

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, 2015

ADVANCING COMMUNITY-ACADEMIC PARTNERSHIPS FOR TRANSLATIONAL RESEARCH: SCIENTIFIC CITIZENS AND CITIZEN SCIENTISTS

AWARD AMOUNT: \$1,659,180 (2011-2016)



MEDICAL SCHOOL

Goal

To support community engagement (CE) and training in clinical and translational research with a focus on communication, dissemination, and public awareness of the benefits of research.

Background

The fourth mission of the Medical College of Wisconsin is to improve the health of the communities that the institution serves. This project seeks to advance that mission by increasing the public's interest in science while also developing faculty capability to partner effectively with communities.

Award Summary

During the reporting period, the Community Engagement Key Function (CEKF) remained active in ongoing efforts within the CTSI and across the national network of CTSAs. The CEKF team has applied for a variety of funding opportunities to enable expansion of expertise, research and partnerships. In addition, the CEKF team has actively presented and published locally, nationally and internationally. The project team also continued to expand community-academic dialogue through the following programs:

Science Cafés: Held 10 Science Cafés focused on "Life is Complicated: Let's Deal with it!" and "Science and a Healthier You".

Students Modeling a Research Topic (SMART) teams: Implemented by MSOE, these included 24 local teams and 250 students who learned about protein structure.

The Inaugural Community Engagement Week: The events were significant for dissemination of

Community Engaged Research (CErR) practice, skill building, and networking to new academic partners and community-based organizations. All sessions of this five-day event were in person, open to the public, and included CME credits.

CEKF published the work related to a retrospective chart review of the past seven years of community-academic partnership grants. The team submitted an NIH X02 (pre-application) to expand and enhance research in collaboration with Marquette University, University of Florida, University of Rochester, Mayo Clinic, University of Minnesota and Northwestern.

In addition, the Community Engagement Learning Repository Phase 1 development has been completed, and communities and researchers conducting CErR will begin to benefit from more accessible resources and products for dissemination for the art and science of CErR.

Principles of CE and CErR (3 credit elective, online) was offered for the second year. Lecturers included faculty at UW-Milwaukee, MCW and CTSI leadership and experts from community-based organizations. The last session was in person, open to the public, and included CME credits.

The team was granted an extension for 2015-2016 to continue to work on evaluation and dissemination via lay publications and poster presentations, peer-reviewed journal articles and presentations.

Relevance

This project seeks to advance MCW's mission to improve the health of the communities that the MCW serves by increasing the public's interest in science while also developing faculty capability to partner effectively with communities.

Significance to Science and Health

Fostering a deeper appreciation of science in the community may inspire youth to pursue careers in science and foster participation in community-engaged research projects. Developing faculty partnership skills may also increase interest in community engagement.



Syed Ahmed, MD, MPH, DrPH, FAAFP
Sr. Associate Dean for Community Engagement, Director of the CTSI Community Engagement Program, Professor of Family Medicine

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

COMMUNITY ENGAGEMENT (CE) CORE PLANNING INITIATIVE

AWARD AMOUNT: \$121,000 (2014-2015)

Goal

To lead coordination of community engagement (CE) across MCW's diverse CE programs and advance the art and science of CE in order to improve the health of Wisconsin communities.

Background

Across multiple disciplines, collaborations between academic and community partners have been shown to improve the translation of new research and discoveries, benefiting communities and improving population health. CE is recognized by the NIH, researchers and community groups as critical to understanding and addressing racial, ethnic, socioeconomic and environmental health disparities. Numerous studies have confirmed that authentic community engagement across sectors is not only central to countering mistrust of research and researchers due to histories of medical experimentation and research abuse, but also to improving the validity, efficacy, and translation of research findings.

MCW is now undergoing unprecedented growth and change. More than ever before, community engagement is emerging as key to advancing quality research and education initiatives.

In the context of this rapid growth in research and education, the CE Core Planning Initiative will ensure intentional and thoughtful alignment and coordination of community engagement across several prominent and new MCW research and education initiatives.

The CE Core will provide the resources and support needed by both community and academic partners to improve and increase community engaged projects and research.

Award Summary

In developing a centralized CE core that is sustainable beyond the funding period, community representatives and MCW stakeholders provided input and support to identify and prioritize the resources needed to address gaps in CE services and further MCW's CE mission to more effectively impact community health.

The effort was also aided by two external consultants with experience in developing CE cores, and who provided important insights regarding the unique challenges faced by MCW when developing CE services.

The outcome of this project was a consensus that resulted in a funding proposal, the MCW Community Engagement Core Implementation Initiative, that will create a centralized community engagement resource, available to community partners and all MCW centers, institutes, programs and departments.



MEDICAL SCHOOL

Relevance

The National Institutes of Health recognize community engagement as essential to understanding and addressing health disparities. Many studies also show that community engagement improves the validity of translational research projects. The MCW CE Core will aid MCW researchers and community partners in bettering the health of Wisconsin residents.

Significance to Science and Health

The CE Core will provide the resources and support needed by both community and academic partners in order to improve and increase community engaged projects and research. This will improve competitiveness for CE grants and increase funded CE projects in Wisconsin communities, which will ultimately improve the health of Wisconsin residents and their communities.



Syed Ahmed, SYED AHMED, MD, MPH, DrPH, FAAFP

Sr. Associate Dean for Community Engagement, Director of the CTSI Community Engagement Program, Professor of Family Medicine

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

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

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



MEDICAL SCHOOL

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 (CVD) is the leading cause of death and disability of men and women in the US and in Wisconsin. This work will improve the health of Wisconsin residents by enhancing 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.

Award Summary

Significant progress has been made in the first year of this award. For Aim 1, the first year has been marked by solidifying and increasing collaborations between basic and clinical scientists across departments and centers at MCW, as well as inter-institutionally. Implementation of the Signature Programs began with the solidification of several Affinity Groups (like-minded researchers) and introduction of new Affinity Groups. Internal and external scientific advisory boards were founded with the purpose of guiding and giving input on several of the initiatives introduced in the past year as well as future endeavors.

Two physician investigators were recruited in two of the three top priority program areas: Shayne

Squires, MD, in Cardio-Oncology and Nicole Lohr, MD, PhD, in Vascular biology. Infrastructure was increased with creation of support positions including an Academic Program & Research Officer, a Research Support Specialist, and a Biostatistician, all of whom work with faculty and staff to establish translational research programs, increase the number of competitive grants, and provide other research support. A pilot funding program was initiated, and the CVC awarded two \$50,000 and two \$25,000 grants designed to enable increased extramural funding from the NIH and non-profit organizations.

Notable progress on Aim 2 included efforts to increase opportunities for faculty and fellow development. In order to further faculty development and increase training opportunities, a "breakfast and learn" forum was initiated for clinical faculty and fellows, as well as a "lunch and learn" series aimed at basic scientists at all levels. A Research Retreat in April 2015 included a keynote presentation from Richard Kitsis, MD, from Albert Einstein College of Medicine, a leader in the field of Cardiovascular Medicine.

Relevance

Cardiovascular Disease is a major concern for individuals in the US and in Wisconsin. 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 at the Medical College of Wisconsin.

ANESTHETIC-INDUCED NEUROAPOPTOSIS: IS ANESTHESIA BAD FOR THE NEWBORN BRAIN?

AWARD AMOUNT: \$600,000 (2012-2015)

Goal

To understand how anesthesia affects developing human nerve cells to ensure safe general anesthesia for newborns.

Background

Studies in developing animals have shown that anesthetic agents administered early in life can lead to neuronal cell death and learning disabilities. A number of studies have suggested that exposure to anesthesia before the age of three may increase a child's risk for developing learning disabilities.

At Children's Hospital of Wisconsin, 10,000 children are anesthetized annually. It is unclear if anesthesia-induced cognitive impairment occurs later in life.

The proposed research seeks to identify the mechanisms involved in anesthetic neurotoxicity, which will allow for the design of molecules that can prevent this toxicity.

Award Summary

Development of human embryonic stem cell (hESC)-derived neurons has provided a valuable tool for understanding the effects of anesthetics on developing human neurons.

Unbalanced fusion or division of mitochondria (the cells "powerplant") leads to various pathological conditions including neurodegeneration.

The aim of this study was to dissect the role of mitochondrial dynamics in anesthetic (propofol)-induced neurotoxicity. Exposure to propofol for six hours increased neuron death and increased mitochondrial fission; this was accompanied by increased

expression of activated dynamin-related protein 1 (Drp1) and cyclin-dependent kinase 1 (CDK1), key proteins responsible for mitochondrial division. Pretreatment of the cells with a mitochondrial division blocker rescued the propofol-induced toxicity. Inhibiting CDK1 reversed the increased mitochondria division, cell death, and the increased expression of Drp1.

These data demonstrate for the first time that propofol-induced neurotoxicity occurs through a mitochondrial division-mediated pathway.

The proposed research has the potential to be clinically relevant, as identifying the mechanisms involved in anesthetic neurotoxicity will allow for drug development that can prevent this toxicity.



MEDICAL SCHOOL

Relevance

A number of studies have suggested that exposure to anesthesia before the age of three may increase a child's risk for developing learning disabilities. This project seeks to reduce any risks to young children from exposure to anesthesia. The work will provide data to guide clinicians in making the most informed decisions possible when anesthetics are used in pediatric patients.

Significance to Science and Health

Through a better understanding of how anesthesia interacts with the developing brain, results from this study will include methods for reducing risk, perhaps even identifying anesthetics that are not toxic for use with newborn infants.



Zeljko Bosnjak, PhD

Professor and Vice Chairman for Research, Anesthesiology

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

FUNCTIONAL PAIN AND AUTONOMIC DISORDERS (FPAD) PROGRAM DEVELOPMENT

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



MEDICAL SCHOOL

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 (things we don't have to think about), and are thus wide-ranging. These common disorders (FPAD) cause patients to experience discomfort and pain in various regions of the body. These and other FPADs affect around 500,000 individuals in Wisconsin. MCW's autonomic disorders clinic is filled with Wisconsin residents who have little access to care.

This project will help better define these disorders, create an educational infrastructure for teaching physicians, and improve treatment options for patients.

Award Summary

During the reporting period, the aim to increase clinical infrastructure was furthered with the recruitment of patients into the autonomic disorders registry, which now exceeds 500 subjects.

Also, projects focusing on the clinical investigation of events underlying pediatric FPADs are advancing in enrollment and completion. These include a neural networks protocol; endocannabinoids protocol (collaboration with Dr. Cecilia Hillard); near-infrared spectroscopy; and the compensatory reserve index.

Two grants were funded, one from the Developmental Disabilities Council (DDC) and another from the Soref Foundation.

In addition, collaboration continues in the investigation of adult pelvic pain disorders.

The aim to increase computational infrastructure, was advanced by Charles Welzig, MD, who completed the rebuild of the core facility and developed machine learning models in several areas. His lab continues to develop infrastructure and new programs for use in diagnostics in other areas such as cardiology. Equipment was purchased to develop new methods to assess brain function in combination with MRI and MEG imaging, and to measure pathways that lead to central and peripheral pain.

The aim to increase genetics infrastructure continues to advance with increased collaboration of local researchers into the role of mitochondria (the cells powerhouse) in FPAD. Work on the epidemiology of FPAD also moved forward and resulted in publications, and forms the basis of future grant proposals.

An additional aim to educate Wisconsin primary care physicians in FPAD continued with the Primary Practice Physician Program for Chronic Pain (4PCP) model, for which the research team hired an educational coordinator. Educational videos for both patients and physicians are being produced, and group visits to MCW are planned.

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 at the Medical College of Wisconsin.

PERSONALIZED MEDICINE PROGRAM: PHASE 1

AWARD AMOUNT: \$2,539,227 (2010-2016)



MEDICAL SCHOOL

Goal

To establish new DNA sequencing and data analysis resources for research and healthcare delivery related to personalized medicine.

Background

This investment helps to establish the infrastructure necessary to deliver personalized medicine – the use of gene sequencing to identify gene variants that underlie disease and that can be used to direct treatments.

Advances in the technologies available to rapidly and accurately identify genomic variants have been made in the past year.

Despite the many advances, the process continues to need refinements as more information is analyzed and the understanding of the limitations of the sequencing technologies are defined.

Award Summary

In the past year, the project team acquired two HiSeq 2500 DNA sequencers, which has had an immediate impact on the timeline from sample processing to analysis.

These two sequencers reduced the total sequencing time from approximately 11 days on the previous instrument (HiSeq 2000) to approximately six days on a HiSeq 2500 in high throughput mode.

The instruments also provided the team with the capacity to run a rapid exome test (sequencing of just protein -encoding parts of the human genome), which takes approximately 27 hours on the new HiSeq 2500 sequencers.

This test has been optimized and is currently being used clinically.

In the past year, the project team's sequencing platforms and clinically validated CarpeNovo software platform was used for nearly 550 individual tests.

The molecular diagnoses resulting from these tests benefited Wisconsin residents and Wisconsin physicians who used these results to improve the treatment plans for their patients.

Relevance

Researchers at MCW were amongst the first in the world to employ DNA sequencing for personalized medicine, and continue to sequence genomes for clinical purposes. Several recent successes in diagnosing and treating children with elusive illnesses have demonstrated the exciting potential of this approach.

Significance to Science and Health

Personalized medicine can be used to improve medical diagnosis of disease, and can improve the selection of therapies with the greatest likelihood of success in treating symptoms or preventing disease in at-risk individuals.



Allen W. Cowley, Jr., PhD

Interim Director of the Human and Molecular Genetics Center, Chairman and Professor of Physiology

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

PROGRAM IN GENOMICS AND ETHICS

AWARD AMOUNT: \$1,642,312 (2011-2016)



Goal

To establish a new research and education program in genomics and ethics to bridge the gap between the application of genomic advances in medicine and the ethical implications that emerge from this new area of exploration in medicine.

Background

Advances in genomics and personalized medicine – tailoring treatments based on human gene signatures – have led the field of medicine into an exciting frontier. This new era also poses many ethical questions for clinicians, researchers, patients and patients' families as the technology for interpreting individual genomes is quickly advancing.

While the technology has allowed for medical successes only once dreamed of, it is important to support rigorous ethical examination that keeps pace with the technology as it evolves.

Award Summary

During this reporting period, the Program in Genomics and Ethics (PGE) continued its work toward discovering new knowledge through conducting innovative research on ethical issues raised by emerging genomic technologies and dissemination of that new knowledge.

Outcomes of this research could lead to recommendations for best practices and guidelines for ethical decision-making among health care providers, researchers and the public.

The PGE's fourth year of funding led to the submission of five grant applications, resulting in two successful proposals that leverage the AHW Endowment's investment.

The study team members continued to publish analysis of data from their innovative research endeavors and

provide expert commentary and recommendations about the ethical, legal and social issues related to the use of genetic and genomic technologies.

The fourth year also brought renewed concentration on exploring new ways to provide education and outreach about genomics and ethics to key stakeholders and new opportunities for research.

The work being done by PGE is benefitting Wisconsin residents by exploring questions related to the ethical, legal and social implications raised by genetic and genomic sequencing technologies.

Data collected and analyzed through the Program's research efforts are continuing to inform the refinement of the informed consent process used by patients/parents considering genome sequencing, and a new collaborative project with the Wisconsin Medical Society that will provide valuable information about the attitudes and needs of the state's medical professionals regarding genomics.

Relevance

Technology for sequencing human genomes is quickly advancing. While this has allowed for medical successes, it is important to support rigorous ethical examination that keeps pace with technology as it evolves.

Significance to Science and Health

Advances in genomics and personalized medicine have led the field of medicine to an exciting frontier. This new era also creates many ethical questions for clinicians, researchers, patients and patients' families regarding the use of such technologies.



Arthur R. Derse, MD, JD

Director of the Center for Bioethics and Medical Humanities, Professor of Bioethics and Medical Humanities

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

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

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



MEDICAL SCHOOL

Goal

To forward our 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:

- i) neurodegenerative diseases like Alzheimer's and Parkinson's diseases,
- ii) nervous system injuries including brain trauma, concussion, and stroke,
- iii) developmental disorders such as autism, cerebral palsy, and attention deficits, and,
- iv) 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 through the hiring of new research talent. The Program hired two faculty members, Christopher M. Olsen, PhD, and Matthew Scaglione, PhD, who have successfully integrated into the research community and are making impacts through their work on how addiction rewires the brain, and how protein aggregates lead to neurodegeneration, respectively.

The Program continued to provide funds, core resources, and opportunities for meeting and discussion, all with the aim of increasing collaboration and capacity for neuroscience research at MCW.

Specific successes include two publications in the prestigious *Journal of Neuroscience*. One, by Nashaat Gerges, PhD, included Dr. Olsen as a co-author; the other was led by Sang Hyeong Lee, PhD, and included both Drs. Liu and Olsen as co-authors. These efforts highlight how important collaborations are to completing impactful, high-quality research studies.

The Program also features pilot awards to spur research, and all accomplished the aims for which they were intended.

Highlights include creation of novel tools to study schizophrenia, and identification of a novel mechanism by which exposure to neglect in early life results in changes in the brain.

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 Pharmacology and Toxicology

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

DEVELOPMENT OF A REDOX BIOLOGY PROGRAM

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

Goal

To 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 defined as the transfer of an electron from a molecule (which is now oxidized) 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 a wide variety of tissues, including the heart, which leads to cardiovascular 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 cardiovascular 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

In the past funding period, the Program has successfully recruited a second Redox Biology faculty member, Shayne Squires, MD, a cardiologist and co-recruit with Ivor Benjamin, MD, Director of the Cardiovascular Center.

Dr. Squires works in the area of redox imaging and is creating new approaches to visually monitor changes in redox status in animals and humans.

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.



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 seek to advance 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 at the Medical College of Wisconsin.

MAGNETOENCEPHALOGRAPHY (MEG) RESEARCH DEVELOPMENT PROGRAM

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



MEDICAL SCHOOL

Goal

To establish a world-class magnetoencephalography (MEG) research program at MCW 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, and thus produce images of the brain. MEG has several advantages over other imaging approaches, including the ability to accurately locate 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.

This program seeks to promote the MEG's potential as a tool in health research. An expanded community of researchers would lead to more opportunities for collaborations and translational science within MCW and between MCW and other institutions.

Award Summary

The MEG Research Program now manages all research being conducted at the MEG scanner at MCW. During this past year, there were over 62 hours of research

scanning completed by three different research groups, which is a significant increase from previous years.

In addition, the research team secured funding of the first NIH grant at MCW to use MEG as a primary measure. This grant 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.

During this period, the Program posted two requests for pilot grant applications.

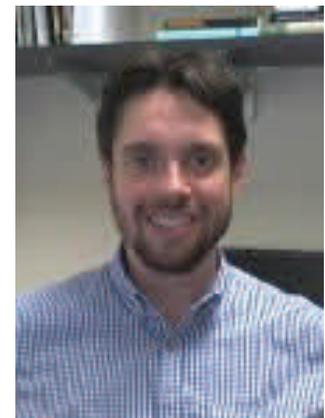
The Program also held an educational workshop and hosted an open house at the MEG scanner to educate the MCW community about MEG.

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 at the Medical College of Wisconsin.

HIGH IMPACT INTEGRATED BEHAVIORAL AND BIOMEDICAL INTERVENTIONS TO ERADICATE AIDS

AWARD AMOUNT: \$999,395 (2014-2017)



MEDICAL SCHOOL

Goal

To 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 onward transmission of HIV disease.

Background

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

Recent groundbreaking clinical trials have shown that early treatment with antiretroviral 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

During the reporting period, the research team made progress on several goals.

The interdisciplinary research team created and established project operations, developed field activity priorities and timelines, finalized an in-depth interview protocol, trained investigators and staff to conduct interviews, initiated analyses of interview data, and prepared presentations of scientific findings for

dissemination at public health conferences.

The research team also established a community advisory panel (CAP) whose members included representatives from HIV-affected communities, leaders of Wisconsin agencies that serve persons living with HIV infection, community constituencies, and community stakeholders.

Many interviews have already been transcribed by project staff and qualitatively analyzed, and more data is still being collected. The team gave two presentations at public health scientific conferences: The International Association of Providers of AIDS Care (IAPAC) Annual Conference and the AIDS IMPACT 2015 Biannual Meeting.

The project's Modeling and Cost Data Workgroup has started to collect relevant HIV epidemiological data needed to undertake modeling analyses, although the analyses themselves are not scheduled until later project years.

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 at the Medical College of Wisconsin.

COMMUNITY MEDICAL EDUCATION PROGRAM: PLANNING PHASE

AWARD AMOUNT: \$4,023,658 (2012-2016)



MEDICAL SCHOOL

Goal

To develop a medical education program that addresses the need for primary care physicians in underserved Wisconsin communities and uses an innovative, immersive teaching model centered on prevention, wellness and inter-professional, team-based learning.

Background

Nationally, there is concern about the adequacy of the primary care workforce in underserved and rural communities. A national shortage of physicians by 2020 is projected, and medical schools have been producing decreasing numbers of primary care physicians and doctors in underserved areas.

A 2011 Wisconsin Hospital Association report concluded that there will be future shortages of primary care doctors and physicians for the underserved. These points underlie the need for MCW's Community Medical Education Program.

Award Summary

During the reporting period, many of the project's goals were achieved and significant strides were made toward achieving the remaining goals.

Through the work of the Medical School's Admissions Committee, and the efforts of the Regional Applicant Advisory Committee (RAAC), the team was able to recruit 26 students (surpassing the goal of 20 students) for MCW-Green Bay.

The curriculum developed for MCW-Green Bay's first year students was evaluated during several distance pilot sessions to test and ensure that delivery would be received well by students.

Another milestone was the Higher Learning Commission's (HLC) and the Liaison Committee on Medical Education's (LCME) approvals of MCW-Central Wisconsin.

The response from the communities with whom the project team is working for both regional campuses has been overwhelmingly positive.

This is evidenced by the creation of the Pathway Community Partner Council for MCW-Green Bay and the formation of several Community Advisory Board working groups focusing on MCW-Central Wisconsin.

Over the next year, the project staff and leaders will work to complete the development of MCW-Central Wisconsin site and the second- and third-year curricula for both campuses.

Relevance

The Association of American Medical College estimates that increases in medical school enrollment and residency positions are needed to prevent a shortage of about 90,000 physicians by 2020. MCW's efforts will help with this problem in rural and underserved areas.

Significance to Science and Health

Physicians trained in underserved areas of Wisconsin are more likely to practice in communities that need more primary care experts, which will increase the health of people in these communities.



Joseph Kerschner, MD, FACS, FAAP

Dean of the MCW Medical School and Executive Vice President of MCW, Professor of Otolaryngology and Communication Sciences

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

HEALTHY WISCONSIN LEADERSHIP INSTITUTE

AWARD AMOUNT: \$731,467 (2011-2015)



MEDICAL SCHOOL

Goal

To build public and community health skills and leadership capacity by facilitating and providing continuing education and training to the public health workforce of Wisconsin.

Background

Calls for innovative approaches to address the nation's increasingly complex public health challenges have placed emphasis on the need to both strengthen the governmental public health infrastructure and build broader partnerships among all sectors working to improve health. This is based on the belief that without highly competent public health professionals in both governmental and non-governmental sectors, the need for programs and policies to combat public health threats and impact major determinants of health will go unmet.

The Healthy Wisconsin Leadership Institute (HWLI) was created as a collaboration between MCW and the University of Wisconsin School of Medicine and Public Health to meet these challenges.

Award Summary

The Institute was identified as one of 15 exceptional public health achievements of the past decade in the state health plan, *Healthiest Wisconsin 2020*. Community Teams trained by the Institute strengthened partnerships, leveraged media coverage, accessed additional resources, mobilized communities, impacted policies, and increased services. During the reporting period, the Healthy Wisconsin Leadership Institute had several accomplishments.

The project team convened a diverse, statewide Advisory Committee that provides guidance,

support, and advocacy for HWLI programming, and revised its mission, vision and values with input from the HWLI Advisory Committee.

The team developed and held workshops, in-community visits, and webinars with the 2014-2015 cohort of five Community Teams (28 participants) that focused on issues including improving mental health access and awareness in minority populations, improving the health of transgender and gender non-conforming individuals, improving food systems, integrating health in planning, and enhancing overall well-being. In addition, the team co-sponsored a pre-conference session, "The Community Readiness Model: A Program Planning Tool for Community Change" at the Wisconsin Public Health Association Annual Conference.

During the reporting period, the research team also revised its evaluation plan, conducted 20-month follow-up assessments with Community Teams Program alumni, redesigned its website, and created a social media presence to facilitate communication and connections with stakeholders.

To further involve the community, the project team participated as a partner in efforts to develop a collective impact infrastructure in Wisconsin. The team provided technical assistance and trainings on topics including implementation of the community-facilitated logic model, conducting a root cause analysis, asset mapping, collective impact, coalition building, and action and evaluation planning. The team also launched COACH (Collaborating, Organizing, and Advocating for Community Health), a new program for Community Teams Program alumni.

Relevance

By providing training, education, and technical assistance to support local agendas for community health improvement, the Institute has enhanced the ability of its participants to advance health and health equity in Wisconsin.

Significance to Science and Health

The Healthy Wisconsin Leadership Institute continues to better train community leaders and statewide multi-sectoral partnerships to more effectively advance health improvement agendas in Wisconsin.



Peter M. Layde, MD, MSc

Co-Director of the Injury Research Center, Associate Chair of Global and Public Health, Professor of Emergency Medicine

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

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

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



MEDICAL SCHOOL

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, held focus groups of 115 adults with diabetes and 15 clinicians, which demonstrated some important themes.

First is improvement in patient and provider communication: patients need encouragement and motivation, relationship building, compassion, and to identify communication preferences for in-person and for MyChart email.

Second was health service delivery: clinicians need support for patient health education, care coordination,

data management, and the financial resources to achieve performance outcomes and cost control.

Third was self-care and management: patients need family and social support of diet/nutrition and physical activity, help with the financing the costs of self-care, and help facing emotional challenges and stigma.

These themes provide a conceptual framework for quality improvements in care coordination initiatives.

Additionally, a value-stream mapping effort in ambulatory care settings for 28 diabetes patient visits significantly improved hemoglobin A1c and micro-albumin testing, as well as patient satisfaction at a pilot clinic, and Dr. Tarima is leading analysis of hypertension and depression in the Clinical Research Data Warehouse sample of 10,000 patients with diabetes.

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 at the Medical College of Wisconsin.

PATIENT-CENTERED OUTCOMES RESEARCH PROGRAM

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



MEDICAL SCHOOL

Goal

To 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 Milwaukee and southeast Wisconsin.

Award Summary

A main purpose of the award is to increase capacity in outcomes research through faculty recruitment. The Program recruited Onur Asan, PhD, who specializes in human factors engineering that advances the understanding of how people interact with technology, which will benefit the citizens of Wisconsin and beyond.

Dr. Asan received extramural support from the Agency for Healthcare Research and Quality and was awarded an MCW President's Faculty Scholar Award. He continues to publish in peer-reviewed journals, and to present his work nationally and internationally.

The Program also furthers outcomes research through seed grants. The three Patient-Centered Outcomes Research (PCOR) Seed Grants that were awarded for FY15 were implemented and successfully completed.

A PCOR Seed Grant for \$15,000 over one year was awarded for FY16 and started July 1, 2015. Awardees included Cynthia Kay, MD, MS, who submitted a manuscript for publication, and presented a poster at the National Society for General Internal Medicine Meeting.

Joan M. Neuner, MD, MPH, leveraged her PCOR Seed Grant to submit an R21 application to the NIH in June 2015, which will examine techniques to overcome a possible barrier that exists in examining patients in Wisconsin who have mild bone loss.

Raj Rao, MD, submitted an abstract to the annual meeting of Orthopaedic Research Society concerning the advantages of yoga therapy over traditional physical therapy in the outcome measurements of physical function, mental function (anxiety and depression), pain intensity and interference. These efforts will help in managing chronic lower back pain at a lower cost, lead to decreased treatment costs while maintaining quality of care, and improve patient examination of osteoporosis (bone loss) in Wisconsin.

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, Lady Riders Professor of Breast Cancer Research, Professor of Medicine

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

CLINICAL EFFECTIVENESS RESEARCH - IMPROVING THE VALUE OF HEALTHCARE

AWARD AMOUNT: \$300,000 (2013-2017)



MEDICAL SCHOOL

Goal

To improve health outcomes for children across the continuum of care by generating, evaluating, synthesizing, and disseminating research findings that ultimately provide the evidence to enhance medical decisions made by patients and their health providers.

Background

Clinical Effectiveness Research (CER) is an area that is designed to address improvements in health care by providing better evidence for what works best for patients.

New evidence will guide health care decisions to improve health care delivery and improve patient outcomes. Because CER research is not limited to a specific disease, there is the possibility for any disease to be studied and treatment approaches improved.

This work will benefit the larger goals of the Center for Clinical Effectiveness Research (CCEF), whose goals are to develop and implement key resources to stimulate, facilitate, and support high-quality, high-impact clinical effectiveness research.

Award Summary

During this project period, an Associate Director, Trafford Crump, PhD, was hired in June 2014, and a clinical research assistant was hired in March 2015. The project team developed 11 new collaborations and strengthened 19 strategic connections. The collaborations were with internal and external groups, and consisted of a national research network workgroup on sickle cell disease; a newly formed sickle cell foundation; internal groups like CTSI and CRI; individual researchers at

MCW; and external groups like the Patient-Centered Outcomes Research Institute (PCORI), NIH and the Cincinnati Children's Hospital Medical Center.

To meet the objective of building a network of clinical effectiveness researchers, the team supported the training of two junior faculty researchers through a workshop focused on patient reported outcomes: the "Patient-Reported Outcomes Measurement Information System (PROMIS®): From Basics to Applications in Clinical Research, Practice, and Population Health" conference held in Philadelphia in May 2015.

The Center continues to distribute monthly newsletters to the campus community to communicate CER activities and highlight publications, conferences, training events, and funding opportunities. In addition to the regular monthly newsletters, the Center sent out five ad hoc mailings to share information about webinars, seminars, presentations and events about CER events on campus and externally.

Relevance

By examining existing data or conducting new studies, clinical effectiveness researchers generate new knowledge that patients and their health providers can use to make informed health decisions.

Significance to Science and Health

Advances in comparative effectiveness research are key to advancing innovation, developing new therapies, and ensuring that optimal health care decisions are made for the people of Wisconsin.



Julie Panepinto, MD, MSPH

Director of the Center for Clinical Effectiveness Research of the Children's Research Institute, Professor of Pediatrics/Hematology

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

NEUROIMAGING RESEARCH PROGRAM- NEUROSCIENCE TRANSLATIONAL RESEARCH INITIATIVE

AWARD AMOUNT: \$749,995 (2011-2017)



MEDICAL SCHOOL

Goal

To build a Neuroimaging Research Program committed to using emerging radiologic techniques to develop new means of diagnosing neurologic disorders and measuring neurological changes following treatment.

Background

The more than 600 known neurological disorders, which include stroke, epilepsy and Parkinson's disease, impact the lives of 50 million Americans each year according to estimates from the National Institutes of Health's Institute of Neurological Disorders and Stroke. The future of both experimental and clinical neuroscience research will increasingly emphasize advanced imaging capabilities. In recent years, rapid evolution of imaging science has made it possible to identify disease in unique ways.

Ultimately, these advances in medical imaging will improve long-term outcome for patients suffering from neurological disease and injury. There is a high likelihood that such techniques will allow clinicians to begin therapies much earlier, and hopefully improve the health of patients in Wisconsin and elsewhere. Furthermore, it will also allow us to evaluate changes associated with disease and treatment, and thus, make decisions that will affect the quality of peoples' lives.

Award Summary

The award allowed recruitment of two researchers whose work stands to improve the health of the people of Wisconsin.

Matthew Budde, PhD, uses brain imaging to detect and monitor injury in the nervous system such as traumatic brain injury (TBI), spinal cord injury, and stroke. Significant progress was made in developing a new MRI imaging technique to rapidly assess the extent of spinal cord injury, which is likely to be able to predict outcomes. Dr. Budde recently obtained extramural funding to investigate the relationship between TBI and drug abuse.

L. Tugan Muftuler, PhD, studies spinal cord anomalies and his work indicates that the deterioration of the disc endplate, which separates the vertebrae, has a direct effect on back pain by affecting blood flow and nutritional delivery to the disc. Endplate degeneration is related to loss of hydration and the structural proteins, which are critical for disc maintenance.

Dr. Muftuler also continues his work to improve MRI imaging technology for neurodegeneration issues such as Alzheimer's disease. The advances improve image resolution and allow rapid scanning. The research team is also applying this technique in studying long-term brain injury after concussion.

Relevance

The researchers are building a Neuroimaging Research Program committed to developing new means of diagnosing neurologic disorders and measuring neurological changes following treatment.

Significance to Science and Health

Each year, 50 million Americans are affected by more than 600 known neurological disorders. Through the Neuroimaging Research Program, these patients will have access to new treatment options and advanced care.



Dennis Maiman, MD, PhD
Professor, Neurosurgery

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

ADVANCING NEW DISCOVERIES IN TRANSLATIONAL RESEARCH THROUGH THE COLLABORATIVE AND PILOT STUDIES PROGRAM

AWARD AMOUNT: \$3,172,764 (2011-2016)



MEDICAL SCHOOL

Goal

To provide a collaborative environment for biomedical researchers, healthcare providers, educators, citizens and industry to work together synergistically to translate fundamental discoveries into better health for the people of Wisconsin.

Background

Innovative collaborations and funding models are necessary to improve Wisconsin's health by increasing the quality and volume of translational research being conducted to turn basic science results into better clinical practice. This research program aims to advance new discoveries in clinical and translational research through the development of new pilot and collaborative funding programs. The program aims to provide a collaborative environment for biomedical researchers, healthcare providers, educators, citizens, and industry.

Award Summary

AHW REP's partnership with the Clinical and Translational Science Institute's (CTSI) Pilot Award Program has been successful in stimulating clinical and translational research among the institutions that comprise the CTSI of Southeast Wisconsin.

Currently there are 25 active pilot awards to support translational projects in the areas of behavioral health, diabetes, cancer, aging, infectious disease, immunology, health disparities and fitness, and genetics.

Highlights include John D. Imig, PhD, whose research team focused on novel therapies to effectively treat and stop the progression of chronic kidney disease. The research team found that a novel drug (EET-A) decreases blood pressure, improves cardiovascular health, and can mitigate radiation-induced kidney injury.

Michael W. Lawlor, MD, PhD, evaluated whether myostatin inhibition can be a potential treatment strategy for nemaline myopathy, a rare pediatric muscle disease in which muscles grow and contract poorly. Myostatin normally blocks muscle growth. This pilot project represents one of the only efforts worldwide to develop treatments for nemaline myopathy.

Vaishnavi Muqheet, MD, and her team study whether light therapy can promote wound healing in spinal cord injured veterans, and have expanded their investigations to include diabetic ulcers and retinal diseases like age-related macular degeneration.

Ru-Jeng Teng, MD, observed that caffeine is useful in treating bronchpulmonary dysplasia (BPD), an oxygen-related lung injury that is very common for extremely premature infants. This may offer a simple and safe medical treatment to protect premature infants against bronchpulmonary dysplasia.

Relevance

Innovative collaborations and funding models are necessary to improve Wisconsin's health by increasing the quality and volume of translational research being conducted to turn basic science results into better clinical practice.

Significance to Science and Health

This research program advances new discoveries in clinical and translational research through the development of new pilot and collaborative funding programs for investigators in clinical and translational research. It provides a collaborative environment for biomedical researchers, healthcare providers, educators, citizens, and industry.



Reza Shaker, MD

Senior Associate Dean and Director, Clinical and Translational Science Institute, Professor and Chief of Gastroenterology and Hepatology

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

CTSI MENTORED CLINICAL TRANSLATIONAL RESEARCH SCHOLARS PROGRAM

AWARD AMOUNT: \$1,980,000 (2011-2017)



MEDICAL SCHOOL

Goal

To improve human health by transforming the research and training environment to expand and enhance the career development of junior faculty as independent investigators through a mentored clinical and translation research experience.

Background

Junior medical faculty members often wish to pursue careers in biomedical research but do not have protected time, research experience, or dedicated research funding. Enhancing the career development of junior medical faculty members through mentored research will establish new investigators focused on clinical and translational science.

Award Summary

During this funding period, the AHW award provided resources for three MCW junior faculty to develop as independent clinical/translational investigators in the Clinical Research Scholars Program (formerly K30).

Venkatesh Sampath, MD, completed his third year of AHW funding and has recently been awarded an NIH-funded R01 grant. In addition, Dr. Sampath published several manuscripts related to his original research project dealing with gene-environment interactions in bronchopulmonary dysplasia, and transitioned to a project studying genetic factors contributing to necrotizing enterocolitis in premature infants. This last project received additional funding by a CTSI pilot award and has recently been funded by an NIH R01 grant.

Arash Babaei, MD, completed his second year of AHW support and is studying the basis for swallowing difficulties (dysphagia) in patients with various clinical disorders. In addition, he was author or co-author of five manuscripts related to studies of dysphagia, and co-investigator of two NIH-funded grants related to mechanisms of dysphagia.

Carmen Bergom, MD, PhD, completed her first year of support and is studying the role of DiRas proteins in protection from breast cancer. In addition, Dr. Bergom co-authored five publications dealing with genetic modifiers of breast cancer.

Relevance

Junior medical faculty members often wish to pursue careers in biomedical research but do not have protected time or dedicated research funding.

Significance to Science and Health

Enhancing the career development of junior medical faculty members through mentored research will establish new investigators focused on clinical and translational science.



Reza Shaker, MD

Senior Associate Dean and Director, Clinical and Translational Science Institute, Professor and Chief of Gastroenterology and Hepatology

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

MCW TISSUE BANK

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



MEDICAL SCHOOL

Goal

To 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 6,321 tissue samples, 18,050 blood samples, and 877 bone marrow samples banked.

In this reporting period, the Bank had 12,344 tissue samples, 42,274 blood samples, and 5,543 bone marrow samples banked.

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

The bank concentrated efforts 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.

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 at the Medical College of Wisconsin.

CANCER BIOMARKERS FOR EARLY DETECTION AND PREDICTION OF CLINICAL OUTCOMES

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



MEDICAL SCHOOL

Goal

To 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

During this year, 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* (Impact factor = 13.9, which is very good) with platinum priority publication.

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 (next-generation sequencing), 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.

The findings were published in the journal *Oncotarget* (impact factor=6.6). Dr. Wang also submitted a manuscript for early detection of lung cancer.

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.

CANCER CENTER INFRASTRUCTURE GRANT

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



MEDICAL SCHOOL

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.

Award Summary

The MCW Cancer Center (MCWCC) has made significant strides in its efforts to develop strong and nationally recognized interdisciplinary programs in cancer-related research, education, clinical care, and community service.

MCWCC recruited Melinda Stolley, PhD as the Associate Director for Prevention and Control. Dr. Stolley is a well-funded, renowned cancer survivorship expert concentrating on the development and implementation of behavioral interventions among underserved populations, in particular African American and Latino women with breast cancer.

MCWCC sponsored the 2015 MCW Cancer Center Scientific Retreat held in March 2015. Cancer genomics and drug discovery were highlighted through presentations by two working groups newly formed at the Cancer Center. Dr. Mark Evers, Director of the recently NCI-designated Markey Cancer Center at the University of Kentucky, and Dr. Scott Weir, a Program Director at the University of Kansas Cancer Center, were the keynote speakers.

Dr. You's team also submitted an NIH Program Project Grant (PPG) on Pancreatic Cancer. MCWCC staff provided preaward support to a PPG led by Dr. Dwinell and involving four projects and three cores.

Dr. You aligned the MCWCC's seed grant structure with research focus areas of breast, pancreas, immunology and disparities. The Request for Applications was revised to align applicants with research focus, as opposed to funding mechanism.

MCWCC has significantly increased both internal and external communications through distribution of the Director's Update, a quarterly electronic newsletter distributed directly to over 750 contacts, improved social media reach of 250% through targeted campaigns, and the development of the Cancer Center Community Advisory Board (CCCAB). Through a partnership with the American Cancer Society Cancer Action Network, Dr. You's team brought in ACS Chief Medical Officer Otis Brawley, MD for a day of talks, events and media opportunities, which garnered widespread media coverage.

The MCWCC communications have reached 25,000+ people throughout Wisconsin and the team continues to collaborate with MCW's, Froedtert's and the CTSI's marketing and public affairs leadership.

There have been several major updates to the MCWCC website including a page for the newly established Cancer Center Community Advisory Board (CC CAB), upgraded Shared Resource and Research Program pages, and a new website for the Pancreatic Cancer Research Program. In addition, the OnCore CTMS clinical trials page was launched. This is

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.

connected to live OnCore data and provides lists of open cancer trials by disease site and trial phase, significantly improving the cancer center's digital reach.



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 at the Medical College of Wisconsin.

HEMATOLOGIC MALIGNANCY & TRANSPLANTATION (HMT)

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



MEDICAL SCHOOL

Goal

To develop new approaches to augment the immune response against cancer and to 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 ultimately die from the disease. Developing new approaches to boost the immune system to fight cancer and to reduce complications associated with bone marrow transplants are highly desirable. Research in this program may lead to clinical applications that improve survival rates and quality of life for patients with cancer and those receiving a bone marrow transplants.

Award Summary

During the past year, the Hematologic Malignancy & Transplantation (HMT) Program recruited Alex Minella, MD, and Nan Zhu, PhD, to MCW and the Program. Both are accomplished researchers who bring prestigious NIH grant funding. Additionally, HMT researchers published 89 articles to share their research findings with the larger scientific community. Several program members actively participated in research with members from other programs, resulting in 16% inter-programmatic publications involving at least one HMT program member.

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. Highlights

include the work of Xiao Chen, PhD, who focuses on graft-versus-host disease (GVHD), which is a serious, frequently fatal complication following bone marrow transplantation. His lab has identified retinoic acid (RA) as a novel and critical factor in the induction of the immune response to the transplanted marrow that attacks the gastrointestinal tract. He also secured the prestigious Amy Strelzer Manasevit Research Award and obtained a 3-year, \$240,000 grant from the National Marrow Donor Program.

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.

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 ultimately die from the disease. Multiple myeloma is a common malignancy that affects many Wisconsin residents. Members of the program have been at the forefront in the treatment of multiple myeloma, which is a cancer of the blood. We are one of the largest programs in the Midwest, and physicians in the program employ state of the art therapies for treatment of this disease.

Significance to Science and Health

Research in 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 at the Medical College of Wisconsin.

CANCER BIOLOGY RESEARCH PROGRAM

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



Goal

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

Background

The American Cancer Society and Wisconsin Division of Public Health estimate that 29,610 Wisconsin residents were diagnosed with cancer in 2010. The program's work to understand the causes and mechanisms of this deadly disease has a significant positive impact on the people of Wisconsin.

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

Cancer Biology researchers published over 51 scientific papers that addressed the goal of identifying unique genetic, signaling, and metabolic features of cancer cells. Nine were published in collaboration with members of other cancer center programs.

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.

In addition, the Program held its second annual Cell Biology retreat in 2015, and will host its third retreat in the winter of 2016 to discuss ongoing

research, develop program themes and priorities and promote translational research.

The Cancer Biology Program also provided technology resources to support scientific advancement. The state-of-the-art Bioenergetics Core Facility is fully operational and supports researchers working to better understand how cancer cells differ from normal in creating and using energy. The Program also provided funding for new research ideas through seed grants.

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. A previous recruit, Dr. Hyeonman Jeong, PhD, continues to successfully develop new models to study skin, prostate, and breast cancer.

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 at the Medical College of Wisconsin.

POPULATION SCIENCES

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

Goal

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

Background

In 2010, cancer replaced heart disease as the 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 68 articles to share their research findings with the larger scientific community.

Several program members actively participate in research with other programs, resulting in 25% inter-programmatic publications involving at least one PS program member. A key function of the Program is to provide members with resources not otherwise available to an individual due to cost or space issues.

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

To bring scientific expertise to MCW, the Program recruited Kristen 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.

To develop mentorship opportunities and collaboration, program leaders and staff held individual mentorship meetings and a series of monthly research presentations. The program also held its third annual research retreat, which focused on cancer disparities, promoting team science, and establishing NCI designation.

The Program also fosters new research through seed grants, which this year will focus on identifying patterns of cancer risk within the Cancer Center catchment area.



MEDICAL SCHOOL

Relevance

In 2010, cancer replaced heart disease as the 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 at the Medical College of Wisconsin.

TUMOR PROGRESSION AND METASTASIS (TPM)

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



MEDICAL SCHOOL

Goal

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

Background

The American Cancer Society and Wisconsin Division of Public Health estimate that, from 1997 to 2007, the overall cancer death rate decreased 11 percent for males and eight percent for females. The groups attribute this decrease partially to earlier detection and improved treatment plans. Progress in imaging sciences and technology that advances the personalized medicine initiative at MCW will lead to better diagnosis and treatment for Wisconsin residents suffering from cancer.

Award Summary

Over the last fiscal year, tumor progression and metastasis (TPM) researchers published 67 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 18% 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. These seed grants are supplemented by mentoring committees that lend additional experience and knowledge to new research projects.

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. Additionally, Dr. Joshi has setup a small-scale synthesis facility for bio-compatible gold, silica, carbon nanotubes, and rare-earth doped nanoparticle-based contrast and therapeutic agents.

Mohit Maheshwari, MD, has continued to enroll subjects in his imaging and neurocognitive data study.

Eric Paulson, PhD, established new collaborations with Elekta, Siemens Healthcare, and Philips Healthcare in his work to develop tools and approaches for MRI-guided radiation therapy.

Peter LaViolette, PhD, focuses on applying imaging technology to detect tumor cells that infiltrate nearby healthy tissue in both brain cancer and prostate cancer, and also on how brain tumors respond to recently approved drugs. This is relevant to local brain tumor patients in Wisconsin, as the drug is extraordinarily expensive and a monetary burden in cases where it is ineffective.

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 throughout the body, and prevent the recurrence of cancer.

Significance to Science and Health

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



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