability to return to pre-stroke activities. Preliminary studies suggest it could be beneficial to perform a reversible tracheostomy procedure earlier than is usually done after severe stroke (within the first 5 days), as opposed to delaying more than 10 days before performing the procedure.

For more information on this study, visit: setpoint2.org

Alexa Craig, MD: Improving Neonatal Care

Dr. Craig, Neonatal and Pediatric Neurologist, was awarded a pilot project in 2018 through the Northern New England Clinical and Translational Research Network (NNE-CTR) to study ways to improve the detection of and treatment for neonatal encephalopathy in rural areas. Neonatal encephalopathy is a type of brain injury that can occur in newborn infants due to lack of oxygen and blood flow to the brain around the time of birth.

Therapeutic hypothermia is the only known treatment for neonatal encephalopathy; this involves placing the baby on a cooling blanket that maintains a temperature of 91 degrees Fahrenheit for 72 hours followed by 12 hours of rewarming. The baby is monitored in an intensive care unit during this treatment and magnetic resonance imaging is then performed to determine presence or absence of brain injury.

Dr. Alexa Craig

One of the clinical challenges of this treatment is that it must be started within the first six hours of life, and earlier treatment is known to be associated with improved outcomes. For the 75 percent of infants treated with hypothermia who are born in rural Maine hospitals, recognizing neonatal encephalopathy and getting the baby cooled quickly are particular challenges, especially for providers in rural locations who do not see these babies all that often.

— Dr. Alexa Craig
Neonatal and Pediatric Neurologist

To combat these challenges, Dr. Craig developed her NNE-CTR pilot study to employ a telemedicine consult, a three-way, real-time interactive communication via video between the rural physician, the neonatologist at MMC and Dr. Craig. For infants and their families, this means faster diagnosis and treatment via a live consultation, thereby improving their chances of a better outcome or avoiding unnecessary treatment. Dr. Craig will assess the results of her pilot project in the next year to determine if the real-time consultations successfully decrease the time to initiate therapeutic hypothermia.

For more information about the NNE-CTR visit: nne-ctr.net

INTERNATIONAL TIES

Scot Remick, MD: Developing Training & Research Infrastructure in Kenya

The burdens of cancer and cerebrovascular disease—a group of conditions that can lead to a cerebrovascular event, such as a stroke—are major causes of morbidity and mortality in Kenya. Kenya's limited research infrastructure and significant scarcity of doctors to address these increasing chronic threats are a major challenge to public health. With funding by the National Institutes of Health Fogarty International Center, an international team of highly interactive and experienced investigators is addressing these issues by developing vital training and research infrastructure, evidence-based approaches for intervention, and public health policy. The team, led by Dr. Scot Remick, Chief of MaineHealth Oncology & Clinical Investigator at Maine Medical Center Research Institute, includes senior Kenyan collaborator Dr. Walter Mwanda, University of Nairobi; Ms. Anne Korir and Dr. Lydia Kaduka at the Nairobi Cancer Registry and Kenya Medical Research Institute in Nairobi; and Dr. Patrick Loehrer at Indiana University and his Kenyan collaborator Dr. Nathan Buziba, Moi University in Eldoret. This diverse team is working to develop sustainable research capacity for cancer and cerebrovascular disease control in Kenya across the lifespan.

Pediatric Palliative Care and End of Life Training Workshop July 2018, Kenyatta National Hospital, Nairobi, Kenya

To date the team has trained 8 stroke [Non-Communicable Disease (NCDs)] registrars; successfully launched and completed the first-ever NCD Stroke Registry in Sub-Saharan Africa; supported one post-doctoral training and PhD candidate for health policy in cerebrovascular disease and cancer epidemiology respectively; supported five early-career Kenyan trainees in the Department of Hematology and Blood Transfusion to satisfy requirements for three Pathology and two Clinical Cytology masters degrees; trained two physicians in palliative care medicine with a focus on end-of-life care in the pediatric setting; and sponsored a workshop that trained more than 30 healthcare professionals in pediatric palliative and end-of-life care. Dr. Remick and his colleagues hope to compete for successor NIH Fogarty International Center funding to build on the success of the current project.

Dr. Miesfeldt and research team during usability testing.

Susan Miesfeldt, MD: Improving Palliative Care in Tanzania

Nearly 80% of those diagnosed with cancer in Tanzania die from their disease due to limited numbers of adequately resourced cancer care facilities. As a result, access to effective palliative care is a critical public health priority in Tanzania, and Africa as a whole, and the need for innovative community-based solutions is highly recognized. Palliative care in the cancer patient is focused on improving quality of life by relieving pain and other distressing symptoms as well as addressing emotional, social and spiritual needs. Although there are few palliative care specialists in Tanzania, mobile technology holds promise in improving community-based access to care by linking the limited pool of

specialists with patients, caregivers, and local health workers. Dr. Susan Miesfeldt, Clinician Investigator at MMCRI, received funding from the National Institutes of Health Fogarty International Center in late 2017, to develop an innovative community-based mobile health solution to a limited palliative care workforce. The overall goal is to develop and test a mobile phone-based symptom assessment/control communication application (m-Palliative Care Link; mPCL) that remotely facilitates symptom self-reporting among late-stage cancer patients and communication between patients, local health workers and specialists, aimed at effective information exchange and reduced symptom burden.

In the first year of funding, partnering with US-based software engineers and Tanzanian researchers and clinicians, the team has completed mPCL development and usability testing. In the second and final year of funding, they will complete an mPCL pilot test among 45 Tanzanian late-stage cancer patients. By working with existing personnel and technology, this work promises to result in a sustainable and scalable means to support high quality, patient-centered symptom assessment and control in Tanzania and other low-resource countries, relevant not only to cancer patients but other chronic diseases patients as well.

INTERNATIONAL TIES

Research Goes Global

Research is a global endeavor at Maine Medical Center Research Institute and the Institute has welcomed research scholars from other countries for many years. In September two scholars from Lund University School of Medicine in Sweden came to participate in a research collaboration with physician scientists in Critical Care Medicine at Maine Medical Center. Ameldina Bilkanovic and Zana Haxhija, who are in their final year of medical school, traveled to Portland to collaborate for three months with David Seder, MD, and the neurocritical care research team on a project related to the International Cardiac Arrest Registry Database. Zana and Ameldina also worked with Sarah Peterson, MD, PhD in the Sawyer Ryzhov Lab on basic science and translational research. Biostatistician Lee Lucas RN, PhD from the Center for Outcomes Research and Evaluation worked with Zana and Ameldina on the biostatistical elements of the project. The students had a robust research experience and felt that their time in the U.S. was well-spent. “We gained so much! We learned a lot about our project and a lot about ourselves, living away from home. Combining research and rounds helped us to see how healthcare works here in the U.S.,” said Zana. “It helped me to confirm that critical care is an area I would like to go into,” says Ameldina. Zana and Ameldina worked on two manuscripts during their time at MMC and will present their research at their home university in Sweden upon their return.

Zana Haxhija (left) and Ameldina Bilkanovic (right)

VISITING SCHOLARS

Ashwani Gupta, PhD Postdoctoral Fellow — Oxburgh Lab

Ashwani came to MMCRI from Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India. He joined the Oxburgh Lab in 2016 to focus on kidney research in an area that may be instrumental in kidney repair or replacement. Specifically the Oxburgh Lab is doing research to make kidney tissue from skin derived cells and testing their functionality. The preliminary data looks promising and Ashwani is looking forward to continuing his work in kidney research.

Ashwani Gupta, PhD

Yosta Vegting — Rosen Lab

Yosta is a medical student from the University of Amsterdam in the Netherlands. She came to MMCRI in 2018 to participate in research collaboration before graduating. Yosta is in the Rosen Lab doing research on a newly discovered hormone called irisin. Irisin is made by muscles when exercising and could help to build our knowledge as to why exercising is healthy. Yosta is looking forward to using the research techniques learned at MMCRI to pursue her PhD.

Yosta Vegting

FOSTERING FUTURE SCIENTISTS

Education & Training Fast Facts

- 14** Rotating & full-time graduate students
- 6** Research fellows
- 40** Academic interns, over:
- 13** labs & research areas
- 5** International visiting scholars
- 3** Maine Medical Center residents
- 5** Student employees

High school student Lucy Hartley gets a chance to experience hands on lab work.

Advancing Maine's High School Science Curriculum

In June 2018, Maine Medical Center Research Institute was awarded \$10K from the Celia Lipton Farris & Victor W. Farris Foundation Home Community of the Maine Community Foundation to expand its current high school program, called NextGen, to other high schools throughout Maine. The grant funding is being used to create a hands-on science and research curriculum pilot program for high school classrooms.

MMCRI currently offers a high school education program to a small number of Maine schools. Students and teachers travel to MMCRI once a month for a seven session-program to learn about biomedical research through experiential learning activities. The program created with this grant funding will allow schools to benefit from the MMCRI program for less money and with less travel.

MMCRI researchers and staff are working collaboratively with several educators and using lessons from the current high school program to create portable kits for classrooms which will include a detailed on-line science curriculum and videos.

Developing and giving access to this curriculum is exciting for us, as are the possibilities that lie ahead for this program. Careers in science and technology are high growth areas in Maine, and programs like these expose and engage students early.

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

MMCRI Summer Student Research Program Expands Opportunities for Underrepresented Students

This past summer MMCRI's Summer Student Research Program (SSRP) had a record number of summer interns. This was in part due to an undergraduate research award in 2018 from the American Heart Association, designed to enhance the diversity of college student research interns at Maine Medical Center. There are many opportunities in Maine to reach students from groups that are underrepresented in STEM careers, which is the focus of this effort. In Maine there are a large number of students from rural and economically disadvantaged communities, a growing immigrant population, and a state university system where approximately one-half of the students are first generation college students. In an attempt to measure diversity, students were provided with an optional demographic information collection sheet. Data was also analyzed to determine if students were from a rural Maine county, from one that has a higher than state average of free or reduced lunch, or from one in which the population has a higher than state average of people with a high school diploma or less. Moving forward, the goal will be to develop proactive measures to continue to help identify students from underrepresented groups, expanding opportunities and engagement for all SRRP students.

2018 Summer Student Research Program Participants

Support Our Research

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 projects that further our understanding of disease processes, which enables us to develop better diagnostics and treatment.

Areas of opportunity for support of our 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.

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