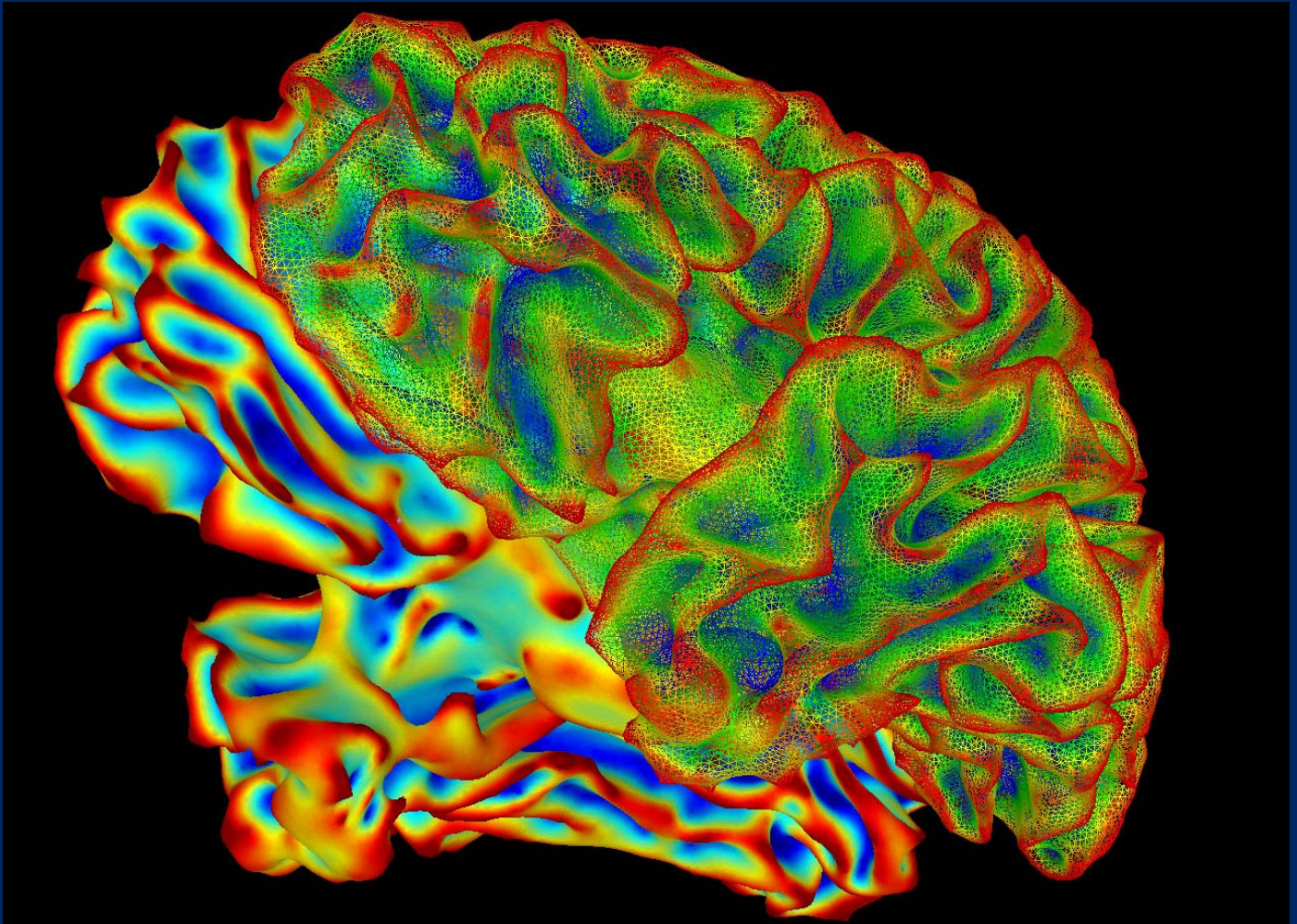




MEDICAL SCHOOL

ADVANCING A HEALTHIER WISCONSIN ENDOWMENT



RESEARCH AND EDUCATION PROGRAM Completed Award Summaries

The following includes summaries of progress for AHW
Research and Education Program awards that completed
during the period ending June 30, 2016

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

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

Goal

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

Award Summary

Through support from the AHW Endowment's Research and Education Program, this award identified and tested several innovative approaches for improving community engagement in and awareness of clinical and translational research.

Key strategies implemented during this award include:

Science Cafés: Held over 10 Science Cafés focused a variety of health and science topics. Topics were prioritized by a council of representatives from community organizations and the Clinical and Translational Science Institute faculty. There were more than 300 registrants for the Science Cafés. Attendees had the opportunity to discuss scientific advances with experts in a public setting. The Science Cafés were successful in encouraging bi-directional dialogue and mutual understanding between scientists, health experts and communities.

The Science Café series received national recognition through an article in the *Clinical Translational Science* journal in June 2014.

Students Modeling a Research

Topic (SMART) teams: Implemented in partnership with the Milwaukee School of Engineering, SMART Teams use an educational outreach approach to foster interest in research. Through SMART Teams, high school teachers and students partner

with scientists to study specific molecular and protein models. During this award, the SMART Teams provided opportunities for 24 local teams and 250 students to engage in principles of scientific research through learning about protein structures.

Annual Community Engagement

Week: To increase public awareness and showcase the benefits of community engaged research, the first Community Engagement week was launched in 2015. The week celebrated community engagement and provided opportunities for dissemination of community-engaged research scholarship and research findings. Sessions focused on community-engaged practice, skill building, and networking to foster new partnerships between researchers and community-based organizations. More than 600 community and academic stakeholders attended.

Community Engagement in Research Graduate level course:

Designed and launched the community engagement graduate level course in 2013. The course continues today to provide faculty with the knowledge and skills necessary to conduct community-engaged research. Lecturers included faculty at UW-Milwaukee, MCW and CTSI leadership and experts from community-based organizations.

The team secured \$830K in extramural support to leverage the AHW investment and continues to apply for funding to expand on its accomplishments. In addition, the leadership team has been successful in dissemination through several local, regional and national publications and presentations.



Relevance

Advanced community-engagement in clinical and translational research by increasing the public's interest in science while also developing faculty capability to partner effectively with communities.

Significance to Science and Health

Identified, tested and launched several new strategies that resulted in increased awareness of the value of community engagement in research as well as improved faculty understanding and skills in working with communities.



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.

COMMUNITY ENGAGEMENT (CE) CORE PLANNING INITIATIVE

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

Goal

Develop a strategic plan for implementing a community engaged research core to align and coordinate all community engaged research activities at the Medical College of Wisconsin.

Background

Across multiple disciplines, strong collaborations between academic and community partners have been shown to improve the translation of research discoveries into improved health. Community engagement 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 experimentation and research abuse, but also to improving the validity, efficacy, and translation of research findings.

The Community Engagement Core Planning Initiative provided dedicated expertise, time and resources to engage MCW faculty, staff and communities in a strategic planning process to identify key priorities for advancing community engagement across several prominent and new MCW research and education initiatives.

Award Summary

Several community representatives and MCW stakeholders provided input and support to identify and prioritize the resources needed to address gaps in community engagement services to more effectively impact community health.

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

As a result of the AHW investment, this planning award:

- established a common agenda and language for community engagement at MCW;
- created the structure for the Community Engagement Core;
- developed principles to guide participation in the Community Engagement Core; and,
- generated an implementation plan for the Community Engagement Core with specific milestones and strategies for sustainability.

As a result of the successful planning phase, an implementation proposal for the Community Engagement Core was submitted in 2015 and funded through the AHW Endowment Research and Education Program. The Community Engagement Core is in the midst of its implementation phase that is expected to complete in 2019.

The Community Engagement Core is will create a centralized community engagement resource, available to community partners and all MCW centers, institutes, programs and departments to advance community engagement in research.



MEDICAL SCHOOL

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.



Syed Ahmed, 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.

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 animals have shown that anesthetic agents administered early in life can lead to neuronal cell death and learning disabilities. Similarly, some research has suggested that exposure to anesthesia in children before the age of three may increase risk for learning disabilities.

At Children's Hospital of Wisconsin, 10,000 children are anesthetized annually. The results of this research study could increase understanding regarding the risk of anesthesia-induced cognitive impairment, and ultimately, inform clinical decision making regarding the use of anesthesia for children.

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.

This study dissected the role of mitochondrial dynamics in anesthetic (propofol)-induced neurotoxicity. The study found that 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.

AHW's investment in this award resulted in the first evidence that propofol-induced neurotoxicity induces death of stem cell-derived neurons and oligodendrocytes (a type of cell in the central nervous system) in vitro.

Specifically, these data demonstrate for the first time that propofol-induced neurotoxicity occurs through a mitochondrial fission-mediated pathway and miR-21 downregulation.

As a result, the study contributed to growing evidence of the potential risks that anesthetics pose to the young developing human brain.

Scientists are using the results of this research to support drug development that can prevent this toxicity.

Based on the team's studies, protective approaches can be identified and used in the future to counteract propofol toxicity in hopes of minimizing any potential brain effects, while still keeping children pain-free during surgery.

In recognition of the significance of this research, the team was awarded more than \$1.4M in NIH funding.

In addition, the team successfully disseminated the research findings through publication in 12 notable journals in the field as well as more than 35 international, national and local presentations.



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 in the MCW School of Medicine.

PERSONALIZED MEDICINE PROGRAM: PHASE 1

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



MEDICAL SCHOOL

Goal

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

Background

Perhaps no discovery has had greater implications in transforming medicine than the human genome project.

Although an overwhelming 98% of the human genome is still unknown, researchers now are able to identify molecular variations in DNA that cause disease.

Gene sequencing has enabled researchers to identify single genes responsible for disease and, as a result, has led to the design of improved strategies for disease prevention and treatment.

Funded in 2010, AHW's investment established the infrastructure necessary to deliver personalized medicine and contributed to positioning Wisconsin as a leader in the use of gene sequencing to identify gene variants that underlie disease and that can be used to target therapies.

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

Award Summary

AHW's investment established the fundamental infrastructure for personalized medicine at MCW, including securing specialized expertise, new technologies and data analysis pipelines.

The resulting infrastructure has had significant and immediate impacts on the ability to move from sample processing to analysis and, in turn, has

speeded the translation of this knowledge for clinical use.

New sequencing technologies 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.

Technologies 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 used clinically today.

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

AHW's investment in the infrastructure for personalized medicine continues to lead to promising lines of discovery with implications for better clinical decision making and treatment.

For example, personalized medicine has led to new tools to detect molecular changes at the early stages of disease development as well as the genetic-based assessment of drug efficacy and adverse drug reactions in patients to name just a few applications.

This investment is expected to continue to benefit Wisconsin residents and their physicians who use these results to improve the treatment plans for their patients.

AHW's investment led to more than \$5M in additional funding.

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 in the MCW School of Medicine

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 that bridges the gap between the application of genomic advances in medicine and the ethical implications that emerge from this new area of medicine.

Background

Advances in genomics and personalized medicine – tailoring treatments based on human gene signatures – have led the field of medicine into an uncharted frontier. This new era 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, it is important to support rigorous ethical examination that keeps pace with the technology as it evolves.

Award Summary

AHW's investment in the Program in Genomics and Ethics (PGE) supported innovative research regarding ethical issues raised by emerging genomic advances and their clinical applications.

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

The study team members continued to publish analysis of data from their innovative research and provide expert commentary and recommendations about the ethical, legal and social issues related to the use of genetic and genomic technologies.

The award also led to education and outreach about genomics and ethics to key stakeholders.

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.

These new frameworks for informed consent address the importance of community engagement to avoid potential healthcare disparities, expand the scope of thinking about risk regarding genetic testing to extend to others who may be affected, and detail an approach to decision-making.

In addition, research has documented convergent and divergent desires for return of genetic test results, highlighted low level of familiarity with genomic science, and identified further needs for education.

A collaborative project with the Wisconsin Medical Society provided valuable information about the attitudes and needs of the state's medical professionals regarding genomics.

Program researchers have provided evidence and arguments justifying emphasis on informed choice, specifically regarding the return of incidental findings and parental authority in a pediatric setting.

The team successfully produced a several publications contributing to new knowledge in the field. In addition, research findings were disseminated through several presentations at local, regional, and national conferences and workshops.

Broadly these endeavors help ensure that the benefits of the advancing technologies in genomics and genetics are maximized and the risks of harm are minimized.



MEDICAL SCHOOL

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 in the MCW School of Medicine

HEALTHY WISCONSIN LEADERSHIP INSTITUTE

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



MEDICAL SCHOOL

Goal

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.

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.

HWLI has offered the Community Teams Program annually since 2006.

Fifty-five teams and approximately 280 individuals participated in this year-long applied learning experience that facilitates sustainable community partnerships through the development of collaborative leadership and public health skills among multisectoral teams working on priority health issues.

In addition, the HWLI developed and held workshops, in-community visits, and webinars 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.

An evaluation and marketing plan was developed and a 20-month follow-up assessments was conducted with Community Teams Program alumni. This resulted in a redesigned website 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 MCW School of Medicine.

COMMUNITY MEDICAL EDUCATION PROGRAM: PLANNING PHASE

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

Goal

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 physician workforce in underserved and rural communities. A national physician shortage by 2020 is projected.

The Community Medical Education Program was designed to ensure access to quality physicians for Wisconsin residents in underserved regions of the state.

Award Summary

Since 2012, AHW's investment in the regional medical campuses has returned significant outcomes that position MCW to help mitigate the physician shortage and address access issues to improve the health of Wisconsin residents.

As a result of AHW's investment, MCW developed two regional medical education campuses: MCW-Green Bay and MCW-Central Wisconsin.

From a pool of more than 2,200 applicants, MCW-Green Bay matriculated its inaugural class of 26 students in July 2015. MCW-Central Wisconsin opened its doors to its first class of 26 students in July 2016 and an additional 30 students matriculated at MCW-Green Bay's campus. On average, eighty percent of the medical students are from Wisconsin.

The first of its kind in Wisconsin, students are trained using an innovative three-year curriculum. The curriculum's shortened duration is

achieved by reducing both the number of electives and the length of breaks, allowing students to graduate sooner and begin practicing medicine one year earlier than traditional four-year programs.

In addition, the MCW-Central Wisconsin campus offers *Physician in the Community*, a scholarly pathway that requires students to work with the community to address specific, health concerns such as obesity, heart disease and other chronic health issues.

An additional innovation launched through this award is the regional admissions advisory committee that enables community members to help evaluate students for fit with each regional medical education campus.

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

By 2022, as many as 200 new physicians could be trained through the new MCW Green Bay and Central Wisconsin campuses. MCW is working with area health systems to help cultivate strong residency programs in these regions as well.

Although still early in realizing its vision, the MCW Green Bay and Central Wisconsin campuses are positioned to successfully increase the number of graduates who remain in northern and central Wisconsin to practice medicine thereby increasing access to care for Wisconsin's rural and underserved communities.

The successful opening of the two new medical school campuses in just four years is a major accomplishment, and could not have been accomplished without support from the AHW Endowment.



MEDICAL SCHOOL

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

Potential to increase access to quality physicians in underserved areas of Wisconsin through the development of two regional medical education campuses and the of an innovative three-year medical education model.



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 in the MCW School of Medicine.

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

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



MEDICAL SCHOOL

Goal

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 awards. The program aims to provide a collaborative environment for biomedical researchers, healthcare providers, educators, citizens, and industry to combine their expertise and speed the translation of scientific discovery into improved patient care.

Award Summary

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

The Pilot Award Program established a competitive RFP process to facilitate and foster research that spans the continuum from bench to bedside, and from bedside to community practice.

As a result of the AHW investment, more than 60 pilot awards were funded to support translational research in the areas of behavioral health, diabetes, cancer, aging,

infectious disease, immunology, health disparities and fitness, population health and genetics.

Awardees disseminated research findings with more than 200 presentations at national and international conferences and published their work in peer-reviewed journals. In addition, 11 researchers reported commercial outcomes, e.g. patents, commercial use, and received more than \$15.4M in extramural funding.

Some of these studies have generated key findings directly impacting diagnostics and patient management.

Additional funds were leveraged through the National Institutes of Health to support 64 translational research awards totaling \$3M with 246 investigators participating.

The Program successfully cultivated a team science approach among its investigators and catalyzed the formation of new, innovative trans-disciplinary research teams. A survey of past awardees showed that more than 90% of awardees were very positive or somewhat positive regarding the benefits of the program to their research.

Among many, selected research outcomes include: improved understanding of the effect of concussion on sensorimotor function in children, the role of gut bacteria in mitigating heart disease, and new approaches to increasing cell membrane permeability to increase efficacy of radiotherapy in cancer treatment.

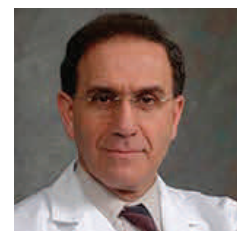
AHW's investment in the CTSI Pilot Awards Program has moved translational research forward by developing novel therapeutics and tools, and improving understanding of diseases that affect Wisconsin residents and beyond.

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 in the MCW School of Medicine.