Biomedical Sciences Research Facilities Funding Program

2020 Report to the Minnesota State Legislature
January 9, 2020

UNIVERSITY OF MINNESOTA

OVERVIEW

The University of Minnesota has set its sights on becoming one of the top public research institutions in the world. Achieving this goal requires state-of-the-art biomedical research facilities that can support leading edge research and attract and retain top-tier research faculty.

To catalyze this effort, the University asked the State of Minnesota to create the Biomedical Facilities Authority as the mechanism to provide a predictable funding source for planning and building research facilities that, in turn, would allow the University to attract and retain the nation's top biomedical research talent.

The State established the $292 million Minnesota Biomedical Research Facilities Funding Program in 2008. This dedicated funding program provided appropriations by the State to the University for up to 75% of the costs to design and construct four new and expanded research buildings on the University's Twin Cities Campus, in the area known as the Biomedical Discovery District (BDD). The State's portion of this funding program is $219 million; while the University's portion is $73 million.

Per the requirements set forth in Minnesota Statue 3.197, the cost to prepare this report was ~$1,500.

PROGRESS TO DATE

Project #1 – Expansion of the Center for Magnetic Resonance Research – Completed July 2010
Project #2 & #3 – Cancer Cardiovascular Research Facility - Completed July 2013
Project #4 – Microbiology Research Facility – Completed October 2015

These four projects comprise 422,000 gross square feet of new research space housing 130 faculty and 729 research support staff.

The Cancer-Cardiovascular research facility also includes 35,000 square feet of shared research commons and support spaces. These areas house common instrumentation and research processing and support facilities, which are available to researchers throughout the district and broader University community, including:

- University Imaging Center
- University Genomics Center
- Mouse Genetics
- Flow Cytometry
- Chronic, long term testing laboratories

In addition, several of the planning principles for the Biomedical Discovery District provided for connectivity and the development of a cohesive research community. This interconnected, collaborative research environment is able to leverage common shared support spaces and resources while allowing for unique opportunities to collaborate across fields and disciplines of research.

The district has now been connected end-to-end by skyway to further enhance and support the principle of cohesiveness and opportunities for collaboration.

Current Occupancy

	Principal Investigators	Other Researchers/Staff	Minnesota Biomedical Research Program Total
Cancer & Cardiovascular Research Building	61	282	343
Center for Magnetic Resonance Research	29	80	109
Microbiology Research Facility	26	125	151
Wallin Medical Biosciences Building	37	271	308
District Support Staff		44	44
TOTAL	153	802	955

Summary Research Programs

Project # 1 – Center for Magnetic Resonance Research (CMRR)

CMRR is focused on advancing methodologies and instrumentation for biomedical imaging using ultrahigh field magnetic resonance imaging and spectroscopy. As an integral part of its mission, CMRR also provides access to its unique instrumentation, technical expertise, and infrastructure through collaborations and service functions to enable the faculty, trainees and staff at the University of Minnesota and in the larger biomedical research community, to carry out basic biomedical, translational and clinical research. Examples of the current large-scale research projects being conducted by CMRR includes a focus on technological developments to usher in the next generation of MR instrumentation, data acquisition and image reconstruction methods, as well as development of new, efficient and safe stimulation paradigms for Deep Brain Stimulation (DBS). The CMRR provides essential resources and synergistic activities with other UMN centers, including the Institute of Engineering in Medicine, as well as several departments outside the Medical School, including Mathematics, Electrical and Computer Engineering, Mechanical Engineering, Chemistry, Physics, and Psychology. There are currently more than 300 collaborators throughout the University. In each of the past five years the CMRR has experienced steady growth, made possible by the investments in infrastructure and resources from the State of Minnesota.

In 2018-2019, CMRR faculty and collaborators made major scientific advances related to MRI and continue to make further program developments. Highlights include:

- Multiple CMRR faculty continue to make ground-breaking developments in neuroimaging, funded by numerous NIH grants, including a competitively renewed NIH P41 center grant, and 4 large BRAIN grants which by themselves total $29.4M. Developments in the BRAIN projects alone include: 1) new techniques and electronics for 10.5 Tesla MRI that will achieve the highest spatial resolution images ever of human brain connectivity and function; 2) a radically new type of head-only 1.5 Tesla MRI scanner that will enhance brain research and, ultimately, enable the diagnosis of neurological diseases in underserved populations throughout the world where MRI scanners are currently unavailable; and 3) novel orientation-selective and field steering stimulation electrodes for neuromodulation.

- In 2015, the Minnesota Legislature committed funding to the University of Minnesota Medical School to support the creation of Medical Discovery Teams (MDT) focused on tackling four major health concerns facing the state and nation. The teams were part of a recommendation by a blue ribbon commission appointed by Gov. Mark Dayton in 2014 to develop strategies for elevating the Medical School's national ranking. CMRR was awarded the MDT on Optical Imaging and Brain Science as a multi-disciplinary effort focused on mapping the detailed circuits that underlie sensation, perception and complex behaviors in the developing and mature brain. This 10-year, $30 million award focuses on a central vision within the BRAIN Initiative for the development of new approaches (microscopes, lasers, scanning methodologies, new fluorescent probes etc.) to overcome the limitation of optical techniques and the development of new computational and theoretical methods to exploit such rich data. This combination of technologies would provide the ability to bridge the scales of organization going from individual neurons to the whole brain envisioned in the BRAIN Initiative. The combined neuroimaging would also provide a bridge to electrophysiological recordings carried out in clinical settings, such as in DBS (Deep Brain Stimulation) surgery and TMS (Transcranial Modulation Stimulation).

- The MDT in Optical Imaging and Brain Science is located within CMRR and has added 3 faculty members (Drs. Prakash Kara, Gordon Smith, and Aaron Kerlin), 2 optical engineers, and 13 postdoctoral fellows, students, and lab staff. Drs. Kara and Smith have built labs in existing renovated CMRR space while Dr. Kerlin is temporarily housed elsewhere on campus due to space constraints in the existing CMRR facility. We are actively recruiting for 2-3 additional faculty members, one computational neuroscientist and one or two experimentalists. These new faculty members will be housed, along with Drs. Kerlin and Smith, in new space that is being built in CMRR that is slated for completion in early 2021. This new construction will add an additional 7,511 ft^2 of lab and office space for this MDT program.

Three year total research expenditures for investigators in CMRR have been $25.4M.

Projects #2 & 3 – Cancer and Cardiovascular Research Building (CCRB)

- Dr. Emilyn Alejandro was recruited to the Department of Integrative Biology and Physiology (IBP) in 2015. The goal of her laboratory is to understand how placental-insufficiency during pregnancy alters the offspring's pancreatic beta-cell function and susceptibility to Type 2 diabetes and to identify the mechanistic link between beta-cell programming and sensitivity to cellular stress involving ER stress, oxidative stress, autophagy and mitochondrial stress in chronic hyperglycemia and hyperlipidemia conditions.

- Dr. Hai-Bin Ruan was recruited to the Department of IBP in 2016. His laboratory is centered on understanding how metabolic homeostasis is maintained by the intercellular, inter-tissue, and inter-organ communication. He aims to define the pathological alterations of metabolic communication in diseases including obesity, diabetes, digestive disease, and inflammation. Ultimately, he hopes to identify targets and to design therapeutics for these diseases.

- Dr. Catherine Kotz was recruited to the Department of Integrative Biology and Physiology (IBP) in 2017and is also the Associate Director for Research at the Geriatric Research, Education and Clinical Center at the Minneapolis VA Hospital. Cathy received a PhD in nutrition at the University of Minnesota in 1993, and maintains a laboratory there and at the Minneapolis VA Medical Center. Her work centers on the central regulation of eating behavior and energy expenditure, which has been funded by the National Institutes of Health and the Department of Veterans Affairs, resulting in more than 100 scientific journal articles, reviews and book chapters. Cathy has directed an NIH funded training program in Obesity Prevention for the last 8 years, and was recently elected to the position of Vice President of The Obesity Society.

- Dr. Xavier Revelo was recruited to the Department of IBP in 2018. His laboratory is centered on understanding the molecular and integrative biology of metabolism and diabetes with emphasis on the immune mechanism that drive inflammation during obesity and non-alcoholic fatty liver disease.

- The Masonic Cancer Center at the University of Minnesota is the only National Cancer Institute-funded comprehensive cancer center in the twin cities and was designated 'Outstanding' by the NCI in 2018. The Masonic Cancer Center's research into cancer exposures led to its inclusion in the national Human Health Exposure Analysis Resource (HHEAR) program led by Drs. Lisa Peterson and Stephen Hecht. The goal of HHEAR is to provide the research community access to laboratory and statistical analyses to add or expand the inclusion of environmental exposures in their research and to make that data publicly available as a means to improve our understanding of the effects of environmental exposures on human health throughout the life course. The Minnesota HHEAR Targeted Analysis Laboratory continues the collaboration between researchers at the Masonic Cancer Center and the Minnesota Department of Health. The team received a 5-year, $2.3M grant to provide specialized analytical services to researchers across the country and around the world. The Masonic Cancer Center is internationally recognized for expertise in measurement of exposures from tobacco products, the environment, and dietary and lifestyle choices.

- Researchers at the Masonic Cancer Center together with collaborators at the Hormel Institute are researching the chemopreventive qualities of watercress. The NCI-funded study led by Drs. Stephen Hecht and Dorothy Hatsukami involves opening a clinical trial to better understand how watercress aids in the detoxification of environmental toxicants and carcinogens. Watercress is a unique and abundant source of PEITC among common vegetables. The glucosinolate precursor to 2-phenethyl isothiocyanate (PEITC) is gluconasturtiin. Researchers are developing methods to freeze-dry watercress and create smoothies that are easy to consume. The results of this study will provide a critical test of the use of watercress as a vehicle for isothiocyanates such as PEITC which can enhance detoxification of environmental toxicants and carcinogens. If the results of the trial support the hypothesis, watercress could emerge as a cheap and convenient food for cancer prevention, consistent with the concepts of "green chemoprevention and frugal medicine."

Figure 1. Watercress-pineapple research smoothie.

- Both highlighted research projects take advantage of the shared resources of the CCRB. One example is the Analytical Biochemistry shared resource which provides state-of-the-art chemistry services and expertise in mass spectrometry, chromatography, and analytical biochemistry. These three complementary specialties afford a center of expertise for a full range of chemical and biochemical services in support of the peer-reviewed research of Cancer Center investigators.

Three year total research expenditures for investigators in CCRB have been $101.9M.

<u>Project # 4 - Microbiology Research Facility (MRF)</u>

The Department of Microbiology and Immunology moved in January of 2016 from the Mayo Memorial Building into the 80,000 sq. ft. **Microbiology Research Facility (MRF)**, the fifth building in the Biomedical Discovery District (BDD), and the first building on campus to be designed and built using new "Smart Lab" technology to reduce energy costs.

The Department of Microbiology and Immunology held its **Centennial Celebration in July of 2019** and was honored, along with the University of Minnesota, by the American Society of Microbiology as a Milestones in Microbiology site. The Milestones in Microbiology Plaque now greets faculty, students and visitors as they enter MRF.

The faculty in MRF share with other investigators in the BDD the objective to "pursue discoveries by bringing together talented investigators and encouraging them to work on the new cures and therapies

for our most challenging and important health conditions." Department of Microbiology and Immunology faculty are the anchor tenants in MRF, but MRF is home as well for the **Infectious Disease Corridor of Discovery (IDC)** whose mission is to understand the microbes and the diseases they cause as the foundations for discovering better ways to prevent, treat and cure infectious diseases with special emphasis on the great killers-HIV/AIDS/TB/influenza/ and other deadly bacterial, fungal and viral infections-on a continuum from fundamental discovery to developing antimicrobials and vaccines.

The guiding principles for MRF and the IDC are encouraging collaborative research through spatial proximity of faculty with expertise in microbiology and immunology and faculty drawn from other departments and colleges along the continuum of team science from fundamental research through clinical translation. So, a snapshot of MRF in 2020 will show microbiologists and immunologists in MRF and the adjoining Center for Immunology (CFI) in WMBB working together by thematic concentration and location with infectious disease physician scientists and a medicinal chemist:

MRF highlights and accomplishments for the last two years include the following:

- **Herpes virus infections and influenza**
    - Participants in Congressionally mandated quest to develop a universal Flu vaccine (Masopust & Langlois)

- **HIV/AIDS/Malaria**
    - Strategies to Cure HIV (Haase/Schacker/Skinner)
    - New approaches to developing an effective HIV Vaccine (Herschhorn/Haase/Jenkins)

- **Lung infections, particularly in Cystic Fibrosis/Candida Infections/Drug Discovery**
    - Understanding microbial communities to better Rx Cystic Fibrosis (Hunter)
    - Candida genetics and drug resistance (Selmecki/Davis)
    - Medicinal Chemistry for new antimicrobials (Aldrich)

- **TB and deadly fungal infections (TB & Cryptococcal meningitis)/ Antimicrobial Resistance**
    - Enterococcal research and antimicrobial resistance (Dunny)
    - TB metabolism and improved drugs (Baughn/Aldrich)
    - TB genetics & immunology and vaccine development (Tischler/Masopust/Jenkins)
    - Cryptococcal and TB Meningitis (Nielsen/Boulware)

Three year total research expenditures for investigators in MRF have been $42.7M.