Biomedical Sciences Research Facilities Funding Program

2022 Report to the Minnesota State Legislature
January 10, 2022

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	Research Associates / Staff / Post Doc / Students	Minnesota Biomedical Research Program Total
Cancer & Cardiovascular Research Building	49	275	324
Center for Magnetic Resonance Research	41	127	168
Microbiology Research Facility	26	140	166
Wallin Medical Biosciences Building	40	240	280
TOTAL	156	782	938

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, the use of these advanced technologies in biomedical research and clinical practice, as well as development of new, efficient and safe stimulation paradigms for Deep Brain Stimulation (DBS). The CMRR provides essential resources and synergistic activities to other UMN centers, including the Institute of Engineering in Medicine, Masonic Cancer Center, and Masonic Institute of the Developing Brain, as well as several departments within the Medical School (e.g. Departments of Radiology, Neurology, Neurosurgery, Medicine, Dentistry, Psychiatry and Neuroscience,) and outside the Medical School (e.g. Mathematics, Electrical and Computer Engineering, Biomedical Engineering, Mechanical Engineering, Chemistry, Physics, and Psychology). There are currently more than 300 collaborators throughout the University supported by CMRR. 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 2020-2021, CMRR faculty and collaborators made major scientific advances related to MRI, despite the challenges posed by the pandemic, 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's Biotechnology Research Center (BTRC) grant, and 4 large grants funded under the national programmatic effort named the BRAIN (**B**rain **R**esearch through **A**dvancing **I**nnovative **N**eurotechnologies) Initiative (https://braininitiative.nih.gov); the 4 BRAIN Initiative grants by themselves total $29.4M in funding. Developments accomplished in these BRAIN Initiative projects alone include: 1) developing what is currently the highest magnetic field (10.5 Tesla) used for imaging humans; in the previous year, this effort accomplished new techniques and electronics for the 10.5 Tesla MRI system 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.

- MRI is an indispensable tool in clinical medicine and biomedical research. Yet, due to its high cost to purchase, site, and maintain, access to MRI is limited to mainly well-funded medical centers or research institutions. During the past 2 years, CMRR researchers have invented a silent MRI technology that simplifies the MRI system in terms of its hardware components, cost, size, weight, and infrastructure requirements. Future portable MRI scanners based on this technology have a chance of empowering communities in remote, resource-limited settings to address health inequities, build local capacity for better health, improve understanding of brain development and degeneration in diverse populations, and enable access to high quality clinical care worldwide.

- 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 (https://braininitiative.nih.gov) 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 networks 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 Magnetic Stimulation).

- The MDT in Optical Imaging and Brain Science is located within CMRR and has added 2 new faculty members in the last 2 years (Drs. Thomas Naselaris and Audrey Sederberg) bringing the total to 5 faculty members, 2 optical engineers, and 16 postdoctoral fellows, students, and lab staff. We are actively recruiting for one additional experimental faculty member and hope to have a candidate identified soon. This new faculty member will be housed, along with the existing faculty, in new space in CMRR that was completed earlier this year. This new construction added 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 $48.48M.

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

- Dr. Eric Batchelor was recruited to the Department of Integrative Biology and Physiology in 2020. His laboratory is focused on understanding how cells detect and respond to stress conditions, with particular interests in different forms of DNA damage and genomic instability. His goal is to determine how the damage responses function in healthy conditions, how they become disrupted in pathological conditions including many forms of cancer, and how they can be targeted therapeutically to restore healthy conditions.

- Dr. Jesse Williams was recruited to the Department of Integrative Biology and Physiology (IBP) and the Center for Immunology (CFI) in 2019. The overarching goal of his laboratory is to understand mononuclear phagocyte heterogeneity and function in cardiovascular and metabolic disease. His group focuses primarily on mechanisms regulating monocyte trafficking, macrophage differentiation within tissues, and cytokine production with the intention to identify therapeutic targets to combat systemic chronic inflammation.

- Dr. Julia Liu was recruited to the Department of Integrative Biology and Physiology (IBP) in 2020. Her lab studies the role of mitochondria in generating, signaling, and responding to cellular stress, particularly in cardiac and skeletal muscle. She currently focuses on the physiological impacts of dysregulated mitochondrial calcium, which plays a critical role in energy production as well as cell death.

- The Masonic Cancer Center (MCC), University of Minnesota is the only National Cancer Institute-designated Comprehensive Cancer Center in the Twin Cities now in its 23rd year of continuous support. At MCC, funded cancer research continues to increase, with over $85.6M in direct cost cancer related research funding in the past year. The CCRB is one of two MCC directed laboratory research facilities. This building was originally designed to house investigators two types of investigators; those with research focused on chemical synthesis and analysis and those

with fundamental work in cancer biology. This unique laboratory space has led to substantial progress in several fields with some examples noted below:

- Under the leadership of Irina Stepanov, PhD, we have created the new "Institute for Global Cancer Prevention Research". The Institute's deputy director is Dorothy Hatsukami, PhD. The goal of this institute is to prevent cancer through research, evidence-based practices and policy changes with three focus areas: tobacco control, environmental causes of cancer and infectious agents and cancer. The initial funding for this institute was provided by the Masonic Cancer Center (MCC), School of Public Health and Medical School at the University of Minnesota. The investigators have already been successful in getting outside funding for their research and a major focus of this global health outreach is based on the analytical biochemistry capabilities that were constructed in the original building design.
- A new multi-PI grant (UG3CA265791) is led by Heather Nelson, PhD, Lisa Peterson, PhD, and Jen Poynter, PhD. The work will focus on three exposures of concern in the state of Minnesota (radon, perfluoryl alkyl substances (PFAS) and glyphosate) and includes partnership with community groups. The long-term goal of the work is to determine whether these exposures of concern are contributing to the excess rates of hematologic cancers in our catchment area. The successful receipt of this grant is directly due to the analytical biochemistry capabilities housed within the CCRB as noted above.
- The laboratory of Branden Moriarity, Ph.D. focuses on genetic engineering to develop T cells with enhanced efficacy in these mechanically complex tumor microenvironments, are poised to make a significant impact in the areas of immune and stromal engineering for enhanced cancer therapy. His work, along with other MCC members, forms the basis of a novel clinical trial "A Study of Metastatic Gastrointestinal Cancers Treated With Tumor Infiltrating Lymphocytes in Which the Gene Encoding the Intracellular Immune Checkpoint CISH Is Inhibited Using CRISPR Genetic Engineering (NCT04426669). In this phase 1 clinical trial, Dr. Moriarity's laboratory is evaluating tumors resected from patients with metastatic colon cancer, identifying immunogenic antigens to select a genetically modified T-cell clone (created in the University's Molecular and Cellular Therapy facility) for administration back to the patient. This ongoing trial shows promise and we are currently discussing expansion of this novel gene modified T-cell study to patients with metastatic lung cancer.

Three year total research expenditures for investigators in CCRB have been $106.5M.

<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 fourth 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 at the beginning of 2020 showed 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 at that time 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)

MRF in the time of the COVID-19 Pandemic

By early spring of 2020, the growing COVID-19 pandemic had forced MRF investigators to restrict their research programs to working remotely with scheduling of critical lab work under conditions that protected the safety of faculty, students and staff. Highlights of essential COVID-19 MRF investigators who redirected their research and activities to responding to the pandemic include the following:

- Identifying rationale treatment strategies for COVID-19 pneumonia: Haase/Schacker/Klatt labs
- Identifying drugs that might be repurposed to treat COVID-19 pneumonia: Langlois and Hunter labs
- Developing serological tests to detect SARS-CoV-2 infection: Jenkins and Herschhorn labs
- Developing a test for antibodies that neutralize SARS-CoV-2: Bold lab
- Developing a T cell vaccine to broadly protect against SARS-CoV-2 and variants: Masopust and Jenkins labs
- Collection, processing and storage of samples for clinical COVID-19 research: Bold/Southern/Schacker
- Processing clinical samples for SARS-CoV-2 PCR diagnosis tests: Langlois lab

Three year total research expenditures for investigators in MRF have been $43.5M. In addition, State Covid-19 research and testing for FY20 and FY21 was $57M.