



RESEARCH AND EDUCATION PROGRAM
Active Award
Progress Summaries

The following includes summaries of progress for AHW Research and Education Program awards active during the period ending June 30, 2017

MCW COMMUNITY ENGAGEMENT CORE IMPLEMENTATION INITIATIVE

AWARD AMOUNT: \$2,399,420 (2015-2019)



MEDICAL SCHOOL

Goal

Establish a central, transformative resource that advances community-engaged research.

Background

Community-engaged research is increasingly recognized by the NIH and other leading research groups as critical to addressing racial, ethnic, socioeconomic, and environmental health disparities.

The Community Engagement Core's planning process identified the need at MCW for a centralized academic resource to enhance MCW's expertise and knowledge in community-engaged research.

AHW's investment in the Community Engagement Core will result in:

- strengthened MCW expertise in community engagement through educational opportunities and mentoring;
- support of promising ideas in community-engaged research through seed grants;
- increased success in extramural funding for community-engaged research through grant support and assistance; and,
- increased community capacity for engaged research.

Input informing the aims and approach of the Center came from a wide group of MCW and community leaders, as well as other academic institutions in the state.

Award Summary

The Community Engagement Core aims to create an accessible,

organized selection of experts and training services to address complex, multi-dimensional community health needs.

By centralizing resources and knowledge in community-engaged research, the Community Engagement Core is positioned to strengthen MCW's academic expertise and position MCW as a national leader.

During this reporting period, Dr. Ahmed and his team launched the Community Engaged Scholars Program, a yearlong mentor award program that works to build capacity for community-engaged research.

The Mentoring Network cohort is comprised of 8 mentees and 3 mentors.

Health Science Square (HSS) events, which brings together MCW and community-based organizations, included a 9-session series of Community Based Participatory Research Roundtables (173 attendees total), among other sessions.

The Core helped to facilitate community-academic research partnerships through its Community Engaged Seed Grants program.

The Community Engagement Core faculty led 12 publications and 23 presentations.

In addition, more than 700 individuals attended the third annual Community Engagement week event.

Relevance

Community-engaged research is increasingly recognized by the NIH and other leading research groups as critical to addressing racial, ethnic, socioeconomic, and environmental health disparities.

Significance to Science and Health

The Community Engagement Core will establish an accessible, organized selection of experts and training services to address complex, multi-dimensional community health needs.



Syed Ahmed, MD, MPH, DrPH, FAAFP

Senior Associate Dean for Community Engagement, Director of the Clinical and Translational Science Institute's Community Engagement Program, Professor of Family and Community Medicine

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

THE CARDIOVASCULAR ROADMAP: BRIDGING OUR FOUNDATIONS TO "SIGNATURE PROGRAMS"

AWARD AMOUNT: \$4,000,000 (2014-2019)



Goal

To improve cardiovascular health in southeastern Wisconsin and beyond through innovative, cutting-edge research and cost-efficient health care by building the foundation for innovation, collaboration, and the translation of research.

Background

Cardiovascular Disease is a leading cause of death and disability in Wisconsin and in the US. AHW's investment in this initiative aims to improve the health of Wisconsin residents by enhancing the capacity of multi-disciplinary translational research teams to adopt and employ new research findings into clinical practice. The award could lead to more effective tools and therapies to enhance clinical decision making and improve patient outcomes.

Award Summary

Significant progress continues to be made in this award. Several strategies have been developed to increase collaborations between basic and clinical scientists for cardiovascular research.

Specific research studies funded through this award have the potential to lead to several promising lines of discovery. For example, research led by Peter Frommelt, MD, is contributing to increased understanding of pediatric heart function. This information will allow cardiologists to more accurately detect when diastolic cardiac function is not normal in a child, leading to a more rapid diagnosis and therapy.

During this reporting period, Dr. Benjamin leveraged AHW's investment through receiving a prestigious, highly-competitive NIH award for \$1.6 million.

In addition, the team received two \$300,000 awards for its research.

There have been more than 45 local and national presentations on the findings generated through this award.

The CVC continues to sponsor initiatives to support its four-pronged mission. Cardiovascular research, which leads to advancements in clinical care in Wisconsin and beyond, were promoted by ongoing CVC services to members, both clinicians and researchers, and new grants to support collaborative teamwork and leverage federal dollars.

Finally, outreach to the community was significantly elevated with the new hire of a community engagement specialist who will work to link the CVC with community-based organizations and citizens of Wisconsin.

Educational workshops and other events were launched to help train the next generation of cardiovascular scientists and physicians who will provide new knowledge and better clinical care to Wisconsin residents.

The team also continued to strengthen the infrastructure for cardiovascular translational research through the recruitment of new faculty and staff.

Relevance

Cardiovascular Disease is a leading cause of death and disability. The associated hospitalizations and economic burden result in significant costs. Part of this is related to inadequate treatments available due to delay in translating benchtop research findings into practice.

Significance to Science and Health

This work will enhance the capacity of multi-disciplinary translational research teams to adopt and employ novel research findings into clinical practice. Investments made in novel research performed in the Cardiovascular Center will provide more effective tools and therapies to enhance clinical decision making and improve patient productivity and outcomes.



Ivor J. Benjamin, MD

Director of the Cardiovascular Center, Professor of Medicine/ Cardiology

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

OPTIMIZING FUNCTIONAL OUTCOMES OF STROKE SURVIVORS THROUGH TRANSLATIONAL RESEARCH

AWARD AMOUNT: \$1,003,673 (2015-2020)



MEDICAL SCHOOL

Goal

Improve functional outcomes for stroke survivors by creating the Stroke Research Center of Southeastern Wisconsin, which will advance translational research in the region.

Background

While significant progress has been made in preventing strokes, fewer resources have been committed to improving rehabilitation for stroke survivors.

Stroke survivors face significant barriers to recover mobility and communication skills after neurologic stroke damage.

While some survivors fully recover, the majority live with chronic post-stroke deficits, which can involve motor skills, speech, thinking, memory, personality and emotional dysregulation. The temporary or permanent loss of independence due to stroke impacts families in addition to survivors.

Improving rehabilitation technology and techniques that lead to better functional outcomes will benefit stroke survivors and their caregivers.

Through dissemination of resources to stroke survivors statewide, the investigators aim to increase adherence to physician recommended home-based rehabilitation, as well as awareness of available advanced rehabilitation technology resources.

Award Summary

Significant progress was made in establishing the core infrastructure to support the new Stroke Research Center of Southeastern Wisconsin.

AHW's investment in the new Center has led to new, cross-disciplinary research collaborations. A key innovation of this work is the engagement of community

members with lived experience in a collaborative environment with researchers and clinicians, facilitating real-time, two-way communication opportunities.

Engaging stroke survivors and their caregivers in the research helps investigators better understand how the proposed new methods might "fit" with the demands and stress experienced by patients and families after a stroke occurs. Working with community members with lived experience is an innovative approach that will make sure new ideas are as implementable in practice as they are in laboratories.

The Stroke Survivor Recruitment Database, which currently has 41 stroke survivors enrolled (52% enrollment rate) was launched. The team has developed the Functional Outcome Measures Toolkit. Through a collaboration with St. Ann's Center - Bucyrus Campus, the team will pilot the toolkit in an urban community clinical setting. All pilot projects have been IRB approved and are actively enrolling subjects.

Our Community Academic Advisory Board (CAAB) has completed 2 projects this reporting period: 1) providing recommendations to improve the information booklet sent home with discharged stroke survivors and inpatient rehabilitation more use friendly, 2) providing input to biomechanical engineers to design a wearable device that will help stroke survivors sense where their affected limb is in space. Future CAAB activities include reviewing consent forms and a collaboration with Ex Fabula, a live storytelling organization in Milwaukee, to feature stroke survivor stories.

The SRC issued a call for proposals in clinical translational stroke rehabilitation research in July 2017. This call will fund two (2) one-year projects at \$50,000 each.

Relevance

While significant progress has been made in preventing strokes, fewer resources have been committed to improving rehabilitation for stroke survivors.

Stroke survivors face significant barriers to recover mobility and communication skills after neurologic stroke damage.

Significance to Science and Health

This award advances research in rehabilitation technology and techniques that could lead to better functional outcomes for stroke survivors and their caregivers.



Diane Braza, MD

Chair and Professor of Physical Medicine and Rehabilitation

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

VASCULAR ODORANT RECEPTORS (ORs): REGULATION AND FUNCTION

AWARD AMOUNT: \$200,000 (2016-2017)



Goal

Identify new approaches to regulate inflammation and cardiovascular disease through increased understanding of the role of odorant receptors (ORs), which are predicted to help blood vessels dilate and improve blood flow in inflammation and blood vessel health.

Background

More than 67.5 million American adults have hypertension, and 11.8% are resistant to current therapies. Hypertension, ischemic heart disease, diabetes, and other cardiovascular diseases associated with inflammation are major causes of death.

Identifying new internal factors and vascular mechanisms that help suppress inflammation is critical to developing new therapies for cardiovascular and inflammatory diseases.

Award Summary

The AHW Endowment's investment in Dr. Campbell and his research team could lead to the identification of vascular ORs and natural and synthetic molecules that activate the receptors. Pathways that are activated by ORs have an impact on human physiology and represent a new avenue for translational research.

Hypertension, ischemic heart disease, diabetes, and heart failure are associated with the vessels' impaired ability to dilate and the presence of inflammation. Cardiovascular diseases are a major cause of death, and while survival has improved, treatment failures remain high.

Because these diseases have vascular and inflammatory components, new approaches to

understanding vascular regulation and function are needed in order to improve treatment and survival.

The identification of new odorant receptors (ORs) has led to new knowledge in areas of vascular biology, inflammation, and cardiovascular disease.

During this reporting period, the research team continued to build from its discovery that the Ms4a family of proteins is expressed in high levels in vascular cells. These proteins are found in nasal tissue and known to sense some odorant. These proteins differ from typical odorant receptors in their structure, and their effects are due to calcium entry into cells. This is a significant and novel finding that suggests an important, unrecognized role for these proteins in vascular biology. This discovery exceeded the research team's expectations for the initiative and poses an exciting new changemaking direction to the research.

The team has learned that human vascular cells express specific odorant receptors as well as the proteins of the intracellular pathway mediating the effects of odorants. These receptors and proteins are found in smooth muscle cells that regulate dilation and constriction of arteries. While more evidence is needed, these studies support the possibility that odorants regulate the blood flow to organs and blood pressure by dilating or constricting arteries.

It is anticipated that AHW's investment in this research could lead to significant publications and extramural funding.

Relevance

More than 67.5 million American adults have hypertension, and 11.8% are resistant to current therapies. Hypertension, ischemic heart disease, diabetes, and other cardiovascular diseases associated with inflammation are major causes of death.

Significance to Science and Health

Identifying new internal factors and vascular mechanisms that help suppress inflammation is critical to developing new therapies for cardiovascular and inflammatory diseases.



William B. Campbell, PhD,

Chair & Professor,
Pharmacology and Toxicology

Co-Investigator: David D. Gutterman, MD, Northwestern Mutual Professor of Cardiology and Senior Director of the Cardiovascular Center

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

FUNCTIONAL PAIN AND AUTONOMIC DISORDERS (FPAD) PROGRAM DEVELOPMENT

AWARD AMOUNT: \$1,943,400 (2013-2018)



Goal

To develop a comprehensive center for clinical excellence, research, teaching, and community outreach for the treatment of functional pain and autonomic disorders (FPADs).

Background

Functional pain is ongoing pain for which there is no known medical explanation. Autonomic disorders affect the autonomic nervous system, which controls our involuntary functions such as heart rate and breathing and are wide-ranging. These disorders (FPAD) cause patients to experience pain in various regions of the body. FPADs affect around 500,000 individuals in Wisconsin.

AHW's investment in the FPAD program will help better define these disorders, educate physicians about new discoveries in FPAD, and improve treatment options for patients.

Award Summary

Establishing the clinical and computational infrastructure to support autonomic disorder research is key to the FPAD program. With the creation of a patient registry database, researchers can collect clinical data and evaluate specific outcomes for FPAD patients. The team has successfully recruited more than 1,000 patients into the autonomic disorders registry, a significant increase in recruitment from the previous year.

Research supported through the FPAD program is progressing well with enrollment. A new research coordinator was recruited to help with analysis of data. To-date, analysis has demonstrated (1) a very novel finding that mitochondrial energy production is very poor in FPADs; (2) a new emphasis on a small area of the brain called the periaqueductal gray

region. The periaqueductal gray region is the place where stress and threat are managed and instructions given to the body as to how to handle these impulses. Research data is showing a likelihood that when these instructions go awry, FPAD develops.

The computational work continues at a steady pace as Charles Welzig, MD, examines brain networks from multiple perspectives including fMRI, MEG, EEG, and Near-infrared regional spectroscopy (NIRS).

The education of Wisconsin primary care physicians in FPADs continues to be a key priority. A survey of over 100 physicians showed a high degree of discomfort in treating FPAD patients. The team has enrolled about 15 practices to provide training and education of how to better diagnose and treat FPAD. To-date, the team has received excellent evaluations regarding the training program.

The website developed to share difficult FPAD cases is getting a large number of participants (about 500 members).

Finally, the FPAD training has gained national attention resulting in a partnership with several Michigan institutions to develop a national program.

Several additional inter-institutional research collaborations have resulted from this award that continue to show promising results.

A collaboration with Sojourner Peace House and Milwaukee Rescue Mission is underway through a separate but related effort to understand the role of chronic pain in opioid abuse.

To-date, the team has received \$3.9M in additional funding to successfully leverage AHW's investment.

Relevance

Functional pain and autonomic disorders (FPADs), such as fibromyalgia and migraines, affect around 500,000 individuals in Wisconsin. Despite a large patient population, understanding of these disorders has progressed slowly.

Significance to Science and Health

By better defining and understanding FPADs, the researchers can create an educational infrastructure for teaching physicians and offer improved treatment options for patients in and outside of Wisconsin.



Thomas Chelimsky, MD
Professor of Neurology/
Autonomic Disorders

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine

DEVELOPING AN ANESTHESIOLOGIST ASSISTANT PROGRAM AT MCW

AWARD AMOUNT: \$969,426 (2015-2018)



MEDICAL SCHOOL

Goal

Increase the number of well qualified anesthesia care providers in Wisconsin through the development of an innovative Master of Science in Anesthesia (MSA) Program at MCW.

Background

In the Midwest, 80 percent of health care facilities report the need for additional anesthesiologists and certified nurse anesthetists. Many rural areas are in especially great need due to a significant proportion of anesthesia providers living and working in urban locations.

Due to the aging population's projected demand for health care services, the current shortage and maldistribution of anesthesia specialists is expected to worsen in coming years.

While the static number of residency positions is a barrier for filling the anesthesia shortage with physicians, anesthesiology assistants are exempt from that requirement and can provide cost-efficient anesthesia care in a physician-led care model.

Currently, Wisconsin residents interested in becoming anesthesiology assistants have to leave the state for training, increasing the likelihood that some graduates may not return to Wisconsin to practice. In total, fewer than 3,000 anesthesiology assistants currently practice in the US.

In order to meet the rising need for cost-effective anesthesia services, however, anesthesiology assistants represent a ripe opportunity to expand the workforce and deliver needed care without sacrificing quality.

Award Summary

Through a focus on interprofessional training, research and patient safety, AHW's investment is helping to build a leading program to train and retain anesthesia providers prepared to meet Wisconsin's evolving needs.

During its reporting period, the leadership team made significant progress in the development of the MSA Program.

Lois Connolly, MD, assumed leadership for the program and AHW award due to the program's past director, David Wartier, MD's retirement.

The program selected 12 students and recruited ten certified anesthesiology assistants as faculty support of its goal of increasing the number of qualified non-physician anesthesia care providers in Wisconsin. Retention of faculty and students in the program is 100 percent.

Faculty development efforts are ongoing and clinical sites for the students have been identified.

It is anticipated that the MSA Program will continue its progress in meeting its long-term outcomes of fostering growth in anesthesia providers in Wisconsin and addressing the anesthesia provider disparity between rural and urban areas of Wisconsin.

Relevance

This program will increase access to quality anesthesia care through an innovative education program for anesthesiology assistants.

Significance to Science and Health

It is anticipated that the MSA Program will continue its progress in meeting its long-term outcomes of fostering growth in anesthesia providers in Wisconsin and addressing the anesthesia provider disparity between rural and urban areas of Wisconsin.



Lois Connolly, MD
Vice Chair and Professor of
Anesthesiology

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

GRADUATE MEDICAL EDUCATION DEVELOPMENT IN CENTRAL AND NORTHERN WISCONSIN

AWARD AMOUNT: \$369,060 (2016-2017)



MEDICAL SCHOOL

Goal

Develop a strategic plan for overcoming barriers to creating and sustaining graduate medical education (GME) expansion in Central and Northern Wisconsin.

Background

There is a pressing need to develop new GME opportunities in order to ensure that there are enough physicians to care for the people of Wisconsin, especially in rural areas.

The Association of American Medical Colleges predicts a US physician shortage due to a steadily expanding older population, high rates of chronic disease, a more diverse population and physicians retiring from practice.

Wisconsin is expected to experience a shortage of more than 2,000 physicians by 2030. However, available data indicate that up to 86% of in-state Wisconsin medical school graduates who also complete GME in the state will remain in Wisconsin to practice. (Wisconsin Hospital Association, 2011).

To-date, there is no formal state or regional GME workforce planning group available for comprehensive consultation to advise, coordinate and facilitate GME expansion or development of new programs in Wisconsin, leaving health systems without ready access to the expertise needed to develop such programs.

Through AHW's investment in GME expansion, a strategic plan will be developed to define the future of GME in the region.

Award Summary

Through this investment, regional

partners have a better understanding of what is needed to make the best decisions for their organizations regarding new and expanded GME opportunities.

With AHW and some regional philanthropic funding, the MCW regional campuses have begun building on MCW traditions and resources to provide a new model of community-engaged undergraduate medical education in Wisconsin.

Linking regional undergraduate medical education (UME) with specific GME opportunities is the next needed step, and additional residency positions are a critical part of accomplishing this goal.

AHW's investment in this effort is helping regional stakeholders in the development of new GME programs and provide opportunities to study and implement methods of linking UME and GME.

During this reporting period, progress has been made in stabilizing family medicine residency programs and information has been gathered to help determine the regional resources available for future GME development.

The consultation available to regional partners will generate the knowledge necessary to implement successful GME expansion.

Once established, graduate medical education opportunities become sustainable through direct and indirect reimbursement from federal Medicare funding, which significantly—but not completely—offsets the cost of graduate medical education for sponsoring health systems.

Relevance

There is a pressing need to develop new GME opportunities in order to ensure that there are enough physicians to care for the people of Wisconsin, especially in rural areas.

Significance to Science and Health

- AHW's investment in this award will develop a strategic plan for graduate medical education in Central and Northern Wisconsin that will lead to increased access to physicians for the people of Wisconsin.



Lisa Dodson, MD
Campus Dean
MCW-Central Wisconsin

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

STEP-UP: STUDENT ENRICHMENT PROGRAMS FOR UNDERREPRESENTED PROFESSIONS IN MEDICINE

AWARD AMOUNT: \$925,915 (2015-2020)



MEDICAL SCHOOL

Goal

Partner with educational institutions to nurture underrepresented in medicine students to better prepare them for success in the field of medicine.

Background

Only fifteen students of African American, Native American, Hispanic or Native Hawaiian descent from Wisconsin matriculated to a medical school last year. MCW has enrolled approximately 30 students considered to be underrepresented in medicine in each of the last three classes. This group constitutes about 15 percent of each class. Many of these students, however, leave Wisconsin for residencies closer to home.

With Wisconsin growing increasingly diverse each year, the need also grows for physicians that can provide culturally competent care and practice effectively within rural and urban areas that have had less access to health care services. To enhance cultural competence and address health disparities, MCW has worked to expand diversity among medical students, residents and faculty members.

AHW's investment in the STEP-UP Program aims to significantly enhance these efforts through in-state community partnerships with educational institutions throughout the instructional spectrum.

Award Summary

Through collaborative enrichment activities, the STEP-UP program leaders are building a strong community-engaged pipeline that will enhance science education and increase interest in medical careers.

This award features extensive

collaboration among MCW's medical school, graduate school and educational institutions in Southeastern, Northeastern and Central Wisconsin.

To-date, the program has been successful in cultivating partnerships with more than twenty partners, including schools and community centers. Examples of participating schools include, University of Wisconsin-Milwaukee, University of Milwaukee- Parkside, University of Wisconsin-Green Bay, Marquette University and Ripon College.

Two open houses with middle schools were held encouraging interest in science, health and medicine in December 2016 and April 2017. Attendance was excellent and participants rotated through various stations to learn more about opportunities.

In addition, two open houses were held for college students in March and April 2017.

The Kaleidoscope film and discussion series continues to be successful with 15 sessions over the last 12 months and average attendance being greater than 100 individuals. Topics ranged from recognizing signs of depression, wellness, and valuing diverse perspectives.

Student engagement of current MCW students has been excellent and they recently formed an official student organization related to this work with more than 50 medical students participating.

Relevance

With Wisconsin growing increasingly diverse each year, the need also grows for physicians that can provide culturally competent care and practice effectively in areas that have less access to health care services.

To enhance cultural competence and address health disparities, programs are needed to help expand diversity among medical students, residents and faculty members.

Significance to Science and Health

The proposed program will develop best practices related to the creation and implementation of a pipeline program across many institutions in Southeastern, Northeastern and Central Wisconsin. The project team will also track the performance of pipeline students over time.



Jose Franco, MD

Associate Dean of Educational Improvement and Professor of Medicine

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

DEVELOPING NOVEL PROGRAMS IN A JOINT BIOMEDICAL ENGINEERING DEPARTMENT

AWARD AMOUNT: \$2,000,000 (2016-2021)



MEDICAL SCHOOL

Goal

Create a Clinical and Translational Biomedical Engineering Program in the MCW/Marquette University joint Department of Biomedical Engineering that addresses unmet needs in health care through biomedical technology development.

Background

As health care reforms continue, it is essential that patients receive high quality care in a safe and cost-effective manner. To achieve this, innovative and transformative approaches to managing health conditions are needed.

This program will advance the creation and application of new technologies to enhance health and help identify clinical solutions to complex health needs more quickly, less expensively, with better outcomes, and with fewer side effects.

Award Summary

Through this program, biomedical engineers work with basic scientists, physicians, and colleagues in industry to take principles from applied and physical sciences and apply them to medicine, directly impacting the triple aim of health care (better health, better care, lower cost). There is an increased demand for professionals who practice at this intersection of disciplines and who are capable of advancing innovations from conception to clinical practice, a process we refer to as Clinical and Translational Biomedical Engineering.

This program is working in the following areas:

- High Value Biomedical Devices (creating high efficiency/ low cost biomedical devices to support community and home-based care initiatives), and
- Cellular Engineering and Bio-manipulation (developing novel approaches to precision medicine based on in vivo and in

vitro cellular manipulation)

During this reporting period, an extensive international search has been conducted for faculty recruits.

As a result of the program's efforts, it is expected that there will be an increase in partnerships between faculty researchers, clinicians, engineers, and experienced industry advisors, who will work together to design, build, and test devices and approaches to solve clinical problems.

The proposed work is planned to establish a strong foundation for progress in two essential areas that will directly impact the health of the people of Wisconsin. Through focus on High Value Biomedical Devices that are both highly efficient and low cost, the program will have immediate bearing on community and home-based care initiatives.

In the long-term, developing programs in Cellular Engineering and Bio-manipulation that support ongoing efforts to develop novel therapeutic options, will afford the people of Wisconsin access to the latest developments in health care.

In addition, this program benefits from the Marquette University and MCW Biomedical Engineering Department, which brings together the engineering education and research expertise of Marquette University and the medical research, technology, and clinical expertise of MCW. The program will engage collaborators with MCW clinicians, graduate students, staff, and connections to industry, made through the Clinical and Translational Science Institute of Southeast Wisconsin and the MCW Office of Technology Development.

Once fully operational, the program plans to be competitive for extramural funding support for new areas of research through federal grants, contracts and foundations.

Relevance

- As healthcare reforms continue in our state and in the nation, it is essential that patients receive high quality care in a safe and cost-effective manner. To achieve this, innovative and transformative approaches to managing health conditions are needed.

Significance to Science and Health

- AHW's investment in this award will develop a new program focused on clinical and translational partnerships that deliver biomedical engineering solutions to clinical problems that impact the health of the people of Wisconsin.



Andrew Greene, PhD

Dr. Robert D. and Dr. Patricia E. Kern Professor in Biotechnology and Bioengineering, Professor of Physiology

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

PROGRAM FOR THE STUDY OF NEURONAL SYNAPTIC PLASTICITY IN HEALTH AND ILLNESS

AWARD AMOUNT: \$3,042,309 (2012-2016)



MEDICAL SCHOOL

Goal

Advance understanding of nervous system function in health and in illness through the creation of a collaborative and translational research program focused on the mechanisms, triggers and consequences of changes in synaptic plasticity (the ability of the brain to rewire over time).

Background

Neurological disorders affect 116 million Americans and it is estimated that Wisconsin residents and businesses incur more than \$10 billion each year in health care and lost productivity due to pain costs.

The Neuroscience Research Center at MCW was established to confront the most complex neurological research problems facing our citizenry, with particular focus on:

- neurodegenerative diseases like Alzheimer's and Parkinson's diseases,
- nervous system injuries including brain trauma, concussion, and stroke,
- developmental disorders such as autism, cerebral palsy, and attention deficits, and,
- mental disorders like schizophrenia, depression, and substance abuse.

This award promotes an innovative team of scientists who study synaptic plasticity, which is the ability of the neurons in our brain to rewire in response to normal activity or pathologic stress. Synaptic plasticity has a role in all neurological disorders and thus, the program has the potential to impact many diseases facing Wisconsin residents.

Award Summary

A primary goal of the award is to increase research capacity and

collaboration for neuronal synaptic plasticity research.

In addition to securing new faculty expertise to advance this area of research, the program has been highly productive in fostering collaboration through educational seminars, networking opportunities, and a pilot award funding program. To-date, the AHW investment of \$3M has leveraged more than \$10.6M in extramural funding through more than 60 grant submissions that build from the AHW-funded research.

In addition, Dr. Hillard's team has advanced knowledge in the field through more than 69 publications in established journals and scholarly texts.

Specific successes include:

- promising findings that suggest imaging of the retina can provide an early diagnosis of Alzheimer's Disease
- findings that certain potassium channels in the brain are involved in seizures
- better understanding of the role of pain receptors in gastrointestinal tissue to explore new ways of treating colitis and related disorders
- Identification of a protein from slime mold that prevents the misfolding of brain proteins. This is an extremely exciting discovery that has implications for several neurodegenerative disorders including Huntington's, Alzheimer's and Parkinson's Diseases.

These efforts highlight how important collaborations are to completing impactful, high-quality research studies.

Relevance

Neurologic disorders affect a large number of Wisconsin residents, and the social and monetary costs of care for neurologic disorders is significant.

Significance to Science and Health

The team's research directly relates to learning and memory disorders, the consequences of addiction, diseases in which neurons are lost, including Parkinson's Disease and ALS, and to chronic pain, all of which are significant problems in Wisconsin.



Cecilia Hillard, PhD

Associate Dean for Research,
Director of the Neuroscience
Research Center, Professor of

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

DEVELOPMENT OF A REDOX BIOLOGY PROGRAM

AWARD AMOUNT: \$1,600,000 (2011-2017)

Goal

Create a premier program in redox biology at the Medical College of Wisconsin (MCW) to foster the sharing of ideas and enhance the ability of researchers to translate basic research discoveries into clinical treatments.

Background

Humans obtain energy from food through "oxidation", which is the transfer of an electron from a molecule to oxygen.

The reverse process of gaining an electron is "reduction", and the study of electron transfer is called "redox" biology.

Some redox processes generate free radicals that can damage tissues, including the heart, which leads to heart disease. Free radicals also play an important role in the development of cancer and its spread.

Researchers in MCW's Redox Biology Program study biological processes involving the transfer of electrons and seek to prevent the damage caused by free radicals by studying how the body produces and controls them.

Such work will help Wisconsin residents suffering from diabetes, cancer, and heart disease. Because of the wide role played by free radicals in human disease, this work may help with designing therapies for other diseases in which free radicals participate.

Award Summary

AHW's investment in the MCW Redox Biology Program expanded expertise and capacity in promising areas of basic science and clinically relevant research through the successful recruitment investigators.

The Redox Biology Program recruited Brian Smith, PhD, whose research advances knowledge of aging and

inflammation in heart disease, as well as cancer, neurodegeneration, diabetes.

Andreas Beyer, PhD, also was recruited through the program. Dr. Beyer combines his expertise in genetics and physiology to advance research in vascular biology that could lead to new therapies to reduce heart disease.

The work of the Redox Biology Program is highly collaborative and researchers have partnered with MCW's Neuroscience Center, Cancer Center, and Cardiovascular Center.

To further collaboration, the researchers have continued the Redox Journal Club and Work-in-Progress program to bring together like-minded faculty, which has been increasingly well attended and is proving a great success.

Through seminar series, symposiums, and journal clubs, AHW's investment in the Redox Biology Program is helping to create a collaborative and fertile environment for the exchange of ideas and experimental data.

Committed to fostering education and training of future generations of researchers in this areas, the Redox Biology Program also has provided training opportunities to graduate, post-doctoral and summer students.

Through this AHW award, Dr. Hogg and his team have garnered more than \$2M in extramural funding and published more than 55 scholarly works contributing to knowledge in the field.



MEDICAL SCHOOL

Relevance

Advances in redox biology have the potential to identify new therapies for several leading causes of death, including diabetes, cancer, and cardiovascular disease.

Significance to Science and Health

The researchers advanced discoveries in the area of redox biology, an exciting area of biomedical research that studies oxidative stress and the body's ability to counteract this stress by using DNA repair enzymes and/or antioxidants. If not regulated properly, oxidative stress can induce a variety of chronic and degenerative diseases.



Neil Hogg, PhD

Associate Dean of Graduate Students, Director of the Redox Biology Program, and Professor of Biophysics

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

MAGNETOENCEPHALOGRAPHY (MEG) RESEARCH DEVELOPMENT PROGRAM

AWARD AMOUNT: \$694,124 (2013-2017)



Goal

Establish a world-class MCW magnetoencephalography (MEG) research program through the support of pilot projects and development of new imaging technologies.

Background

Magnetoencephalography (MEG) is a technique for measuring small changes in magnetic fields produced by the electrical activity of neurons in the brain that can help to produce neural images. MEG has several advantages over other imaging approaches, including the ability to accurately locate specific areas of activity within the brain.

The Froedtert MEG scanner is currently used to evaluate patients in the MCW epilepsy and brain tumor programs. Unfortunately, only a small number of projects so far have used the facility for research. Several factors, including the unavailability of funds for pilot projects, lack of familiarity with MEG methodology among local scientists, and a relatively steep learning curve for MEG data analysis have contributed to this low level of adoption.

AHW's investment in the MEG Research Development Program seeks to promote the MEG's potential as a tool in health research.

Award Summary

AHW's investment in the MEG Research Program has supported a competitive pilot funding program to foster use of the MEG for health research. In addition, Dr. Humphries and his team have developed education and training tools as well as enhanced data analysis and software programs regarding use of the MEG for health research.

Through the pilot funding program, eight awards were funded that advance investigations using the MEG as a research tool.

Examples include a project dedicated to identifying the biomarkers of concussion and a project that explores the spatiotemporal dynamics of attention control.

Due to the complexity of MEG data, projects are still in the early stages of data analysis. However, emerging findings suggest differences in brain activation related to attention focus and differences in brain activation between athletes with recent concussions and matched controls. Several technical advances were also made through the funded projects including one of the first studies in the world to use simultaneous MEG and NIRS, a non-invasive method of optical imaging.

A new MEG Users Group was formed to continue to educate researchers about MEG and foster future collaborations beyond the duration of the AHW investment.

Several members of the MEG Research Group represented MCW in a NIH-sponsored initiative to create a new scientific community focused on MEG in North America.

In addition, the research team secured funding of the first NIH grant at MCW to use MEG as a primary measure. This award aims to study brain connectivity in Epilepsy using fMRI and MEG is part of the NIH Human Connectome Project. According to NIH guidelines, all collected data for this project will be released to the public, providing a high degree of publicity for MEG research in Wisconsin.

Relevance

Brain imaging studies are an important tool researchers use to continue exploring the brain's role in health and in disease, and magnetoencephalography (MEG) offers advantages over other imaging approaches.

Significance to Science and Health

Expanding the use of MEG technology will improve research projects that use imaging to better understand how the brain works.



Colin Humphries, PhD

Director of MEG Research,
Assistant Professor of Neurology

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

TREATMENT OF PANCREATIC DUCTAL ADENOCARCINOMA WITH COMBINED IMMUNOTHERAPY, NOX INHIBITION, AND ALTERED CHEMOKINE SIGNALING

AWARD AMOUNT: \$200,000 (2016-2017)



Goal

Test therapies that alter the normal cells surrounding a tumor (called the tumor microenvironment) in pancreatic ductal adenocarcinoma (PDAC) so that tumor-killing immune cells can reach the tumor and be activated to kill the cancer cells.

Background

Milwaukee County has one of the highest rates of pancreatic cancer mortality in the U.S., 15 percent higher than the national average. Our immune system has the ability to kill cancer cells, but solid tumors alter the microenvironment such that immune cells poorly penetrate the tumor and are inactivated by inhibitory substances. Recent advances to harness the power of the human immune system to fight cancer (called immune therapy) has shown success for leukemia (blood cancer), but not for solid tumors. This research seeks to improve infiltration of immune cells into the tumor using a "homing" molecule called CXCL12, and to reduce production of immune suppressive molecules by inhibiting the enzyme Nox (NADPH oxidase).

It is critical that scientists with diverse backgrounds and expertise work together to develop novel treatments, such as immune therapy.

Award Summary

The AHW Endowment's investment in this initiative enabled Dr. Johnson and his research team to investigate the potential of immune therapy to halt pancreatic cancer progression when used in combination with repurposed FDA-approved Nox inhibitors and a novel immune cell homing molecule produced at MCW.

There is a critical need for new treatments to limit pancreatic cancer progression. Immune therapy is increasingly recognized as a powerful

tool in fighting cancer, but it has not worked well with solid tumors, such as pancreatic cancer.

The research approaches undertaken through this initiative are changemaking and have not been previously used for any cancer. The research has the potential to advance to clinical trials using clinical protocols at MCW.

Completion of the proposed work is expected to reveal new strategies and approaches to limit the devastating effects of pancreatic cancer and improve patient survival, especially in areas with high mortality rates, such as Milwaukee County.

During this reporting period, Dr. Johnson's team completed a series of studies to improve detection of tumor reactive lymphocytes in pancreatic cancer.

These approaches include detection of T cells within the central immune tissues (bone marrow), peripheral immune tissues (liver, spleen) and pancreatic tumor parenchyma. The team has discovered that recombinant chemokines continue to have powerful use as a biologic therapy, with effects on tumor cells and tumor reactive T cells. While these results have been largely in preclinical animal models, they should be readily translatable to the clinic.

Further studies are underway. These studies are laying the critical groundwork to a combinatorial approach to activate the immune system and improve its killing of pancreatic cancer.

Relevance

There is a critical need for new treatments to limit pancreatic cancer progression. Immune therapy is increasingly recognized as a powerful tool in fighting cancer, but it has not worked well with solid tumors, such as pancreatic cancer.

Significance to Science and Health

Completion of the proposed work is expected to reveal new strategies and approaches to limit the devastating effects of pancreatic cancer and improve patient survival, especially in areas with high mortality rates, such as Milwaukee County.



Byron Johnson, PhD

Professor, Pediatrics and Microbiology and Molecular Genetics

Co-Investigators: Michael Dwinell, PhD, Professor, Microbiology and Molecular Genetics; Director of the Bobbie Nick Voss Laboratory; Leader of the Tumor Progression and Metastasis Program

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

HIGH IMPACT INTEGRATED BEHAVIORAL AND BIOMEDICAL INTERVENTIONS TO ERADICATE AIDS

AWARD AMOUNT: \$999,395 (2014-2018)



MEDICAL SCHOOL

Goal

Support research to develop and test the efficacy of novel interventions designed to reach HIV-positive persons in the community, connect them to medical care, increase treatment adherence, and thereby reduce transmission of HIV disease.

Background

In the first thirty years of AIDS prevention, campaigns to reduce risk have limited the growth of the HIV epidemic, but have not stopped it.

Recent groundbreaking clinical trials have shown that early treatment with anti-retroviral drugs is now the best available treatment and method of prevention.

Approximately 8,500 Wisconsin residents live with HIV infection.

Significant racial disparities exist among those living with the disease, as new infections disproportionately impact Milwaukee's African American community.

Efforts to decrease HIV transmission will be beneficial to Wisconsin residents and beyond.

Award Summary

The interdisciplinary research team tested an intervention to deliver pre-exposure prophylaxis (PrEP) to a sample of approximately 70 high-risk men who have sex with men (MSM) community volunteers in Milwaukee.

The innovative approach combined behavioral and biomedical interventions culturally tailored to the needs of African American MSM in Milwaukee to learn if such approaches are effective in addressing this critical challenge.

A community advisory panel guided the research efforts whose members included representatives from HIV-affected communities, among other key stakeholders.

Consistent with Wisconsin's HIV epidemiology and incidence trends, interviews were primarily undertaken with men who have sex with men especially young African American men in Milwaukee.

Over the past several years, large-scale medical trials have unequivocally demonstrated that MSM who are presently uninfected but at high behavioral risk for contracting HIV infection can be substantially protected from contracting HIV if they follow a daily oral prophylaxis medication regimen.

Based on data showing over 92% protection from HIV afforded by the use of PrEP regimens, the CDC and the Wisconsin Department of Health (DOH) now recommend PrEP for MSM at high risk for contracting HIV infection.

However, PrEP uptake in Wisconsin is very low. MCW's Division of Infectious Diseases estimate that only about 50 persons in Wisconsin are on PrEP regimens even though the Wisconsin DOH (2016) estimates that over 8,000 residents are high-risk MSM.

Interventions that can increase uptake of PrEP by high-risk but still uninfected MSM carry the potential to dramatically reduce HIV transmissions in Wisconsin.

This research study identified several reasons for low PrEP use, including a close link with the presence of other co-existing life problems including alcohol and other substance abuse, unaddressed mental health needs, housing instability, stigma associated with both HIV and homosexuality, and other unmet service needs.

This study also identified several concerns that exist in the community about PrEP's benefits, risks, reliability, and cost. The study finds that a population-level intervention is needed to help ensure PrEP uptake among high-risk MSM. The research team aims to evaluate community intervention strategies to increase awareness and accurate understanding of PrEP among community members where its use could have great benefit.

Relevance

Decreasing HIV transmission requires an understanding of why HIV positive persons are not receiving regular HIV care, do not adhere to medication regimens, or do not seek HIV testing, among other areas that will be addressed through this investment.

Significance to Science and Health

This work will benefit the health of Wisconsin by identifying and testing strategies that: 1) maintain health and decrease HIV-related morbidities and mortality, and 2) prevent downstream HIV incidence by engaging HIV positive persons in care, thereby reducing viral load infectivity, and the likelihood of HIV transmission to others.



Jeffrey A. Kelly, PhD

Director of the Center for Aids Intervention Research, Professor of Psychiatry and Behavioral Medicine

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

ROLES OF SUBCUTANEOUS ADIPOSE TISSUE AND ADIPONECTIN ON THE PATHOGENICITY OF VISCERAL ADIPOSE TISSUE

AWARD AMOUNT: \$200,000 (2016-2017)



MEDICAL SCHOOL

Goal

Identify how peripheral adipose tissue (SAT, or subcutaneous fat) protects against metabolic diseases compared to visceral adipose tissue (VAT, or central/abdominal fat) in healthy obese persons, resulting in lower rates of metabolic diseases, such as diabetes.

Background

Visceral obesity with VAT accumulation is associated with type 2 diabetes, cardiovascular disease, and other diseases caused in part by inflammation.

To help control and prevent these emerging health conditions, emphasis has largely been put on weight loss. However, adipose tissue distribution in peripheral skin depots may not be as harmful as previously thought, and may, in fact, be protective. If findings do point to this, they may suggest that “all obesity is not equal.” Less emphasis could be placed on weight loss for certain individuals and instead limited health care resources could be shifted to better control other cardiovascular risk factors, such as smoking, hypertension, and type 2 diabetes, which can be present independent of obesity.

Award Summary

The AHW Endowment investment in this initiative enabled Dr. Kidambi and her research team to identify innovations in obesity treatment by suggesting that “not all fat is equal” and that adipose tissue distribution determines the contribution of obesity to type 2 diabetes and cardiovascular risk.

The research team aims to increase understanding of how different body

fats influence metabolic diseases and how SAT may be protective. Ultimately, this knowledge can shift emphasis from weight loss to other measures in order to control inflammatory diseases.

During this reporting period, the research team has recruited 55 subjects to participate in the study.

Significant progress was made in completing the sequencing for small molecules called microRNAs that control other genes.

Preliminary research findings are showing differences in expression of 46 molecules between visceral and subcutaneous adipose tissue depots.

The team also found three microRNAs that were associated with a protective hormone secreted by fat tissue called adiponectin. Of these researchers picked four molecules (miRs 33b, 199a, 141, and 142a) to further test their association with metabolic pathways and ultimately their role in obesity-related diseases.

In addition, the research team found seven microRNAs changed in relation to a subject’s body mass index.

Further research is underway to learn more about the metabolic pathways and their association with obesity-related diseases.

To-date, the team has shared three presentations.

Relevance

Visceral obesity with VAT accumulation is associated with type 2 diabetes, cardiovascular disease, and other diseases caused in part by inflammation.

To help control and prevent these emerging health conditions, emphasis has largely been put on weight loss.

However, adipose tissue distribution in peripheral skin depots may not be as harmful as previously thought, and may, in fact, be protective.

Significance to Science and Health

Researchers are learning how peripheral adipose tissue (SAT, or subcutaneous fat) protects against metabolic diseases compared to visceral adipose tissue (VAT, or central/abdominal fat) in healthy obese persons, resulting in lower rates of metabolic diseases, such as diabetes.



Srividya Kidambi, MD, MS

Associate Professor of Medicine—
Endocrinology

Co-Investigators: Daisy Sahoo, PhD,
Associate Professor of Medicine and Vice
Chair for Research; Jon Gould, MD, Chief,
Professor, Surgery; Pengyuan Liu, PhD,
Associate Professor, Physiology; Leah
Solberg Woods, PhD, Associate Professor,
Pediatrics

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

IMPROVING CLINICAL IMAGING DIAGNOSTICS THROUGH USE OF CUTTING-EDGE MRI TECHNOLOGY

AWARD AMOUNT: \$500,000 (2015-2018)



MEDICAL SCHOOL

Goal

Improve high-strength magnetic resonance imaging (MRI) technology and techniques to better assess cancer, inflammation, brain degeneration and brain injury.

Background

The implantation of metallic devices has become increasingly common, especially with the rise of joint replacements. The need is projected to continue rising with the age of the population, as 3.5 million knee replacements are projected to be done in 2030. And that is just the prediction for the United States.

Better imaging techniques are needed to assess complications due to tissue inflammation near the implant, as well as to better check for any cancer recurrence near the implant site after treatment for osteosarcoma.

In addition, the researchers aim to implement a number of newly designed techniques to improve clinical monitoring of brain degeneration and traumatic brain injury, among other conditions.

Award Summary

By improving MRI images near metal implants, physicians will be better able to test for a number of potential post-implantation complications, including local tissue inflammation, loosening of the implant, infection and recurrence of osteosarcoma.

These improved tests will enable physicians to assess the status of an implant and make more informed treatment decisions if any problems arise.

Dr. Koch and his team have made excellent progress toward

implementing new techniques to improve the images taken by MCW's most powerful MRI machine, which will enhance imaging for Alzheimer's disease, traumatic brain injury and cancer. Currently, work is underway to develop and refine techniques to help physicians look for abnormal iron levels that will help in imaging of cancer and micro-bleeds in the brain indicative of head trauma.

During this reporting period, the research team provided the first demonstration of distortion free diffusion-weighted MRI near metal implants, which resulted in one publication and an NIH award. In addition, the team developed technology that allows for advanced tissue measurements near failed total hip replacements. With hospital collaborators, the team demonstrated that this technology could be an early predictor of tissue death in those cases.

In addition, the team has made progress in learning more about how the brain recovers from sports concussion. An important public health concern, these studies will continue to inform best practices in managing sports concussion at the juvenile through professional levels.

The research team disseminated its findings through seven international presentations and publication efforts. A total of \$775,000 has been leveraged through extramural resources through this award.

This award features collaboration within the Departments of Biophysics and Radiology. The team also includes members from the Departments of Neurosurgery and Orthopedic Surgery.

Relevance

Better imaging techniques are needed to assess complications due to tissue inflammation near the implant, as well as to better check for any cancer recurrence near the implant site after treatment for osteosarcoma.

Significance to Science and Health

By improving MRI images near metal implants, physicians will be better able to test for a number of potential post-implantation complications, including local tissue inflammation, loosening of the implant, infection and recurrence of osteosarcoma.



Kevin Koch, PhD

Associate Professor
Biophysics and Radiology

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

AN INNOVATIVE MODEL FOR EDUCATING THE PHARMACISTS OF THE FUTURE: PHARMACY SCHOOL DESIGN AND DEVELOPMENT

AWARD AMOUNT: \$3,024,132 (2015-2017)



MEDICAL SCHOOL

Goal

Design and develop a School of Pharmacy at the Medical College of Wisconsin to address workforce needs in rural and urban underserved communities in Wisconsin.

Background

In Wisconsin, there is a continuing maldistribution of pharmacists in medically-underserved communities. MCW aims to emphasize student clinical training in these locales. With an aging population and health care changing to emphasize team-based preventive care, pharmacists must adapt and deliver primary care to meet the rising need. MCW aims to prepare pharmacists to provide quality care in a team setting.

AHW's investment in the School of Pharmacy aims to reshape pharmacist training in Wisconsin to focus on the pharmacist of the future.

The proposed School of Pharmacy will train pharmacists to provide patient-centered care in a team-based model, enabling pharmacists to provide direct support to address community health needs.

MCW will explore a three-year curriculum that is rigorous yet time efficient, allowing pharmacists to enter residency or the workforce more quickly. The program will emphasize interprofessional education to prepare pharmacists that deliver cost-efficient primary care within a team-based model of care.

Award Summary

To-date, the School of Pharmacy has made significant progress in creating the Pharmacy School curriculum.

Highlights of accomplishments include:

- Recruitment of key faculty to teach in the School of Pharmacy
- Established two academic departments (Biopharmaceutical Sciences and Clinical Sciences)
- Successfully completed the first phase of accreditation processes through Accreditation Council for Pharmacy Education
Launched the Doctor of Pharmacy (PharmD) curriculum
- Developed the course schedule and delivery methods
- Developed student and educational services
- Ensuring quality introductory pharmacy practice experiences (IPPEs) and applied pharmacy practice experiences (APPEs)
- Continuing to coordinate inter-professional education experiences
- Continuing to refine evaluation methods for the students and faculty

In addition, Dr. MacKinnon and the School of Pharmacy team established best practices for admission processes, student services, and educational support. The Student Affairs Office conducted 30 visits to regional colleges and universities since November 2016.

During this reporting period, the School of Pharmacy leveraged AHW's investment with the addition of \$205,000 in extramural funding.

Relevance

In Wisconsin, there is a continuing maldistribution of pharmacists in medically-underserved communities. MCW aims to emphasize student clinical training in these locales. With an aging population and health care changing to emphasize team-based preventive care, pharmacists must adapt and deliver primary care to meet the rising need.

Significance to Science and Health

Through the development of a School of Pharmacy at MCW, the project team will innovate by emphasizing interprofessional education to prepare Wisconsin's pharmacists of the future.



George MacKinnon III, PhD, RPh
Founding Dean and Professor
MCW School of Pharmacy

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

DEFINING THE NATURE AND EXTENT OF NERVOUS SYSTEM TRAUMA AND ITS MODIFICATIONS: NEW STRATEGIES

AWARD AMOUNT: \$1,053,108 (2015-2020)



MEDICAL SCHOOL

Goal

Improve the diagnosis and treatment of brain injuries, including concussions, and other forms of nervous system trauma.

Background

Wisconsin has a higher rate of per capita brain injuries than the national average, which makes improving diagnosis and treatment even more important in Wisconsin.

Concussions are a significant source of nervous system trauma. While much continues to be learned about concussions, results to-date indicate that patients lacking appropriate care may develop post-concussion syndrome and potentially suffer long lasting effects on functionality, learning and behavior. Even minor brain injuries, if repeated, may lead to the accumulation of nervous system trauma and cause permanent brain damage.

Award Summary

Recent research has demonstrated that mild traumatic brain injuries, including concussions, alter the metabolism of blood flowing in the brain. While this metabolism problem normalizes relatively quickly in most patients, abnormalities after one month are associated with more severe post-concussion symptoms.

By better understanding this phenomenon, the investigators aim to develop methods for using blood samples to diagnose the presence and severity of injury.

Two talented researchers were recruited with expertise that can advance this important area of study.

Timothy Meier, PhD, studies the metabolic pathways associated with head injury. Antje Kroner-Milsch, MD, PhD, has worked extensively in studying the characterization of

specific cells involved in spinal cord injury and has published in the most prominent journals in the field of neuroscience.

These scientists are studying the effects of repeated concussions. Chronic concussions may lead to brain tissue loss due to the blood containing abnormal amounts of a substance that destroys nerve tissue. This research may lead to new treatments for major nervous system traumas and those that are minor but repeated.

As a result of the AHW investment, the research team have established a database of existing data and analyzing inflammatory markers to help better establish the neurophysiological mechanisms of mild traumatic brain injury in patients that do not show typical recovery.

While the investigators will continue to advance research in this area and to work to improve MRI brain scans related to nervous system trauma and concussion, they also aim to develop a new, simplified procedure for diagnosing concussions, assessing their severity and monitoring patient recovery. The protocol is likely to include a neurological exam and a blood test. In addition, the researchers aim to create methods for enhancing healing after a patient suffers major nervous system damage. Many patients would benefit from new methods to slow or reverse progression of dysfunction from serious nervous system damage.

During this award period, the research team garnered \$443,000 in additional funding, conducted three presentations, and submitted two manuscripts for publication.

Relevance

Wisconsin has a higher rate of per capita brain injuries than the national average, which makes improving diagnosis and treatment important for the people of Wisconsin.

Chronic concussions may lead to brain tissue loss due to the blood containing abnormal amounts of a substance that destroys nerve tissue.

Significance to Science and Health

AHW's investment in this award supports research that may lead to new treatments for major nervous system traumas and those that are minor but repeated.



Dennis Maiman, MD, PhD
Professor of Neurosurgery

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

POPULATION HEALTH IMPROVEMENT: RESEARCH AND EDUCATION TO HELP PATIENTS AND EMPLOYEES WITH DIABETES OR CANCER

AWARD AMOUNT: \$1,800,000 (2013-2017)

Goal

To establish a research infrastructure to improve population health, initially focused on diabetes control for patients and employees through better coordinated, patient-centered care to ultimately increase affordable, equitable access to quality services.

Background

26 million Americans have diabetes. Another 79 million have pre-diabetes in which heart complications begin.

Despite prevention and treatment options, many individuals lack education, motivation, and support in modifying their lifestyle.

Through a focus on diabetes control, the project aims to help participating patients and employees make improvements toward achieving stable blood sugar, normal cholesterol and blood pressure, decreased tobacco use and lower body-mass index.

Award Summary

During the reporting period, the project team, led by Staci Young, PhD, disseminated results of focus groups of 115 adults with diabetes and 15 clinicians, which have informed systems improvement. Focus group findings demonstrated that patients and providers would benefit from greater education regarding diabetes self-management in partnership with support networks.

Working with biostatisticians, the team has studied clinical records of 10,000 patients with diabetes served to predict groups at-risk for complications. Peripheral vascular disease, insulin treatment, and previous hospitalization substantially increase the risk of hospitalization for patients with diabetes. A new

statistical method was developed for testing in quantile regression in the team's recently accepted manuscript (Tarima et al).

The implication of the team's research reinforces that ambulatory clinic and community interventions to prevent diabetes and improve self-management can significantly improve well-being and reduce health care costs.

During this reporting period, the research team has produced three publications in scholarly journals in diverse areas of population health management, sociology, ethics, diabetes self-management, ambulatory care, among other areas.

In addition, AHW's investment in the Population Health Improvement initiative advanced capacity building efforts to expand education and training opportunities in population health management. Through a series of lunch and learn sessions with community centers, such as Silver Spring Neighborhood Center, Next Door, and Neighborhood House.

The research team continues to make progress in launching new studies regarding depression management in partnership with seven community physician sites as well as blood pressure measurement and control at specialty clinics.



MEDICAL SCHOOL

Relevance

26 million Americans have diabetes, and many also have cancer. Another 79 million have pre-diabetes in which heart complications begin. Despite prevention and treatment options, many individuals lack education, motivation, and support in modifying their lifestyle.

Significance to Science and Health

Through a focus on diabetes control, the project aims to help participating patients and employees make improvements toward achieving stable blood sugar, normal cholesterol and blood pressure, decreased tobacco use and lower body-mass index. The project also aims to decrease the cost of diabetes care and optimize the rate of needed referrals.



John Meurer, MD, MBA

Professor and Director, Institute for Health and Society

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

PATIENT-CENTERED OUTCOMES RESEARCH PROGRAM

AWARD AMOUNT: \$900,000 (2012-2017)



Goal

Advance the health of Wisconsin populations through improving methods for conducting patient-centered outcomes research, and applying those methods to key Wisconsin health issues.

Background

Treatment and prevention for chronic diseases and conditions such as obesity, diabetes, and cardiovascular disease have experienced significant advancement over the last few years. The adoption of these discoveries into real-life practice continues to lag behind, particularly for underserved patients and populations, and the impact of these gaps on treatment outcomes is substantial. This program has the potential to improve the diagnosis, treatment, and adoption of best treatment practices of a number of chronic conditions relevant to people in southeast Wisconsin.

Award Summary

A main purpose of the award is to increase capacity in outcomes research through recruitment of faculty expertise.

The Program successfully recruited two faculty to advance patient-centered outcomes research.

Onur Asan, PhD, specializes in human factors engineering. His research advances understanding of how technology influences people and health outcomes in health systems. For example, Dr. Asan's research has led to new knowledge regarding the impact of the electronic health record on health system workflow, quality of patient/physician interactions, patient safety, among other areas.

Dr. Asan's published his research findings in peer-reviewed journals.

In addition to Dr. Asan, the Program recruited Cynthia Kay, MD, a VA-supported researcher who studies the way chronic non-cancer pain is managed with an emphasis on the role of opioids in pain management.

The Program also furthers outcomes research through a small seed research grants program. Seed research grants were awarded through three funding cycles to a total of five investigators for \$15,000 one-year research awards.

During this reporting period, two seed research awards completed their work.

For example, Dr. Kathlyn Fletcher's seed award led to a new tool to help patients in decision-making to address infertility. Although widespread testing of the aid with patients is ongoing preliminary findings suggest that the decision aid is comprehensible and useful. One publication was generated through this research.

To-date, AHW's investment in the Patient-Centered Outcomes Research Program has garnered \$2M in extramural funding and more than 20 publications in scholarly journals.

Relevance

This program has the potential to improve the diagnosis, treatment, and adoption of best treatment practices of a number of chronic conditions relevant to people in Milwaukee and southeast Wisconsin.

Significance to Science and Health

This project will help narrow the gap between what is known to improve patient outcomes and how health care providers and patients act upon this knowledge to improve health. Data generated by this project will also inform how healthcare can be redesigned to achieve better outcomes with reduced spending.



Ann Butler Nattinger MD, MPH, MACP
Senior Associate Dean for Research,
Director of the Center for Patient
Care and Outcomes Research
Professor of Medicine

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

COLLABORATIVE FOR HEALTHCARE DELIVERY SCIENCE (CHDS)

AWARD AMOUNT: \$5,000,000 (2017-2022)



MEDICAL SCHOOL

Goal

Create a collaborative of multi-disciplinary experts dedicated to developing, testing, and disseminating health care practice, organization and delivery strategies to improve the quality, experience, and value of care in Wisconsin.

Background

While health care spending has been rising at an unsustainable rate, the quality of US health care remains suboptimal. The health care system in Wisconsin has been identified as one of the most expensive in the US.

Much of health outcomes lie in behavior that health care systems address unreliably, if at all, such as smoking, physical inactivity, and poor nutrition. However, little is known about how best to integrate medical and nonmedical sectors to achieve improved population health and reduce disparities.

Furthermore, existing approaches often do not consider the patient perspective in efforts to improve care delivery.

Organized, systematic efforts are needed to inform the development and adoption of efficient, affordable strategies to improve the quality, experience, and value of the care provided to Wisconsin's population.

Award Summary

The Collaborative addresses the challenge of delivering higher value, more efficient health care by using a population health approach.

Three key areas form the foundation of the Collaborative's work.

- Development of infrastructure to

support population health approaches to improve outcomes and decrease costs, including recruitment of experts in areas such as economics, informatics, social science, and human factors engineering.

- Cultivation of research to create and implement scientifically-sound practices that solve real world problems facing populations.
- Increased capacity for using population health approaches through education and dissemination programs.

The Collaborative uses state-of-art methods and tools in areas such as behavioral economics, behavioral health, engineering, predictive analytics, and econometric modelling, to improve quality, value, patient experience, and efficiency.

Examples of anticipated outcomes over time include:

- improvements in the quality of care, patient satisfaction, and value provided by partners;
- development of programs incorporating community needs for disease prevention; and,
- enhanced population health knowledge among MCW faculty, staff, partner institutions, and community members.

During this reporting period, the Collaborative established key committees, established a regular meeting structure, recruited faculty expertise in clinical informatics, developed a needs assessment, and initiated two pilot projects.

Relevance

Organized, systematic efforts are needed to inform the development and adoption of efficacious, affordable strategies to improve the quality, experience, and value of the care provided to Wisconsin's population.

Significance to Science and Health

AHW's investment in this initiative will result in increased opportunities to achieve the Triple Aim of Health Care—better care, lower cost and healthier people.



Ann Nattinger, MD, MPH, MACP

Senior Associate Dean and Associate Provost for Research, Professor of Medicine

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

MICROBIAL APPROACHES FOR THE TREATMENT OF MULTI-DRUG RESISTANT ENTEROCOCCUS

AWARD AMOUNT: \$200,000 (2016-2017)



MEDICAL SCHOOL

Goal

Eradicate multi-drug resistant strains of enterococci bacteria from the gastrointestinal tract without disrupting host microbiota in order to prevent systemic infection from, and spread of, drug-resistant organisms.

Background

Enterococci bacteria are among the three most common causes of hospital-acquired infection. Many of these infections are caused by multi-drug resistant enterococci (MDRE), rendering antibiotics ineffective.

Antimicrobial resistance has been increasing rapidly. While the current approach has been to use multiple combinations of antibiotics, this may be ineffective and result in massive disruption of the intestinal microbiome.

Using multiple combinations of antibiotics may also exacerbate the disease and cause secondary complications, such as increased susceptibility to intestinal and system infections, and increased local and systemic inflammation.

Led by Dr. Salzman, the research team is testing a new approach to prevent and reduce MDRE infections.

Award Summary

The AHW Endowment's investment in this initiative enabled Dr. Salzman and her research team to use a new approach for preventing and reducing MDRE infections.

Rather than attempting to eliminate resistant infections once they have occurred, the researchers aim to prevent infections and reduce the spread of MDRE, by preventing MDRE from colonizing and spreading from the gut. Using targeted microbial therapy to achieve this goal is a new approach that will prevent undesirable collateral damage to the

GI tract and preserve beneficial microbes that reside there.

This approach is expected to prevent the infection and curtail the spread of MDRE within hospitals and other environmental contamination.

During this reporting period, Dr. Salzman and the research team made excellent progress toward testing a therapeutic strain of enterococcus that is capable of eliminating MDRE in GI tract of mice. This strain of bacteria has shown to be effective in vivo to eliminate enterococcal colonization and reduce enterococcal expansion.

Efforts to use enterococcal phages to decolonize enterococci from the gut, or to prevent expansion upon administration of antibiotics, are also underway. In initial experiments, the team has established a phage dosing regimen that is capable of preventing enterococcal population expansion in the gut upon antibiotic administration. Attempts at decolonizing the gut of a target strain of *E. faecalis* have not yet been successful. Future experiments are planned to troubleshoot the possibility that indigenous enterococci in the mouse gut are interfering with the ability of the phage to attack the target enterococci.

Findings from this research could be applied to benefit susceptible hospitalized populations, but could also be applied agriculturally, to prevent transmission of these organisms into food. The rapid increase in multi-drug resistant bacteria, combined with the lack of effective antibiotics, supports the need for novel and effective approaches, such as those proposed and validated by this work.

Relevance

Antibiotic resistance is growing yet development of new antibiotics effective against resistant strains lags behind. Therefore, there is an urgent need for new approaches to address antibiotic-resistant infections.

Significance to Science and Health

Rather than attempting to eliminate resistant infections once they have occurred, the researchers aim to prevent infections and reduce the spread of MDRE, by preventing MDRE from colonizing and spreading from the gut.



Nita H. Salzman, MD, PhD
Professor, Pediatrics and Microbiology and Molecular Genetics

Co-Investigators: Christopher Kristich, PhD, Associate Professor, Microbiology and Molecular Genetics; Michele Battle, PhD, Associate Professor, Cell Biology, Neurobiology and Anatomy

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

CTSI MENTORED CLINICAL AND TRANSLATIONAL RESEARCH TRAINING PROGRAM AND PILOT AND COLLABORATIVE CLINICAL AND TRANSLATIONAL RESEARCH PROGRAM

AWARD AMOUNT: \$5,327,956 (2015-2020)



Goal

Improve health by transforming the research and training environment for junior physician-scientists and advance discovery in clinical and translational research through the Clinical and Translational Science Institute of Southeastern Wisconsin (CTSI).

Background

Translational research is one of the most promising fields of medical research today. Ultimately, translational research leads to new clinical treatments by translating scientific knowledge into new tools and methods to improve patient care. The translational spectrum moves from research into the biological basis of health and disease to interventions that improve the health of individuals and populations.

While biomedical research has led to extraordinary improvements in many areas of medicine, effective therapies to address several diseases are still greatly needed. By preparing a stronger workforce skilled in research along the translational spectrum, the CTSI can advance more research aimed at bringing optimal interventions and practices into clinics and communities.

The KL2 mentorship program recruits and cultivates young investigators who would otherwise lack protected research time and have limited access to funds for conducting translational research.

Using separate funding strategies for basic science and population health, the innovative pilot and collaborative grants program will support the testing and growth of promising ideas in clinical and translational science to turn basic scientists' laboratory results into better clinical practice.

By enhancing career development opportunities for early career

scientists, the KL2 mentored training program will expand the breadth and depth of clinical and translational research being conducted by CTSI members.

By fostering a positive environment for biomedical researchers, healthcare providers, educators, citizens, and members of industry, the pilot and collaborative grant program facilitates diverse groups working together to translate fundamental discoveries into better health for Wisconsin.

Award Summary

Translational research, broadly defined, aims to find and test new or improved therapies derived from basic science discoveries. AHW's investment supports two programs within CTSI.

To-date, 23 junior faculty (12 past cycle and 11 this cycle) were selected to develop as independent clinical and translational investigators.

During this reporting period, eleven new research awards were launched that bring together interdisciplinary research teams to enhance discoveries leading to better treatments and cures for Wisconsin's leading diseases. This represented a strong response to the funding opportunity.

In addition, national recognition and partnerships were formed with other CTSA's in the US.

This award has the potential to leverage an estimated \$20+ million in NIH funding. Also, both programs support future extramural grant applications.

The long-term goal for both programs is to support and enhance clinical and translational research to improve community health.

Relevance

NIH recognizes increasingly recognizes community engagement as essential to addressing health disparities. Many studies also show that community engagement in research improves the translation of research discoveries into the improved health of communities.

Significance to Science and Health

The MCW Community Engagement Core will advance community engagement in research by creating a core resource center that provides expertise, training, and other resources to aid MCW researchers and community partners in bettering the health of Wisconsin residents.



Reza Shaker, MD

Senior Associate Dean and Director, Clinical and Translational Science Institute and Professor and Chief, Medicine (Gastroenterology)

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

MCW TISSUE BANK

AWARD AMOUNT: \$5,219,068 (2010-2020)



Goal

Centralize the collection, storage, and distribution of human specimens to be used for research at the Medical College of Wisconsin and partnering institutions, and to sponsor cooperative research programs, specimen-based basic research, and translational research.

Background

Having access to human tissue specimens is crucial for advances in biomedical science and developing disease therapies.

Cancer is a health priority for Wisconsin due to it being an important contributor to mortality in Wisconsin, and the second most common cause of death in the United States.

Cancer is a primary area of research supported by the MCW Tissue Bank, which serves as the Tissue Procurement Core for the MCW Cancer Center to meet the scientific needs and objectives to become a National Cancer Institute designated Cancer Center.

The central tissue bank provides the resources necessary for individual faculty members to acquire tissue samples for research, expediting MCW's tissue-based translational research.

Award Summary

During this reporting period, the MCW Tissue Bank continued to grow its consent program and overall collection of specimens.

In the prior reporting period, the MCW Tissue Bank had grown to 12,344 tissue samples, 42,274 blood samples, and 5,543 bone marrow samples banked.

This represented a significant increase of 6,023 tissue samples (49% increase), 24,224 blood samples (57% increase), and 4,666 bone marrow samples (84% increase).

The bank continues to grow its Cord Blood Banking Program. In addition to consenting more participants and training OBGYN clinic staff to obtain consent for the Cord Blood Banking Program, the Bank broadened the scope of the program to include banking of discard placenta, umbilical cord, and a one-time peripheral blood draw in addition to cord blood collection.

In addition, during this reporting period, the Tissue Bank leadership submitted presentations to two national conferences and received \$250,000 in additional funding from the Johnson Controls Foundation.

The ongoing efforts of the MCW Tissue Bank to collect, store, and distribute human specimens to basic and clinical researchers is a clear benefit Wisconsin residents. The project team will continue working toward its goal through the next reporting period.

Relevance

Cancer continues to be a national disease focus and is an area of research that benefits tremendously from access to patient specimens. The MCW Tissue Bank serves as the Tissue Procurement Core for the MCW Cancer Center to meet the scientific needs and objectives of a National Cancer Institute designated Cancer Center.

Significance to Science and Health

A central tissue bank provides the resources required for individual faculty members to acquire tissue samples for research, and the MCW Tissue Bank continues to expedite MCW's tissue-based translational research.



Saul Suster, MD

Chairman and Professor, Department of Pathology and Laboratory Medicine

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

CANCER BIOMARKERS FOR EARLY DETECTION AND PREDICTION OF CLINICAL OUTCOMES

AWARD AMOUNT: \$1,309,260 (2012-2017)



MEDICAL SCHOOL

Goal

Strengthen critical research fields of cancer genetics and translational research in the Medical College of Wisconsin Cancer Center.

Background

Small noncoding RNAs that are 19-23 nucleotides long, known as microRNAs (miRNAs), are involved in almost all biological mechanisms during carcinogenesis.

Recent studies show that miRNAs released from live cells are detectable in body fluids and may be taken up by other cells to confer cell-cell communication. These released miRNAs (here referred to as extracellular miRNAs) are often protected by RNA-binding proteins or embedded inside circulating microvesicles.

Due to their relative stability, extracellular miRNAs are believed to be promising candidates as biomarkers for diagnosis and prognosis of disease, or even as therapeutic agents for targeted treatment.

In addition, studies have shown that DNA released into the blood from dead tumor cells is detectable. Due to frequent DNA variations in tumor cells, detection of tumor-related DNA is believed to be an attractive approach for early diagnosis of cancer and outcome prediction.

Award Summary

The research team validated 2 miRNA markers for prediction of overall prostate cancer survival in an additional 100 advanced prostate cancer patients.

The team built a multivariate statistical model to estimate survival. This model showed better performance in risk assessment than a clinical factor-based model. This result was published in the journal *European Urology*, a highly regarded journal in the field.

In addition, Dr. Wang's team tested the plasma in 20 advanced prostate cancer patients and eight early stage lung cancer patients for tumor DNA.

With the use of advanced DNA sequencing technology, the team detected gene signatures indicative of tumor DNA; these sequences were sensitive biomarkers for prediction of treatment effectiveness.

The research team also found that early detection of lung cancer is possible by using the plasma DNA.

Based on Dr. Wang's data, the team developed a plasma genomic abnormality (PGA) score system to predict tumor burden in cancer patients.

The findings of this research were published in the scientific journal *Oncotarget*.

Dr. Wang has 16 manuscripts that he has prepared for publication to disseminate his research findings in the field. In addition, he has secured more than \$3.8M in extramural funding to leverage AHW's investment in expanding this important area of cancer research.

Relevance

Prostate cancer is the most common non-skin cancer among male Wisconsin residents, accounting for 28 percent of new cases diagnosed in Wisconsin men between 2003 and 2007. The work could lead to early detection and treatment advances in prostate as well as other cancers.

Significance to Science and Health

This may be the first study to employ next-generation sequencing technology to identify biological markers in micro-vesicles, which are containers of genetic information residing in human plasma and other fluids. This advance may help physicians detect and treat prostate cancer.



Liang Wang, MD, PhD
Professor of Pathology

This award was funded by the Advancing a Healthier Wisconsin Endowment at the Medical College of Wisconsin.

INNOVATIVE APPROACHES TO PRECISION MEDICINE (IAPM)

AWARD AMOUNT: \$1,500,000 (2017-2021)



MEDICAL SCHOOL

Goal

Use innovative approaches to advance precision medicine and facilitate individualized care for patients with common diseases, such as hypertension, kidney and heart disease.

Background

Recent progress in genomics and big data has led to precision medicine, a new approach for disease prevention and treatment that considers the variability in genes, environment, and lifestyle for each person.

Current efforts in precision medicine focus primarily on genome sequences. This approach could be productive for diseases such as congenital diseases and cancer where a small number of genome sequence variations play a major role in the disease of a patient.

However, genome sequences alone are unlikely to be useful for common diseases such as heart disease, hypertension, and kidney disease.

In these common diseases, the number of genome sequence variations involved in a patient may be large, but the effect of each sequence variation on the disease is likely small. Adding to the complexity are several environmental and lifestyle factors that greatly influence these diseases.

The role of environmental and lifestyle factors has been largely neglected in precision medicine, in part due to the complexity of quantifying and analyzing the inter-relationship between genetic and non-genetic factors.

Award Summary

Through AHW's investment in this award, the IAPM initiative is addressing two critical challenges in precision medicine: 1) how to understand the link between disease and genetic variations that do not change protein structure, and 2) how to measure and account for the influence of environmental and lifestyle factors.

The first challenge is being addressed by focusing on studying non-coding genetic variants associated with human hypertension. The second challenge is being addressed by analyzing biopsy samples of kidneys and small blood vessels from patients with kidney disease or cardiovascular disease risk factors.

During this reporting period, Dr. Liang focused on developing and improving several highly complex research methods that are essential to the program. Human research samples have been obtained with additional requests under review by the Institutional Review Board to recruit additional human subjects for the IAPM program.

Several publications benefited from research initiated in this award, including a publication in the top-ranked journal in nephrology.

Advancing the understanding of environmental, lifestyle and genetic factors for disease could lead to better strategies for preventing, diagnosing, and treating disease.

In addition, this initiative could lead to findings that would be readily translatable to clinical practice.

Future studies that build upon the success of this initiative could lead to significant extramural funding.

Relevance

There is a pressing need to better understand the role of environmental and lifestyle factors in precision medicine and analyze the inter-relationship between genetic and non-genetic factors.

Significance to Science and Health

- AHW's investment in this award will result in increased knowledge regarding the inter-relationship between a patient's genetic make-up and the influence of lifestyle and environmental factors on disease.



Mingyu Liang, MB, PhD

Professor, Physiology | Eminent Scholar, Director, Center of Systems Molecular Medicine

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

GASEOUS INTOXICATION BY BACTERIAL INFECTION: A MECHANISM FOR ABSCESS FORMATION

AWARD AMOUNT: \$200,000 (2016-2017)



MEDICAL SCHOOL

Goal

Develop new non-antibiotic treatments that limit damage and accelerate recovery from deep tissue infections.

Background

Many bacteria produce a gaseous environmental toxicant—hydrogen sulfide. Exposure to toxic substances such as hydrogen sulfide is a common cause of injury and death in the workplace. Being freely diffusible, hydrogen sulfide can intoxicate across tissue boundaries, much like thermal burns or radiation, causing abscesses. Antibiotic therapy cannot modify the effects of the gas, resulting in prolonged disease and poor outcomes, including death.

The research team has identified a novel virulence mechanism in the hydrogen sulfide gas that explains the severe and prolonged complications that are unresponsive to antimicrobials. Using their novel detection method, they plan to develop new, non-antibiotic treatments that limit damage and accelerate recovery from deep infections.

Award Summary

The AHW Endowment's investment in this initiative enabled Dr. Willoughby and his research team to capitalize on their unique detection method for hydrogen sulfide to develop non-antibiotic treatments that effectively limit damage and speed recovery from infections resulting from contact with the gas.

The outcome of bacterial infections has not changed for decades, despite regular increases in potency and spectrum of antimicrobials and major advances in critical care.

The team offers a changemaking shift of treating these infections as environmental toxins. AHW's investment in this research could translate into applications in inflammation and immunology, neurodegenerative diseases, cancer, and cardiovascular medicine.

For example, despite being treated with antibiotics, meningitis in a 4-year-old patient continued to progress. The patient improved dramatically when the research team began treating the child with nitrate and hyperbaric oxygen to reduce hydrogen sulfide. This case highlights the potential for immediate translation into medical practice.

By conducting this research, the team is uniquely positioned to leverage expertise in genetics, physiology, and biochemistry to achieve the goals of the proposed research, and ultimately, improving the lives of patients who have been affected.

During this reporting period, the team made excellent progress in cloning and expressing the bacteria and human versions of enzymes that produce hydrogen sulfide gas.

However, technical difficulties in some of the team's tools have posed some setbacks in the expected progress.

To-date, the team has effectively excluded current known inhibitors of hydrogen sulfide production as therapeutic agents -- they are far more toxic to humans than to bacteria. The team also has identified vitamin B12 as a novel binder of hydrogen sulfide, a safe inhibitor in humans yet to be tested in bacteria.

Relevance

Many bacteria produce a gaseous environmental toxicant—hydrogen sulfide. Exposure to toxic substances such as hydrogen sulfide is a common cause of injury and death in the workplace.

Antibiotic therapy cannot modify the effects of the gas, resulting in prolonged disease and poor outcomes, including death.

Significance to Science and Health

Using a novel detection method, as well as an advanced animal model, researchers plan to develop new, non-antibiotic treatments that limit damage and accelerate recovery from deep infections.



Rodney Willoughby, MD

Professor, Pediatrics and Program Director for Antibiotic Stewardship at Children's Hospital Wisconsin

Co-Investigators: Brian Smith, PhD, Assistant Professor, Biochemistry; Chris Kristich, PhD, Associate Professor, Microbiology and Molecular Genetics

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

CANCER CENTER INFRASTRUCTURE GRANT

AWARD AMOUNT: \$5,366,551 (2010-2021)

Goal

Develop strong and nationally recognized interdisciplinary programs in cancer-related research, education, clinical care, and community service in order to become a National Cancer Institute (NCI)-Designated Cancer Center.

Background

Through NCI designation, MCW can further develop strong and nationally recognized interdisciplinary programs in cancer-related research, education, clinical care, and community service.

Wisconsin's highest rates of cancer are in the Southeastern Wisconsin area, including Milwaukee, Kenosha, Ozaukee, Racine, Walworth, Washington, and Waukesha counties. Through AHW's investment in the MCW Cancer Center, AHW is advancing the translation of cancer-related discoveries to improve outcomes, decrease rates of incidence, and reduce cancer disparities in underserved populations.

Award Summary

During this reporting period, the MCW Cancer Center continued to make significant progress toward its program goals.

Building from AHW's investment in the MCW Cancer Center, Dr. You and his fellow researchers submitted several applications for extramural funding to support promising lines of research discovery. These included two NIH program project grant applications. A grant application support program has been established to help increase submissions. As a result of this enhancement, eleven applications were submitted.

Dr. You aligned the MCW Cancer Center seed grant structure with research focus areas of breast,

pancreas, immunology and disparities. The pilot funding program Request for Applications was revised to better position recipients for success through strengthening mentorship in research. In addition, REDCAP, an online survey/data collection tool, was adapted to create further efficiencies in the review process.

In support of its goal to create a strong, vibrant research community to advance discovery of new cancer therapies and treatments, the MCW Cancer Center sponsored several individual program retreats. The retreats provided opportunities for researchers to share knowledge and foster cross-disciplinary research collaborations.

In addition, work continued to refine the MCW Cancer Center website, in preparation for a total site transformation in late 2017 and early 2018. This included culling pages and content, consolidating key information and adding new tools and data, including heat maps of cancer incidence, late-stage incidence and mortality in our catchment area.

The MCW Cancer Center has significantly increased both internal and external communications as demonstrated by more than 10 notable media items during this reporting period. MCW Cancer Center communications continues to reach more than 25,000 people throughout Wisconsin, and the team continues to collaborate with MCW's, Froedtert's and the MCW Clinical and Translational Science Institute's marketing and public affairs leadership.



MEDICAL SCHOOL

Relevance

Through this project, the researchers seek to develop strong and nationally recognized interdisciplinary programs in cancer-related research, education, clinical care, and community service in order to obtain NCI designation.

Significance to Science and Health

Through NCI designation, MCW can further develop strong and nationally recognized interdisciplinary programs in cancer-related research, education, clinical care, and community service.



Ming You, MD, PhD

Senior Associate Dean for Cancer Research, Director of the MCW Cancer Center, Professor of Pharmacology and Toxicology

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

HEMATOLOGIC MALIGNANCY & TRANSPLANTATION (HMT)

AWARD AMOUNT: \$4,329,820 (2011-2021)



MEDICAL SCHOOL

Goal

Develop new approaches to augment the immune response against cancer and reduce complications associated with bone marrow transplantation so that this therapy is more effective.

Background

Over 2,500 new cancer cases in Wisconsin each year are cancers of the blood. Many patients who develop these diseases are in the prime years of their life, and almost half die from the disease. New approaches are needed to boost the immune system's ability to fight cancer and reduce complications associated with bone marrow transplants. Research in this program may lead to clinical applications that improve survival rates and quality of life for patients with cancer and those receiving bone marrow transplants.

Award Summary

During the past year, the Hematologic Malignancy & Transplantation (HMT) Program researchers published significantly resulting in more than 100 articles from inception through this reporting period that share their research findings with the larger scientific community.

Several program members actively participated in research with members from other programs. Eleven percent of the publications were collaborative within MCW, and 86% collaborative with external researchers.

The Program also awarded MCW Cancer Center seed grants to several scientists to spur research and provide

preliminary data for grants to outside agencies, including the National Cancer Institute of the NIH.

Lily Wang, PhD, was recruited to MCW and the HMT program in 2014 from Dartmouth University. She discovered a novel role of an immune suppressive protein called VISTA in the activation of immune cells. VISTA may be a useful target to inhibit in developing "immunotherapy" – training the immune system to attack cancer cells – which may be useful to treat hematological malignancies.

Dr. Wang published a new study regarding the role of VISTA in regulating inflammation in psoriasis. Dr. Wang is also preparing for a manuscript regarding how VISTA regulates TLR signaling.

The program's accrual to clinical trials focused on the treatment of patients with hematological malignancies. Clinical trial participation increased substantially in this reporting period resulting in MCW being positioned as one of the highest accruing institutions in the United States to bone marrow transplant clinical trials.

In addition, the AHW Endowment's investment in the HMT program of the Cancer Center resulted in significant additional leveraged dollars for Wisconsin cancer research through extramural funding. There were more than 30 applications for extramural funding in 2017, with six awards totaling \$2.23M.

Relevance

Over 2,500 new cancer cases in Wisconsin each year are cancers of the blood. Many patients who develop these diseases are in the prime years of their life, and almost half die from the disease.

New approaches are needed to boost the immune system's ability to fight cancer and reduce complications associated with bone marrow transplants.

Significance to Science and Health

Research through this program may lead to clinical applications that improve survival rates and quality of life for patients receiving bone marrow transplants.



Ming You, MD, PhD

Senior Associate Dean for Cancer Research, Director of the MCW Cancer Center, Professor of Pharmacology and Toxicology

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

CANCER BIOLOGY RESEARCH PROGRAM

AWARD AMOUNT: \$5,097,898 (2011-2021)



MEDICAL SCHOOL

Goal

Determine the biological and chemical causes of cancer, and promote outstanding research aimed at identifying new therapeutic targets and developing more effective therapies to treat cancer for the citizens of Wisconsin.

Background

In 2016, the American Cancer Society and Wisconsin Division of Public Health estimated that 285,000 Wisconsin residents are living with a cancer diagnosis. This is a significant increase from 2013.

While much of this increase is attributed to improved cancer screening rates, survivorship is also on the rise because of improved treatments, and the rate of cancer mortality in Wisconsin is falling.

AHW's investments in cancer research through this and other initiatives are leading to a transformative impact in improving health for Wisconsin residents suffering from cancer.

The Cancer Biology program serves the citizens of Wisconsin by supporting research to develop new ways to eradicate tumors after cancer has been diagnosed, halt the spread of tumors throughout the body, and prevent the recurrence of cancer.

Award Summary

During this reporting period, Cancer Biology researchers contributed to several publishing efforts that addressed the goal of identifying unique genetic, signaling, and metabolic features of cancer cells. As of this reporting period, this represents more than 360 publishing efforts through this program.

To further these efforts, the Program established an interactive community

of investigators through participation in the Cancer Cell Biology Research Forum, which meets weekly to promote the sharing of ideas and collaboration.

To increase cancer research expertise, the Program recruited two new team members: Carmen Bergom, MD, PhD, an internal candidate with expertise in radiation oncology and Laura Kresty, PhD, whose expertise lies in chemoprevention.

Dr. Bergom's research continues to advance knowledge regarding the role of the DiRas family of tumor suppressors in breast and brain cancers.

Dr. Kresty's research studies the benefits of cranberry extracts on esophageal cancer cells. Preliminary studies show that cranberry extracts appear to increase reactive oxygen resulting in the death of esophageal adenocarcinoma cells.

To further expand cancer research expertise, the program recruited additional leading scientists in the field. Halgeir Rui, PhD, and Dr. Marya Nevalainen, PhD, whose expertise lies in breast and prostate cancer respectively, continue to be strong contributors and mentors for the program.

During this reporting period, there were more than 95 local, national or international presentations on discoveries related to this work and the program has garnered more than \$33M in additional funding.

In addition, several researchers funded through this program are continuing to advance discovery in cancer prevention and treatment strategies.

Relevance

More than 29,000 Wisconsin residents were diagnosed with cancer in 2010. The program can have a significant positive impact on the people of Wisconsin through better understanding of the causes and mechanisms of cancer.

Significance to Science and Health

The Cancer Biology program supports Wisconsin residents by developing new ways to eradicate tumors after cancer has been diagnosed, halt the spread of tumors throughout the body, and prevent the recurrence of cancer.



Ming You, MD, PhD

Senior Associate Dean for Cancer Research, Director of the MCW Cancer Center, Professor of Pharmacology and Toxicology

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

POPULATION SCIENCES

AWARD AMOUNT: \$4,991,871 (2012-2021)

Goal

Conduct outstanding research aimed at influencing the implementation of improved prevention, screening, and therapeutic strategies for cancer, and reducing disparities in care.

Background

Cancer is a leading cause of death among Wisconsin residents.

Although the development of new technology is important to preventing and treating cancer in the Wisconsin population, better use of existing tools could decrease morbidity and mortality from cancer more quickly.

The most common cancers all have methods available for prevention, screening, treatment, and/or improving survivorship care, but unfortunately these methods are known to be underused.

Increasing our cancer knowledge will improve outcomes, decrease rates of incidence, and reduce cancer disparities in underserved populations.

Award Summary

During this reporting period, the Population Sciences (PS) researchers published more than 85 articles to share their research findings with the larger scientific community.

Several program members actively participate in research with other programs. A key function of the Program is to provide members with resources not otherwise available.

Biostatisticians from the Observational Methods Core assist in developing new prevention and population health research projects. The Core is heavily used and assists in grant development for outside funding opportunities.

To bring scientific expertise to MCW, the Program recruited Kirsten M. Beyer, PhD, MPH, who examines how

cancer burdens segregate geographically in our communities, and the causes of the segregation.

Also recruited was Kathryn Flynn, PhD, who focuses on patient-reported outcomes measures with the goal of standardizing the measures across disease populations, and Melinda Stolley, PhD, who focuses on obesity, health behaviors, cancer disparities, and survivorship.

Dr. Flynn, in collaboration with Dr. Ehab Atallah in the Division of Hematology/Oncology, received a large extramural funding award from the National Cancer Institute that leverages AHW's investment in her work. The study explores recurrence and quality of life for patients with leukemia who stop taking their medication under medical supervision. Work on understanding and improving decision making for these same patients is ongoing.

Dr. Stolley's work increased cancer prevention, screening and education efforts through a series of presentations and community-based efforts. Dr. Stolley continues to research methods for increasing understanding of community perspectives on cancer disparities.

The program provided a funding opportunity through seed grants. In the past year, four seed grants were awarded to generate important preliminary data and initiate partnerships to advance cancer research.

During this reporting period, there were more than 50 leveraging efforts that led to \$61M in leveraged funding. In addition, there were 25 local, national or international presentations with more than 280 presentation overall through this program.



MEDICAL SCHOOL

Relevance

Cancer is a leading cause of death among Wisconsin residents. Wisconsin's highest rates of cancer are in the MCW Cancer Center's eight-county catchment area, and breast cancer mortality rates for minority women in Milwaukee County are some of the highest in the nation.

Significance to Science and Health

This program facilitates the translation of cancer-related discoveries to all residents within the state. Increasing knowledge about the impact of cancer will improve outcomes, decrease rates of incidence, and reduce cancer disparities in underserved populations.



Ming You, MD, PhD

Senior Associate Dean for Cancer Research, Director of the MCW Cancer Center, Professor of Pharmacology and Toxicology

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.

TUMOR PROGRESSION AND METASTASIS (TPM)

AWARD AMOUNT: \$4,856,491 (2012-2021)



MEDICAL SCHOOL

Goal

Promote and support cancer-related basic, translational, and clinical research in imaging sciences and technology that result in improved diagnostic and therapeutic approaches.

Background

In 2016, the American Cancer Society and Wisconsin Division of Public Health estimated that 285,000 Wisconsin residents are living with a cancer diagnosis. This is a significant increase from 2013.

While much of this increase is attributed to improved cancer screening rates, survivorship is also on the rise because of improved treatments, and the rate of cancer mortality in Wisconsin is falling.

It is estimated that one-third of all cancer deaths would be prevented if no one smoked, and another third could be prevented if everyone maintained a healthy weight and active lifestyle.

AHW's investments in cancer research through this and other initiatives are leading to a transformative impact in improving health for Wisconsin residents suffering from cancer.

Award Summary

During this reporting period, tumor progression and metastasis (TPM) researchers published 96 articles to share their research findings with the larger scientific community. Several program members actively participate in research with other cancer center programs, resulting in 51% inter-programmatic publications involving at least one TPM Program member.

Through seed grants, the program provides the funding needed to jumpstart collaborations among Cancer Center members and support future funding applications to outside

agencies, including the National Institutes of Health.

Scientific expertise was expanded by recruitment of faculty.

Amit Joshi, PhD, established an optical molecular imaging laboratory and facilities to use nanoparticles for cancer imaging and treatment.

Eric Paulson, PhD, strengthened collaborations with Elekta, Siemens Healthcare, and Philips Healthcare in his work to develop tools and approaches for MRI-guided radiation therapy. Several patents have been submitted based on the new technology developed through Dr. Paulson's contributions to this award.

Peter LaViolette, PhD, focused on applying imaging technology to detect tumor cells that infiltrate nearby healthy tissue in both brain and prostate cancer, and also on how brain tumors respond to recently approved drugs. Dr. LaViolette's research led to findings that patients with tumors showing a decrease in abnormal vessels categorized by imaging technology survived longer than those with an increase following treatment.

Adriano Marchese, PhD, explored how the interaction of the cell surface receptor known as CXCR4 with its extracellular ligand CXCL12 activates intracellular signal transduction cascades that lead to cell survival.

Dr. Marchese's experiments reveal that in addition to signaling initiated at the plasma membrane, signaling also occurs from an intracellular compartment that is distinct from the plasma membrane. This suggests that the signal instigated from this intracellular compartment promotes cell survival, which may be a contributing factor to cancer progression.

Relevance

The Tumor Progression and Metastasis Research program serves the citizens of Wisconsin by supporting research to develop new ways to eradicate tumors after cancer has been diagnosed, halt the spread of tumors in the body, and prevent the recurrence of cancer.

Significance to Science and Health

Progress in imaging sciences and technology that advances personalized medicine approaches to cancer will lead to better diagnosis and treatment for Wisconsin residents suffering from cancer.



Ming You, MD, PhD

Senior Associate Dean for Cancer Research, Director of the MCW Cancer Center, Professor of Pharmacology and Toxicology

This award was funded by the Advancing a Healthier Wisconsin Endowment in the MCW School of Medicine.