

POSITION AND CANDIDATE SPECIFICATION



MEDICAL COLLEGE OF WISCONSIN

CHAIR, ANESTHESIOLOGY

Prepared by: Mark I. Furman, M.D.
Deborah Prothrow-Stith, M.D.

Assignment: 16777-005

Date: November 2015

Confidential: This document and the information contained within is confidential and is provided to the named recipient. This information has been prepared in good faith by Spencer Stuart but may require future verification or correction. Distribution or reproduction of this document and/or its contents is strictly prohibited.

Amsterdam
Atlanta
Barcelona
Beijing
Bogota
Boston
Brussels
Budapest
Buenos Aires
Calgary
Chicago
Copenhagen
Dallas
Dubai
Frankfurt
Geneva
Hong Kong
Houston
Istanbul
Johannesburg
London
Los Angeles
Madrid
Melbourne
Mexico City
Miami
Milan
Minneapolis/St. Paul
Montreal
Moscow
Mumbai
Munich
New Delhi
New York
Orange County
Paris
Philadelphia
Prague
Rome
San Francisco
Santiago
Sao Paulo
Seattle
Shanghai
Silicon Valley
Singapore
Stamford
Stockholm
Sydney
Tokyo
Toronto
Vienna
Warsaw
Washington, D.C.
Zurich

SpencerStuart

Page 1

POSITION SPECIFICATION

MEDICAL COLLEGE OF WISCONSIN

The Medical College of Wisconsin (MCW) is a private, academic institution whose mission is to be a national leader in the education and development of the next generation of physicians and scientists; to discover and translate new knowledge in the biomedical sciences; to provide cutting-edge, interdisciplinary and compassionate clinical care of the highest quality; to improve the health of the communities we served. MCW and its key clinical affiliates, Froedtert Hospital and the Children's Hospital of Wisconsin, are located on a beautiful, fully integrated campus in west suburban Milwaukee.

MCW began as the Wisconsin College of Physicians and Surgeons, founded on May 20, 1893. The following year, the Milwaukee Medical College opened. On January 14, 1913, the Wisconsin College of Physicians and Surgeons and the Milwaukee Medical College merged to become the Marquette University School of Medicine. On September 30, 1967, Marquette University, due to financial constraints, terminated its sponsorship of the medical school. The name was changed on October 14, 1970, to the Medical College of Wisconsin.

As of 2015, there are more than 1,200 students pursuing M.D., Ph.D., M.S., M.P.H. and M.A. degrees. In addition, there are more than 670 physicians and 250 physician fellows in residency and fellowship training.

The MCW Medical School in Milwaukee and new campuses in Green Bay and Central Wisconsin provide an innovative, rigorous and immersive curriculum that prepares our graduates with a deep understanding of the healthcare needs in their communities. MCW-Green Bay opened in July 2015. MCW-Central Wisconsin is targeted for a July 2016 opening.

AFFILIATED HOSPITALS

MCW physicians and practitioners see patients at three major affiliates – Froedtert Hospital, Children's Hospital of Wisconsin, and the Zablocki VA Medical Center – and many other hospitals and clinics in Eastern Wisconsin, including Community Memorial Hospital in Menomonee Falls and St. Joseph's Hospital in West Bend.

Approximately 1,510 Medical College of Wisconsin physicians and approximately 600 nurse practitioners, physician assistants, and other healthcare practitioners care for more than 500,000 patients, representing more than 2.2 million patient visits annually.

**For additional information about each hospital, please see Appendix A.*

MEDICAL COLLEGE PHYSICIANS AND CHILDREN'S SPECIALTY GROUP

The MCW has two physician practices - Medical College Physicians and Children's Specialty Group. Medical College Physicians (MCP) is MCW's adult physician group practice, which consists of physicians providing care in every specialty of medicine and is one of the largest academic practices in the United States. Children's Specialty Group (CSG) is a joint venture of MCW and Children's Hospital of Wisconsin and consists of specialty physicians providing care to children.

MCW physicians also teach, conduct research and collaborate with other faculty scientists to develop new ways of preventing and treating diseases. Patients of Medical College Physicians and Children's Specialty Group have access to some of the finest, most advanced care available.

RESEARCH AT MCW

As a major national research center, MCW faculty received more than \$154 million in external support for research, teaching, training and related purposes in fiscal year 2013-2014, of which \$138 million was for research. In the federal government's FY 2014, MCW received approximately \$79.5 million in NIH funding and ranked 46th among the nation's 137 medical schools receiving NIH research funding. This represents dramatic growth and development over the past 15 years, with the formation of extremely strong basic science and clinical departments leading to a tremendous improvement in NIH ranking. More than 2,500 research studies, including clinical trials, were conducted in FY 2013-2014. Nearly 1,450 scientific papers by MCW faculty are published in peer-reviewed medical journals.

MCW, together with eight institutions in Southeastern Wisconsin, is the lead institution for the Clinical Translational Science Institute (CTSI). NIH awarded a \$20 million grant to CTSI. The five-year award is being used to create a borderless, synergistic biomedical research enterprise that will accelerate the translation of research discoveries into new and improved medical treatments.

**For additional information about research at MCW, please see Appendix A.*

COMMUNITY ENGAGEMENT

MCW invests significantly in expanding its community mission to build strategic community-academic partnerships that have the greatest impact on Wisconsin's most critical health needs. More than 280 faculty are involved in more than 480 community outreach activities to advance public and community health in the metro Milwaukee area and throughout Wisconsin, according to a campus-wide survey conducted in 2015 by the Office of the Senior Associate Dean for Community Engagement.

**For additional information about community engagement, please see Appendix C.*

DEPARTMENT OF ANESTHESIOLOGY

Clinical Services

The Department of Anesthesiology at MCW is one of the largest in the United States with 132 faculty members and 13 additional physicians in the community division. Established in 1957 as a division of the Department of Surgery, Anesthesiology became an independent department in 1965. Since then, the scope of resident and fellowship training, research, and patient care have continually increased. Affiliated clinic sites include Froedtert Hospital, Children's Hospital of Wisconsin (CHW), Zablocki Veterans Administration Medical Center (VAMC), Wheaton Franciscan St. Joseph's Hospital, Community Memorial Hospital, Froedtert Surgery Center, Surgery Center of Greater Milwaukee, Menomonee Falls Surgery Center, the Medical College of Wisconsin Pain Management Center, and the Reproductive Medicine Clinic. Additionally, faculty staff a pain clinic at the VAMC, a pediatric pain medicine clinic at CHW, and two intensive care units. The number of anesthetic administration conducted by the faculty exceeds 63,000 annually, providing an excellent educational environment. Unique cases in patients with significant comorbidities are commonplace at the hospitals. The anesthesiologists manage more than 100 anesthetizing locations on any given day, considering all affiliate hospitals, operating rooms, and out-of-the-OR locations.

Education and Training

The resident class size is 22 per year, and the department offers 17 categorical positions a year. An ACGME-approved combined Medicine/Anesthesiology and Pediatric/Anesthesiology residencies complete the traditional training program. ACGME-approved fellowships include pediatric anesthesia (8 fellows), pain medicine (4 fellows), a combined 2-year pediatric anesthesia/pain medicine (1 fellow), cardiac anesthesia (1 fellow), critical care (2 fellows), and OB anesthesia (1 fellow). In addition, fellowships are available in neuroanesthesia and patient safety/quality. The total number of house staff at any time approaches 100.

The education team includes an educational specialist with a PhD degree, supported by three coordinators. Each year, typically 10% to 15% of the fourth year medical school class (~ 205 students) at MCW enters anesthesiology residencies. The department provides the largest number of students choosing anesthesia of any medical school in the U.S.

The Department of Anesthesiology offers simulation programs for medical students, interns, residents, fellows, team training and workshops. Additionally, the Medical College of Wisconsin Anesthesia Simulation Program is offering simulation courses to fulfill the

training requirement for Part IV (Practice Performance Assessment & Improvement) of Maintenance of Certification in Anesthesiology Program (MOCA®).

Master of Science in Anesthesia

The MCW recently announced a new, 28-month, Master of Science in Anesthesia – Anesthesiologist Assistant Program, the first program in the state, and one of only 11 nationwide, to train anesthesiologist assistants, who will work under the direction of leading physician anesthesiologists after graduation. The program is anticipated to welcome its inaugural class in August of 2016, with a capacity of 10 – 16 students.

The initial funding for the development of the new program is provided by a grant from the Advancing a Healthier Wisconsin endowment (AHW). The AHW endowment, stewarded by MCW, has provided more than 300 awards totaling more than \$160 million to advance the health of Wisconsin through community health improvement, research and education.

Research

With a robust and international reputation, the research division fills greater than 20,000-square feet of research space at MCW and the VAMC. There are 12 basic scientists and 15 physician scientists who conduct basic science research. The department is perennially in the top ten for NIH funding and has had three members awarded the American Society of Anesthesiologists' Excellence in Research Award. In addition, the department has a large, active, program project grant for the study of myocardial ischemia and reperfusion injury, and an NIH T32 Training Grant that funds anesthesia residents and fellows who wish to pursue research training, providing a path for a productive academic career.

**For additional information about community engagement, please see Appendix D.*

SpencerStuart

Page 5

Position Summary

The Chair of Anesthesiology will create a platform for sustainable success in clinical and scholarly endeavors and provide sound fiscal leadership for the department that will afford the financial fuel necessary for success. All clinical department chairs within MCW are expected to work collegially with the other chairs and center directors at the school, as well as the leadership at the affiliated and partner hospitals.

The next Chair of Anesthesiology will be responsible for overseeing and maintaining excellence in the department's educational programs and growing significantly the clinical and research programs in collaboration with MCW and its affiliated hospitals. The position requires excellent interpersonal skills and the ability to bring together a diverse group of individuals to advance the common goals of the department and the institution. The successful candidate will be a strong leader and have a proven track record in administration, clinical care, education and research, as well as an acute understanding of the complexities of an academic Department of Anesthesiology and the ability to lead the further growth and development of the department in all missions.

Key Relationships

Reports to:	Joseph E. Kerschner, MD, Dean of the School of Medicine, Executive Vice President, MCW
Direct reports:	Faculty of the Department Department Administrator
Other key relationships:	Chairs of other clinical and basic science departments Senior leaders within the system Associate and Assistant Deans Adult Anesthesiology and Pediatric Anesthesiology Service Line Leadership

Major Responsibilities

- In collaboration with the leadership of MCW, define the mission and establish the strategic direction for the department, ensuring the necessary financial and human resources to achieve the agreed upon objectives.
- Provide the vision and leadership to achieve and maintain superior clinical programs within the Department of Anesthesiology. Work with the leadership of other departments and at the various clinical sites to build and grow areas of acknowledged excellence.

- Define and lead the department's research strategy by expanding basic, translational and clinical research. Support principal investigators and other faculty within the department in efforts to secure NIH and other grant funding to support research priorities. Ensure a deliberate investment into research activities and priorities within the department.
- Assure delivery of excellent clinical education and advanced training to the medical students, residents and fellows. Provide leadership and oversight to the residency and fellowship programs within the department.
- Supervise, prepare, implement and monitor the department budget that encompasses all funding sources and ensures compliance with grant, legislative and institutional guidelines. Effectively work to manage limited resources. Encourage ethical medical and financial practice across the department and support compliance activities as necessary.
- Recruit, hire, and retain outstanding faculty within specialty areas of anesthesiology. Ensure an atmosphere of support, collaboration and mentorship. Help monitor and develop the careers of junior faculty.
- Ensure alignment of individual goals with the mission, vision, strategy and goals of the department and institution.

CANDIDATE SPECIFICATION: KEY SELECTION CRITERIA

Ideal Experience

Candidates for the position of Chair of Anesthesiology will be selected from a pool reflecting gender/racial diversity and will be evaluated according to the following criteria:

- Clinical excellence within a subspecialty of anesthesiology.
- A record of personal academic accomplishments and credentials within Anesthesiology. The experience and reputation necessary to ensure the continuation and enhancement of the clinical, research, and educational missions of the department.
- A full appreciation of the factors that support the growth of research in an academic environment. Experience in leading or developing a successful research program.
- Demonstrated managerial and business acumen. Experience in and demonstrated knowledge of the complex financial pressures facing academic medical centers and

SpencerStuart

Page 7

healthcare delivery organizations today. Ability to manage a large and complex faculty and staff in a matrixed environment.

- Successful administrative and leadership experience at a highly performing healthcare organization or academic institution, such as a vice chair, division chief /division head or clinical or research program director. Experience in cultivating academic leaders through mentorship of trainees and development of junior faculty.
- An M.D., M.D./Ph.D. or an equivalent degree is required with an academic rank of Associate Professor or Professor. The candidate must be board certified in anesthesiology.

Critical Competencies for Success

Leadership: The successful candidate must possess the requisite leadership skills to take a strong clinical and research department to the next level of academic and operational excellence. The successful candidate will do this through:

- Developing and instituting a strong and impassioned vision for excellence in all aspects of the academic mission;
- Earning the respect and confidence of all who provide care in the perioperative environment;
- Understanding the current trends in the field of anesthesiology and the implications this has for a successful academic department; and by,
- Effectively managing across multiple sites.

Relationship Building: The successful candidate must be able to build strong relationships with others in an environment where MCW and the hospital are partners and where the department must collaborate with other departments to ensure mutual achievement. The successful candidate will:

- Have an outgoing but personable demeanor, an orientation towards strong collaboration, and create win-win relationships;
- Develop cohesiveness amongst individuals and groups across a large department, and bring together multiple diverse constituencies (physicians, surgeons CRNAs, anesthesia assistants) and align them in a common vision; and
- See the bigger picture of issues, as opposed to taking sides.

SpencerStuart

Page 8

Capacity building: The successful candidate must build and sustain outstanding programs. He/she will accomplish this through:

- Developing, in collaboration with other departmental and institutional leadership, clinical and research areas of expertise; and by,
- Recruiting, mentoring, and developing trainees and the next generation of superior faculty members.

Other Personal Characteristics

- A dynamic, highly credible leader.
- Highly developed skills and personal diplomacy; emotionally intelligent with absolute integrity.
- A consensus builder, yet decisive and bold.
- An effective communicator. Someone who is open, direct and favors transparency.
- Demonstrates grace under pressure.

SpencerStuart

Page 9

FOR FURTHER INFORMATION, PLEASE CONTACT:

Mark I. Furman, M.D.

Office telephone: 617.531.5701
Office fax: 617.531.5732
Mobile telephone: 508.361.3629
E-mail address: mfurman@spencerstuart.com

Assisted by: Kristy Morais
617.531.5707
kmorais@spencerstuart.com

Deborah Prothrow-Stith, MD

Office telephone: 617.531.5730
Office fax: 617.531.5732
Mobile telephone: 617.797.4844
E-mail address: dprothrowstith@spencerstuart.com

Assisted by: Tyler Huntington
617.897.3305
thuntington@spencerstuart.com

APPENDIX A – AFFILIATED HOSPITALS

Froedtert Hospital

Froedtert Hospital is the primary adult hospital affiliate of the MCW and is staffed by MCW physicians providing care in all medical specialties and sub-specialties. A 500-bed academic medical center, Froedtert delivers advanced care and is nationally recognized for exceptional physicians and nurses, research leadership, specialty expertise, and state-of-the-art treatments and technology.

Froedtert is a member of the University Health Systems Consortium (UHC) and in 2015 was ranked fifth in the 2015 The Bernard A. Birnbaum, MD, Quality Leadership Award – formerly the UHC Quality Leadership Award. This award is given to members that demonstrate excellence in delivering high-quality care based on five key organizational characteristics identified by the Quality and Accountability Study. Froedtert and MCW are at the forefront of new technology and care in many areas, including cancer, genetics, heart disease and stroke, brain injury and disorders, spinal cord injury, limb reattachment, epilepsy, gastrointestinal diseases, diabetes, hearing disorders, and women's health. Froedtert is recognized as high performing in six medical specialties. The transplant center is the only provider of all adult organ transplants (liver, kidney, pancreas, heart, and lung) in eastern Wisconsin. Froedtert has been awarded Magnet status – the highest award for excellence in nursing from the American Nurses Credentialing Center. In addition, both the National Research Corporation's Consumer Choice Awards and Truven Analytics recognized Froedtert as one of the best hospitals in the U.S.

Froedtert Hospital has been designated as a Level One Trauma Center by the American College of Surgeons, one of only two adult hospitals so recognized in Wisconsin. Froedtert's location in the Milwaukee MSA and its state-wide reputation contribute to it being the busiest Level 1 trauma center in the state, with over 68,000 emergency room visits and 2,900 trauma cases per year. Collaboration with emergency medical services (EMS) and Flight for Life crews offers patients rapid, safe transport to our expert care from across the Milwaukee region, state and beyond.

Children's Hospital of Wisconsin

MCW pediatric specialists are on the staff of the magnet status Children's Hospital, the principal pediatric hospital affiliate of MCW. Founded in 1894, Children's Hospital is the only Wisconsin hospital dedicated solely to the care of children, and serves children with all types of illnesses, injuries, birth defects and other disorders. Children's Hospital of Wisconsin is ranked all ten specialty areas in *U.S. News & World Report's* Best Children's Hospitals report in 2014-2015; #5 in Heart, #11 in Orthopaedics, #12 in Nephrology, #14 in Neurology and Neuroscience, #16 in Pulmonary, #18 in Urology, #19 in Gastroenterology, #21 in Neonatology, #26 in Diabetes/Endocrine, and #34 in Cancer. CHW also has a level 4 Epilepsy program and has one of only a few Level I trauma centers in the country devoted to pediatrics.

SpencerStuart

Page 11

Children's Hospital is one of the busiest pediatric hospitals in the nation. Last year, 24,085 infants, children and adolescents were admitted and 332,211 were seen in the hospital's specialty outpatient clinics and urgent care sites. The Emergency Department/Trauma Center treated 61,732 children, and 15,559 surgical procedures were performed at the hospital. An additional 9,292 surgeries were performed at the outpatient surgery center. In addition, the primary care clinics supported 241,897 patient visits.

More than 70 specialty clinics provide outpatient diagnosis and treatment for a wide variety of pediatric disorders. The Children's Hospital facility has 296 beds. Patient care units include a Pediatric Intensive Care Unit (72 beds), Neonatal Intensive Care Unit, Cardiac Intensive Care Unit, Cancer and Blood Disorders Unit, Epilepsy Monitoring Unit and Short Stay Unit.

Clement J. Zablocki VA Medical Center

MCW physicians are on staff at the Clement J. Zablocki VA Medical Center, a major hospital affiliate of MCW since 1946. The VA Medical Center provides 168 acute care hospital beds. Annually, it admits 6,400 patients and records more than 533,000 outpatient visits. It is one of the busiest and most comprehensive centers operated by the Department of Veterans Affairs. Approximately \$15.3 million in research (funded primarily by the VA and the NIH) is conducted by MCW faculty at the Zablocki VA Medical Center.

Community Memorial Hospital

Community Memorial Hospital (CMH) enjoys a national reputation of excellence as a provider of top quality health care services and has received many awards for innovations. CMH regularly rank as one of the top hospitals accredited by the Joint Commission on Accreditation of Healthcare Organizations.

APPENDIX B – PUBLIC AND COMMUNITY ENGAGEMENT

MCW invests significantly in expanding its community partnerships and building strategic community-academic relationships that have the greatest impact on Wisconsin's most critical health needs. More than 150 faculty are working with more than 100 diverse community groups to advance public and community health in the metro Milwaukee area and throughout Wisconsin.

The efforts of the MCW around public and community health is complemented by the Healthier Wisconsin Partnership Program, part of a special endowment to MCW of \$300 million from the State of Wisconsin dedicated to improving the health of the people of Wisconsin. The Program awards funding and supports community-medical school partnerships. During the first two funding cycles, 78 urban, rural, and statewide projects were funded for more than \$17 million, involving more than 100 community and MCW partners.

The Advancing a Healthier Wisconsin (AHW) Endowment launched its first funded initiatives in community health, research and education in 2004. The Endowment was established through funds resulting from the Blue Cross/Blue Shield United of Wisconsin's conversion to a for-profit corporation.

- As of May 2015, the Endowment's initial value of \$318 million has increased to more than \$400 million through MCW's stewardship.
- As of May 2015, the AHW Endowment has awarded more than \$175 million to more than 315 initiatives dedicated to improving the health of the people of Wisconsin.

Healthier Wisconsin Partnership Program

The Endowment supports community health improvement and community-academic partnerships through the Healthier Wisconsin Partnership Program:

- More than 155 community-based health initiatives have received funding to advance strategic interventions, health promotion and systems changes since 2004.
- These initiatives contributed to health improvement efforts in more than 45 of Wisconsin's 72 counties and more than 20 statewide initiatives.

Research and Education Program

Through the Research and Education Program, the AHW Endowment contributes to improved health through support for research discoveries and innovative educational initiatives:

SpencerStuart

Page 13

- More than 200 MCW faculty members have contributed to new discoveries in identifying genes underlying complex diseases, understanding and treating pancreatic cancer, and developing new technologies and methods for treating cardiac abnormalities, among other achievements.
- Funded the development of MCW's new medical school campuses in Green Bay and Central Wisconsin to help address the physician shortage in Wisconsin, as well as the development of a school of pharmacy to train the pharmacists of the future with a focus on interprofessional education and team-based care. In addition, support for innovative doctoral and master's degrees in public and community health increased professional development opportunities for public health professionals and researchers.

Oversight

The MCW Consortium on Public and Community Health provides stewardship for the AHW Endowment. It has authority over the 35 percent of the AHW Endowment funding dedicated for the Healthier Wisconsin Partnership Program and provides advice and comment on the 65 percent committed to the Research and Education Program. The MCW Consortium meets on a monthly basis and conducts itself in accordance with its bylaws and Wisconsin Open Meetings and Public Records Laws.

The Research and Education Advisory Committee serves as the oversight body for the Research and Education Program. In that capacity, the Research and Education Advisory Committee makes recommendations regarding the Research and Education Program's funding initiatives, application criteria, processes, program administration policies and ensures compliance with supplanting and other guidelines.

APPENDIX C – RESEARCH AT MCW

MCW has several Centers that greatly enhance research capacity. The Center for Imaging Research (**CIR**), directed by Shi-Jiang Li, PhD, facilitates collaboration between imaging scientists and clinicians at academic institutions within the Milwaukee region as well as nationally and internationally. In addition, it manages, develops, and maintains MCW's imaging facilities that include an ultra-high frequency GE High-Field Actively Shielded 7T/90-cm Whole-Body Imaging System - the first actively shielded GE 7T MRI scanner. It is currently one of only five GE 7T MRI scanners in North America. Other resources include a 3.0 T GE 750 MRI System, a 3.0 T GE Long-Bore Excite MRI System, a 9.4 T Bruker Biospec 94/30 USR In-Vivo Spectroscopy Imaging System, and a Gamma Medica MicroSPECT/CT, Preclinical Imaging System.

MCW was one of three institutions to develop fMRI in 1992. Since then, Froedtert and MCW have become international leaders in neuro-imaging, as reflected by more than \$44 million dollars in federal and foundation grants. Recently, MCW fMRI investigators have begun to apply innovative imaging techniques to diagnose and monitor patients with a variety of neurological and psychiatric disorders, including brain tumors, stroke, epilepsy, drug abuse, Alzheimer's disease, Parkinson's disease, Huntington's disease, attention deficit disorder, multiple sclerosis, head injury, post-traumatic stress disorder, visual disorders, gastrointestinal disorders, and schizophrenia.

Founded in 2004, the Children's Research Institute (CRI) is a collaborative effort between MCW and Children's Hospital of Wisconsin (CHW) to advance state-of-the-art pediatric health care practice through dedicated laboratory and clinical research. Through scientific discovery, CRI seeks to prevent and cure disease while improving the health outcomes of children and their families as they wait for cures. CRI is the only research center in Wisconsin dedicated solely to issues of children's health. The CRI further supports the full continuum of interdisciplinary pediatric research. The proximity of the CRI to CHW improves access for both researchers and patients to the latest and best developing therapies available in treating pediatric conditions and interventions to assist individuals and families dealing with these health conditions. There are 220 investigators within the CRI, participating in over 1,000 active clinical trials, an increase of more than 80% since the institute first launched in 2003. The Department of Pediatrics at the MCW has risen in National Institutes of Health funding ranking from No. 35 to No. 17, and received nearly \$35 million in external funding in fiscal year 2012. CRI is nationally known for premie and newborn care, heart care, and cancer care, among other critical areas.

In January 2007, CHW dedicated a new, \$140 million biomedical and translational research facility. The research center, a collaborative project of CHW and the MCW, is located on Watertown Plank Road in Wauwatosa, close to research partners and collaborators on the Milwaukee Regional Medical Center campus. The 298,000 square foot, state-of-the-art research facility includes space for bench laboratory research and vivarium space, as well as other shared service support space and administrative support.

SpencerStuart

Page 15

Additional research laboratories are located throughout the Milwaukee Regional Medical Center campus.

APPENDIX D- ANESTHESIOLOGY RESEARCH

The Research Division of the Anesthesiology Department began in 1968 with a small laboratory in the Physiology Department in the Cramer Building of what was then Marquette Medical School. With a robust and international reputation, the research division now fills greater than 20,000 square feet of research space at MCW and the VAMC. There are 12 basic scientists and 15 physician scientists who conduct basic science research.

Stem cell biology laboratories (Zeljko Bosnjak, PhD)

Research in Dr. Bosnjak's laboratory over the past 30 years has been directed toward an understanding of the cellular mechanisms of anesthetic action. His research is supported by PPG and R01 grants from the NIH and Advancing a Healthier Wisconsin grants. Over the past six years, he has developed strategies in regenerative medicine that include: a) deriving patient-specific cardiac cells to study anesthetic preconditioning; b) developing an *in vitro* model of stem cell-derived human neural cell lines to test the effects of commonly used anesthetics; and c) designing novel therapies for repairing damaged cardiac tissue by using autologous adipose tissue-derived stem cells.

Patient-derived stem cells. Researchers have developed and validated a clinically relevant model of cardiac preconditioning using human cardiomyocytes derived from embryonic stem cells (hESCs) and induced pluripotent stem cells (iPSCs), derived from both normal iPSCs (N-iPSCs) and type 1 and 2 diabetes mellitus iPSCs. This *in vitro* model of human disease will enable developmental and comparative studies of normal and diabetic cardiomyocytes to address genetic and environmental mechanisms responsible for attenuation of preconditioning efficacy in diabetics. Importantly, the proposed experiments will also yield new insights into how diabetes might alter the potential efficacy of stem cells for future use in regenerative medicine.

Developmental neurotoxicity (Xiaowen Bai, MD, PhD) Dr. Bai has developed an *in vitro* model of stem cell-derived human neural cell lines to test the effects of commonly used anesthetics under control conditions and during intense synapse formation. The ultimate goal is not only to find the trigger for developmental neurotoxicity, this catastrophic chain of events, but also to prevent cell death itself. These are very clinically relevant studies that are exciting and at the forefront of this field. As far as we know, nobody has this *in vitro* model, and one could use this approach to test various conditions and drugs on a developing human neuronal network. If this research allows us to mitigate risks in pediatric patients, or find novel drugs that are less likely to cause neurotoxicity, major advances will have been made toward assuring the safety of anesthesia for children. These translational research studies will set the stage for future studies to rapidly test the effects of various conditions and anesthetics on developing human neurons, which will lead to major advances toward assuring the safety of anesthesia in the developing brain.

Cardiac regeneration (Xiaowen Bai, MD, PhD) The focus of this research is on isolating and identifying universal stem cells in different tissues or organs and to explore their potential clinical applications, with a particular emphasis on the effect of human adipose tissue-derived stem cells on cardiac function after myocardial infarction, and the promotion of wound healing. Results will guide the design of novel therapies for repairing damaged cardiac tissue by increasing the ability of injected adipose tissue-derived stem cells (ASCs) to migrate from the peri-infarct zone into the

infarcted myocardium and survive in injured hearts. Steps involved in ASC-based treatment of injured hearts include injection of ASCs into the peri-infarct zone, migration of ASCs through the infarcted myocardium, engraftment and survival of ASC at the site of injury, differentiation of stem cells to heart cells, and secretion of paracrine factors for myocardium regeneration. Since improved cardiac function is dependent on higher numbers of ASCs surviving in the injured myocardium, increasing the migration, engraftment, and survival rate of injected ASCs in target myocardium is of critical importance for effective implementation of stem cell-based therapy.

Cardioprotection with light (Martin Bienengraeber, PhD; Wai-Meng Kwok, PhD)

The impact of far red/near infrared light on the heart and mitochondria during cardiac ischemia and reperfusion injury is being studied. Exposure of the ischemic heart with a LED light source at the time of reperfusion reduces injury. Mitochondria may play a crucial role in the mechanism behind this phenomenon. In addition, nitric oxide derived from unconventional sources such as myoglobin or hemoglobin is involved. Interestingly, light treatment at reperfusion protects under disease conditions (e.g., diabetes) where many other strategies against ischemia and reperfusion injury fail.

Pain Management (Quinn Hogan, MD; Bin Pan, MD)

Two topics, supported by separate grants, are being explored in this laboratory. First, the pathophysiology of neuropathic pain using rodent models of nerve injury, electrophysiology by intracellular, patch, and dorsal horn recording techniques, and microfluorimetry, with a focus on calcium signaling is being investigated. Second, molecular therapies at the level of the dorsal root ganglion, including genetic modulation of sensory neurons using viral vectors (lentivirus and AAV), and implantation of genetically engineered mesenchymal stem cells are being developed. The ultimate goal is to better understand mechanisms of pain and provide new treatment options.

Volatile anesthetic-induced cardioprotection (Judy Kersten, MD; David Warltier, MD, PhD)

This lab has found that the HIF1 α -VEGF-NO axis is crucial for cardioprotection produced by anesthetic preconditioning. Further studies are being conducted to determine the contribution of NO synthase isoforms and the role of microRNA in modulation of the HIF1 α -VEGF-NO axis during anesthetic preconditioning.

Hyperglycemia-induced myocardial injury (Judy Kersten, MD; David Warltier, MD, PhD)

Significant progress has been made in the mechanistic investigation of impaired myocardial protection during hyperglycemia and diabetes mellitus. Decreased tetrahydrobiopterin plays a pivotal role in hyperglycemia-induced myocardial injury. An investigation is underway to elucidate the effect of increased endothelial tetrahydrobiopterin by pharmacological and genetic approaches to mitigate hyperglycemia-induced myocardial injury.

Cardioprotection mechanisms (David Stowe, MD, PhD; Amadou Camara, PhD)

The Stowe/Camara laboratory focuses on integrative heart research, particularly development of protective mechanisms against ischemia-reperfusion (IR) injury. This includes the effects of age, hypothermia, ischemic and pharmacologic preconditioning (volatile anesthetics and other cardioprotective agents), sodium hydrogen and sodium calcium exchange inhibitors, and nanoparticle based cardioplegic formulations on electrophysiology, contractility, vascular reactivity, reactive

species formation, ion fluxes, metabolism, and tissue damage. Of particular interest is the protective role of small conductance Ca^{2+} -sensitive K^+ channels, which we recently discovered exist in the cardiac mitochondrial membrane.

Experiments are conducted in isolated, intact hearts, isolated heart tissue, and in isolated mitochondrial and their sub-particulate proteins to attain information on ischemic heart disease in an integrative, mechanistic approach from the whole organ to the molecular and atomic levels. In this effort, the primary research focus is the regulation of mitochondrial bioenergetics in cardiac myocytes after IR injury. The effects of drugs, hypothermia, toxic injury, and ischemia on mitochondrial respiration, membrane potential, electron transfer reactions, enzyme activities, redox potential, hydrogen, potassium, and calcium fluxes are examined to understand generation and scavenging of beneficial and deleterious reactive oxygen and nitrogen species. Of particular interest is locating the specific sites of oxidative/nitrosative damage to amino acids in mitochondrial proteins that are essential for mitochondrial energy production, e.g. complex I, the voltage dependent anion channel (VDAC), and the adenine nucleotide translocator (ANT). One such irreversible and deleterious post-translational modification is nitration of tyrosine residues. These sites are located using proteomics and mass spectroscopy and then site-directed mutagenesis is utilized to convert the susceptible tyrosine to alanine, which cannot be nitrated, to determine if this site must be protected during IR injury. Electron paramagnetic resonance is used to determine how IR stress impacts the transfer of electrons among the atoms within and between the mitochondrial complexes/enzymes. There also is an ongoing interaction with the Bioengineering and Biotechnology Center to model, test, and predict variations in mitochondrial trans-membrane ion fluxes due to activity of mitochondrial cation exchangers, ion channels, and respiratory complexes.

Cardiac extracellular matrix (Dorothee Weihrauch, DVM, PhD)

Investigations on the impact of altered cardiac extracellular matrix in diseases like diabetes, hyperglycemia, left ventricular hypertrophy and cardioprotection are ongoing. And in collaboration with Dr. Ninomiya, Department of Orthopedic Surgery, novel therapeutic modalities in fracture healing and osteoporosis are being sought.

Anesthesiology Research at VA mcw.edu/anesthesiology/research.htm

The Department's faculty members focus their research on various aspects of cardiovascular and respiratory function and control along with the effects of anesthetics on this regulation. Anesthesia faculty members are principal or co-investigators in several grants from various agencies including National Institutes of Health (NIH), VA Merit Review, American Heart Association, National Science Foundation, American Diabetes Association, and other industry grants. Combined, these investigators have more than 460 publications derived from grant-funded studies.

Nine faculty members have been leading advanced studies in the VAMC MCW Anesthesia Research Lab with collaborative support of staff and partnering sponsorships. The following research efforts have led to new discoveries and to the beginning of more advanced studies.

Focusing on the neural regulation of the central control and integrative aspects of the sympathetic nervous system, studies by **Dr. Caron Dean-Bernhoft** include electrophysiological, neuropharmacological, and neuroanatomical approaches to examine synaptic mechanisms and central pathways underlying the control of regional sympathetic outflow. Current studies are

examining the integration of inputs to neurons in the brainstem that utilize different transmitters to evoke an increase in blood pressure associated with acute stress

Developing viral vectors for treating chronic pain is initiated by introducing new genes into sensory neurons that have the potential of correcting disordered function that contributes to pain following nerve injury. The research, led by **Dr. Quinn Hogan**, is expanding by developing a technique of transplanting mesenchymal stromal cells into the sensory nerves after genetically engineering them to produce analgesic peptides; this may provide the means for long-term therapy for chronic pain using a single injection.

Dr. Astrid Stucke is exploring whether the differences seen in sites of action of opioids may be related to maturity of the central respiratory control system, developmental aspects of opioid-induced respiratory depression.

Research in **Dr. Ekehard Stuth's** lab is focused on characterizing the mechanisms by which volatile anesthetics alter neural function in the intact, spontaneously active mammalian respiratory system in vivo. Volatile anesthetics such as isoflurane and sevoflurane have profound effects on upper airway patency at subanesthetic concentrations. Motor neurons in the hypoglossal motor nucleus of the brainstem control the upper airways and are depressed by anesthetics. The goal of the current study is to determine whether this effect is due to altered neurotransmission to these motor neurons and the mechanisms behind the altered neurotransmission.

The main focus behind **Dr. Edward Zuperku's** research is to elucidate mechanisms within the respiratory areas of the brainstem that generate and control breathing. This includes delineating the neurotransmitter/modulators that underlie the discharge patterns of the various types of inspiratory and expiratory neurons in the respiratory network and then to understand the mechanisms by which volatile anesthetics and opioids depress breathing.