Duke Anesthesiology
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Volume 4 | 2013

ARCTIC WONDERS

A TEAM OF RESEARCHERS HAS BEEN STUDYING THE HIBERNATING ARCTIC GROUND SQUIRREL'S NATURAL DEFENSE MECHANISMS AGAINST ISCHEMIA-REPERFUSION INJURY

Duke Anesthesiology

Volume 4 | 2013

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WELCOME

From the Chair

Greetings Family and Friends,

I am pleased to present the 2013 edition of our BluePrint publication. In this year's edition, we included several videos to accompany our articles, which can be viewed on our BluePrint website at http://blueprint.duhs.duke.edu.

When I think about our department and what we have accomplished, I find myself overwhelmed by the level of dedication, teamwork, and unfettered ambition that it has taken to get to where we are today. We are consistently looking ahead to what's next in the field of anesthesia and how we can improve the lives of patients for generations to come.

In 2012, we received $9 million in grants to support research that focuses on many areas, such as pain management for our veterans, organ protection during heart surgery, stroke, and genomics. To date, five of our DREAM Innovation Grant (DIG) recipients have received $1,180,944 in extramural funding. We were also honored to see several of our faculty recognized for their achievements, including Dr. Richard Moon, who received the 2012 Leonard Palumbo Jr., MD, Faculty Achievement Award; Dr. Catherine Kuhn, who received the 2012 Master Clinician/Teacher Award; and Dr. Cecil Borel, who received the Robert N. Sladen Teacher of the Year Award. In addition, I'd like to congratulate Dr. Catherine Kuhn for being selected to take on the roles of Director of Graduate Medical Education and Designated Institutional Official for the Duke University Hospital and Health System. Finally, we said a fond farewell to Dr. Katherine Grichnik, who served in the department for over 22 years, as she takes on the new role as the Director of Research, Education, and Quality for American Anesthesiology.

As we continue to press forward, we rely both on the commitment from our tenured faculty to share their leadership and wisdom with younger generations of physicians as well as the innovations in education that younger physicians bring to the department. We count on the resilience of our researchers who are committed to searching for new medical discoveries. Last but not least, we are grateful for the unwavering support from our family, friends, alumni, faculty, staff, and donors who make what we do possible.

Sincerely,

Mark F. Newman, MD
Merel H. Harmel Professor of Anesthesiology
and Professor of Medicine
Chair, Department of Anesthesiology

Featured Stories

DIG

The 2012 DREAM Innovation Grant (DIG) recipients reveal what they have discovered during the one-year funding period of the DIG, as well as what the future holds for their promising research studies. Also, meet the 2013 DIG recipients as they share what brought them to Duke and what they hope to accomplish.

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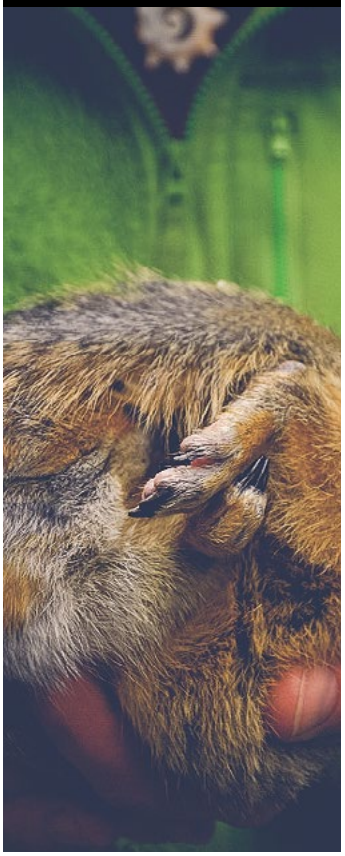
RESEARCH



The team of researchers from Duke provides a snapshot of a recent trip to Alaska, where the team has been studying the hibernating arctic ground squirrel's natural defense mechanisms against ischemia-reperfusion injury.

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MENTORSHIP

The department has formalized a mentorship process to attract and retain the brightest physicians from around the country. To attest to the benefits of mentorship, faculty, including the newly awarded DIG recipients as well as the chair of the department, give their testimonies on how mentorship has brought them to where they are today.

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TRAINING

A team of physicians within the Division of Cardiothoracic Anesthesiology and Critical Care Medicine at Duke has developed a way of utilizing the iPad as a tool for real-time TEE instruction in the operating room.

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DREAM Innovation Grant

The DREAM Innovation Grant (DIG) program was started in 2011 at Duke to support innovative research in the field of anesthesia. Applicants are encouraged to submit unique, high-risk ideas that have the potential for positively impacting the field of anesthesia and pain management. The grant provides investigators with one-year pilot funding, enabling them to develop their hypotheses and collect data that will be submitted for long-term funding from other prestigious agencies. Winners of the DIG are announced at the annual ASA Duke Anesthesia Alumni Reception.

2011-2013 DIG Recipients

To date, five of our ten DIG recipients have received $1,180,944 in extramural funding! That's $150,000 in donations that have led to over a million dollars in external grants!

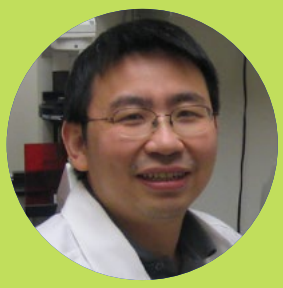
- Joseph P. Mathew, MD - 2011

Functional Neuroimaging to Assess Cognitive Function after Cardiac Surgery

In August 2011, Dr. Mathew was awarded a two-year, $431,750 Exploratory/Developmental research grant from the National Heart, Lung, and Blood Institute.

- Michael "Luke" James, MD - 2011

Gender-based Differences in Genetic Expression after Acute Brain Injury in Mice



- Wei Yang, PhD- 2011

Role of SUMO2/3 Conjugation Pathway in Cerebral Ischemia/ Stroke

Dr. Yang was awarded a four-year, $308,000 NCRP Winter 2012 Scientist Development Grant from the American Heart Association.

- Mihai V. Podgoreanu, MD- 2012

Elucidating Adaptive Mechanisms of Perioperative Cardioprotection Following Ischemia-reperfusion in Hibernating Arctic Ground Squirrels

In the Spring of 2012, Dr. Podgoreanu was awarded a $75,000 Foundation for Anesthesia Education and Research Grant, and a $10,000 Duke SOM voucher award.

- Joern A. Karhausen, MD - 2012

Determinants of Intestinal Epithelial Wound Healing

- Huaxin Sheng, MD - 2012

Effect of an Mn-Porphyrin in Neuropathic Pain

- Karthik Raghunathan, MD, MPH - 2013

Comparative effectiveness in Perioperative and Critical Care Medicine: Crystalloid Fluid Therapy

-In the Summer of 2013, Dr. Raghunathan was awarded a $206,944 grant from the Baxter Healthcare Corporation Fluids franchise.
-In the Fall of 2013, Dr. Raghunathan was awarded the $100,000 APSF/ASA Endowed Research Award from the APSF Scientific Evaluation Committee.

- Miklos Kertai, MD, PhD - 2013

Pharmacogenomics of β-blockers: Implication for Postoperative Atrial Fibrillation

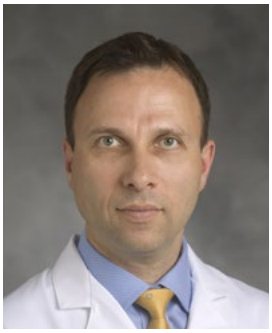
- Michael Manning, MD, PhD - 2013

Cardiopulmonary Bypass Induced Inflammatory Changes in the Atrial Wall: The Novel Role for Cardiac Chymase produced Angiotensin II in the Development of Atrial Fibrillation

In the Spring of 2013, Dr. Manning was awarded a two-year, $50,000 Society of Cardiovascular Anesthesiologists (SCA) Starter Grant.

- Steve Melton, MD- 2013

Neurointerventional Regional Anesthesia to Improve Hand Rehabilitation in Stroke



2012 Final DIG Report: Mihai Podgoreanu, MD

Elucidating Adaptive Mechanisms of Perioperative Cardioprotection Following Ischemia-reperfusion in Hibernating Arctic Ground Squirrels

The overall goal of this study is to understand how hibernating animals have developed natural defense mechanisms to withstand extremes of environment, and to ultimately apply this knowledge for organ protection in humans undergoing heart surgery. Three broad categories of regulatory mechanisms used by hibernating mammals to support long-term viability and organ preservation have relevance to perioperative cardioprotection. These include a controlled depression of the global metabolic rate, a shift in fuel utilization away from glucose towards fatty acids and ketones, and attenuation in the inflammatory response.

Findings

Our study began investigating the last two mechanisms, testing the joint hypothesis that changes in hibernation–specifically myocardial expression/activity of PPARα nuclear receptors following cardiac surgery–provide cardioprotection by increasing myocardial fatty acid oxidation (transactivation effects) and inhibiting NF-κB regulated pro-inflammatory responses (transrepression effects). The rationale for our study is that if endogenous activation of PPARα, or one of its target genes, in hibernators improves mitochondrial fatty acid utilization and avoids accumulation of incompletely oxidized lipid species while attenuating myocardial inflammation following cardiac surgery, then novel pharmacological cardioprotective approaches for perioperative metabolic optimization and reprogramming could be devised.

We conducted deep hypothermic/cardioplegic arrest (45 min, 18°C) followed by sham surgery, reperfusion for 3 hours, or reperfusion for 24 hours in adult hibernating arctic ground squirrels (AGS), summer active AGS, and rats. Compared to rats, AGS displayed robust tolerance of myocardial ischemia following DHCA as evidenced by reduced myonecrosis and apoptosis (fig. 1).

This cardioprotective phenotype in AGS was associated with preservation of myocardial PPARα activity, and a metabolic phenotype consistent with the development of mitochondrial substrate flux "bottlenecks" in rats (accumulation of acylcarnitines and ceramides) (fig. 2).

Furthermore, the hibernator cardioprotective phenotype was also associated with reduced myocardial NF-κB activity (fig. 3),

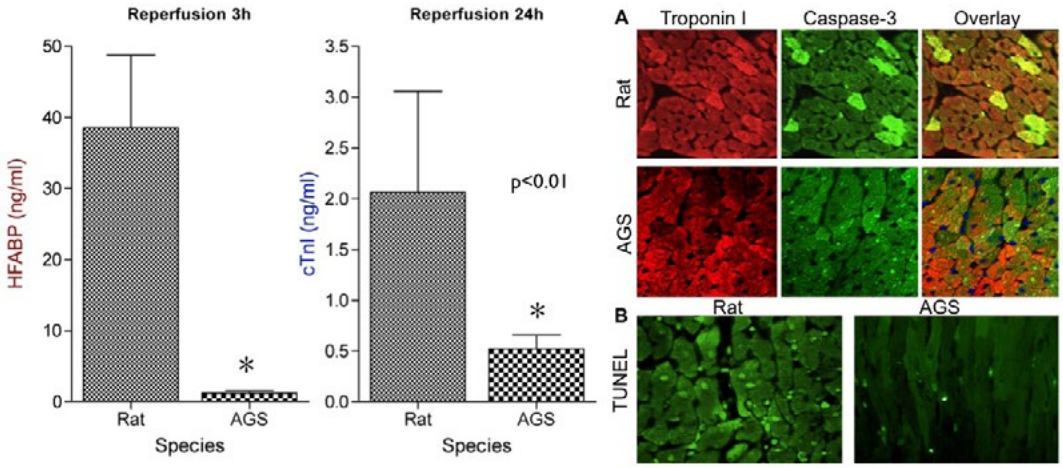


Figure 1: *We conducted deep hypothermic/cardioplegic arrest (45 min, 18°C) followed by reperfusion for 3h, 24h or sham surgery in adult hibernating arctic ground squirrels (AGS), summer active AGS, and rats. Compared to rats, AGS displayed robust myocardial ischemic tolerance following DHCA as evidenced by reduced myonecrosis and apoptosis.*

Figure 2: *This cardioprotective phenotype in AGS was associated with preservation of myocardial PPARα activity, and a metabolic phenotype consistent with the development of mitochondrial substrate flux "bottlenecks" in rats (accumulation of acylcarnitines and ceramides), compared to AGS.*

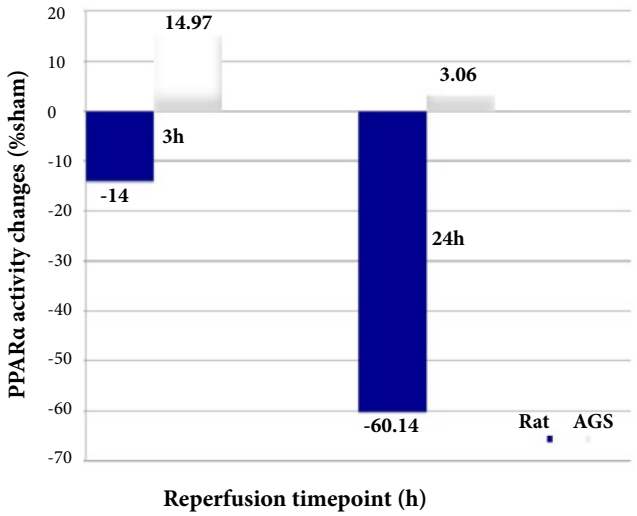
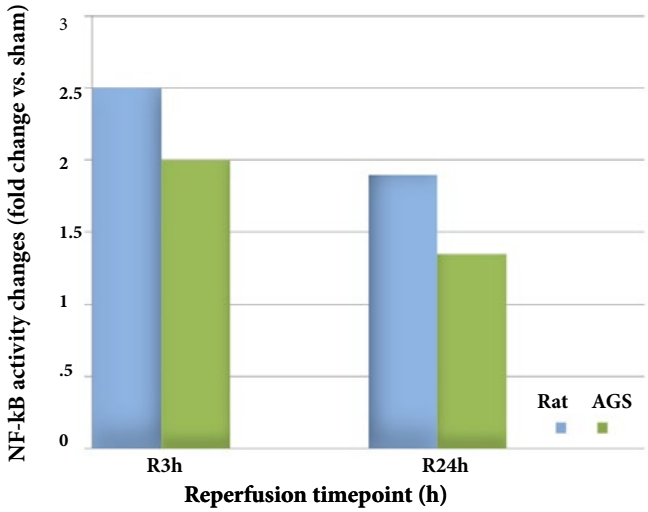


Figure 3*: Furthermore, the hibernator cardioprotective phenotype was also associated with reduced myocardial NF-κB activity, reduced expression of downstream cytokines (TNFα, IL6), and neutrophil extravasation (MPO) following cardiac surgery.*



reduced expression of downstream cytokines (TNFα, IL6), and neutrophil extravasation (MPO) following cardiac surgery.

These findings are novel because they challenge the current paradigm for metabolic optimization in human ischemic heart disease and heart failure that involves promoting glucose oxidation at the expense of fatty acid oxidation during reperfusion, by attempting to induce an "adaptive" substrate switch that is the exact opposite of that demonstrated by natural hibernators.

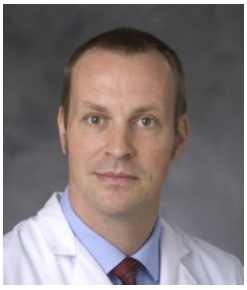
Funding

We have received funding from the Foundation of Anesthesia Education and Research and the Duke School of Medicine Voucher Program, and have recently submitted an NIH Transformative-R01 grant. Our results have been selected for podium presentations at various local, national, and international meetings, including the annual scientific sessions of the American Society of Anesthesiology and the American Heart Association.

Next Steps

Our future directions include mechanistic studies to follow-up on the relationship between deregulation of PPARα and several of its specific target genes using in vivo pharmacological modulation as well as gain and loss of function experiments in cardiomyocytes.

Of note, one of these target genes (FGF21) has already been shown to induce torpor (a hibernation-like hypometabolic state) when injected into mice, but its role in cardioprotection remains unclear. We further aim to characterize changes in the abundance of the full spectrum of proteins expressed in the heart using proteomic analyses, as well as in the repertoire of inflammatory cells responsible for heart damage following cardiac surgery using flow cytometry analyses.



2012 Final DIG Report: Joern A. Karhausen, MD

Determinants of Intestinal Epithelial Wound Healing

Overview

This study is aimed at unraveling compensatory mechanisms that help the intestinal mucosa respond to injury due to ischemia (interruption of blood flow) and reperfusion (restoration of blood supply). In cardiac surgery, pronounced abnormalities of blood flow are observed particularly in the small blood vessels within the intestinal wall. In the past, it has been repeatedly hypothesized that the resulting lack of tissue oxygenation leads to breaches of intestinal barrier integrity, bacterial translocation, activation of gut resident inflammatory cells, and consequently, to systemic inflammatory responses. Based on my previous work, I had hypothesized that the intestinal epithelium is not only uniquely susceptible to such ischemic injury, but also uniquely equipped to respond to it.

Findings

In a mouse model, our research team observed that the intestinal lining was profoundly injured immediately after ischemia, but that within three to five hours after reperfusion, epithelial cells had spread out to fully cover the wound. This swift recovery of epithelial integrity did not seem to be immediately dependent on the regulatory cycle identified in our initial proposal, consisting of the zinc finger E-box binding homeobox factors 1 and 2 (ZEB-1, -2) and the miR-200 family of micro RNAs. Extensive research based on protein and RNA profiles did not reveal significant changes in these components, and an attempt to recapitulate these conditions under cell culture conditions using genetically modified cell lines showed no functional differences to unmodified (wild type) cells.

As we investigated possible explanations and alternatives, we observed a significant increase of protein SUMOylation in the intestinal epithelium following ischemia-reperfusion (fig. 1). SUMO, or Small Ubiquitin-like Modifiers, are small proteins that alter the function of other cellular proteins by direct binding, and thus modifying their function, cellular localization, or stability. Changes in SUMOylation have been observed in an ischemia-reperfusion setting and are thought to predominantly contribute to tissue-protective anti-inflammatory responses.

Next Steps

As a consequence of these results, I have begun collaborating with Wulf Paschen, PhD, and Wei Yang, PhD, of Duke University.

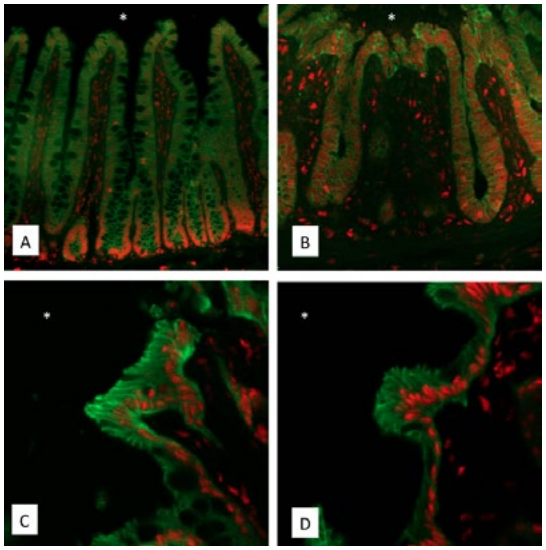


Figure 1*: Colonic SUMO expression in a rat model of deep hypothermic circulatory arrest (DHCA). Immunofluorescence change of SUMO2/3 distribution from exclusively basal expression in Sham (A) to broad-spread epithelial in DHCA treated animals (B). In contrast SUMO1 staining does not change between Sham (C) and DHCA treated animals (D). Magnification 400x, Red: Sumo, Green: E-cadherin (intestinal epithelial marker). Asterisks denotes intestinal luminal side.*

Both are experts in research on SUMO-modifications in ischemia, and over the last few years have developed innovative tools to study these modifications in cell culture and animal models. With their support, I have generated SUMO-deficient cell lines and am characterizing the pattern of SUMOylation in the context of intestinal ischemia-reperfusion injury. Preliminary data gathered through this work has served to apply for both internal (Duke Chancellor`s Development Fund) and external (American Gastroenterological Association, Pilot Grant) pilot funding. Important aspects of these results have also been incorporated in a K08-Mentored Clinical Scientist Career Development Award application, which I have just submitted to the National Institutes of Health. The DIG has funded important observations central to my research endeavors, and I expect significant returns of this investment through the initiated projects.

2012 Final DIG Report: Huaxin Sheng, MD

Effect of an Mn-porphyrin in Neuropathic Pain

Overview

Clinical investigations indicate that 60% to 80% of spinal cord injury (SCI) patients experience pain, which is severe in nature in at least one-third of them. My DIG research was to examine the efficacy of Mn-porphyrin, a catalytic oxidoreductant, in treating SCI-induced neuropathic pain in mice, and explore its potential for therapeutic development.

Our laboratory has a long history of studying central nervous system (CNS) injury, but neuropathic pain was new to us. With the support of the DIG, we were able to establish the animal models, purchase the equipment for behavioral tests, and do preliminary experiments; allowing expansion of our research to a new domain.

Findings

The first experiment explored spinal cord ischemia, a common complication from surgical repair of thoracoabdominal aortic aneurysms. Mice were subjected to either 10 minutes of thoracic aorta clamping or sham surgery, and then observed for pain-like behavioral responses. The injured mice that were subject to clamping became less tolerant to fine von Frey filament stimulus, compared to sham surgery mice (p=0.02, fig. 1), which was consistent with the development of neuropathic pain. This response persisted for eight weeks and beyond, and represented a new model for studying this disorder.

Next, we examined whether the Mn-porphyrin, BuOE2, decreased the activity of NF-kB, a key transcription factor in the inflammation pathway. Mice were subjected to 10 minutes of clamping of the thoracic aorta, and then received 0.25 mg/kg BuOE2 or saline. The NF-kB activity was measured at 24 hours post-injury. We found that the BuOE2 suppressed SCI-induced NF-kB activity (p=0.03, fig. 2).

Our second experiment was related to lumbar spinal cord injury, a condition of acute traumatic injury or a central type of lumbar disc herniation. Mice were subjected to left lumbar spinal cord hemisection and then received saline, 0.05 and 0.15 mg/kg BuOE2, one hour after injury, twice per day, for two weeks. As a normal reference, 10 mice then received sham surgery. Pain-like responses were observed weekly for eight weeks. After the eight-week period, we observed that injury-induced neuropathic pain was slightly reduced by BuOE2 (fig. 3), which was not statistically significant due to low drug dose or severe hemisection.

Figure 1

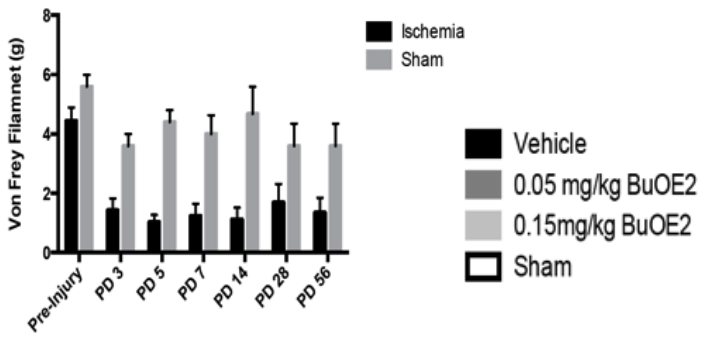


Figure 2

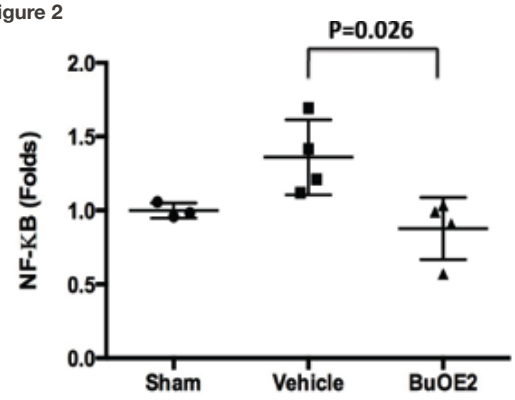
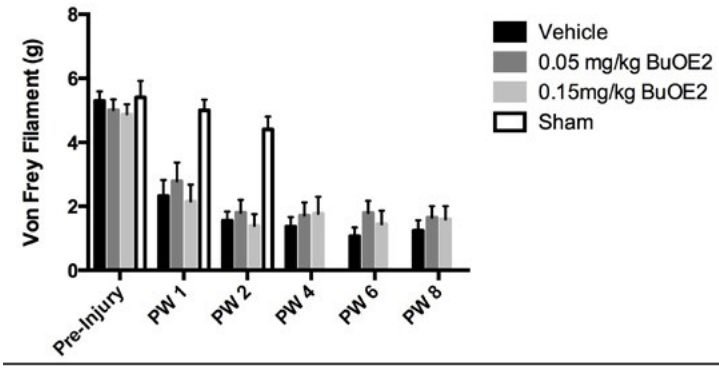


Figure 3



Next Steps

To further explore BuOE2 efficacy, we plan to try a higher dose of the compound and investigate a spinal cord contusion injury model. We are hopeful that this will allow us to collect sufficient data for a translational NIH R21 proposal.

2013 DIG Research Projects

Karthik Raghunathan, MD, MPH

Comparative effectiveness in Perioperative and Critical Care Medicine: Crystalloid Fluid Therapy

Background

I was born and raised in India. I completed my basic medical education and initial training there, and immigrated to the United States in 1999. As a graduate student at the State University of New York in Albany, I studied epidemiology while interning at the Albany Medical College and the New York State Department of Health. Anesthesiology afforded me an opportunity to pursue my twin passions: applied pathophysiology and pharmacology at the bedside; and clinical epidemiology.

By the summer of 2002, I was accepted into an anesthesiology training program in Philadelphia, where I trained over the next three years. My family and I moved to Springfield, MA, to complete my training within the Tufts University system, as my wife, a neurologist, took up a job in a medically underserved area. My fellowship in critical care medicine served to further my understanding of acute illness and by July 2007, I had begun working as a staff anesthesiologist at the Baystate Medical Center. This academic tertiary community hospital provided me with opportunities to work as an educator, engage in research, and provide care to patients from all over western Massachusetts and eastern New York. After five years at this location, I met Andrew Shaw, MD, MBBS, at an anesthesiology conference, and this led to an offer to join the anesthesiology team at Duke.

The promise of collaboration with committed and capable peers at the highest level was impossible to turn down. A family of five at this point, we moved to Duke in July of 2012. A few months later, I found out that I was a DIG recipient!

Research

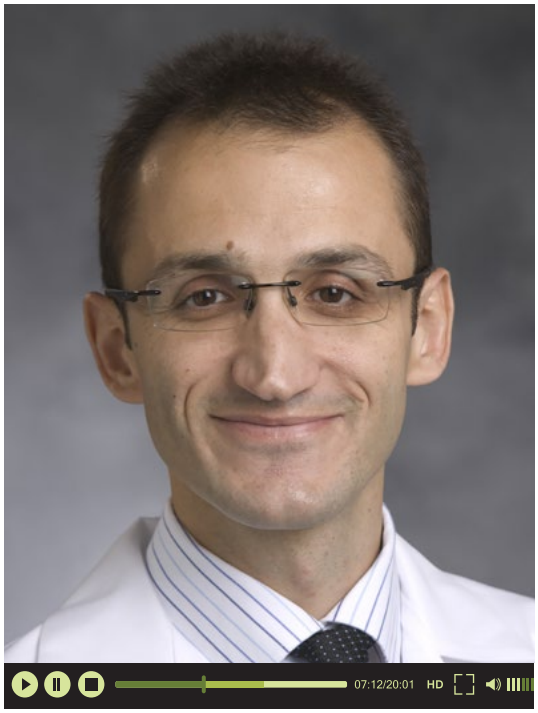
My research project aims to answer the following question: “What is the right kind of intravenous crystalloid fluid to use during severe illness and surgery?” Intravenous fluids are used to support circulation when patients are admitted to the hospital for major surgery or during critical illness. Despite nearly universal use, the fundamental question of “what fluid is best in which situation” remains unresolved. There is wide variation across various populations and our study is going to examine the results of using different combinations of fluids. At the population level, since intravenous fluid use is so common, even small differences in important outcomes will have immense consequences.

I decided to work on this question since my epidemiologic training prepared me for the study of patterns of disease across different populations. Also, as an anesthesiologist and intensive care specialist, I use these fluids every day. This was a practical question directly relevant to my patients.

The DREAM Campaign gives investigators the critical support they need to make the leap from an interesting idea to a pilot project early in their careers. Pilot data is pivotal in testing hypotheses and to subsequent, continued support for promising avenues of research. As a testament to this, in the Spring of 2013, we were awarded a $206,944 extramural grant from the Baxter Healthcare Corporation Fluids franchise, and in the Fall of 2013, we were awarded the $100,000 APSF/ASA Endowed Research Award from the APSF Scientific Evaluation Committee. This could not have happened without the initial funding from the DIG award and Dr. Shaw’s tremendous mentorship.

Personal

Outside of work, our three daughters, ages seven years, three years, and five months old, keep us happily busy.



Miklos Kertai, MD, PhD

Pharmacogenomics of β-blockers: Implication for Postoperative Atrial Fibrillation

Background

I was born and raised in Hungary, where I completed most of my undergraduate studies. I received my medical degree from Semmelweis University in Budapest, Hungary, and my PhD degree from Erasmus University in Rotterdam, the Netherlands. I completed my residency in anesthesiology and intensive care medicine at Semmelweis University. Subsequently, I went on to complete my fellowship training in cardiothoracic anesthesiology at Royal Brompton and Harefield Hospital in Harefield, the United Kingdom, prior to taking a position as faculty at Washington University School of Medicine in St Louis, Missouri. Two years ago, I was fortunate to be invited to join the Department of Anesthesiology at Duke University Medical Center to pursue my research career in clinical and translational research. It was the unparalleled resources of a community of clinical collaborators and geneticists that brought me to Duke.

Currently, as an assistant professor in the Department of Anesthesiology, I serve as a cardiothoracic anesthesiologist. My research interests include perioperative and long-term cardiac risk assessment and management, genomics, perioperative cardiac risk profiling, and perioperative pharmacogenomics. I am the author and co-author of several book chapters in the field of cardiovascular anesthesiology and surgery. I have been a frequent speaker at international conferences about the importance of perioperative cardiac risk assessment and management, and have published over 60 peer-reviewed articles as a first author or as a co-author in scholarly journals with national and international circulation. Many of my peer-reviewed publications have been selected and used by national and international guidelines to formulate recommendations for the assessment and prevention of cardiovascular complications after surgery.

Research

My study is designed to test blood and small specimens of tissue from the atrium of human hearts to learn how to prevent and treat a serious complication following heart surgery. Approximately 25% to 40% of heart surgery patients experience dangerously high irregular heart rates (postoperative atrial fibrillation), and are, therefore, in danger of congestive heart failure, kidney failure, stroke, and even death. The purpose of the proposed study is to analyze the genetic material from the stored blood and heart tissue samples to learn why some patients experience postoperative atrial fibrillation despite treatment with beta-blockers, which are used routinely to protect patients against this very serious complication. This knowledge will help physicians predict which patients will benefit from beta-blockers and which ones will not. For those who will not benefit, other treatments can be developed and used to prevent or treat postoperative atrial fibrillation, thereby further reducing the number of patients who have this potentially life-threatening complication.

The DREAM Campaign has a noble mission to support academic research within the Department of Anesthesiology at Duke. As a part of this wonderful undertaking, the DIG program provides a unique opportunity to accelerate anesthesia research. In this era of financial constraints, it can be very challenging to obtain extramural research funding unless one has sufficient preliminary data or peer-reviewed scientific publications. However, with the support of the DIG, it is now possible to achieve these goals with a future potential for successfully applying for societal and federal grant opportunities.

Personal

I have been married to my beautiful wife, Monika, for 11 years, and we have three lovely children; David (ten years old), Sara (six years old), and Lily (two years old), all born in different countries. We share a great passion for travel, which is not surprising since we have lived in so many different cities and countries. We also share the passion for the beauty of nature, which is why North Carolina is a very special place for us.

Michael Manning, MD, PhD

Cardiopulmonary Bypass Induced Inflammatory Changes in the Atrial Wall: The Novel Role for Cardiac Chymase produced Angiotensin II in the Development of Atrial Fibrillation

Background

I am a Kentucky native. I attended the University of Kentucky for all of my education, beginning with my undergraduate studies, to my graduate work, continuing through my medical school, and residency training.

As an undergraduate, I was introduced to David Randall, PhD. A cardiac physiologist, Dr. Randall was the director for an introductory course in systems physiology. He fostered my scientific curiosity by first introducing me to research. He mentored and encouraged me to follow my growing interest in biomedical research by attending graduate school. As I moved through my doctoral studies, I found myself becoming more interested in the clinical applications of the research we were conducting. Medical school seemed to be the logical extension. Toward the end of medical school, as I began to explore residencies and specialties, it was my wife who encouraged me to look hard at anesthesiology. An anesthesiologist herself, she reminded me of the love I had for physiology, and detailed her experiences in the operating room. What she described was everything that I had been looking for! It allowed me to blend my physiology background with clinical medicine, and I quickly joined her in residency.

Our anesthesia residency director at the University of Kentucky, Randall Schell, MD, a Duke alumnus, serving both as a role model and advisor, encouraged me to explore my interest in cardiovascular research and anesthesia. He directed me to Drs. Mark Newman and Mark Stafford-Smith, and the fellowship program at Duke. Once again, following my love of both cardiac physiology and anesthesia, I moved to Duke for the Cardiothoracic Anesthesia Fellowship. During my interview at Duke, I was blown away by the level of interest and support for research within the Department of Anesthesiology. I had found an environment that would strongly support my clinical education and development, as well as my growth as a scientist. I happily joined the Duke team. Last year, I completed my clinical training as a cardiothoracic anesthesia fellow, and am now working as a research fellow and medical instructor within the Division of Cardiothoracic Anesthesia.

Research

Under the mentorship of Mihai Podgoreanu, MD, and Tom Coffman, MD, I am looking at the inflammatory processes that occur as a consequence of the cardiopulmonary bypass (heart-lung machine) during open-heart surgery. We believe that Angiotensin II, a small protein that normally controls blood pressure, becomes elevated to the point of stimulating this inflammatory response. Consequences of this inflammation may result in atrial fibrillation and kidney injury following surgery. Our goal is to better understand these pathways and to pinpoint ways to prevent this damage and identify patients that are most at risk for this damage. In the Spring of 2013, we received a two-year, $50,000 Society of Cardiovascular Anesthesiologists (SCA) starter grant, which will allow us to continue making progress in our study.

This research is very special to me for multiple reasons. First, it is a spinoff of work that I did under the guidance of Alan Daugherty, PhD, on Angiotensin II-induced inflammation. More importantly, my own father is facing open-heart surgery, as are many “baby-boomers.” Anything that we can do as physician-scientists to make this major operation safer with better outcomes is my personal and professional passion.

Personal

My wife, Erin, is now a faculty member in the Department of Anesthesiology, and is involved in her own research as well. Together, we are so proud to be a part of this incredible group of people as well as the larger Duke University community. The commitment to research here at Duke is so important. To be able to answer questions, develop solutions, and bring better care to our patients is an absolute must, especially within the specialty of anesthesia. Support to the DREAM Campaign provides new and established investigators the opportunity to begin asking those critical questions. By funding initial experiments and clinical studies, the DIG provides us the chance to develop new insights to problems that will revolutionize patient care, and truly make a difference.

Steve Melton, MD

Neurointerventional Regional Anesthesia to Improve Hand Rehabilitation in Stroke

Background

Before coming to Duke, I completed an undergraduate degree from Arizona State University, near my hometown of Phoenix, Arizona. I left the sunny Southwestern skies to attend Loyola Stritch School of Medicine in Chicago. Despite the change in climate, I enjoyed my time and training in the Windy City and stayed at Loyola to complete my anesthesiology residency. Upon completing my residency, I pursued a regional anesthesiology fellowship at the Hospital for Special Surgery in New York. Anesthesiology and regional anesthesia were a natural pursuit for me because I enjoyed the operating room setting, the ability to practice acute care in critical situations among a diverse patient population, and the opportunity to comfort patients in a small but crucial window of time. These interests made Duke an ideal place for me, giving me the opportunity to practice in a renowned regional anesthesiology program, to work among talented faculty, and to pursue Duke's unique and unrelenting focus on improving patient care and outcomes.

Upon joining the anesthesiology department and Ambulatory Division at Duke, I was surrounded by an amazing team that provided ideas, input, and support, which led to our current research pursuit. Our research focuses on investigating how peripheral nerve blockade, or regional anesthesia, can be used to improve hand rehabilitation after stroke. Peripheral nerve blockade involves depositing local anesthetic, or numbing medication, around peripheral nerves, or groups of nerves, to anesthetize, or block, regions of the body for surgical anesthesia and/or postoperative pain management. Peripheral nerve blockade temporarily blocks the transmission of messages along the nerve from the blocked body part to the brain. Research by our group and others has demonstrated that brain activity and organization transiently changes subsequent to peripheral nerve blockade of these messages. Subsequent to stroke, there are also changes that occur in the brain, both from the injury itself and the brain's effort to adapt to that injury. While the brain's efforts are intended to be adaptive, they can unfortunately be maladaptive, thereby further limiting hand rehabilitation after stroke. We propose that peripheral nerve blockade can be used to facilitate adaptive changes in the brain, optimizing brain activity and reorganization for improved hand rehabilitation after stroke.

Research

The proposed model of Neurointerventional Regional Anesthesia challenges the current paradigm of hand rehabilitation in stroke patients. Given the increasing prevalence of stroke and its high level of disability, this novel rehabilitation strategy has the potential to significantly improve hand rehabilitation in stroke, ultimately leading to faster and more complete recovery.

The DREAM Campaign is providing our group the opportunity to pursue this area of study. Without the generous contributions of DREAM supporters, the initial financial support for this project would be challenging. I encourage you to consider supporting the DREAM Campaign and giving innovative new ideas a chance to be explored!

Personal

My time outside of anesthesiology is spent with my family. With two boys, my wife and I are always busy, always entertained, and always grateful for the time we have together.

Photo credit: Photodune.com

Scientists at Duke are hard at work to unravel how arctic ground squirrels hibernate through the harsh Alaskan winter. They hope to gain a deeper understanding about the ways arctic ground squirrels have adapted—their ability to lower their metabolism, utilize energy, and suppress their immune system—and apply this knowledge toward organ protection for humans undergoing heart surgery.

Arctic Wonders

These tiny creatures spend the winter months hibernating under layers of snow and ice. Through the years, arctic ground squirrels have adapted unique, natural defense mechanisms during hibernation to withstand the extremes of the Alaskan winter. Mihai Podgoreanu, MD, an anesthesiologist in the Division of Cardiothoracic Anesthesiology and Critical Care Medicine at Duke, and his research team, including his mentee, Quintin Quinones, MD, PhD, and assistant research professors, Qing Ma, MD, and Zhiquan Zhang, PhD, have just completed their third trip to the University of Alaska Fairbanks (UAF) to study these mechanisms.

Preparation

Since the experiments in Alaska study "deep hypothermic arrest," the pop-up lab, located in the basement of UAF, had to be set up as a small rodent operating room and intensive care unit. Prior to the trip, the team's lab technician, Michael Smith, prepared shipments for both procedural and research equipment, including a cardiopulmonary bypass pump, small membrane oxygenator, life support equipment, such as ventilators and infusion pumps, materials for arterial and venous lines, and molecular equipment so that after the experiments were concluded, they could gather the organs of the animals, freeze them, and ship them back to Duke for molecular analyses.

A Day in the Life

On January 22, 2013, after everything was shipped and coordinated, Dr. Podgoreanu, Dr. Quinones, Dr. Zhang and Dr. Ma flew to Alaska to embark on a 12-day research journey. Their days would usually begin by meeting in the lobby of their hotel, Sophie Station, at 7 a.m. They would let the car, which had been plugged in all night to avoid freezing, warm up, and grab a cup of coffee before heading out to the lab. On the short, 10-minute commute in the dark from their hotel, the temperature gauge would more often than not read -45°F!

The Research

The four researchers involved in the study multitasked. The experiments consisted of anesthetizing and intubating the arctic hibernating ground squirrel, putting it on cardiopulmonary bypass,

cooling it to 18 degrees centigrade, arresting the heart, stopping the pump, and after 45 minutes of no blood flow or oxygen, using reperfusion to reanimate the animal. Dr. Ma was responsible for inserting the arterial and venous lines, connecting to the perfusion pump, and performing any other surgical procedure under an operating microscope. A critical part of the experimental preparation was to place a balloon-tipped catheter down the right carotid, brachiocephalic artery and into the ascending aorta, where the balloon would be inflated, and cardioplegia injected to stop the heart. This required millimeter precision adjustments under echocardiographic guidance.

Drs. Podgoreanu and Quinones were the anesthesiologists during the procedures. They also did echocardiographic monitoring and recorded data. After the procedures were concluded, Dr. Quinones and Dr. Zhang conducted the molecular part of the work. For the first time ever during their experiments, Dr. Quinones was able to harvest live white blood cells from the spleen, bone marrow, blood, as well as white blood cells that were digested out of the heart and lungs during the surgically-induced ischemia-reperfusion event.

Dr. Zhang's role was to isolate live adult ventricular cardiomyocytes, characterize them using fluorescence microscopy, and conduct hypoxia-reoxygenation experiments. Although these experiments have previously been successful in both rats and summer arctic ground squirrels, attempts to isolate cardiomyocytes from hibernating arctic ground squirrels have proved to be very challenging.

Back at Duke

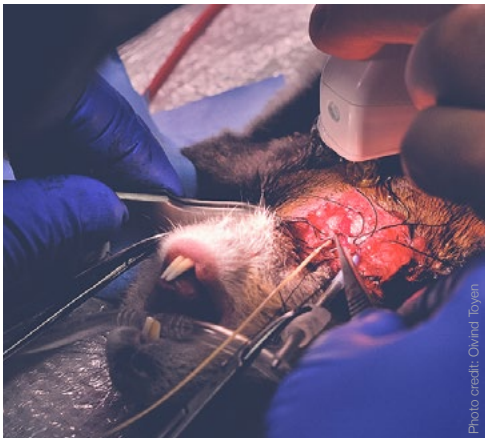
Back at Duke, the team is focused on analyzing three years' worth of samples collected from hibernating arctic ground squirrels during their Alaska trips, along with those gathered from summer active arctic ground squirrels and rats (non-hibernating mammals) in experiments conducted at Duke. The main areas of interest are: the mechanisms that allow the arctic ground squirrels to decrease their metabolic rate during hibernation, how energy is used during a hibernating versus non-hibernating state, and how hibernating animals are able to suppress their immune system.

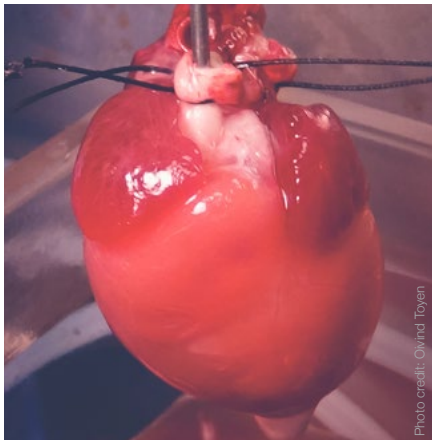
Metabolic Suppression During Hibernation

Unlike other animals, hibernating ground squirrels have the ability to lower their metabolism to 2% of their baseline prior to cooling, subsequently shutting down bodily functions that are not necessary and making them incredibly resistant to ischemia-reperfusion injury. In contrast, therapeutic applications of hypothermia in humans reverse this chicken-egg relationship by cooling first to an internal temperature of 33 degrees centigrade (or lower) before their metabolism slows. Since this method is inefficient and takes time, Dr. Podgoreanu's lab is studying the metabolic differences in the samples obtained from three types of animals with the hope of finding the switch that allows the arctic ground squirrel to actively suppress its metabolic rate prior to cooling.

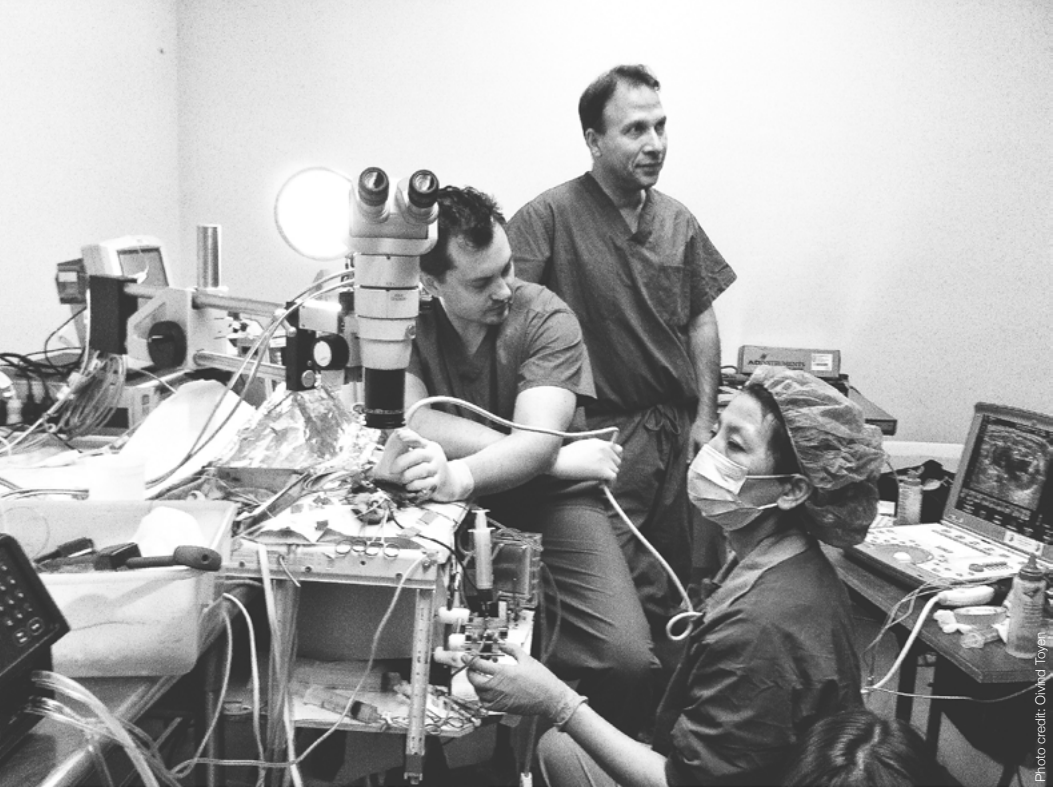
Efficient Energy Use

The team is also focusing on the type of fuel that hibernating ground squirrels use as energy for their organs. In healthy human hearts, 70% of our fuel comes from fat





From left to right: (a) An arctic ground squirrel being held in a hibernation (torpid) state by Franziska Kohl, MS, of the Institute of Arctic Biology at UAF (b) Performing microvascular cannulation on a hibernating arctic ground squirrel (c) Isolated heart preparation for isolation of cardiomyocytes (cardiac cells) from an arctic ground squirrel



From top to bottom: (a) Dr. Mihai Podgoreanu and Dr. Quintin Quinones provide echocardiographic guidance to Dr. Qing Ma as she positions a balloon-tipped catheter into the aorta of an arctic ground squirrel (b) Dr. Qing Ma performing experimental heart surgery on an arctic ground squirrel under an operating microscope (c) Dr. Quintin Quinones harvesting live white blood cells digested out of the heart and lungs of an arctic ground squirrel after a surgically-induced ischemia reperfusion event

and 30% from glucose. During stress, surgery, or ischemia, hearts have the ability to switch to using glucose as energy, yet this flexibility is lost in sick or failing hearts. This has lead to an entire therapeutic paradigm aimed at enhancing glucose and reducing fat use as a fuel in sick hearts. Arctic ground squirrels, on the other hand, maintain obligate fat use during hibernation, and burn it very efficiently until nothing is left. Discovering how they do this would have huge implications on how caregivers could induce or promote effective fat use in humans during surgery to improve patient outcomes. To accomplish this, the team has partnered with experts in metabolic regulation from the Duke Stedman Center for Nutrition and Metabolism – Christopher Newgard, PhD; James Bain, PhD; and Michael Muehlbauer, MD, PhD – to study the simultaneous regulation of 135 metabolites involved in energy production in the heart.

Immunity at Rest During Hibernation

The last adaptation being studied is how arctic ground squirrels suppress their immune system effectively during hibernation. If the immune system in humans is inappropriately activated when stressed, which is very common during cardiac surgery, organ damage and even sepsis can occur. Thanks to the white blood cells harvested by Dr. Quinones, the team is able to use a multi-color flow cytometer approach, which allows them to look at the differences between various components of white blood cells in hibernating versus non-hibernating mammals. These include a panel of 27 specific proteins on the surface of white blood cells,

Hibernating ground squirrels have the ability to lower their metabolism to 2% of their baseline prior to cooling, subsequently shutting down bodily functions that are not necessary and making them incredibly resistant to ischemia-reperfusion injury.

Photo credit: Olvind Toyen

such as pattern recognition receptors (seeking to identify any hibernation effects on danger sensing and signaling), which are an essential part of innate immune responses to injury. If they are able to determine how arctic ground squirrels suppress their immune system, the same process could be adapted for humans undergoing surgery.

In addition to the three areas above, the team is also trying to determine why, for the second year in a row, Dr. Zhang's attempts to isolate adult ventricular cardiomyocytes from hibernating arctic ground squirrels have remained very challenging, despite being successful in active summer animals. Singling out these cardiomyocytes is necessary to determine what mechanisms are being used in the survival process arctic ground squirrels have developed to overcome a lack of oxygen. To show how certain molecules are functionally important, they must be able to take a single heart cell and either increase or decrease certain molecules. But this remains uncharted territory, and every step of the process requires optimization. It seems that the very adaptations that allow the hibernator's heart to continue beating at cold temperatures, such as increased cell-to-cell connections or an intolerance to calcium, are some of the reasons why they cannot easily isolate these cardiomyocytes from hibernating arctic ground squirrels, yet are able to do so in the same species during the summer months as well as in rats.

What the Future Holds

With plans afoot for the 2014 Alaska trip, Dr. Podgoreanu and his team are eager to continue their research with these fascinating mammals. Dr. Quinones is in his last year of residency, and will begin his clinical anesthesia fellowship in critical care medicine at Duke while continuing his research with Dr. Podgoreanu. He firmly believes that there is potential in uncovering the mysterious biology of hibernation and applying it to medicine.

In addition, Dr. Podgoreanu's research lab is planning to collaborate with Anne Yoder, PhD, a professor of biology and director of the Lemur Center at Duke, to study two species of hibernating lemurs. This is particularly exciting since lemurs are primates, thus, very close to humans.

The team members hope that with continued support from the Department of Anesthesiology, the University of Alaska-Fairbanks, and extramural funding, they will be able to continue their investigations that would ultimately improve patient outcomes and benefit future generations.

THE POWER OF MENTORSHIP

Above: Andrew Shaw, MD (left) with Karthik Raghunathan, MD, MPH **(right) Top Right:** Jerry Reves, MD (center with striped tie), is surrounded by some of the grateful physicians he has mentored over the years. From left to right are: Jeffrey Balser, MD, vice chancellor for Health Affairs and dean of Vanderbilt University School of Medicine; Peter S. A. Glass, MD, HS '87-'88, chair of the Department of Anesthesiology at the State University of New York at Stony Brook; Scott Reeves, MD, chair of the Department of Anesthesiology at the Medical University of South Carolina; Dr. Reves; Mark Newman, MD, HS '88-'89, chair of the Department of Anesthesiology at Duke; David Lubarsky, MD, chair of the Department of Anesthesiology at the University of Miami; Debra Schwinn, MD, HS '86-'89, dean of the University of Iowa Roy J. and Lucille Carver College of Medicine; and William Greeley, MD, HS '76-'80, chair of the Department of Anesthesiology and Critical Care Medicine at Children's Hospital of Philadelphia.

Photo credit: Elizabeth T. Perez

"A lot of times, mentors see more in you than you see in yourself. They create opportunities for those coming behind them and then those people take advantage of it and hopefully take it to even higher levels than you would expect or hope when you're the leader."

- Mark F. Newman, MD

In 2009, Tong-Joo Gan, MD, MHS, vice chair of faculty development, took over the responsibility to help the anesthesiology department establish a formalized mentorship program that would attract and retain the best and brightest physicians and put them on a pathway to success. Under this program, mentors encourage mentees to push the envelope a little further and look for innovative ways to improve patient care.

According to Dr. Gan, studies have shown that the first five years of a new faculty member's career in an academic setting are critical to their overall success and satisfaction in academic medicine. Keeping this in mind, a formalized mentorship program was put in place at Duke to pair new and associate faculty members with world-class experts who could guide them in their pursuits.

Process

After faculty members are paired with a mentor, they are placed within a "mentorship committee" that consists of the mentee, the mentor, and the division chief. Mentors meet with their mentees quarterly to review their current and future goals. The meetings help the mentor keep the mentee on track by developing short-term goals (six to twelve months), intermediate-term goals (one to three years, such as a manuscript or program), and long-term goals for career development.

At the six-month mark, the mentor creates a formal report that outlines the mentee's goals, achievements, and aspirations for the future. The mentor works with the mentee to identify obstacles and determine the resources needed for success. The mentorship committee then meets with the department chair to evaluate the success of the mentoring relationship and discuss future plans.

Next Steps

The department now has plans to expand this initiative to include residents and fellows. A formalized plan will allow trainees to benefit from guidance much earlier in their careers and set a path for themselves from the outset.

Dr. Gan believes that a formalized training program should be implemented for mentors as well. He feels that symposiums and educational programs would give mentors the opportunity to fine-tune their leadership skills and allow them to become a better resource for their mentees.

Mark F. Newman, MD
Chair of the Department of Anesthesiology

When Mark Newman, MD, came to Duke as a cardiac anesthesiology fellow in 1988, he had plans to go into private practice. "I came and I enjoyed the process so much that I was totally confused when I left," recalls Dr. Newman. During his fellowship, Dr. Newman had two mentors, Jerry Reves, MD, and John Leslie, MD. "Dr. Reves showed me what I could do, trained me, put me on a pathway where I could succeed and gave me the credit for that success. Dr. Leslie made me feel a part of the team and allowed me to pick up and run some of my own projects at an early time, which made me realize that this is something that I can do."

After three years of service in the United States Air Force as chief of cardiac anesthesiology at Wilford Hall, Dr. Newman made his way back to Duke in 1992. A few years later, there was an opportunity for a transition in leadership in the Division of Cardiothoracic Anesthesiology. "We did a national search for a new chief, then Dr. Reves came and talked to me one day and asked me if I would consider the position. A lot of times, mentors see more in you than you see in yourself. I thought it was a little early, but I had a lot of support from the faculty and other people."

As Dr. Newman progressed in his career at Duke, he found himself following in the footsteps of Dr. Reves. "Obviously, I had a good role model. Dr. Reves had been the chief of the cardiac division, then, over time, he allowed me to learn as vice chair of the department. When he went on to become dean, it was an opportunity for me to become interim chair, and then chair of the department. I think that's what mentors do, they create opportunities for those coming behind them and then those people take advantage of it, and hopefully, take it to even higher levels than you would expect or hope when you're the leader."

Karthik Raghunathan, MD, MPH
2013 DREAM Innovation Grant Recipient

In July 2012, Karthik Raghunathan, MD, MPH, left his job in private practice at Baystate Medical Center, joined Duke, and moved his young family of five to start a new life in Durham. "Mentorship is a big reason why I moved to Duke," says Dr. Raghunathan. He found that unlike his previous experiences, Duke celebrated a culture of curiosity and questioning. "Part of mentorship is being able to comfortably ask questions without fear. You want someone who is willing to listen even if you are raising something that seems very fundamental."

As a fellow, Dr. Raghunathan had Tom Higgins, MD, an anesthesiologist, intensivist, and vice-chair for the Department of Medicine at Baystate Medical Center, as a mentor. Dr. Higgins inspired him to think about his role in medicine globally. "I don't think of what I do as being restricted to just the operating room, but how it impacts patients around the world," Dr. Raghunathan explains.

After five years of practicing anesthesia at Baystate Medical Center, Dr. Raghunathan met Andrew Shaw, MD, MBBS, who is an anesthesiologist at the Durham VA Hospital. Sharing similar research interests, Dr. Shaw encouraged Dr. Raghunathan to come to Duke, where his passion for research would be fostered by an innovative and collaborative environment. Once he joined Duke, Dr. Raghunathan was put under the able mentorship of Dr. Shaw. "This place has exceeded my expectations in terms of

Photo credit: Elizabeth T. Perez

"This place has exceeded my expectations in terms of having almost daily access to my mentor, and not just professionally, but also personally."

- Karthik Raghunathan, MD, MPH

having almost daily access to my mentor, not just professionally, but also personally," says Dr. Raghunathan.

Steve Melton, MD
2013 DREAM Innovation Grant Recipient

In 2007, Steve Melton, MD, joined the ambulatory anesthesia faculty at Duke. "From the start, you're surrounded by great people who want to get involved with your career beyond the clinical practice," says Dr. Melton. While Dr. Melton found many clinical mentors within his division, including Stephen Klein, MD, chief of the Division of Ambulatory Anesthesia and Medical Director of the Ambulatory Surgery Center, Karen Nielsen, MD, and Marcy Tucker, MD, PhD, he also reached out to Ricardo Pietrobon, MD, PhD, as part of the department's Research and Innovation Coaching Program, and Richard Moon, MD, chief of the Division of General, Vascular, and Transplant Anesthesia and Medical Director of the Hyperbaric Center, to serve as his research mentors.

Drs. Klein, Nielsen, and Tucker fostered Dr. Melton's interest in utilizing peripheral nerve blockades that are used in ambulatory surgery and applying them to rehabilitate stroke patients. Drs. Pietrobon and Moon showed Dr. Melton how to conduct research and obtain funding and turned his research aspirations into reality. Dr. Melton was awarded a 2013 DREAM Innovation Grant as a result of the support he received from his mentors.

Michael Manning, MD, PhD
2013 DREAM Innovation Grant Recipient

Michael Manning, MD, PhD, is a firm believer in the power of mentorship and has had several mentoring relationships throughout his career. During his undergraduate years at the University of Kentucky, he had a budding interest in research, something that David Randall, PhD, professor of cardiac physiology, noticed early on. "He quickly brought me into his lab and started introducing me to research and research techniques…and he really became a father figure to me," says Dr. Manning fondly. Dr. Randall guided Dr. Manning to pursue his career in research by encouraging him to attend graduate school followed by medical school. While in residency, Dr. Manning's residency director, Randall Schell, MD, served as both his role model and advisor. Dr. Schell completed his cardiothoracic anesthesia training at Duke, and encouraged Dr. Manning to explore his interest in cardiovascular research and anesthesia at this institution.

Photo credit: Elizabeth T. Perez

"Together, this mentoring team is going to bring me forward in my career and allow me to really look at angiotensin and the interplay between the heart and the kidney, especially centered around cardiopulmonary bypass."

- Michael Manning, MD

Above: Michael Manning, MD, working on his research project with his mentor, Mihai Podgoreanu, MD

When Dr. Manning came to Duke for his clinical fellowship, he was put under the mentorship of Mihai Podgoreanu, MD, a basic research scientist and anesthesiologist in the Division of Cardiothoracic Anesthesiology and Critical Care Medicine, and Tom Coffman, MD, chief of the Division of Nephrology and a well-known expert in the angiotensin function in the kidney. "Together, this mentoring team is going to bring me forward in my career and allow me to really look at angiotensin and the interplay between the heart and the kidney, especially centered around cardiopulmonary bypass," says Dr. Manning.

Dr. Manning advises new faculty to take the first step in the mentoring program and build on it. "Once [you] get comfortable with the program, look for other people outside and build on those mentorship relationships," adds Dr. Manning.

Miklos Kertai, MD, PhD
2013 DREAM Innovation Grant Recipient

Miklos Kertai, MD, PhD, assistant professor in the Division of Cardiothoracic Anesthesiology and Critical Care Medicine, was drawn to Duke because of the formalized mentorship program that he knew was critical to his career development. He was at a point in his professional and scientific career where he wanted to dig deeper into the reasons why certain patients suffer postoperative atrial fibrillation, a serious complication following heart surgery.

Dr. Kertai was placed under the mentorship of Dr. Podgoreanu and Dr. Joseph Mathew, chief of the Division of Cardiothoracic Anesthesiology and Critical Care Medicine. "Dr. Podgoreanu was instrumental in helping me develop my research idea as well as getting the tools necessary that developed into a successful [grant] application, while Dr. Mathew was critical in reintroducing the importance of atrial fibrillation."

Dr. Kertai attributes his ability to obtain a DREAM Innovation Grant and pursue his research interests to his mentors, support of the division, and to Dr. Newman's vision of establishing a formalized mentorship program.

Photo credit: Jared Lazarus

Above: (From right) Steve Melton, MD, with his mentor, Stephen Klein, MD, performing a peripheral nerve blockade at Duke Ambulatory Surgery Center

TEE meets iPad

Brandi Bottiger, MD, and a team of talented physicians from the Department of Anesthesiology at Duke are changing the way trainees look at the heart.

Photo credit: Elizabeth T. Perez

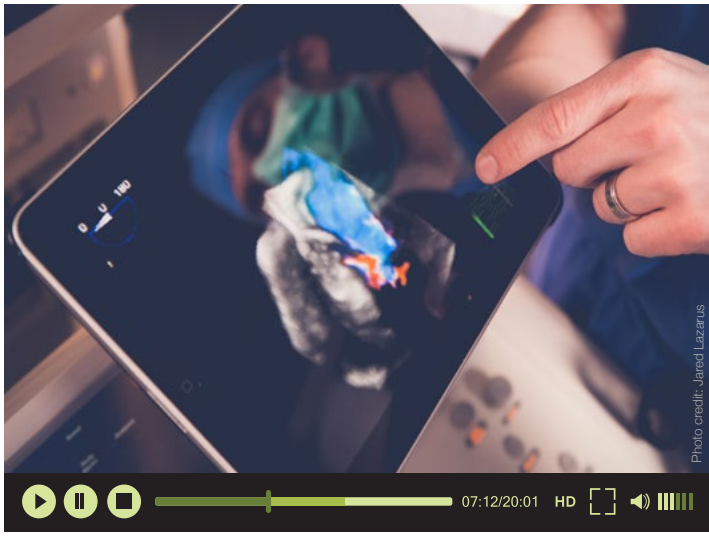


Photo credit: Jared Lazarus

Left to right: Madhav Swaminathan, MD, MBBS, instructing residents on the use of TEE in the OR; Close-up of the real-time TEE instruction given on the iPad in the operating room; James (Alex) Feix, MD, and Brandi Bottiger, MD, use the iPad for real-time TEE instruction in the operating room

As a pioneer of transesophageal echocardiography (TEE) during cardiac surgery, the department has always used traditional didactic methods to teach residents and fellows how to become the best in the field. For Dr. Bottiger, the best isn't good enough. She believes that a combination of didactic methods and the use of the iPad as an instructional and reporting tool in the operating room would not only give residents and trainees a higher level of education, but it would also ensure better perioperative care for patients. She is determined to make the TEE program at Duke advance even further.

TEE at Duke

Fiona Clements, MD, who became chief of cardiothoracic anesthesiology in 1991, pioneered TEE during cardiac surgery at Duke. TEE is a way of producing echocardiograms of the heart by guiding a transducer down the patient's esophagus and placing it directly behind the heart. The transducer uses ultrasound to generate images of the heart. This is more efficient than standard methods because first, the heart is directly visualized with the echocardiogram, and second, images are obtained during surgery so surgeons can evaluate the success of repair.

Today, Madhav Swaminathan, MD, MBBS, and Alina Nicoara, MD, are the forces behind the TEE program at Duke. Dr. Swaminathan joined Duke as a cardiothoracic anesthesia fellow in 2000, and is known worldwide for his expertise in TEE education and identifying echocardiographic predictors of adverse outcome. Under his leadership, Duke Anesthesiology was one of the first departments to use a TEE simulator to further the fellowship training experience. Dr. Nicoara completed her fellowship in cardiothoracic anesthesia at Duke in 2007, and went on to become faculty in the cardiac division in July 2010. Last year, she was appointed as the Director of the TEE Education Program for Cardiothoracic Anesthesia at Duke.

Dr. Swaminathan describes Duke's TEE program as the most advanced echo-training program in the country. He is adamant that, "No one even comes close to the instruction they (trainees) get at Duke in echo." The program trains 12 fellows every year. They are exposed to an extensive curriculum, including didactics, rotations in the echo lab, case diversity, reviews, lectures, seminars, quizzes, and additional training necessary to complete the program and graduate as experts. Dr. Swaminathan and Dr. Nicoara have been heavily involved with Dr. Bottiger's iPad study and believe that the use of the new iPad technology in the operating room would advance the TEE program even further.

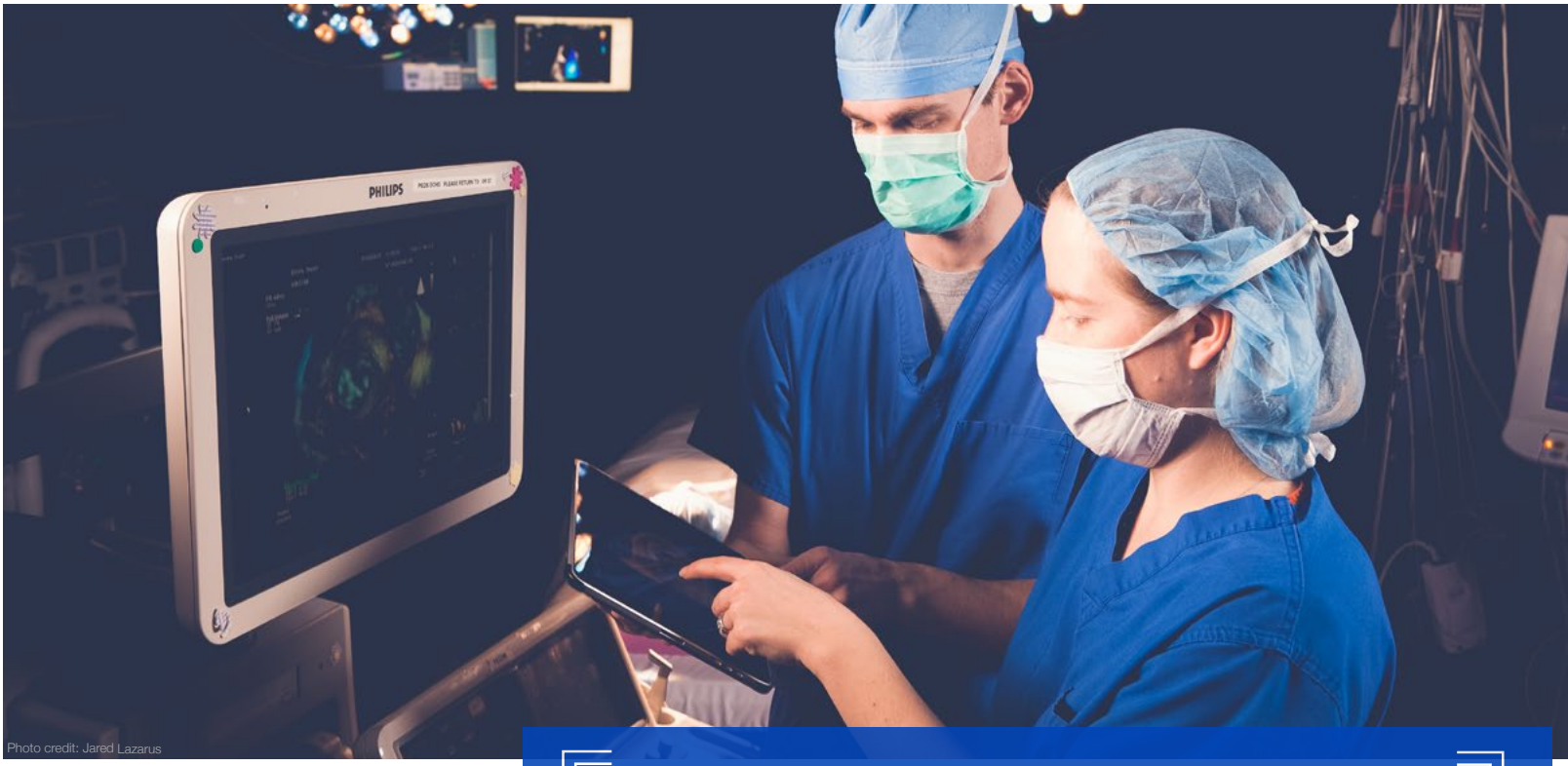


Photo credit: Jared Lazarus

> "Here at Duke, we are always trying to implement the next level and how we can get better." - Brandi Bottiger, MD

An Idea is Born

Dr. Bottiger completed her fellowship in cardiothoracic anesthesiology at Duke University in 2011. During her training, a combination of workshops, hands-on didactics, instruction in the operating room, and lectures were the primary methods used to teach fellows how to obtain and interpret TEE images.

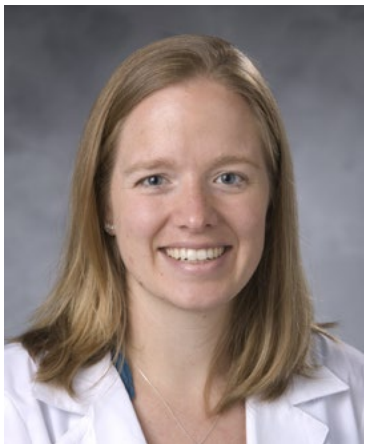
It was in the TEE simulation center, during a trial funded by the Foundation for Anesthesia Education and Research, where Dr. Bottiger and her Duke colleague, Dr. Atif Raja, came up with the idea of employing the iPad as an educational tool. During the trial, the iPad was being used to display 2-D TEE images. With the high quality 3-D TEE images that Dr. Raja had obtained, they agreed that the iPad could be used for real-time instruction in the operating room.

Using the iPad

During surgery, a Philips X-72t TEE probe with an iE33 XMatrix system™ is used to capture 3-D images. Loops of the images are then downloaded to the Xcelera Phillips Imaging Management System™ for post processing, and iMovie™ is used to annotate the loops with instructional education on how to acquire and interpret 3-D images, as well as highlight normal and abnormal structures. Each video is approximately three to five minutes long, and takes approximately two to three hours to acquire, edit, annotate, and post.

Once the videos are complete, they are uploaded and indexed onto the iPad, which is set up next to the echo machine. Through the Movies application, the videos can be pulled up at any time to allow trainees to see the procedure while it is being performed. Currently, there are two iPads that circulate among trainees. These iPads are used exclusively in the operating room to eliminate the risk of altering video or software settings. While having just two iPads can be limiting, it is hoped that with incoming residents receiving iPads, the use of this technology will be expanded.

To date, 17 videos have been created with the ACGME objectives and TEE Board content requirements in mind. Through feedback from trainees, the team is still determining which videos are the most useful for educational purposes and what content is necessary for educational advancement.



(From left): TEE faculty Madhav Swaminathan, MD, MBBS; Brandi Bottiger, MD; and Alina Nicoara, MD

Trial Period

In order to fully implement the iPad as a training tool in the TEE program, Dr. Bottiger and her team, which has grown to include Alina Nicoara, MD; Katherine Grichnik, MD; Madhav Swaminathan, MD, MBBS; Manuel Fontes, MD; Mark Stafford-Smith, MD; Catherine Kuhn, MD; and George Whitener, MD, will need to make a strong case for the use of the iPad as an educational device in the perioperative setting. Two groups of residents and fellows in the TEE program at Duke will be tested over a two-year period to determine if the use of the iPad improves their accuracy and timing in both written and simulated tests.

The team is hoping that the iPad will help trainees get a better educational experience as well as improve the proficiency of perioperative care. A preliminary analysis is being carried out to assess how the iPad in the operating room will make TEE reporting more efficient. Currently, fellows perform the TEE exam on patients in the operating room and return to their office or desktop to enter the data. This data is then relayed to the attending and is entered into the patient's electronic medical record (EMR). With the iPad, the fellow could enter the data in the operating room, and the information could be electronically sent to the attending and entered into the patient's EMR before the patient ever leaves the operating room. This process would also allow healthcare providers in the intensive care unit (ICU) to view current patient data in the post-operative phase of care. They would have access to the data before the patient even arrives in the ICU.

While there are many benefits of using the iPad as a learning tool, Dr. Bottiger and her team also anticipate some obstacles during their two-year study period. The initial cost of providing iPads, servicing expenses, technology support, and the replacement of lost or stolen iPads are issues that will need to be addressed. Also, some believe that the presence of an iPad in the operating room could lead to distractions and misuse. However, citing the successful use of tablet devices by several academic institutions recently, the team is confident that this is the technology of the future and its benefits will greatly outweigh any drawbacks.

The Future of Education

Dr. Bottiger and her team are eager to discover how the use of the iPad in the perioperative setting will advance the learning of health care professionals trained at Duke. They are already looking at new opportunities to expand the capabilities of the iPad. The creation of an application that contains videos and articles is just the beginning. Eventually, they would like to produce videos that are not only available for internal consumption, but would also represent the face of Duke outside. Though they are in the infancy of analyzing tablet technology in the realm of TEE, they feel there are endless possibilities of its use as a training tool in other divisions of anesthesiology as well. Dr. Bottiger: "Here at Duke, we are always trying to implement 'the next level' and 'how we can get better.'" It is clear that she is well on her way to do that.

Medical Alumni Association Awards
DISTINGUISHED FACULTY AWARD

Mark F. Newman, MD, HS '88-'89

Having grown up on a farm in Owensboro, Ky., with a full complement of cattle, hogs, and sheep, a natural career path for Mark Newman could easily have been veterinary medicine. But the hard-working farmer's son sought more intimate connections with his patients and chose the human variety instead.

Anesthesiology grabbed his interest early and his impact on the field has been profound. Best known for his two decades of far-reaching research on neurocognitive decline after surgery, Newman, the chair of the Duke Medicine Department of Anesthesiology, has helped to identify pre- and post-operative risk factors for cognitive decline following surgery. His discoveries regarding the management of body temperature and glucose levels to improve cognitive outcomes are widely used today.

He earned a medical degree at the University of Louisville in Kentucky and completed residency in anesthesiology at Wilford Hall United States Air Force Medical Center in San Antonio, Texas. He came to Duke in 1988 for a cardiac anesthesia fellowship under pioneering anesthesiologist Joseph "Jerry" Reves, MD, who ignited Newman's passion for neurological outcomes research. Newman returned to Wilford Hall to serve as director of research and chief of cardiothoracic anesthesiology. During that time, he also held an appointment at the University of Texas Health Sciences Center as a clinical assistant professor. He returned to Duke in 1992 to lead the Division of Cardiothoracic Anesthesiology and Critical Care Medicine to international prominence. Newman went on to become a pioneer in the field, having largely defined the now widely accepted demographic, procedural, and genetic risk factors for outcomes-based research.

He became full professor of anesthesiology and vice-chairman of the Department of Anesthesiology in 1999, and was named chair of the department in 2001. Also in 2001, Newman was recognized for his expertise by his appointment as the first medical director of the Global Perioperative Research Organization, a joint venture between the International Anesthesia Research Study Society and Duke University's Clinical Research Institute.

In 2004, he was named the Merel H. Harmel Distinguished Professor of Anesthesiology. In 2006, he was awarded The Bernard H. Eliasberg Medal for significant contributions to the field of anesthesia, critical care, and pain management. He currently is principal investigator on the largest perioperative study ever conducted to reduce mortality and stroke in patients undergoing cardiac surgery. More than 10,000 patients are enrolled worldwide.

Dr. Newman and his wife Susan live in Durham and have three children, Sarah, T'07, Jack, a senior at Trinity University in San Antonio, Texas, and Catherine, a Duke freshman.

Mark F. Newman, MD, HS'88-'89
Education: Western Kentucky University, Bowling Green, Ky.; University of Louisville, Kentucky
Training: Wilford Hall United States Air Force Medical Center, San Antonio, Texas; Duke University Hospital
Current titles: Merel H. Harmel Professor of Anesthesiology, Chair of the Department of Anesthesiology, Professor of Medicine, Duke University School of Medicine; Medical Director, Global Perioperative Research Organization, Director, Perioperative Organ Protection Consortium, Duke University Medical Center

Class Notes

Brett Gutsche, MD
Residency 1965

I am still practicing anesthesiology part-time at the Hospital of the University of Pennsylvania, but will be retiring on May 31, 2013. At that time, I would have been on the faculty at Penn Medicine for 43 and a half years.

I have never regretted the day, during my surgical internship at Duke, I told Ron Stephen, MD, that I wanted to be an anesthesiologist. On completing my residency at Duke in June 1965, I spent two years in the Public Health Service (PHS) in Anchorage, AK, which were two of the most enjoyable years of my life. Then, I went to the University of Tennessee in Memphis, where I was the anesthesiologist in-house the night Martin Luther King, Jr. was shot. On January 2, 1969, I joined the anesthesia staff at the University of Pennsylvania, where Robert D. Dripps was the chair.

While I still miss Alaska and visit the state often, I never regret going to Penn Medicine and entering an academic career as a clinician and a clinical teacher.

Debra Schwinn, MD
HS 1986-1989

Debra A. Schwinn, MD, began her appointment as dean of the University of Iowa Roy J. and Lucille A. Carver College of Medicine on October 31, 2012. She is also the 2012-2014 chair of the Board of Trustees for the International Anesthesiology Research Society.

Scott Howell, MD
HS 1992-1995

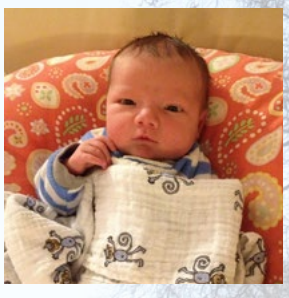
My family continues to enjoy living in Florida. My group practice also continues to do well and remains busy.

In Spring 2012, my wife, Ann, and youngest son, Finn, now in eighth grade, travelled to Nairobi, Kenya, for their second trip in as many years to produce a video for the American Embassy. It was quite an experience and they had a great time exploring that part of the world.

My oldest son, Sebastian, now a sophomore in college, and I raced dirt bikes in a 24-hour event last summer. We won our "Family Duo" class where we both had to "tag- team" for 24 hours. Might I say it was really tough getting back on the bike at 3 a.m.! Competition was strong and we were in last place at one point, but managed to move into first place by 5 a.m. the next day and held it to the end. We miss Durham and Duke!

Andy Katz, MD
Residency 2009

I am enjoying my job at Children's Healthcare of Atlanta, Scottish Rite Campus. Karen and the kids are all doing well.



Robert H. Thiele, MD
HS 2012

In December 2012, I was awarded $43,780 from the Ivy Biomedical Innovation Fund for a project entitled, "Pre-Animal Development of a NIRS Device to Monitor the Mitochondrial Redox and Tissue Oxygen State of Mucosal Tissue." This is an internal grant focused on the development of biomedical devices with strong commercialization potential.

My wife, Dana, gave birth to our second child, and first son, Turner Coons Thiele, on January 5, 2013.

Burkhard Mackensen, MD, PhD, FASE
HS 2000

Dr. Burkhard Mackensen is serving as acting chair of the Department of Anesthesiology and Pain Medicine at the University of Washington.

Moeen Panni, MD, PhD
Duke Faculty 2002-2005

Following faculty positions at Duke University and the University of Texas, Houston, Dr. Panni was appointed chair of anesthesiology and promoted to professor at the University of Florida College of Medicine, Jacksonville.

Dr. Panni has received several educational awards, including the Society of Obstetric Anesthesiology and Perinatology's Research in Education Award and the national "Teacher of the Year" award.

Mount Everest Project

The sudden lack of tissue oxygen is a major problem for the critically ill, as well as those who scale high altitudes. However, it has been seen that experienced mountaineers adapt to low oxygen environments found at higher elevations. If we find the underlying mechanisms of this adaptive response, we could help critically sick patients survive the harmful effects of tissue oxygen deprivation. Efforts are afoot at Duke in this direction.

CLUES TO SURVIVING LOW OXYGEN ENVIRONMENTS

During its development in the womb, a fetus thrives in a low-oxygen environment. This ability, however, is lost shortly after birth. Interestingly, it has been seen that some mountaineers seem to regain some of this capacity when they ascend high mountains slowly.

The summit of Mount Everest has about one-third of the oxygen supply found at sea level. If people were to suddenly be transported there from sea level, they would lose consciousness within a few minutes. The only way to stay alive would be to breathe extra oxygen from a tank. However, some people have been able to climb Mount Everest without extra oxygen. By climbing slowly, they have been able to adapt to this decreased oxygen environment. A conclusive explanation for this adaptation, however, remains elusive.

OUR PLAN

We plan to learn how humans successfully adapt to altitude and low oxygen environments in a series of experiments over the next few months. The attempt is to understand this adaptive mechanism and accelerate the adaptation process from a few weeks to a few hours or minutes. This is a first step in figuring out new ways of adapting to altitude as well as developing new therapies for illnesses, like heart attack, stroke, and lung disease, in which the lack of oxygen can be devastating to the patient's brain and other organs. We will be studying people in an altitude chamber at Duke that simulates the environment of people trekking to the Mount Everest Base Camp. We will be examining changes in metabolism and DNA while people acclimatize to the low oxygen levels at higher altitudes.

Earlier this year, a simulated climb was performed in the altitude chambers at the Center for Hyperbaric Medicine and Environmental Physiology at Duke to obtain preliminary measurements on the effects of altitude on genes. Afterwards, the team made a trek to the Mount Everest Base Camp to study adaptation to altitude in a large number of people in conjunction with the Xtreme Everest 2 team from University College, London, UK. An updated report of their climb will be featured in the next BluePrint edition.

FOLLOW US

You can follow the team's blog by visiting the BluePrint website: http://anesthesiology.duke.edu/?page_id=228144.

SPECIAL THANKS TO OUR DONORS

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