Biomedical Sciences Research Facilities Funding Program

2014 Report to the Minnesota State Legislature

January 15, 2014

UNIVERSITY OF MINNESOTA

OVERVIEW

The University of Minnesota has established the goal of becoming one of the top public research institutions in the world. To achieve this goal, the University needs new, state-of-the-art biomedical research facilities to support leading-edge research and to attract and retain top tier research faculty.

To assist with 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, will allow the University to attract and retain the nation's top research talent.

The State established the $292 million Minnesota Biomedical Research Facilities Funding Program in 2008. This dedicated funding program provides 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 now known as the Biomedical Discovery District (BDD). The State's portion of the funding program is $219 million; while the University's portion is $58 million.

PROGRESS TO DATE

Since the program was established, the University has made significant progress:

- Project #1 – Expansion of the Center for Magnetic Resonance Research – Completed July 2010
- Projects #2 & #3 – Cancer and Cardiovascular Research Facility - Completed July 2013; occupied beginning in September 2013
- Project #4 – Microbiology Research Facility – In design; occupancy scheduled for late fall 2015.

When the final project is completed, these four projects will provide 425,700 gross square feet of new research space housing 79 faculty and 746 research support staff.

The Cancer and 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 the broader University community, including:

- Microscopy and specialized imaging facilities
- Biomedical genomic facilities
- Animal genetics facilities
- Long term testing laboratories
- Flow cytometry facilities.

One of the core principals in the planning and design of the Biomedical Discovery District has been the importance of collaboration in developing new and innovative approaches to research. The new research environment encourages interaction among interdisciplinary teams, and the facilities allow for creative and flexible design of lab space. Enabling researchers from different fields of research to collaborate with each other will lead to breakthrough thinking that would not have been possible in a traditional siloed research environment.

The buildings have already helped the University secure additional research dollars in areas such as brain mapping, where our facilities have placed us at a significant advantage over other institutions.

When the Microbiology Research Facility is completed and the Cancer-Cardiovascular Research Facility fully occupied, the Minnesota Biomedical Research Program will have provided an estimated 3100 construction jobs and will house 825 faculty and research staff in the Biomedical Discovery District.

Project	Construction Jobs	Principal Investigators	Other researchers/staff	Minnesota Biomedical Research Program Total
Center for Magnetic Resonance Research	560	10	90	660
Cancer- Cardio Vascular Research	1630	43	350	2023
Microbiology (predicted)	900	26	208	1134
District support staff			98	98
TOTAL	3090	79	746	3915

Summary of Appropriation Spending & Research Programs

Project # 1 - Center for Magnetic Resonance Research

Research Programs: The University of Minnesota's Center for Magnetic Resonance Research (CMRR) is now one of the top imaging facilities in the world. In the last two decades, advanced imaging techniques, including magnetic resonance imaging (MRI) and Positron Emission Tomography (PET) have come to play an indispensable role in biomedical research. Advances in imaging technology and capabilities have made an impact on every discipline and department in the Medical School, as well as research and clinical practice in other health sciences schools such as pharmacy, nursing and veterinary medicine. These technologies have also been leveraged in departments outside of the health sciences including Mathematics, Electrical Engineering, Biomedical Engineering, Nanotechnology, Chemistry, and Economics.

2013 was another banner year for the CMRR facility.

Highlights include:

- The long-awaited **10.5T MRI** was delivered in December 2013. The 110-ton whole body imaging magnet was ordered in 2009. The magnet is the world's most powerful whole body MRI to date and is housed in a 600-ton iron-shielded box built during the CMRR Expansion construction. The scanner will be used to create detailed maps of the human brain and body, showing brain structures with an expected resolution of a half-millimeter or less. The magnet should be ready for pre-clinical research in July 2014.

- Interdisciplinary and interdepartmental collaborative work done within CMRR was the basis for receiving a University of Minnesota Infrastructure Investment Initiative Award to fund a **new 3T MRI system**. The new scanner is located in shell space built during the CMRR expansion and was operational January 2013. This scanner has vastly improved access to imaging services to University researchers, as well as community medical practices and medical device manufacturers.

- CMRR continued to lead **global advanced neuroscience research** through ground-breaking research and leadership on the Human Connectome Project, a five-year initiative funded by the National Institutes of Health Blueprint for Neuroscience Research. This grant will help researchers comprehensively map human brain circuitry, which will yield information about brain connectivity and its relationship to genetic, environmental and behavioral factors. In addition to the original grant and two supplements, a new Lifespan project was awarded in October 2013 to study brain circuitry differences across age groups. This award relies on facilities and equipment funded through the CMRR Expansion.

- CMRR's leadership in neuroscience imaging is playing a major role in President Obama's **Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative**. In March 2013, Kamil Ugurbil, Director of CMRR, was appointed to the BRAIN Working Group, which was charged with articulating the short-, mid- and long-term scientific goals for achieving the vision of the BRAIN Initiative, as well as developing a scientific plan. CMRR hosted the BRAIN Working Group session in August 2013, which included four hours of presentations from top scientists from across the globe. In that same month, U.S. Senator Amy Klobuchar hosted a roundtable discussion on the BRAIN Initiative which was attended by community groups, local media, the general public and University researchers and staff. These events, and other research, education and community events, were made possible with expanded CMRR facilities for large group meetings.

- A **Radiochemistry Lab,** capable of producing novel radioisotopes for preclinical and clinical studies, was completed in November 2013. This lab was envisioned during the planning of the CMRR Expansion, but due to funding considerations, was omitted from the final building design. Additional funds were subsequently identified from foundation gifts and internal funds. This lab will capitalize on major BDD investments in PET scanners as well as the existing cyclotron facility and CMRR building infrastructure. The lab will begin producing radioisotopes for preclinical research in February 2014.

- The investment in CMRR continues to **expand beyond the building** to the greater University community, as well as Minnesota, U.S. and global communities.
    - In 2013, 378 University researchers, including 108 Principal Investigators, utilized CMRR facilities.
    - Several major Minnesota-based medical device companies began research collaborations with CMRR for device testing across the product development lifecycle, including prototype testing, preclinical research and clinical research.
    - On a global scale, patent filings and technology licensing saw significant activity. In 2013, CMRR researchers and their collaborators filed 7 nonprovisional and 4 provisional patents. In August 2013, a 15-patent package, authored by CMRR faculty, was licensed to a multinational conglomerate. Finally, a CMRR-developed multiband accelerated EPI MRI imaging program was distributed and supported without charge to 98 research and clinical imaging sites worldwide.
    - The cyclotron facility, leased and operated by PETNET Solutions, a wholly owned subsidiary of Siemens Healthcare, rolled out clinical production of Amyvid, an FDA-

approved PET scanning radiopharmaceutical. This compound is a diagnostic tool for Alzheimer's disease and is available to PET imaging centers at the University of Minnesota and throughout the Twin Cities.

Total Cost = $51.5 million, including $14 million for research magnets and imaging equipment

- Square Feet = 62,000 GSF
- Research Dollars = $5,322,866 for the entire CMRR facility in FY 2013

Projects # 2 & 3 – Cancer and Cardiovascular Research Building

Research Programs: With the opening of the Cancer and Cardiovascular Research Building (CCRB) in September 2013, the Masonic Cancer Center and the Lillehei Heart Institute have to date moved 31 faculty researchers and their research teams (254 individuals) into the new facility. Space has been reserved for an additional ten to twelve faculty researchers who are currently being actively recruited to join the University.

The benefits of the CCRB extend beyond the walls of the building. These researchers are teaming with colleagues from throughout the University and around the world to move discoveries forward, and to fast track the timeline of bringing new cures from the lab to patients in need.

Cancer and cardiovascular researchers at the University have seen significant success with new lines of investigation and discovery in recent years.

Highlights include:

- Cancer specialists from the Masonic Cancer Center, University of Minnesota, have launched a Phase 1 clinical trial designed to assess the toxicity of **Minnelide, a University of Minnesota-developed drug that has successfully disrupted pancreatic cancer development in laboratory tests**. The drug is a type of injectable chemotherapy designed to target tumor cells. The drug works by inhibiting a heat shock protein, HSP 70, which has been proven to aid the growth of tumor cells. By stopping HSP 70 from working, Minnelide disperses the cells integral to the tumor's growth and the cancer disintegrates.

- Masonic Cancer Center researchers continue to pioneer research within the field of **immuno-based therapies**, particularly in the area of using the body's natural killer (NK) cells against cancer. NK cells help make up our immune system and, in part, can recognize cancer and destroy cancerous cells before they can lead to problems. An interdisciplinary team within the Masonic Cancer Center lead projects that have led to new cancer therapies and treatment options for hundreds of patients in clinical trials for conditions such as acute myeloid leukemia and ovarian cancer. Future goals include engineering large numbers of NK cells with anti-tumor and antiviral receptors to provide off-the-shelf products for cancer treatments.

- **Masonic Cancer Center researchers have found new genetic links to infant leukemia**, which will likely provide new insights into identifying both the causes of infant leukemia and new treatment strategies. After examining the entire coding DNA in healthy cells of 23 infant leukemia patients and their mothers, they found the infants had an enrichment of potentially harmful variants in their healthy DNA making them especially susceptible to developing the disease.

- Recent research out of the Lillehei Heart Institute has shown that by turning on a single gene, Mesp1, different cell types including the heart, blood and muscle can be created from stem cells. Stem cell researchers have been trying to generate different cell types for regenerative medicine for years. Now, by understanding what Mesp1 does, researchers are more likely to make different cell types from stem cells more efficiently and **Lillehei Heart Institute faculty have pushed modern medicine one step closer to using stem cell technology for regenerative medicine**.

- Researchers at the University of Minnesota's Lillehei Heart Institute have combined genetic repair with cellular reprogramming to generate stem cells capable of muscle regeneration in a mouse model for Duchenne Muscular Dystrophy (DMD). The research, which provides proof-of-principle for the feasibility of combining induced pluripotent stem cell technology and genetic correction to treat muscular dystrophy, could **present a major step forward in autologous cell-based therapies for DMD** and similar conditions and should pave the way for testing the approach in reprogrammed human pluripotent cells from muscular dystrophy patients.

- Investigations are underway at the Masonic Cancer Center, University of Minnesota, to **determine the level of nicotine and toxin exposures caused by the use of e-cigarettes**, a category of products with no established baseline. E-cigarette use has doubled in just the last three years, with sales for 2013 expected to reach $1.6 billion worldwide. Many users have begun supplementing or substituting regular cigarette use with these products, in an attempt to cut back on toxicants. This will be one of the first major research projects designed to determine whether e-cigarettes are safer or limit exposure to toxicants.

Total Cost = $180.7 million

- Square Feet = 274,000 GSF
- Current Research Funding of Faculty in the Facility
  - Masonic Cancer Center: $10,641,194
  - Lillehei Heart Institute: $ 7,413,070

Project #4 – Microbiology Research Facility

Research Programs: The Microbiology Research Facility (MRF) will house and facilitate research by faculty in the Medical School's Department of Microbiology as well as faculty drawn from many disciplines, colleges and schools throughout the University. Researchers in this building will focus on better ways to treat, cure and prevent infectious diseases. The building will be home to faculty in Microbiology, Immunology, Infectious Diseases, and Drug and Vaccine Discovery, and will promote and enhance collaboration among all of these teams. The new building will also provide "hotel" lab space for

investigators wanting a collaborative environment for specific research projects. This type of research space will support the state's interest in "facilitating research collaboration between the University of Minnesota and other private and public institutions in this state." (Minnesota Statutes 2013, Sec 137.61: Purpose, Biomedical Science Research Funding).

The main emphasis of the work in the Microbiology Research Facility will be on particularly deadly illnesses such as HIV/AIDS/TB and fungal diseases that extract an enormous toll on life and health worldwide. Researchers will also take on microbiological problems such as antibiotic-resistant bacteria and viruses that cause cold sores and life-threatening infections in transplant recipients.

Research will include:

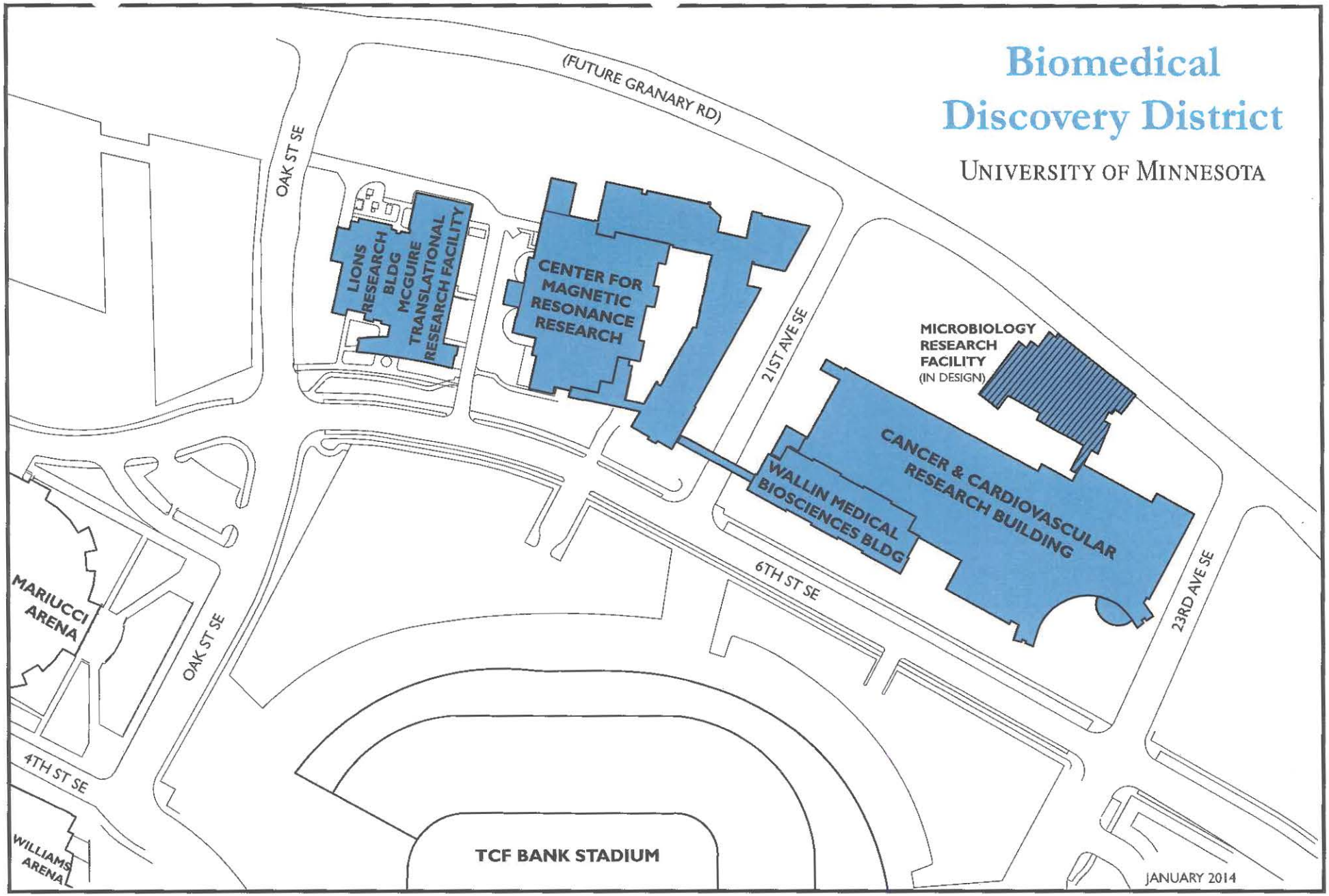
- Research to design new, targeted treatments for M. tuberculosis.
- Efforts to understand iron acquisition mechanisms of Bordetella pertussis, the bacterial agent of pertussis or whooping cough.
- A project aimed at improving treatment strategies, counter drug resistance, and improved drug susceptibility testing for tuberculosis.
- An investigation into the genetic basis of pheromone-inducible transfer of antibiotic resistance plasmids in Enterococcus faecalis.
- An analysis of HIV Reservoirs and Immune Reconstitution to help design more effective treatments.
- Research around how microbial communities co-evolve with the chemical environment of the Cystic Fibrosis airways to better understand the disease and potentially develop new therapeutic targets.

The Microbiology Research Facility will begin construction in February 2014 with occupancy planned for late fall 2015. The 89,700 gross square foot facility is budgeted to cost $59.8 million.

Attachments:

- Map of the Biomedical Discovery District

- "Margin of Excellence," Medical Bulletin, Fall 2013, published by the University of Minnesota Medical School and Foundation


Biomedical
Discovery District
UNIVERSITY OF MINNESOTA
(FUTURE GRANARY RD)
OAK ST SE
LIONS RESEARCH BLDG
MCGUIRE TRANSLATIONAL RESEARCH FACILITY
CENTER FOR MAGNETIC RESONANCE RESEARCH
21ST AVE SE
MICROBIOLOGY RESEARCH FACILITY
(IN DESIGN)
CANCER & CARDIOVASCULAR RESEARCH BUILDING
WALLIN MEDICAL BIOSCIENCES BLDG
6TH ST SE
23RD AVE SE
MARIUCCI ARENA
OAK ST SE
4TH ST SE
WILLIAMS ARENA
TCF BANK STADIUM
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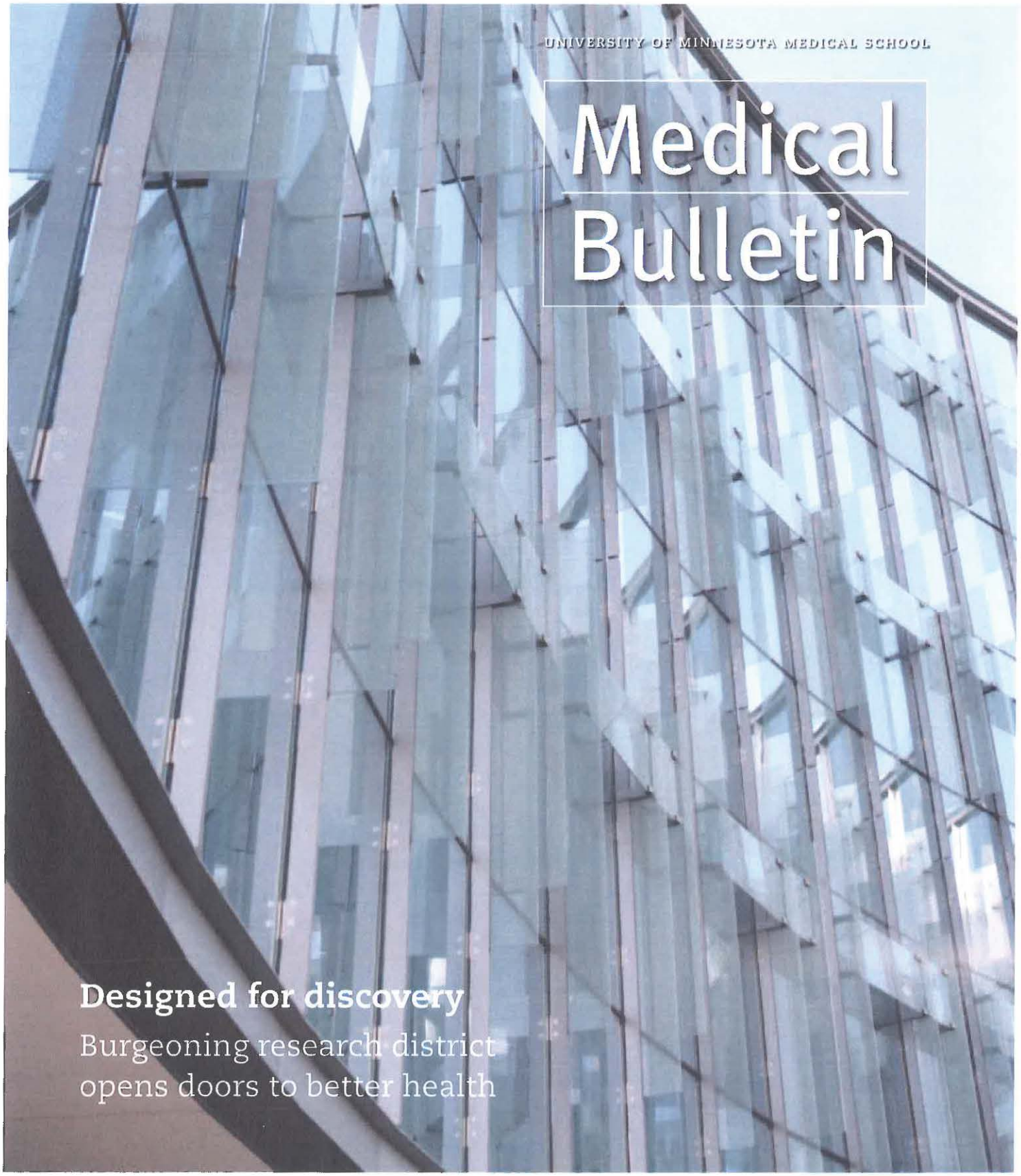
UNIVERSITY OF MINNESOTA MEDICAL SCHOOL

Medical Bulletin



Designed for discovery

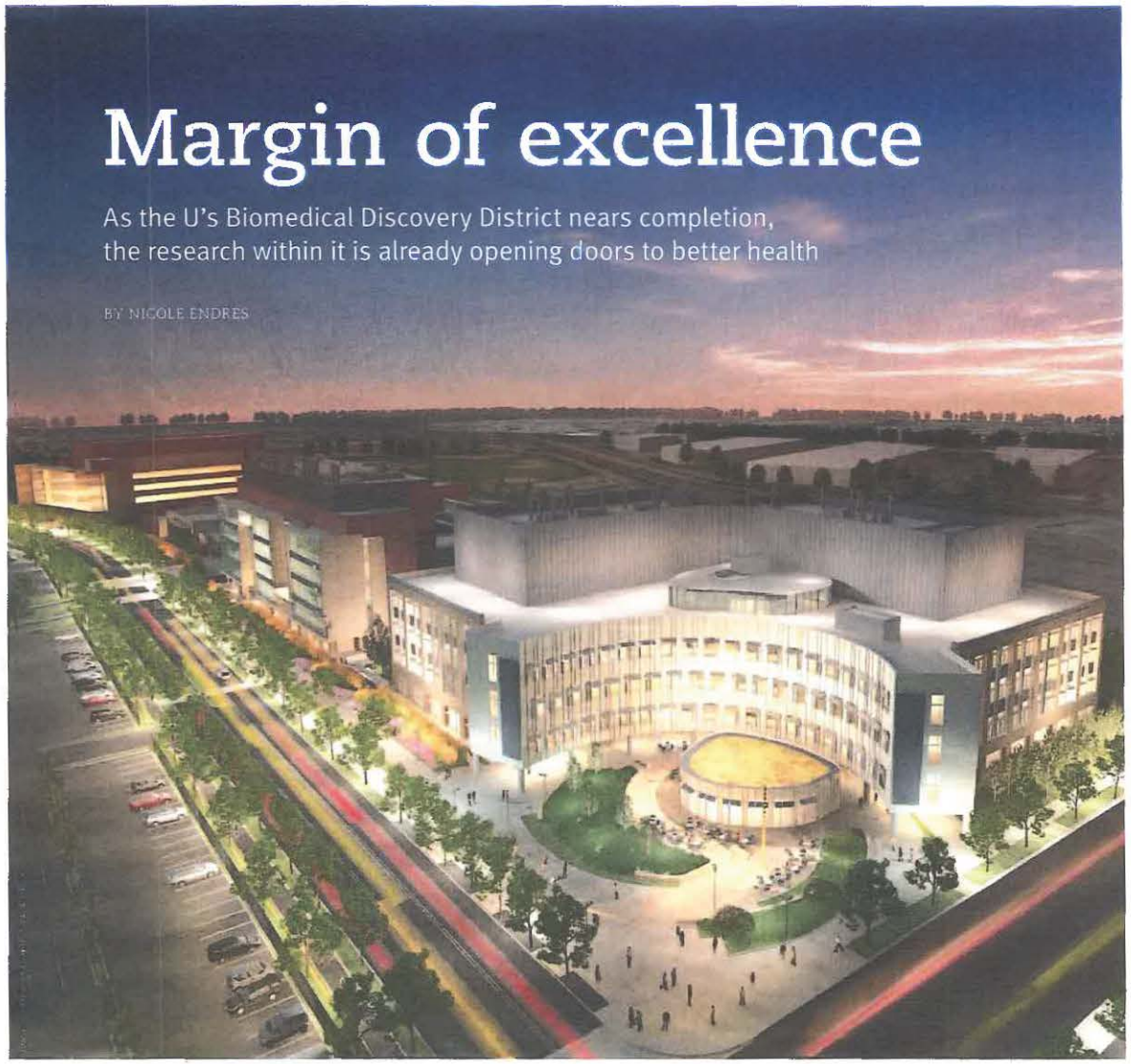
Burgeoning research district opens doors to better health

FALL 2013 What happens to kids when a parent goes to prison? ▭ Pioneering center maps a new frontier—the human brain ▭ New admissions deans focus on the right student mix

Margin of excellence

As the U's Biomedical Discovery District nears completion, the research within it is already opening doors to better health

BY NICOLE ENDRES



In a state with a thriving biosciences industry and rich history of innovation, it only made sense for the 2008 Minnesota Legislature to invest in a state-of-the-art research park at the University of Minnesota. The Biomedical Discovery District's six buildings—the last one will open in 2015—will provide 700,000 square feet of space for more than 1,000 investigators and personnel to collaborate on research leading to lifesaving discoveries in cancer, cardiovascular diseases, diabetes, brain sciences, vision, hearing, immunology, and infectious diseases.

PHOTO: SCOTT STREBLE

THE FULL SPECTRUM

Research in the Biomedical Discovery District covers the lifespan and a wide range of diseases.

MOLECULAR TO CELLULAR, CARDIOLOGY TO NEUROLOGY

Working across disciplines ensures that even small discoveries in one area have the maximum impact on research happening throughout the district.

Accelerating discovery

A groundbreaking idea can come from anywhere—from silence, from a brainstorm, from a chance encounter with someone new. That's why the Biomedical Discovery District purposefully incorporates flexible, open laboratory spaces and common areas for those who work there: to make collaboration easier. By sharing knowledge and building one another's discoveries, basic science researchers and clinicians working side by side here can find new treatments for some of today's most challenging and complex health conditions, faster than ever before.

IMAGE: COURTESY OF BMBR

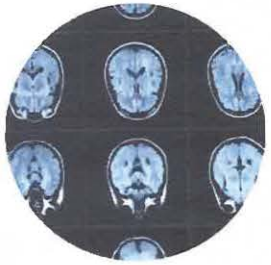
By clustering and interconnecting all buildings in the Biomedical Discovery District—including the 80,000-square-foot Microbiology Research Facility (6), now under construction—the University is maximizing resources and fostering collaboration among disciplines.

1 LIONS RESEARCH BUILDING

Built in 1992 as the initial anchor to the Biomedical Discovery District, this facility is home to researchers focused, for example, on creating a brain cancer vaccine, understanding and treating age-related hearing loss, and examining how changes in the eye can cause macular degeneration.

2 McGUIRE TRANSLATIONAL RESEARCH FACILITY

Scientists in this building, which opened in 2005, are devoted to "translational research," which bridges basic science discoveries and breakthrough clinical care. It houses the Stem Cell Institute (led by Jakub Tolar, M.D., Ph.D.), Orphan Drug Center, and Center for Infectious Diseases and Microbiology Translational Research.



3 CENTER FOR MAGNETIC RESONANCE RESEARCH

Opened in 1999 and expanded in 2010, this internationally acclaimed center contains some of the most powerful human and animal imaging magnets in the world, upholding its reputation as the preeminent center of its kind. It also houses the Center for Clinical Imaging Research, where both research and patient care happen.

4 WINSTON AND MAXINE WALLIN MEDICAL BIOSCIENCES BUILDING

Named in honor of two steadfast University supporters, this is home to world-leading research into Alzheimer's disease (led by Karen Hsiao Ashe, M.D., Ph.D.), ataxia, muscular dystrophy, and other neurodegenerative disorders, as well as the Center for Immunology, where investigators are figuring out how to help the immune system fight off disease.

5 CANCER AND CARDIOVASCULAR RESEARCH BUILDING

Designed as the gateway to the Biomedical Discovery District, this building, which opened in June, features advanced laboratories, instrumentation, and support facilities for research programs focused on cancer prevention, genetic mechanisms of cancer, tumor biology, vascular biology, heart tissue repair, and hypertension. Its first floor is open to the public.

BY THE NUMBERS

12

Football fields worth of state-of-the-art research space in the Biomedical Discovery District

50

Years since the University campus has seen an expansion this large

40

Millions of dollars the Biomedical Discovery District is expected to attract in new annual research funding

4

Displays of public art incorporated into the district's design

WEB EXTRAS

Visit www.give.umn.edu/mb/bdd to find:

- an interactive map of the BDD
- a special feature about the district's public art
- video interviews with cancer expert David Largaespada, Ph.D., about the new labs, and a family that has participated in BDD research

To learn how you can support research in the Biomedical Discovery District, contact Patricia Porter at 612-626-6703 or pkporter@umn.edu.

Fulfilling the promise

At the very core of the Biomedical Discovery District is translational research—bringing breakthroughs in the laboratory to patients as quickly as possible. Ultimately, that's the value of the work that happens here. And that's the goal driving the University's best and brightest thinkers to keep pursuing better treatments and cures.

PHOTO: SCOTT STEELE

PHOTO: SCOTT STEELE

PART OF THE SOLUTION

The world-renowned Center for Magnetic Resonance Research specializes in pushing the limits of imaging technologies to get previously unattainable information. Using the center's high-field spectroscopy technologies and expertise, Gülin Öz, Ph.D., and colleagues James Cloyd, Pharm.D., and Paul Tuite, M.D., found that a natural product that's available over the counter increases antioxidant levels in the brains of people who have Parkinson's disease—which could eventually slow the course of the disease. Öz says the medication needs further study, "but it could be part of the solution and keep patients healthy a little longer."

EXPONENTIAL IMPACT

Working in the University-affiliated Adult Congenital and Cardiovascular Genetics Center, Cindy Martin, M.D., sees how heart and blood vessel abnormalities affect her patients' quality of life. And through her lab investigations in the new Cancer and Cardiovascular Research Building, she aims to make their lives better. Martin acknowledges that she's just one physician and can treat only a finite number of patients. "But the beauty of science and innovation," she says, "is that what we can potentially discover has the capacity of logarithmically affecting people."

A SPECIAL CONTRIBUTION

Ten-year-old Caroline Schlehuber remembers the day that she and her mother volunteered to have a "cookie cutter" punch small skin samples out of their arms. Caroline summoned her bravery to make a donation to stem cell research focused on type 1 diabetes at the University with a larger goal in mind: "In any way I can, I always want to help find a cure." Mom Michelle takes pride in the tiny scars that she and Caroline took away from the experience. "She and I both have that badge of honor that we contributed in a very unique way," she says of the research, which will use stem cells made from skin samples to look for clues about why some people develop diabetes while their relatives don't. "We have high hopes for the work they're doing."

PHOTO: BRADY WILLETTE

PHOTO: JIM BOVIN

LOCATION, LOCATION, LOCATION

For cancer geneticist David Largaespada, Ph.D., moving into the new Cancer and Cardiovascular Research Building means moving into a better "scientific neighborhood" in which to conduct his work. "We have a world-class imaging facility near us, we have immunologists, we have cancer chemistry, we have cancer genetics—all in one place," he says. "I think this will be a fantastic, synergistic environment for new research that will allow us to take the best and most logical steps [toward therapies for] human patients. Given how difficult and time-consuming and expensive it is to do that, we must take the absolute best steps and the best shots we can when we bring something to the clinic."

PHOTO: JIM BOVIN