



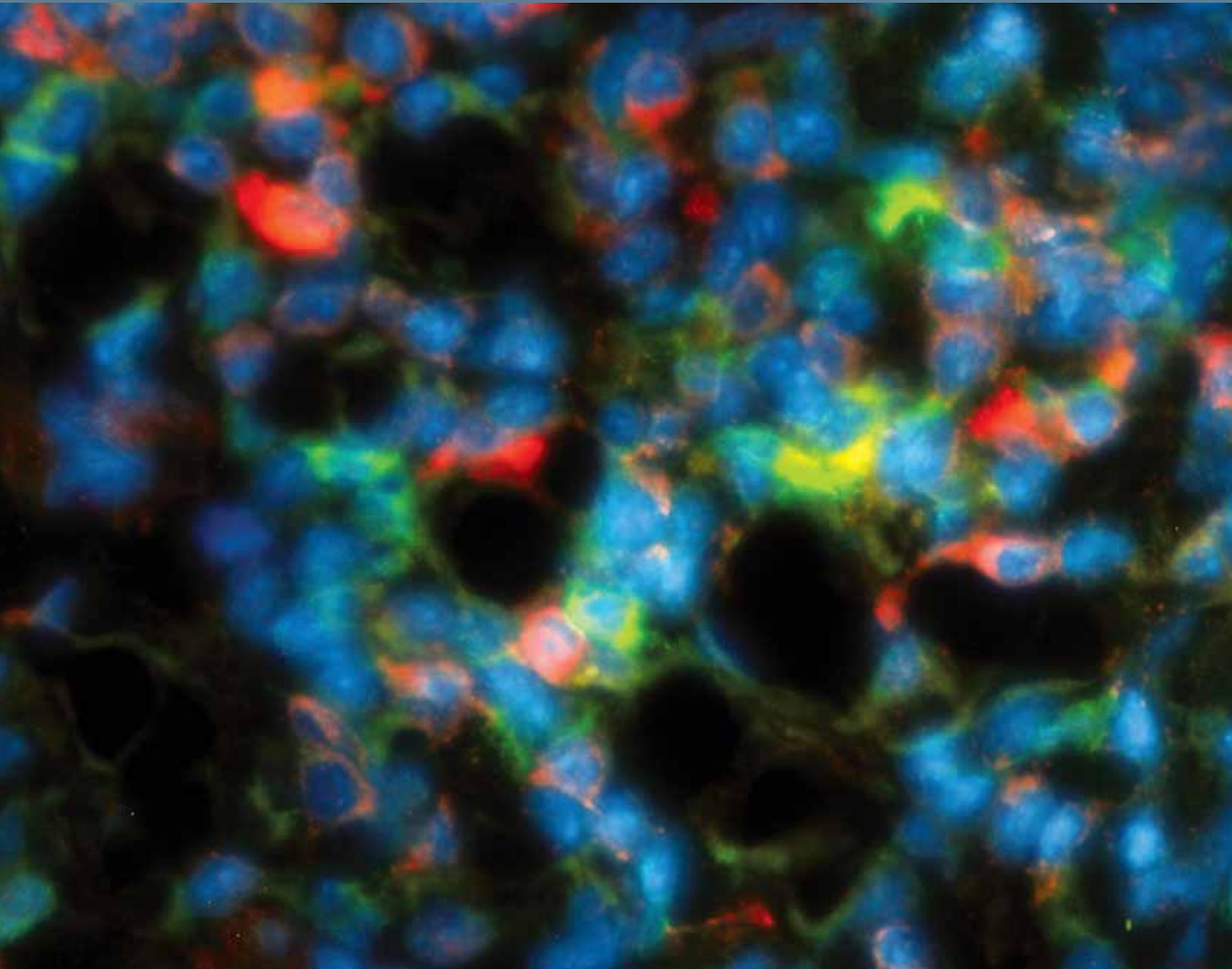
Beth Israel Deaconess
Medical Center



HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

Roberta and Stephen R. Weiner Department of Surgery

2018 SURGERY RESEARCH REPORT



◀ COVER IMAGE:

The Wegiel research group (see page 98, was selected to provide the cover image of *Cancer Research* in July 2017, to accompany the paper, "Deletion of Lactate Dehydrogenase-A in Myeloid Cells Triggers Antitumor Immunity." The paper describes research which suggests that lactic acid, expressed by macrophages, is a major contributor to the suppression of T cells in the tumor microenvironment. Not only does this research add to the understanding of how immunosuppression encourages tumor growth, but it also suggests new targets for treatment.

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From the Chair



Innovation and discovery occur at the interface of disciplines – where diverse viewpoints interact, problems are examined from different perspectives, and ideas germinate into new solutions to intractable clinical problems.

The Department of Surgery at Beth Israel Deaconess Medical Center (BIDMC) is committed to fostering innovation and discovery, by providing a research environment that nurtures intellectual diversity, embraces individual freedom, encourages flexibility, and promotes spontaneity and originality. By embracing these values, we are able to further our mission to develop more effective approaches for the promotion of health, the prevention of illness, and the treatment of disease.

The 2018 issue of our Surgery Research Report highlights research that spans from bench to bedside. Our robust research platform has nearly \$20 million in funding from the NIH and other federal sources, major philanthropic organizations, and private industry. We conduct laboratory-based investigations that define the molecular basis of disease; develop novel surgical approaches, tools, and devices; and evaluate the effectiveness of clinical interventions on large populations of patients. We also carry out studies that shed light on disparities in the delivery of surgical care or access to treatment for our most vulnerable citizens.

This research has international impact. Our faculty and residents have published hundreds of papers in peer-reviewed scientific journals. Many of our faculty also serve as editors and reviewers for high-impact journals such as *JAMA*, *The New England Journal of Medicine*, and *Nature* – among others. They participate in leading medical and scientific organizations.

We are also committed to training and mentoring the next generation of surgeon-investigators – master-surgeons who will change the practice of medicine. We offer both exceptional clinical training in surgery and novel educational opportunities that promote innovative problem finding and problem solving.

The individuals whose research is highlighted in this report represent the very best of our department and the medical center. They are dedicated to fulfilling our mission, of serving our communities, improving health through innovation and discovery, and preparing future leaders in American medicine.

Elliot L. Chaikof, MD, PhD

Johnson and Johnson Professor of Surgery
Chair, Department of Surgery
Surgeon-in-Chief

Introduction

In addition to delivering outstanding patient care, translational and clinical research constitutes one of the cornerstones and missions of the Department of Surgery. Research programs in Surgery at the Beth Israel Deaconess Medical Center (BIDMC) are focused in five thematic areas – Cancer Biology, Innate and Adaptive Immunity, Regenerative Medicine, Nutrition and Metabolism, and Health Services Research. Important cross cutting platforms include the Center for Drug Discovery, the Harvard Surgical Program in Innovation (SPIN), Surgical Informatics, and the FIRST (**F**acilitating **I**nnovative **R**esearch and **S**urgical **T**rials) program, which supports clinical research and surgical trials.

All divisions and nearly all faculty have active translational or clinical research programs. In FY17, over 40 faculty had research programs with dedicated research space, postdoctoral fellows, graduate students and surgical residents, as well as research nurses and clinical coordinators. Many of these programs include undergraduates and medical students pursuing research electives and fellowships.

Our clinical research initiatives range from clinical trials focused on the development and assessment of new drugs and surgical technology, to health services research focused on the development of effective clinical decision tools, addressing challenges in health inequities and global health, and the novel applications of machine learning and recent innovations in the field of data science. Our faculty are principal investigators of more than 250 open clinical research protocols.

Collectively, the common thread that weaves through all of these research projects is the drive to advance scientific discovery and foster the translation of research into clinical practice to improve the health and wellbeing of our patients. In the process, the department has expanded its clinical research mentorship program for faculty, research fellows, and surgical residents. Preparing future leaders in American surgery, who excel as master clinicians, own a question, and embrace the notion of life-long scholarship, remains a core mission of the department.

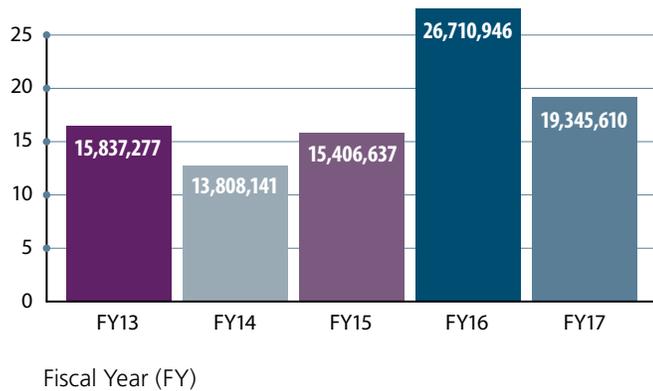
Leadership

Research programs in the Department of Surgery are led by Richard R. Cummings, PhD, Vice Chair for Basic and Translational Research, James Rodrigue, PhD, Vice Chair for Clinical Research, and Raul Guzman, MD, Vice Chair for Resident Research. Dr. Cummings is Professor of Surgery at Harvard Medical School, Director of the NIH-funded National Center for Functional Glycomics, and Director of the Harvard Medical School Center for Glycoscience, all based in the department. In addition, he serves as Associate Director of our Center for Drug Discovery and Translational Research. Dr. Rodrigue is Professor of Surgery at Harvard Medical School and oversees the FIRST program, the Faculty Clinician-Investigator Mentorship Program, and the Clinical Scholarship Program. He also serves as Chair of the Academic Promotions Committee in the Department of Surgery. Dr. Guzman is Associate Professor of Surgery in the Division of Vascular Surgery and an NIH-funded investigator. He oversees resident pre-research advising, resident research mentorship and career development, and our resident and fellow research community.

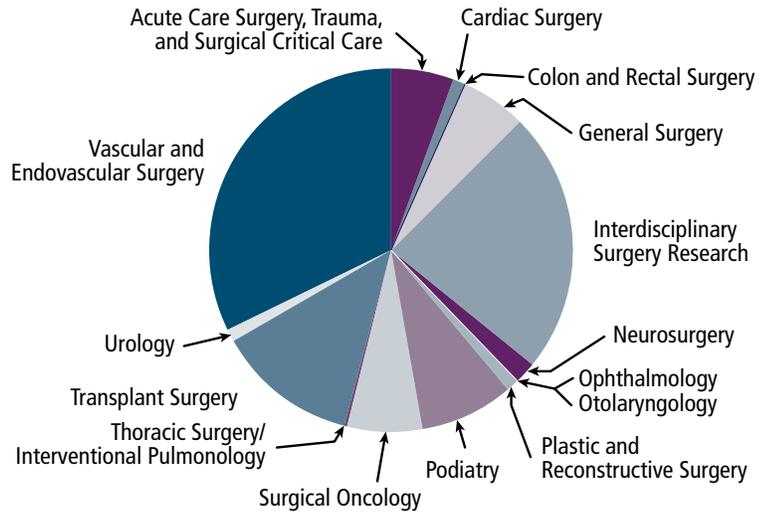
Research Funding

The Department of Surgery holds numerous federal awards from the National Institutes of Health, Department of Defense, Department of Health and Human Services and the Patient-Centered Outcomes Research Institute (PCORI). Grants included a total of 43 federally funded grants and 73 non-federal awards. In addition, the Department faculty were Principle Investigators of two NIH T32 and one NIH T35 training grants. Total research funding was more than \$19.3 million dollars in FY17 (Figure 1) with a broad distribution of awards among our divisions (Figure 2).

▼ FIGURE 1: Total (federal, non-federal, other-federal, and training) research dollars awarded per year during the 5-year period, 2013-2017.



▼ FIGURE 2: Total (federal, non-federal, other-federal, and training) research dollars awarded in FY17 by division.



Acute Care Surgery, Trauma, and Surgical Critical Care	8	\$1,102,573
Cardiac Surgery	4	\$204,218
General Surgery	10	\$1,154,142
General Surgery	20	\$4,486,854
Neurosurgery	7	\$378,075
Plastic and Reconstructive Surgery	3	\$184,492
Podiatry	7	\$1,639,947
Surgical Oncology	6	\$1,298,120
Transplant Surgery	13	\$2,436,066
Urology	5	\$207,184
Vascular and Endovascular Surgery	34	\$6,228,756

▲ FIGURE 3: Total number and amounts of research awards in FY17 by division.

T32 Training Grants

The Department of Surgery continues its longstanding NIH Training Grant in Vascular Biology and Surgery (PI: Frank LoGerfo, MD) and an NIH T35-funded program directed at providing research opportunities for medical students. In addition, we hold an NIH-funded T32 training grant in Inflammation and Trauma (PI: Wolfgang Junger, PhD). Surgical faculty are also participating mentors in the GI Surgery Research Training Grant, which is a joint NIH-funded T32 training grant among the three Harvard Medical School teaching hospitals.

Surgical Residents, Post-doctoral Fellows, and Research

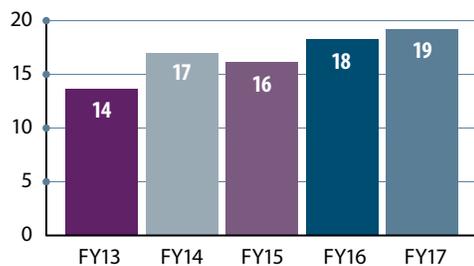
Clinical Scholarship Program

The Clinical Scholarship Program pairs first-year surgery residents with a faculty member who provides mentorship and guidance required for the development of the skills and tools necessary to conduct clinical investigations. Residents are also provided with a one month period for focused advanced study in clinical trial and research design related to their project area in the latter portion of their internship year.

Directed by James Rodrigue, PhD, the core objective of the Clinical Scholarship Program is to provide residents with a robust foundation for scholarship early in training and accelerate their development as future leaders in American Surgery. The program also allows residents to develop a mentorship relationship with additional faculty in the department in order to explore potential areas of clinical interest.

Within the structure of the Clinical Scholarship Program, residents meet regularly with research mentor(s), participate in research meetings, receive informal and formal feedback from faculty on project proposals, and are provided with focused reading and self-study material. They also attend presentations including topics such as clinical study design, biostatistics, communicating research, ethics, regulatory issues, and grant writing.

Residents are expected to prepare, submit, and present their research at the annual Department of Surgery George H. Clowes Surgery Research Day, and at the annual Harvard Medical School Surgery Research Day, as well as submit abstracts for presentations at national and international conferences, and manuscripts for publication in peer-reviewed scientific journals.

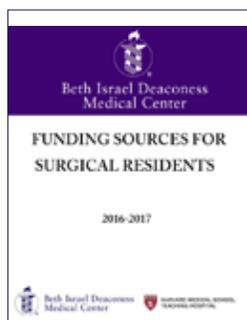


▲ FIGURE 4: Number of surgical residents per fiscal year spending time (2-3 years) in a research elective.

Residents' Research Rotation

Nearly all of our residents pursue a two to three year research fellowship in translational or clinical research as part of their surgical training, typically after their second or third clinical years (Figure 4).

The majority of residents perform research in laboratories within the Department of Surgery, but have also pursued research experiences at MIT, Harvard, Oxford University, NIH, or other leading institutions in the United States or abroad. In addition to funding through NIH training grants, society fellowships, or principle investigator research support, the department has also established five Richard and Sandra Cummings Surgical Resident Research Scholarships, which provides a minimum of \$25,000 of annual funding in support an approved research fellowship.



◀ FIGURE 5: "Funding Sources for Surgical Residents" aids in identifying fellowship awards for surgical research training.

George H. A. Clowes, MD, Surgery Research Day

The annual George H. A. Clowes, MD Surgery Research Day is open to all postdoctoral research fellows, surgical residents, graduate students, as well as medical students and undergraduates working in research labs in the Department of Surgery. Allan Kirk, MD, PhD, Professor and Chair of Surgery at Duke University served as the 2017 George H. A. Clowes Visiting Professor. Participants in 2017 included:

Basic Science

Christopher D. Barrett, MD

"Human neutrophil elastase mediates fibrinolysis shutdown through competitive degradation of plasminogen and generation of angiotatin"

Mentor: Michael B. Yaffe, MD

Christopher S. Digesu, MD

"A mechanistic case for paclitaxel-eluting polymer films in chondrosarcoma"

Mentor: Yolanda Colson, MD

Eliza Lee, MD

"Neuropilin-1 and its potential role in organ transplantation"

Mentor: Heung Bae Kim, MD

Qing Zhao Ruan, MD

"Large animal model of modified lymphatic microsurgical preventative healing approach"

Mentor: Bernard T. Lee, MD

Clinical Research

Ana Sofia Ore, MD

"Comparing the treatment burden of minimally invasive and open gastrectomy after neoadjuvant chemotherapy for locally-advanced gastric cancer"

Mentor: A. James Moser, MD

Daniel H. Buitrago, MD

"Perioperative Outcomes in 161 consecutive patients undergoing tracheobronchoplasty for severe diffuse tracheobronchomalacia"

Mentor: Sidhu P. Gangadharan, MD

Gyulnara Kasumova, MD

"Surgical management of gallbladder cancer: simple versus extended cholecystectomy and the role of adjuvant therapy"

Mentor: Jennifer F. Tseng, MD

Rouzbeh Motiei Langroudi, MD

"Modified park bench position for superior vermian arteriovenous malformations; a case series"

Mentors: Christopher Ogilvy, MD, and Ajith Thomas, MD

Theochardis Georgis, PhD

"Inflammation and neuropeptides in diabetic wound healing"

Mentor: Aris Veves, MD

Surgical Horizons Seminars Series

The Surgical Horizons Seminar Series hosts emerging and senior leaders whose endeavors promise to dramatically alter the landscape of care for the surgical patient.

- November 14, 2016 Heung Bae Kim, MD
Assistant Professor of Surgery, Harvard Medical School
Director, Pediatric Transplant Center at Boston Children's Hospital
"Patient Inspired Surgical Innovation: Where Do We Go From Here?"
- December 8, 2016 Allan M. Goldstein, MD
Surgeon-in-Chief, MassGeneral Hospital for Children
Director, Pediatric Neurogastroenterology Program, MassGeneral Hospital for Children
"Hirschsprung Disease: From Embryology to Therapy"
- January 30, 2017 Michael B. Yaffe, MD
David H. Koch Professor in Science and Professor of Biological Engineering, MIT
Acute Care Surgery, Department of Surgery, BIDMC
"Cross Talk between Neutrophils and the Blood Clotting System Modulates Inflammation after Traumatic Injury"
- February 13, 2017 Barbara A. Kahn, MD
Chief of Endocrinology, Diabetes and Metabolism, BIDMC
George A. Minot Professor of Medicine, HMS
"Discovery of a Novel Class of Endogenous Lipids with Anti-diabetic and Anti-inflammatory Effects"
- March 20, 2017 Elena Aikawa, MD
Director, Vascular Biology Program, Center for Interdisciplinary Cardiovascular Diseases, BWH
Associate Professor of Medicine, HMS
"Recent Advances in Cardiovascular Calcification Research"
- April 24, 2017 Suvranu De, ScD
J. Erik Jonsson '22 Distinguished Professor of Engineering
Head, Department of Mechanical, Aerospace and Nuclear Engineering, Rensselaer Polytechnic Institute (RPI)
Professor of Engineering, RPI
"Virtual Reality for Surgical Education: Some Recent Advances"
- May 15, 2017 Darrell J. Irvine, PhD
Professor of Materials Science & Engineering and Bioengineering, MIT
"Engineering Immunotherapies for Cancer and Infectious Disease"
- June 19, 2017 Daniel G. Anderson, PhD
Associate Professor, Department of Chemical Engineering and Institute for Mechanical Engineering and Science,
David H. Koch Institute for Integrative Cancer Research, MIT
"In Vivo Delivery of Nucleic Acid Genome Editing Tools and Cells"

FIRST Program

A robust research infrastructure is necessary to support the myriad tasks associated with study design and implementation, data collection, biostatistics and data analysis, within a complex regulatory environment. The FIRST (Facilitating Innovative Research and Surgical Trials) program was established to provide a core platform of resources to catalyze innovative and impactful clinical research and to educate and train the next generation of surgeon-investigators focused on patient-centered research.

Led by James Rodrigue, PhD, Professor and Vice Chair of Clinical Research, and Aaron Fleishman, MPH, the FIRST Program represents a comprehensive effort to:

- Advance scientific discovery and foster the translation of research into clinical practice to improve the lives of our patients
- Provide Department of Surgery faculty, fellows and residents with robust and comprehensive clinical research support
- Employ dedicated clinical research staff with extensive experience in all facets of clinical research conducted in the Department of Surgery
- Consolidate clinical research resources and expertise in the department
- Provide mentorship and guidance to clinical investigators and research staff
- Position the Department of Surgery to compete successfully for industry, federal, and private foundation funding
- Serve as a formal liaison between the Department's clinical research programs and regulatory agencies, including the Institutional Review Board, Office of Human Research Protections, and Clinical Trials Office, among others

The FIRST Program is designed to handle a full assortment of activities that are an essential part of most clinical research programs. These activities include, but are not necessarily limited to, research mentorship, protocol guidance and development, regulatory support, industry engagement, biostatistics support, study coordination, data collection and analysis, and grant application preparation and review. The FIRST Program is staffed by clinical trials specialists, clinical research assistants and coordinators, research nurses, and biostatisticians.

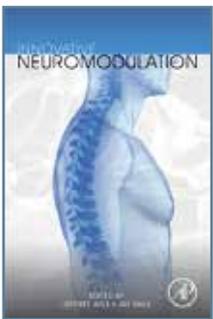
Research Facilities and Space

Research in the Department of Surgery currently occupies approximately 25,000 square feet (sf) of space, including basic science laboratories and clinical research activities in the Center for Life Science, Dana/Research West Building, Research North, among other sites. The overall dollar density for research space in the Department of Surgery is approximately \$260 per square foot.

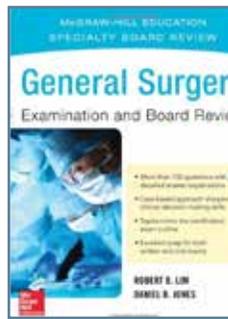
National and International Impact

Faculty members in the Department of Surgery have national and international impact through their research published in many high-impact journals such as *JAMA*, *New England Journal of Medicine*, *Nature*, *PNAS*, and *PLoS One*, among others (see Bibliography, page 13). In addition, our faculty have published books and textbooks that influence surgical practice. Members of our faculty also hold leadership positions in influential medical societies and serve on editorial boards or are editors for national and international journals. (See examples below.)

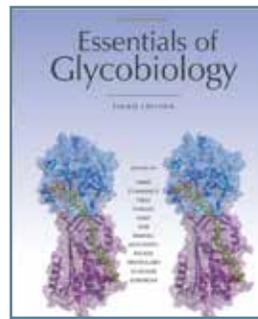
Books and Textbooks



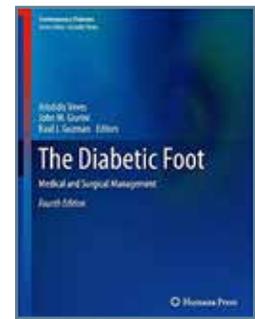
Arle JE, Shills JL. Innovative Neuromodulation. Academic Press 2017.



Lim RB, Jones DB. General Surgery: Examination and Board Review. McGraw-Hill Education 2016.



Varki A, Cummings RD, Esko JD, Stanley P, Hart G, Aebi M, Darvill AG, Kinoshita T, Packer NH. Essentials of Glycobiology, Third Edition. Cold Spring Harbor Laboratory Press 2017.



Veves A, Giurini JM, Guzman RJ. The Diabetic Foot: Medical and Surgical Management, Fourth Edition. Humana Press 2017.

Leadership positions

- Co-chair, Research and Scientific Policy Committee , International Neuromodulation Society (Arle)
- Board Member, International Society of Intraoperative Neurophysiology (Arle)
- Member, Policy and Advocacy Committee, North American Neuromodulation Society (Arle)
- President-Elect, Boston Surgical Society (Callery)
- President-Elect, Society for Surgery of the Alimentary Tract (Callery)
- President of the Americas Hepato-Pancreato-Biliary Association (AHPBA) Foundation (Callery)
- Executive Council member, International Hepato-Pancreato-Biliary Association (Callery)
- Vice-Chair for Section 01 in the National Academy of Medicine (Physical Sciences, Mathematical Sciences, Computer/Information Sciences, Biomedical Engineering, Engineering Sciences) (Chaikof)
- Co-Chair, Mapping the Human Glycome in Health and Disease, Radcliffe Institute for Advanced Studies (Chaikof)
- Member, Convening on the Physician Scientist Workforce, National Institutes of Health (Chaikof)
- Chair, Strategic Planning Committee, Surgical Infection Society (Cook)
- Director, National Center for Functional Glycomics (Cummings)
- President, Cell Transplant and Regenerative Medicine Society (Fisher)
- Member, Board of Directors, American Foundation for Donation and Transplantation (Fisher)
- Scientific Review Committee member, 2020 International Head and Neck Conference (Jalisi)
- Program Committee member, Academic Surgical Congress (James)
- President, Society of American Gastrointestinal and Endoscopic Surgeons (Jones)
- Trustee-at-Large, Society for Surgery of the Alimentary Tract (Jones)
- Chair, Essentials Task Force, www.Essentials.ASMBS.org (Jones)
- Chair, Education and Training Committee, Americas Hepato-Pancreato-Biliary Association (Kent)
- Member of In-Service Examination, Scientific Program and Instructional Course, Health Policy, and Healthcare Delivery committees, American Society of Plastic Surgeons (Lee)
- Treasurer-Elect, American Society for Reconstructive Microsurgery (Lee)
- Program Committee member, American Association of Plastic Surgeons (Lee)
- Co-chair, Performance Measures Work Group on Autologous Breast Reconstruction, American Society of Plastic Surgeons (Lee)
- Living Donor Committee member, American Society of Transplant Surgeons (Rodrigue)
- Member, Vascular Quality Initiative (a cooperative of 18 regional quality groups in the U.S. and Canada) (Schermerhorn)
- Member, Executive Committee and Research Advisory Committee, Society for Vascular Surgery (Schermerhorn)
- Member, Constitution and Bylaws Committee, and Continuing Medical Education Committee, Society of Surgical Oncology (Sharma)
- Associate Member, Broad Institute (Thomas)

Editors

- Associate Editor, *Frontiers in Eating Behavior* (Alonso-Alonso)
- Associate Editor, *Neurosurgery* (Arle)
- Associate Editor, *Neuromodulation* (Arle)
- Editor, *HPB* (Callery)
- Associate Editor, *Science Advances* (Cummings)
- Associate Editor, *Metabolism* (Hasselgren)
- Associate Editor, *Purinergic Signalling* (Junger)
- Editor-in-Chief, *Journal of Reconstructive Microsurgery* (Lee)
- Academic Editor, *Public Library of Science (PLOS One)* (Lin)
- Associate Editor, *Plastic and Reconstructive Surgery* (Lin)
- Associate Editor, *Plastic and Reconstructive Surgery-Global Open* (Lin)
- Associate Editor, *Clinical Transplantation* (Rodrigue)
- Editor in Chief, *Science Signaling* (Yaffe)
- Editor, *Frontiers in Biosciences* (Zhou)
- Editor-in-Chief, *Nutrition and Metabolic Insights* (Zhou)
- Editor-in-Chief, *Journal of Health Sciences* (Zhou)

Editorial board members

- *Liver Transplantation* (Fisher)
- *Liver Disease Review Letters* (Fisher)
- *Medscape* (Fisher)
- *Nutrition* (Hasselgren)
- *International Journal of Interferon* (Hasselgren)
- *Cytokines* (Hasselgren)
- *Mediator Research* (Hasselgren)
- *Journal of Surgical Research* (James)
- *Surgical Endoscopy* (Jones)
- *Bariatric Times* (Jones)
- *UpToDate* (Jones)
- *Surgery for Obesity and Related Disorders* (Jones)
- *Shock: Injury, Inflammation* (Junger)
- *Sepsis: Laboratory and Clinical Approaches* (Junger)
- *Journal of Surgical Education* (Kent)
- *Annals of Plastic Surgery* (Lee)
- *Journal of Plastic, Reconstructive, & Aesthetic Surgery* (Lee)
- *ePlasty* (Lee)
- *Journal of Genetic, Molecular and Cellular Biology* (Zhou)
- *Journal of Disease and Global Health* (Zhou)
- *Single Cell Biology* (Zhou)
- *World Journal of Clinical Oncology* (Zhou)
- *International J. Tropical Disease & Health* (Zhou)

Bibliography

Acute Care Surgery, Trauma, and Surgical Critical Care

Acosta D, Castillo-Angeles M, Garces-Descovich A, **Watkins AA, Gupta A, Critchlow JF, Kent TS**. Surgical practical skills learning curriculum: implementation and Interns' confidence perceptions. *J Surg Educ* 2017; in press.

Barrett CD, Moore HB, Banerjee A, Silliman CC, Moore EE, **Yaffe MB**. Human neutrophil elastase mediates fibrinolysis shutdown through competitive degradation of plasminogen and generation of angiotensin. *J Trauma Acute Care Surg* 2017; in press.

Bauer KA, Johnston JEW, Wenzler E, Goff DA, **Cook CH**, Balada-Llasat JM, Pancholi P, Mangino JE. Impact of the NAP-1 strain on disease severity, mortality, and recurrence of healthcare-associated *Clostridium difficile* infection. *Anaerobe* 2017;48:1-6.

Braun CJ, Stanciu M, Boutz PL, Patterson JC, Calligaris D, Higuchi F, Neupane R, Fenoglio S, Cahill DP, Wakimoto H, Agar NYR, **Yaffe MB**, Sharp PA, Hemann MT, Lees JA. Coordinated splicing of regulatory detained introns within oncogenic transcripts creates an exploitable vulnerability in malignant glioma. *Cancer Cell* 2017; in press.

Castillo-Angeles M, **Watkins AA**, Acosta D, Frydman JL, Flier L, Garces-Descovich A, **Cahalane MJ, Gangadharan SP**, Atkins KM, **Kent TS**. Mistreatment and the learning environment for medical students on general surgery clerkship rotations: What do key stakeholders think? *Am J Surg* 2017;213(2):307-12.

Coimbra R, Kozar RA, Smith JW, Zarzaur BL, **Hauser CJ**, Moore FA, Bailey JA, Valadka A, Jurkovich GJ, Jenkins DH, Davis KA, Price MA, Maier RV. The Coalition for National Trauma Research supports the call for a national trauma research action plan. *J Trauma Acute Care Surg* 2017;82(3):637-45.

Farmer D, Tessier JM, Sanders JM, Sawyer RG, Rotstein OD, Dellinger EP, Lipsett PA, Cuschieri J, Miller P, **Cook CH**, Guidry CA, Askari R, Moore BJ, Duane TM. Age and its impact on outcomes with intra-abdominal infection. *Surg Infect (Larchmt)* 2017;(2):77-82.

Griessler M, Gutknecht M, **Cook CH**. Determination of suitable reference genes for RT-qPCR analysis of murine Cytomegalovirus *in vivo* and *in vitro*. *J Virol Methods* 2017; in press.

Hassinger TE, Guidry CA, Rotstein OD, Duane TM, Evans HL, **Cook CH**, O'Neill PJ, Mazuski JE, Askari R, Napolitano LM, Namias N, Miller PR, Dellinger EP, Coimbra R, Cocanour CS, Banton KL, Cuschieri J, Popovsky K, Sawyer RG. Longer-duration antimicrobial therapy does not prevent treatment failure in high-risk patients with complicated intra-abdominal Infections. *Surg Infect (Larchmt)* 2017;18(6):659-63.

Irizarry D, **Odom SR**. Appendix surgery. In: Mazer LM, Lagisetty K, Butler KL, editors. *Essential articles in general surgery*. New York, NY: McGraw Hill; 2017: 287-307.

Itagaki K, Riça I, Zhang J, Gallo D, DePrato M, Otterbein LE, **Hauser CJ**. Intratracheal instillation of neutrophils rescues bacterial overgrowth initiated by trauma damage-associated molecular patterns. *J Trauma Acute Care Surg* 2017; 82(5):853-60.

Kamine TH, **Odom SR**, King BT. Major burns and smoke inhalation. In: Lim RB, Jones DB, editors. *General surgery: examination and board review*. New York, NY: McGraw Hill; 2017: 297-300.

Ledderose C, Hefti MM, Chen Y, Bao Y, Seier T, Li L, Woehrle T,

Zhang J, Junger WG. Adenosine arrests breast cancer cell motility by A3 receptor stimulation. *Purinergic Signal* 2016;12(4):673-85.

Li X, Kondo Y, Bao Y, Staudenmaier L, Lee A, **Zhang J, Ledderose C, Junger WG**. Systemic adenosine triphosphate impairs neutrophil chemotaxis and host defense in sepsis. *Crit Care Med* 2017;45(1):e97-e104.

Mansfield SA, **Cook CH**. Antiviral prophylaxis of cytomegalovirus reactivation in immune competent patients—the jury remains out. *J Thorac Dis* 2017;9(8):2221-3.

Maung AA, Johnson DC, Barre K, Peponis T, Mesar T, Velmahos GC, McGrail D, Kasotakis G, Gross RI, Rosenblatt MS, Sihler KC, Winchell RJ, Cholewczynski W, Butler KL, **Odom SR**, Davis KA; ReCONNECT MRI C-SPINE Study Group. Cervical spine MRI in patients with negative CT: A prospective, multicenter study of the research consortium of New England Centers for Trauma (ReCONNECT). *J Trauma Acute Care Surg* 2017;82(2):263-9.

Odom SR. Blood products and transfusion. In: Lim RB, Jones DB, editors. *General surgery: examination and board review*. New York, NY: McGraw Hill; 2017: 304-7.

Qi B, Yu T, Wang C, Wang T, Yao J, Zhang X, Deng P, Xia Y, **Junger WG**, Sun D. Shock wave-induced ATP release from osteosarcoma U2OS cells promotes cellular uptake and cytotoxicity of methotrexate. *J Exp Clin Cancer Res* 2016;35(1):161.

Saliba L, **Cook CH**, Dungan KM, Porter K, Murphy CV. Medication-induced and spontaneous hypoglycemia carry the same risk for hospital mortality in critically ill patients. *J Crit Care* 2016;36:13-7.

Sanders JM, Tessier JM, Sawyer RG, Lipsett PA, Miller PR, Namias N, O'Neill PJ, Dellinger EP, Coimbra R, Guidry CA, Cuschieri J, Banton KL, **Cook CH**, Moore BJ, Duane TM. Inclusion of vancomycin as part of broad-spectrum coverage does not improve outcomes in patients with intra-abdominal infections: a post hoc analysis. *Surg Infect (Larchmt)* 2016;17(6):694-9.

Seshadri A, **Brat GA**, Yorkgitis BK, Keegan J, Dolan J, Salim A, Askari R, Lederer JA. Phenotyping the immune response to trauma: a multiparametric systems immunology approach. *Crit Care Med* 2017;45(9):1523-30.

Sullivan E, **Gupta A, Cook CH**. Cost and consequences of surgical site infections: A call to arms. *Surg Infect (Larchmt)* 2017;18(4):451-4.

Trgovcich J, Kincaid M, Thomas A, Griessler M, Zimmerman P, Dwivedi V, Bergdall V, Klenerman P, **Cook CH**. Cytomegalovirus reinfections stimulate CD8 T-memory inflation. *PLoS One* 2016;11(11):e0167097.

Watkins AA, Gondek SP, Lagisetty KH, Castillo-Angeles M, **Gangadharan SP, Cahalane MJ, Kent TS**. Weekly e-mailed teaching tips and reading material influence teaching among general surgery residents. *Am J Surg* 2017;213(1):195-201.

Wernick B, Cipriano A, **Odom SR**, MacBean U, Mubang RN, Wojda TR, Liu S, Serres S, Evans DC, Thomas PG, **Cook CH**, Stawicki SP. Temporal changes in hematologic markers after splenectomy, splenic embolization, and observation for trauma. *Eur J Trauma Emerg Surg* 2017;43(3):399-409.

Yaffe MB. Highlight: Understanding radiation sialadenitis. *Sci Signal* 2017;10(482).

Yorkgitis BK, Bryant EA, **Brat GA**, Kelly E, Askari R, Ra JH. Ultrasonography training and utilization in surgical critical care fellowships: a program director's survey. *J Surg Res* 2017; in press.

Bibliography

Yorkgitis BK, Bryant E, Raygor D, **Brat G**, Smink DS, Crandall M. Opioid prescribing education in surgical residencies: A program director survey. *J Surg Educ* 2017; in press.

Van Berkel MA, MacDermott J, Dungan KM, **Cook CH**, Murphy CV. Tiered protocol implementation improves treatment of hypoglycaemia in a neurosciences critical care and surgical intensive care unit. *Intensive Crit Care Nurs* 2017; in press.

Cardiac Surgery

Bardia A, **Khabbaz K**, Mueller A, Mathur P, Novack V, Talmor D, **Subramaniam B**. The association between preoperative hemoglobin A1C and postoperative glycemic variability on 30-day major adverse outcomes following isolated cardiac valvular surgery. *Anesth Analg* 2017;124(1):16-22.

Carroll BJ, Pemberton H, Bauer KA, **Chu LM**, Weinstein JL, Levargue BL, Pinto DS. Initiation of a multidisciplinary, rapid response team to massive and submassive pulmonary embolism. *Am J Cardiol* 2017; in press.

Dearani JA, Gold M, Leibovich BC, Ericsson KA, **Khabbaz KR**, Foley TA, Julsrud PR, Matsumoto JM, Daly RC. The role of imaging, deliberate practice, structure, and improvisation in approaching surgical perfection. *J Thorac Cardiovasc Surg* 2017; in press.

Deeb GM, Chetcuti SJ, Reardon MJ, Patel HJ, Grossman PM, Schreiber T, Forrest JK, Bajwa TK, O'Hair DP, Petrossian G, Robinson N, Katz S, Hartman A, Dauerman HL, Schmoker J, **Khabbaz K**, Watson DR, Yakubov SJ, Oh JK, Li S, Kleiman NS, Adams DH, Popma JJ. 1-Year results in patients undergoing transcatheter aortic valve replacement with failed surgical bioprostheses. *JACC Cardiovasc Interv* 2017;10(10):1034-44.

Jeganathan J, Knio Z, Amador Y, Hai T, Khamooshian A, Matyal R, **Khabbaz KR**, Mahmood F. Artificial intelligence in mitral valve analysis. *Ann Card Anaesth* 2017;20(2):129-34.

Kaza AK, Wamala I, Friehs I, Kuebler JD, Rathod RH, Berra I, Ericsson M, Yao R, Thedsanamoorthy JK, Zurakowski D, **Levitsky S**, Del Nido PJ, Cowan DB, McCully JD. Myocardial rescue with autologous mitochondrial transplantation in a porcine model of ischemia/reperfusion. *J Thorac Cardiovasc Surg* 2017;153(4):934-43.

Khamooshian A, Amador Y, Hai T, Jeganathan J, Saraf M, Mahmood E, Matyal R, **Khabbaz KR**, Mariani M, Mahmood F. Dynamic three-dimensional geometry of the aortic valve apparatus—A feasibility study. *J Cardiothorac Vasc Anesth* 2017;31(4):1290-1300.

Knio ZO, Montealegre-Gallegos M, Yeh L, Chaudary B, Jeganathan J, Matyal R, **Khabbaz KR**, **Liu DC**, **Senthilnathan V**, Mahmood F. Tricuspid annulus: A spatial and temporal analysis. *Ann Card Anaesth* 2016;19(4):599-605.

Mahmood F, Knio ZO, Yeh L, Amir R, Matyal R, Mashari A, Gorman RC, Gorman JH 3rd, **Khabbaz KR**. Regional heterogeneity in the mitral valve apparatus in patients with ischemic mitral regurgitation. *Ann Thorac Surg* 2017;103(4):1171-7.

Mashari A, Montealegre-Gallegos M, Znio Z, Yeh L, Jeganathan J, Matyal R, **Khabbaz KR**, Mahmood F. Making three-dimensional echocardiography more tangible: a workflow for three-dimensional printing with echocardiographic data. *Echo Res Pract* 2016; in press.

Nagy E, Lei Y, Martínez-Martínez E, Body SC, Schlotter F, Creager M, Assmann A, **Khabbaz K**, Libby P, Hansson GK, Aikawa E.

Interferon- γ released by activated CD8(+) T lymphocytes impairs the calcium resorption potential of osteoclasts in calcified human aortic valves. *Am J Pathol* 2017;187(6):1413-25.

Nemec U, Heidinger B, Sokas C, **Chu L**, Eisenberg RL. Diagnosing sarcopenia on thoracic computed tomography: Quantitative assessment of skeletal muscle mass in patients undergoing transcatheter aortic valve replacement. *Acad Radiol* 2017;24(9):1154-61.

Popma JJ, Reardon MJ, **Khabbaz K**, Harrison JK, Hughes GC, Kodali S, George I, Deeb GM, Chetcuti S, Kipperman R, Brown J, Qiao H, Slater J, Williams MR. Early clinical outcomes after transcatheter aortic valve replacement using a novel self-expanding bioprosthesis in patients with severe aortic stenosis who are suboptimal for surgery: Results of the Evolut R U.S. study. *JACC Cardiovasc Interv* 2017;10(3):268-75.

Reardon MJ, Van Mieghem NM, Popma JJ, Kleiman NS, Søndergaard L, Mumtaz M, Adams DH, Deeb GM, Maini B, Gada H, Chetcuti S, Gleason T, Heiser J, Lange R, Merhi W, Oh JK, Olsen PS, Piazza N, Williams M, Windecker S, Yakubov SJ, Grube E, Makkar R, Lee JS, Conte J, Vang E, Nguyen H, Chang Y, Mugglin AS, Serruys PW, Kappetein AP; SURTAVI Investigators including **Khabbaz KR**. Surgical or transcatheter aortic-valve replacement in intermediate-risk patients. *N Engl J Med* 2017;376(14):1321-31.

Sun R, Peng XY, You QS, Jiao LQ, **Liu DC**. Branch retinal artery occlusion following carotid stenting: a case report. *Exp Ther Med* 2016;12(4):2183-6.

Colon and Rectal Surgery

Eskander MF, Bliss LA, McCarthy EP, de Geus SW, Chau Ng S, **Nagle D**, **Rodrigue JR**, **Tseng JF**. Massachusetts healthcare reform and trends in emergent colon resection. *Dis Colon Rectum* 2016;59(11):1063-72.

Feuerstein JD, Alvarez D, **Curran T**, Lerner A, **Cataldo TE**, Falchuk KR, **Poylin V**. Surgery for ulcerative colitis in geriatric patients is safe without increased risks compared to younger patients who undergo surgery for ulcerative colitis. *Gastroenterology* 2017;152(5):S782.

Feuerstein JD, Lerner A, Alvarez D, **Curran T**, **Cataldo TE**, Falchuk KR, **Poylin V**, Nagle DA. Symptomatic venous thromboembolism is rare following elective and non-elective surgery for ulcerative colitis. *Gastroenterology* 2017;152(5):S782-83.

Poylin V, **Curran T**, Alvarez D, Nagle D, **Cataldo T**. Erratum to: Primary vs delayed perineal proctectomy—there is no free lunch. *Int J Colorectal Dis* 2017;32(8):1213.

Poylin V, **Curran T**, Alvarez D, Nagle D, **Cataldo T**. Primary vs. delayed perineal proctectomy—there is no free lunch. *Int J Colorectal Dis* 2017;32(8):1207-12.

Tillou J, **Poylin V**. Functional disorders: slow-transit constipation. *Clin Colon Rectal Surg* 2017;30(1):76-86.

General Surgery

Abbott DE, Tzeng CW, McMillan MT, **Callery MP**, **Kent TS**, Christein JD, Behrman SW, Schauer DP, Hanseman DJ, Eckman MH, Vollmer CM. Pancreas fistula risk prediction: Implications for hospital costs and payments. *HPB (Oxford)* 2017;19(2):140-6.

Acosta D, Castillo-Angeles M, Garces-Descovich A, **Watkins AA, Gupta A, Critchlow JF, Kent TS**. Surgical practical skills learning curriculum: implementation and Interns' confidence perceptions. *J Surg Educ* 2017; in press.

Alam R, Abdolmaleky HM, **Zhou JR**. Microbiome, inflammation, epigenetic alterations, and mental diseases. *Am J Med Genet B Neuropsychiatr Genet* 2017;174(6):651-60.

Beavers KM, Leng I, Rapp SR, Miller ME, Houston DK, Marsh AP, Hire DG, Baker LD, Bray GA, **Blackburn GL**, Hergenroeder AL, Jakicic JM, Johnson KC, Korytkowski MT, Dorsten BV, Kritchevsky SB; Action for Health in Diabetes Movement and Memory Ancillary Study Research Group. Effects of longitudinal glucose exposure on cognitive and physical function: Results from the action for health in diabetes movement and memory study. *J Am Geriatr Soc* 2017;65(1):137-45.

Beqari J, Lembo A, **Critchlow J, Hamden A, Kent MS**. Pseudoachalasia secondary to thoracic aortic aneurysm. *Ann Thorac Surg* 2017;103(6):e517-8.

Castillo-Angeles M, **Watkins AA**, Acosta D, Frydman JL, Flier L, Garces-Descovich A, **Cahalane MJ, Gangadharan SP**, Atkins KM, **Kent TS**. Mistreatment and the learning environment for medical students on general surgery clerkship rotations: What do key stakeholders think? *Am J Surg* 2017;213(2):307-12.

de Geus SW, **Eskander MF**, Bliss LA, **Kasumova GG**, Ng SC, **Callery MP, Tseng JF**. Neoadjuvant therapy versus upfront surgery for resected pancreatic adenocarcinoma: A nationwide propensity score matched analysis. *Surgery* 2017;161(3):592-601.

Digesu CS, Wiesel O, Vaporciyan AA, Colson YL. Management of sarcoma metastases to the lung. *Surg Oncol Clin N Am* 2016;25(4):721-33.

Ecker BL, McMillan MT, Allegrini V, Bassi C, Beane JD, Beckman RM, Behrman SW, Dickson EJ, **Callery MP**, Christein JD, Drebin JA, Hollis RH, House MG, Jamieson NB, Javed AA, **Kent TS**, Kluger MD, Kowalsky SJ, Maggino L, Malleo G, Valero V 3rd, Velu LKP, **Watkins AA**, Wolfgang CL, Zureikat AH, Vollmer CM Jr. Risk factors and mitigation strategies for pancreatic fistula after distal pancreatectomy: Analysis of 2026 resections from the International, Multi-institutional Distal Pancreatectomy Study Group. *Ann Surg* 2017; in press.

Ecker BL, McMillan MT, Asbun HJ, Ball CG, Bassi C, Beane JD, Behrman SW, Berger AC, Dickson EJ, Bloomston M, **Callery MP**, Christein JD, Dixon E, Drebin JA, Castillo CF, Fisher WE, Fong ZV, Haverick E, Hollis RH, House MG, Hughes SJ, Jamieson NB, Javed AA, **Kent TS**, Kowalsky SJ, Kunstman JW, Malleo G, Poruk KE, Salem RR, Schmidt CR, Soares K, Stauffer JA, Valero V, Velu LKP, **Watkins AA**, Wolfgang CL, Zureikat AH, Vollmer CM Jr. Characterization and optimal management of high-risk pancreatic anastomoses during pancreatoduodenectomy. *Ann Surg* 2017; in press.

Ecker BL, McMillan MT, Maggino L, Allegrini V, Asbun HJ, Ball CG, Bassi C, Beane JD, Behrman SW, Berger AC, Bloomston M, **Callery MP**, Christein JD, Dickson E, Dixon E, Drebin JA, Castillo CF, Fisher WE, Fong ZV, Haverick E, Hollis RH, House MG, Hughes SJ, Jamieson NB, **Kent TS**, Kowalsky SJ, Kunstman JW, Malleo G, Salem RR, Soares KC, Valero V 3rd, **Watkins AA**, Wolfgang CL, Zureikat AH, Vollmer CM Jr. Pancreatogastrostomy vs pancreateojejunostomy: A risk-stratified analysis of 5316

pancreatoduodenectomies. *J Gastrointest Surg* 2017; in press.

Gardner AK, Steffes CP, Nepomnayshy D, Nicholas C, Widmann WD, Fitzgibbons SC, Dunkin BJ, **Jones DB**, Paige JT. Selection bias: Examining the feasibility, utility, and participant receptivity to incorporating simulation into the general surgery residency selection process. *Am J Surg* 2017;213(6):1171-7.

Gouma DJ, **Callery MP**. Bile duct injury: examining results of early repair by the index surgeon. *HPB (Oxford)* 2017;19(1):1-2.

Hagen SJ. Non-canonical functions of claudin proteins: Beyond the regulation of cell-cell adhesions. *Tissue Barriers* 2017;5(2):e1327839.

Jones DB, editor. Pocket surgery, 2nd edition. Philadelphia:Wolters Kluwer; 2017 in press.

Jones DB, Stefanidis D, Korndorffer JR Jr, Dimick JB, Jacob BP, Schultz L, Scott DJ. Erratum to: SAGES University MASTERS Program: a structured curriculum for deliberate, lifelong learning. *Surg Endosc* 2017; in press.

Jones DB, Stefanidis D, Korndorffer JR Jr, Dimick JB, Jacob BP, Schultz L, Scott DJ. SAGES University MASTERS Program: a structured curriculum for deliberate, lifelong learning. *Surg Endosc* 2017;31(8):3061-71.

Jones SB, Munro MG, Feldman LS, Robinson TN, Brunt LM, Schwaitzberg SD, **Jones DB**, Fuchshuber PR. Fundamental Use of Surgical Energy (FUSE): An essential educational program for operating room safety. *Perm J* 2017;21.

Kasumova GG, Eskander MF, Kent TS, Ng SC, **Moser AJ**, Ahmed M, Pleskow DK, **Callery MP, Tseng JF**. Hemorrhage after pancreaticoduodenectomy: does timing matter? *HPB (Oxford)*. 2016;18(10):861-9.

McMillan MT, Allegrini V, Asbun HJ, Ball CG, Bassi C, Beane JD, Behrman SW, Berger AC, Bloomston M, **Callery MP**, Christein JD, Dickson E, Dixon E, Drebin JA, Fernandez-Del Castillo C, Fisher WE, Fong ZV, Haverick E, Hollis RH, House MG, Hughes SJ, Jamieson NB, **Kent TS**, Kowalsky SJ, Kunstman JW, Malleo G, McElhany AL, Salem RR, Soares KC, Sprys MH, Valero V 3rd, **Watkins AA**, Wolfgang CL, Zureikat AH, Vollmer CM Jr. Incorporation of procedure-specific risk into the ACS-NSQIP surgical risk calculator improves the prediction of morbidity and mortality after pancreatoduodenectomy *Ann Surg* 2017;265(5):978-86.

McMillan MT, Ecker BL, Behrman SW, **Callery MP**, Christein JD, Drebin JA, Fraker DL, **Kent TS**, Lee MK, Roses RE, Sprys MH, Vollmer CM Jr. Externalized stents for pancreatoduodenectomy provide value only in high-risk scenarios. *J Gastrointest Surg* 2016;20(12):2052-62.

Nguyen BM, Fitzpatrick E, **Jones DB**. Barriers to implementation of the FUSE program. *Surg Endosc* 2017; in press.

Palmer CJ, Bruckner RJ, Paulo JA, Kazak L, Long JZ, Mina AI, Deng Z, LeClair KB, Hall JA, Hong S, Zushin PH, Smith KL, Gygi SP, **Hagen SJ**, Cohen DE, Banks AS. Cdkal1, a type 2 diabetes susceptibility gene, regulates mitochondrial function in adipose tissue. *Mol Metab* 2017; in press.

Patriarca L, Magerowski G, **Alonso-Alonso M**. Functional neuroimaging in obesity. *Curr Opin Endocrinol Diabetes Obes* 2017;24(2):154-9.

Patriarca L, Magerowski G, **Alonso-Alonso M**. Functional

Bibliography

neuroimaging in obesity. *Curr Opin Endocrinol Diabetes Obes* 2017;24(3):260-5.

Puri PM, **Watkins AA**, **Kent TS**, Maggino L, Jeganathan JG, **Callery MP**, Drebin JA, Vollmer CM. Decision-making for the management of cystic lesions of the pancreas: how satisfied are patients with surgery? *J Gastrointest Surg* 2017; in press.

Rapp SR, Luchsinger JA, Baker LD, **Blackburn GL**, Hazuda HP, Demos-McDermott KE, Jeffery RW, Keller JN, McCaffery JM, Pajewski NM, Evans M, Wadden TA, Arnold SE, Espeland MA; Look AHEAD Research Group. Effect of a long-term intensive lifestyle intervention on cognitive function: action for health in diabetes study. *J Am Geriatr Soc* 2017; in press.

Smetana GW, **Jones DB**, Wee CC. Should this patient have weight loss surgery?: Grand Rounds discussion from Beth Israel Deaconess Medical Center. *Ann Intern Med* 2017;166(11):808-17.

Tabatabaie O, **Kasumova GG**, **Eskander MF**, **Critchlow JF**, **Tawa NE**, **Tseng JF**. Totally implantable venous access devices: A review of complications and management strategies. *Am J Clin Oncol* 2017;40(1):94-105.

Tabatabaie O, **Kasumova GG**, **Kent TS**, **Eskander MF**, **Fadayomi AB**, **Ng SC**, **Critchlow JF**, **Tawa NE**, **Tseng JF**. Upper extremity deep venous thrombosis after port insertion: What are the risk factors? *Surgery* 2017;162(2):437-44.

Telem DA, Majid SF, Powers K, DeMaria E, Morton J, **Jones DB**. Assessing national provision of care: variability in bariatric clinical care pathways. *Surg Obes Relat Dis* 2017;13(2):281-4.

Watkins AA, Gondek SP, Lagisetty KH, Castillo-Angeles M, **Gangadharan SP**, **Cahalane MJ**, **Kent TS**. Weekly e-mailed teaching tips and reading material influence teaching among general surgery residents. *Am J Surg* 2017;213(1):195-201.

Watkins AA, **Kent TS**, Gooding WE, Boggi U, Chalikhonda S, Kendrick ML, Walsh RM, Zeh HJ 3rd, **Moser AJ**. Multicenter outcomes of robotic reconstruction during the early learning curve for minimally-invasive pancreaticoduodenectomy. *HPB (Oxford)* 2017; in press.

Wee CC, **Jones DB**, Apovian C, Hess DT, Chiodi SN, Bourland AC, Davis RB, **Schneider B**, **Blackburn GL**, Marcantonio ER, Hamel MB. Weight loss after bariatric surgery: Do clinical and behavioral factors explain racial differences? *Obes Surg* 2017; in press.

Interdisciplinary Surgery Research

Bai S, Nagai M, Koerner SK, **Veves A**, **Sun L**. Structure-activity relationship study and discovery of indazole 3-carboxamides as calcium-release activated calcium channel blockers. *Bioorg Med Chem Lett* 2017;27(3):393-7.

Brazil JC, Sumagin R, Stowell SR, Lee G, Louis NA, **Cummings RD**, Parkos CA. Expression of Lewis-A glycans on polymorphonuclear leukocytes augments function by increasing transmigration. *J Leukoc Biol* 2017;102(3):753-62.

Byrd-Leotis L, **Cummings RD**, Steinhauer DA. The interplay between the host receptor and influenza virus hemagglutinin and neuraminidase. *Int J Mol Sci* 2017;18(7):1541.

Collins BC, Gunn RJ, McKittrick TR, **Cummings RD**, Cooper MD, Herrin BR, Wilson IA. Structural insights into VLR fine specificity for blood group carbohydrates. *Structure* 2017; in press.

Hanes MS, Moremen KW, **Cummings RD**. Biochemical characterization of functional domains of the chaperone Cosmc. *PLoS One* 2017;12(6):e0180242.

Jernigan FE, Hanai JI, Sukhatme VP, **Sun L**. Discovery of furan carboxylate derivatives as novel inhibitors of ATP-citrate lyase via virtual high-throughput screening. *Bioorg Med Chem Lett* 2017;27(4):929-35.

Jernigan FE, **Sun L**. *In silico* discovery and therapeutic potential of IDO1 and TDO2 inhibitors. *Future Med Chem* 2017;9(12):1309-11.

Koerner SK, Hanai JI, Bai S, Jernigan FE, Oki M, Komaba C, Shuto E, Sukhatme VP, **Sun L**. Design and synthesis of emodin derivatives as novel inhibitors of ATP-citrate lyase. *Eur J Med Chem* 2017;126:920-8.

Kudelka MR, Hinrichs BH, Darby T, Moreno CS, Nishio H, Cutler CE, Wang J, Wu H, Zeng J, Wang Y, Ju T, Stowell SR, Nusrat A, Jones RM, Neish AS, **Cummings RD**. Cosmc is an X-linked inflammatory bowel disease risk gene that spatially regulates gut microbiota and contributes to sex-specific risk. *Proc Natl Acad Sci U S A* 2016;113(51):14787-92.

Laan LC, Williams AR, Stavenhagen K, Giera M, Kooij G, Vlasakov I, Kalay H, Kringel H, Nejsum P, Thamsborg SM, Wuhrer M, Dijkstra CD, **Cummings RD**, van Die I. The whipworm (*Trichuris suis*) secretes prostaglandin E2 to suppress proinflammatory properties in human dendritic cells. *FASEB J* 2017;31(2):719-31.

Sardar MYR, Krishnamurthy VR, Park S, Mandhapaty AR, Wever WJ, Park D, **Cummings RD**, Chaikof EL. Synthesis of Lewis(X)-O-Core-1 threonine: A building block for O-linked Lewis(X) glycopeptides. *Carbohydr Res* 2017; in press.

Schneider C, Wicki S, Graeter S, Timcheva TM, Keller CW, Quast I, Leontyev D, Djoumerska-Alexieva IK, Käsermann F, Jakob SM, Dimitrova PA, Branch DR, **Cummings RD**, Lünemann JD, Kaufmann T, Simon HU, von Gunten S. IVIG regulates the survival of human but not mouse neutrophils *Sci Rep* 2017;7(1):1296.

Tiemeyer M, Aoki K, Paulson J, **Cummings RD**, York WS, Karlsson NG, Lisacek F, Packer NH, Campbell MP, Aoki NP, Fujita A, Matsubara M, Shinmachi D, Tsuchiya S, Yamada I, Pierce M, Ranzinger R, Narimatsu H, Aoki-Kinoshita KF. GlyTouCan: An accessible glycan structure repository. *Glycobiology* 2017; in press.

Varki A, **Cummings RD**, Consortium of Glycobiology, editors. *Essentials of glycobiology*, 3rd edition. NY: Cold Spring Harbor Laboratory Press; 2017.

Wang Y, Hedblom A, Koerner SK, Li M, Jernigan FE, Wegiel B, **Sun L**. Novel synthetic chalcones induce apoptosis in the A549 non-small cell lung cancer cells harboring a KRAS mutation. *Bioorg Med Chem Lett* 2016;26(23):5703-6.

Zhong AH, Gordon Jiang Z, **Cummings RD**, Robson SC. Various N-glycoforms differentially upregulate E-NTPDase activity of the NTPDase3/CD39L3 ecto-enzymatic domain. *Purinergic Signal* 2017; in press.

Neurosurgery

Adeeb N, **Griessenauer CJ**, Foreman PM, **Moore JM**, **Motiei-Langroudi R**, **Chua MH**, Gupta R, **Patel AS**, Harrigan MR, Alturki AY, **Ogilvy CS**, **Thomas AJ**. Comparison of stent-assisted coil embolization and the pipeline embolization device for endovascular

treatment of ophthalmic segment aneurysms: a multicenter cohort study. *World Neurosurg* 2017;105:206-12.

Adeeb N, **Griessenauer CJ**, Foreman PM, **Moore JM**, Shallwani H, **Motiei-Langroudi R**, **Alturki A**, Siddiqui AH, Levy EI, Harrigan MR, **Ogilvy CS**, **Thomas AJ**. Use of platelet function testing before pipeline embolization device placement: A multicenter cohort study. *Stroke* 2017;48(5):1322-30.

Adeeb N, **Griessenauer CJ**, **Moore JM**, Foreman PM, Shallwani H, **Motiei-Langroudi R**, Gupta R, Baccin CE, **Alturki A**, Harrigan MR, Siddiqui AH, Levy EI, **Ogilvy CS**, **Thomas AJ**. Ischemic stroke after treatment of intraprocedural thrombosis during stent-assisted coiling and flow diversion. *Stroke* 2017;48(4):1098-1100.

Adeeb N, **Griessenauer CJ**, **Patel AS**, Foreman PM, Baccin CE, **Moore JM**, Gupta R, **Alturki A**, Harrigan MR, **Ogilvy CS**, **Thomas AJ**. The use of single stent-assisted coiling in treatment of bifurcation aneurysms: A multicenter cohort study with proposal of a scoring system to predict complete occlusion. *Neurosurgery* 2017; in press.

Adeeb N, **Griessenauer CJ**, **Patel AS**, **Moore J**, Dolati-Ardejani P, Gupta R, **Motiei-Langroudi R**, **Ogilvy CS**, **Thomas AJ**. Reliability of dual- vs single-volume reconstruction of three-dimensional digital subtraction angiography for follow-up evaluation of endovascularly treated intracranial aneurysms. *Interv Neuroradiol* 2016;22(6):687-92.

Adeeb N, **Griessenauer CJ**, Shallwani H, Shakir H, Foreman PM, **Moore JM**, Dmytriw AA, Gupta R, Siddiqui AH, Levy EI, Snyder K, Harrigan MR, **Ogilvy CS**, **Thomas AJ**. Pipeline embolization device in treatment of 50 unruptured large and giant aneurysms. *World Neurosurg* 2017;105:232-7.

Adeeb N, **Moore JM**, **Griessenauer CJ**, Foreman PM, Shallwani H, Dmytriw AA, Shakir H, Siddiqui AH, Levy EI, Davies JM, Harrigan MR, **Thomas AJ**, **Ogilvy CS**. Treatment of tandem internal carotid artery aneurysms using a single pipeline embolization device: Evaluation of safety and efficacy. *AJNR Am J Neuroradiol* 2017;38(8):1605-9.

Adeeb N, **Moore JM**, Wirtz M, **Griessenauer CJ**, Foreman PM, Shallwani H, Gupta R, Dmytriw AA, **Motiei-Langroudi R**, Alturki A, Harrigan MR, Siddiqui AH, Levy EI, **Thomas AJ**, **Ogilvy CS**. Predictors of incomplete occlusion following pipeline embolization of intracranial aneurysms: Is it less effective in older patients? *AJNR Am J Neuroradiol* 2017; in press.

Arle JE, Shils JL. *Innovative neuromodulation*. London: Academic Press; 2017.

Arle JE, Carlson KW, Mei L. Investigation of mechanisms of vagus nerve stimulation for seizure using finite element modeling. *Epilepsy Res* 2016;126:109-18.

Ascanio LC, Alturki AY, **Griessenauer CJ**, **Motiei-Langroudi R**, Kumar S, **Ogilvy CS**. Medullary decompression by sling repositioning of vertebral artery with operative video. *World Neurosurg* 2017; in press.

Alterman RL. A trial of focused ultrasound thalamotomy for essential tremor. *N Engl J Med* 2016;375(22):2201.

Alterman RL. Commentary: Utilization of quantitative susceptibility mapping for direct targeting of the subthalamic nucleus during deep brain stimulation surgery. *Oper Neurosurg (Hagerstown)* 2017; in press.

Alterman RL. One step backward: Magnetic resonance guided focused ultrasound thalamotomy for the treatment of medically refractory tremor. *Ann Neurol* 2017;81(3):348-50.

Ardaillon H, Laviv Y, **Arle JE**, **Kasper EM**. Lumbar disk herniation during pregnancy: A review on general management and timing of surgery. *Acta Neurochir (Wien)* 2017; in press.

Bayoumi AB, Chen JX, Swiatek PR, Laviv Y, **Kasper EM**. Primary pituitary fibrosarcoma with previous adenoma. *World Neurosurg* 2017;105:1032.e7-1032.e11.

Boone MD, Jinadasa SP, Mueller A, Shaefi S, **Kasper EM**, Hanafy KA, O'Gara BP, Talmor DS. The effect of positive end-expiratory pressure on intracranial pressure and cerebral hemodynamics. *Neurocrit Care* 2017;26(2):174-81.

Chang YM, Kim G, Peri N, **Papavassiliou E**, Rojas R, Bhadelia RA. Diagnostic utility of increased STIR signal in the posterior atlanto-occipital and atlantoaxial membrane complex on MRI in acute C1-C2 fracture. *AJNR Am J Neuroradiol* 2017;38(9):1820-5.

Chua MH, **Griessenauer CJ**, **Thomas AJ**, **Ogilvy CS**. In reply to "Patients with multiple intracranial aneurysms presenting initial worse clinical condition as a result of a ruptured aneurysm". *World Neurosurg* 2016;96:606.

de Almeida CC, Boone MD, Laviv Y, Kasper BS, Chen CC, **Kasper EM**. The utility of routine intensive care admission for patients undergoing intracranial neurosurgical procedures: a systematic review. *Neurocrit Care* 2017; in press.

de Almeida CC, Uzuner A, **Alterman RL**. Stereotactic drainage of brainstem abscess with the BrainLab Varioguide™ System and the Airo™ Intraoperative CT scanner: A technical case report. *Oper Neurosurg (Hagerstown)* 2017; in press.

Deer TR, Lamer TJ, Pope JE, Falowski SM, Provenzano DA, Slavin K, Golovac S, **Arle J**, Rosenow JM, Williams K, McRoberts P, Narouze S, Eldabe S, Lad SP, De Andrés JA, Buchser E, Rigoard P, Levy RM, Simpson B, Mekhail N. The neurostimulation appropriateness consensus committee (NACC) safety guidelines for the reduction of severe neurological injury. *Neuromodulation* 2017;20(1):15-30.

Germano IM, **Kasper EM**. The changing landscape of ependymomas: Diagnostic and treatment approaches. *J Neurosurg Sci* 2017; in press.

Griessenauer CJ, Adeeb N, Foreman PM, Gupta R, **Patel AS**, **Moore J**, Abud TG, **Thomas AJ**, **Ogilvy CS**, Baccin CE. Impact of coil packing density and coiling technique on occlusion rates for aneurysms treated with stent-assisted coil embolization. *World Neurosurg*. 2016;94:157-66.

Griessenauer CJ, **Chua MH**, Hanafy KA, Baffour YT, Chen R, LeBlanc RH 3rd, **Patel AS**, Salem M, Karumanchi SA, Xu D, Thadhani R, **Ogilvy CS**, **Thomas AJ**. Soluble Fms-like tyrosine kinase-1 (sFlt-1) and risk of cerebral vasospasm after aneurysmal subarachnoid hemorrhage. *World Neurosurg* 2017; in press.

Griessenauer CJ, Gupta R, **Moore J**, **Thomas AJ**, **Ogilvy CS**. Ex-vivo release of Pipeline Embolization Device Polytetrafluoroethylene (PTFE) sleeves for improved distal landing zone accuracy in-vivo: a technical note. *Interv Neuroradiol* 2016;22(6):679-81.

Griessenauer CJ, Gupta R, Shi S, Alturki A, **Motiei-Langroudi R**, Adeeb N, **Ogilvy CS**, **Thomas AJ**. Collar sign in incompletely

Bibliography

occluded aneurysms after pipeline embolization: evaluation with angiography and optical coherence tomography. *AJNR Am J Neuroradiol* 2017;38(2):323-6.

Griessenauer CJ, Ogilvy CS, Foreman PM, Chua MH, Harrigan MR, He L, Fusco MR, Mocco JD, Stapleton CJ, Patel AB, Sonig A, Siddiqui AH, Thomas AJ. Pipeline embolization device for small intracranial aneurysms: evaluation of safety and efficacy in a multicenter cohort. *Neurosurgery* 2017;80(4):579-87.

Griessenauer CJ, Ogilvy CS, Foreman PM, Chua MH, Harrigan MR, Stapleton CJ, Patel AB, He L, Fusco MR, Mocco J, Winkler PA, Patel AS, Thomas AJ. Pipeline Embolization Device for small paraophthalmic artery aneurysms with an emphasis on the anatomical relationship of ophthalmic artery origin and aneurysm. *J Neurosurg* 2016;125(6):1352-9.

Griessenauer CJ, Patel AS, Gupta R, Adeeb N, Foreman PM, Shallwani H, Moore JM, Harrigan MR, Siddiqui AH, Ogilvy CS, Thomas AJ. In reply to the letter to the editor regarding "safety and efficacy of noncompliant balloon angioplasty for the treatment of subarachnoid hemorrhage-induced vasospasm: A multicenter study". *World Neurosurg* 2017;105:1023.

Griessenauer CJ, Piske RL, Baccin CE, Pereira BJA, Reddy AS, Thomas AJ, Abud TG, Ogilvy CS. Flow diverters for treatment of 160 ophthalmic segment aneurysms: Evaluation of safety and efficacy in a multicenter cohort. *Neurosurgery* 2017;80(5):726-32.

Griessenauer CJ, Shallwani H, Adeeb N, Gupta R, Rangel-Castilla L, Siddiqui AH, Levy EI, Boone MD, Thomas AJ, Ogilvy CS. Conscious sedation versus general anesthesia for the treatment of cerebral aneurysms with flow diversion: A matched cohort study. *World Neurosurg* 2017;102:1-5.

Gupta R, Adeeb N, **Griessenauer CJ, Moore JM, Patel AS, Kim C, Thomas AJ, Ogilvy CS.** Evaluating the complexity of online patient education materials about brain aneurysms published by major academic institutions. *J Neurosurg* 2017;127(2):278-83.

Gupta R, Adeeb N, **Griessenauer CJ, Moore JM, Patel AS, Thomas AJ, Ogilvy CS.** Removal of symptomatic titanium fixation plates after craniotomy. *Acta Neurochir (Wien)* 2016;158(10):1845-8.

Gupta R, Adeeb N, **Moore JM, Motiei-Langroudi R, Griessenauer CJ, Patel AS, Ogilvy CS, Thomas AJ.** Validity assessment of grading scales predicting complications from embolization of cerebral arteriovenous malformations. *Clin Neurol Neurosurg* 2016;151:102-7.

Gupta R, Ascanio LC, Enriquez-Marulanda A, **Griessenauer CJ, Chinnadurai A, Jhun R, Alturki A, Ogilvy CS, Thomas AJ, Moore JM.** Validation of a predictive scoring system for ventriculo-peritoneal shunt insertion following aneurysmal subarachnoid hemorrhage. *World Neurosurg* 2017; in press.

Gupta R, **Griessenauer CJ, Adeeb N, Chua MH, Moore JM, Patel AS, Thomas AJ, Ogilvy CS.** Evaluating imaging follow-up strategies and costs of unruptured intracranial aneurysms treated with endovascular techniques: A survey of academic neurovascular centers in the United States. *World Neurosurg* 2016;94:360-7.

Gupta R, **Griessenauer CJ, Moore JM, Adeeb N, Patel AS, Ogilvy CS, Thomas AJ.** An analysis of malpractice litigation related to the management of brain aneurysms. *J Neurosurg* 2016; in press.

Gupta R, **Moore JM, Adeeb N, Griessenauer CJ, Patel AS, Chua MH, Thomas AJ, Ogilvy CS.** Clinical presentation, progression, and treatment outcomes of Moyamoya disease in the elderly. *Acta*

Neurochir (Wien) 2016;158(12):2409-14.

Gupta R, **Moore JM, Griessenauer CJ, Adeeb N, Patel AS, Youn R, Poliskey K, Thomas AJ, Ogilvy CS.** Assessment of dual-antiplatelet regimen for Pipeline Embolization Device placement: A survey of major academic neurovascular centers in the United States. *World Neurosurg* 2016;96:285-92.

He L, Griessenauer CJ, Fusco MR, Chua MH, Stapleton CJ, Guidal BT, Thomas AJ, Ogilvy CS. Lazic aneurysm clip system for microsurgical clipping of cerebral aneurysms: Transition to a new aneurysm clip system in an established cerebrovascular practice. *World Neurosurg* 2016;96:454-9.

Horn A, Kühn AA, Merkl A, Shih L, **Alterman R, Fox M.** Probabilistic conversion of neurosurgical DBS electrode coordinates into MNI space. *Neuroimage* 2017;150:395-404.

Jinnah HA, **Alterman R, Klein C, Krauss JK, Moro E, Vidailhet M, Raïke R.** Deep brain stimulation for dystonia: A novel perspective on the value of genetic testing. *J Neural Transm (Vienna)* 2017;124(4):417-30.

Kasper BS, Dörfler A, Di Donato N, **Kasper EM, Wiczorek D, Hoyer J, Zweier C.** Central nervous system anomalies in two females with Borjeson-Forssman-Lehmann syndrome. *Epilepsy Behav* 2017;69:104-9.

Kasper EM, Ippen FM, Maragkos GA, Anderson MP, Rojas R, Mahadevan A. Tanycytic ependymoma of the brain stem, presentations of rare cystic disease variants and review of literature. *J Neurosurg Sci* 2017; in press.

Kasper BS, **Kasper EM.** New classification of epilepsy-related neoplasms: The clinical perspective. *Epilepsy Behav* 2017;67:91-7.

Khatami D, **Kasper EM, Bhadelia R, Rojas R.** Radiologic characteristics of ependymomas: A case-based approach. *J Neurosurg Sci* 2017; in press.

Koch MJ, Stapleton CJ, Agarwalla PK, Torok C, Shin JH, Coumans JV, Borges LF, **Ogilvy CS, Rabinov JD, Patel AB.** Open and endovascular treatment of spinal dural arteriovenous fistulas: A 10-year experience. *J Neurosurg Spine* 2017;26(4):519-23.

Krishnan V, Stoppel DC, Nong Y, Johnson MA, Nadler MJ, Ozkaynak E, Teng BL, Nagakura I, Mohammad F, Silva MA, Peterson S, Cruz TJ, **Kasper EM, Arnaout R, Anderson MP.** Autism gene Ube3a and seizures impair sociability by repressing VTA Cbln1. *Nature* 2017;543(7646):507-12.

Laviv Y, Bayoumi A, Mahadevan A, Young B, Boone M, **Kasper EM.** Meningiomas in pregnancy: Timing of surgery and clinical outcomes as observed in 104 cases and establishment of a best management strategy. *Acta Neurochir (Wien)* 2017; in press.

Laviv Y, Germano IM, Mahadevan A, **Kasper EM.** Surgery for posterior fossa ependymomas in adults. *J Neurosurg Sci* 2017; in press.

Laviv Y, Kasper BS, **Kasper EM.** Vascular hyperpermeability as a hallmark of phacomatoses: Is the etiology angiogenesis comparable with mechanisms seen in inflammatory pathways? Part I: historical observations and clinical perspectives on the etiology of increased CSF protein levels, CSF clotting, and communicating hydrocephalus: a comprehensive review. *Neurosurg Rev* 2017; in press.

Laviv Y, Kasper BS, **Kasper EM.** Vascular hyperpermeability as a hallmark of phacomatoses: Is the etiology angiogenesis related to

or comparable with mechanisms seen in inflammatory pathways? Part II: angiogenesis- and inflammation-related molecular pathways, tumor-associated macrophages, and possible therapeutic implications: a comprehensive review. *Neurosurg Rev* 2017; in press.

Laviv Y, Neto S, **Kasper EM**. Management of quadrigeminal arachnoid cyst associated with obstructive hydrocephalus: Report on stereotactic ventricular-cystic stenting. *Br J Neurosurg* 2017; in press.

Laviv Y, **Thomas A, Kasper EM**. Hypervascular lesions of the cerebellopontine angle: The relevance of angiography as a diagnostic and therapeutic tool and the role of stereotactic radiosurgery in management. A comprehensive review. *World Neurosurg* 2017;100:100-17.

Moore JM, Caplan L, Hwang P, Mandan A, **Ogilvy CS, Thomas AJ**. Dementia resulting from expansion of basilar artery aneurysm: Two case reports and a review of the literature. *Acta Neurochir (Wien)* 2016;158(10):1901-5.

Motiei-Langroudi R, Adeeb N, Foreman PM, Harrigan MR, Fisher WS Rd, Vyas NA, Lipsky RH, Walters BC, Tubbs SR, Shoja MM, **Moore JM**, Gupta R, **Ogilvy CS, Thomas AJ**, Griessenauer CJ. Predictors of shunt insertion in aneurysmal subarachnoid hemorrhage. *World Neurosurg* 2017;98:421-6.

Motiei-Langroudi R, Adeeb N, Foreman PM, Harrigan MR, Fisher WS Rd, Vyas NA, Lipsky RH, Walters BC, Tubbs RS, Shoja MM, **Moore JM**, Gupta R, **Ogilvy CS, Thomas AJ**, Griessenauer CJ. Corrigendum to 'predictors of shunt insertion in aneurysmal subarachnoid hemorrhage' [*World Neurosurgery* 98 (2017) 421-426]. *World Neurosurg* 2017;104:1043.

Motiei-Langroudi R, Griessenauer CJ, Alturki A, Adeeb N, **Thomas AJ, Ogilvy CS**. Bow hunter's syndrome from a tortuous V1 segment vertebral artery treated with stent placement. *World Neurosurg* 2017;98:878.e11-878.e15.

Ogilvy CS, Motiei-Langroudi R, Ghorbani M, Griessenauer CJ, Alturki AY, **Thomas AJ**. Flow diverters as useful adjunct to traditional endovascular techniques in treatment of direct carotid-cavernous fistulas. *World Neurosurg* 2017;105:812-7.

Patel AS, Griessenauer CJ, Gupta R, Adeeb N, Foreman PM, Shallwani H, **Moore JM**, Harrigan MR, Siddiqui AH, **Ogilvy CS, Thomas AJ**. Safety and efficacy of noncompliant balloon angioplasty for the treatment of subarachnoid hemorrhage-induced vasospasm: A multicenter study. *World Neurosurg* 2017;98:189-97.

Phan K, Dmytriw AA, Maingard J, Asadi H, **Griessenauer CJ**, Ng W, Kewagamang K, Mobbs RJ, **Moore JM, Ogilvy CS, Thomas AJ**. Endovascular thrombectomy alone versus combined with intravenous thrombolysis. *World Neurosurg* 2017; in press.

Phan K, Dmytriw AA, Teng I, **Moore JM, Griessenauer C, Ogilvy C, Thomas A**. A direct aspiration first pass technique vs standard endovascular therapy for acute stroke: A systematic review and meta-analysis. *Neurosurgery* 2017; in press.

Phan K, Moore JM, **Griessenauer C**, Dmytriw AA, Scherman DB, Sheik-Ali S, Adeeb N, **Ogilvy CS, Thomas A**, Rosenfeld JV. Craniotomy versus decompressive craniectomy for acute subdural hematoma: Systematic review and meta-analysis. *World Neurosurg* 2017;101:677-85.

Phan K, **Moore JM, Griessenauer CJ, Ogilvy CS, Thomas AJ**. Aspirin and risk of subarachnoid hemorrhage: Systematic review and

meta-analysis. *Stroke* 2017;48(5):1210-7.

Phan K, **Moore JM, Griessenauer CJ**, Xu J, Teng I, Dmytriw AA, Chiu AH, **Ogilvy CS, Thomas A**. Ultra-early angiographic vasospasm after aneurysmal subarachnoid hemorrhage: Systematic review and meta-analysis. *World Neurosurg* 2017;102:632-8.

Pirio Richardson S, Altenmüller E, Alter K, **Alterman RL**, Chen R, Frucht S, Furuya S, Jankovic J, Jinnah HA, Kimberley TJ, Lungu C, Perlmutter JS, Prudente CN, Hallett M. Research priorities in limb and task-specific dystonias. *Front Neurol* 2017;8:170.

Schmalz PGR, Alturki A, **Ogilvy CS, Thomas AJ**. Ruptured distal anterior choroidal artery aneurysm treated with superselective provocative testing and coil embolization. *World Neurosurg* 2017;105:1032.e19-1032.e22.

Shi S, Gupta R, **Moore JM, Griessenauer CJ**, Adeeb N, **Motiei-Langroudi R, Thomas AJ, Ogilvy CS**. De novo AVM formation following venous sinus thrombosis and prior AVM resection in adults: report of 2 cases. *J Neurosurg* 2017;10:1-5.

Stippler M, Liu J, **Motiei-Langroudi R**, Voronovich Z, Yonas H, Davis RB. Complicated mild traumatic brain injury and the need for imaging surveillance. *World Neurosurg* 2017;105:265-9.

Vespa P, Hanley D, Betz J, Hoffer A, Engh J, Carter R, Nakaji P, **Ogilvy C**, Jallo J, Selman W, Bistran-Hall A, Lane K, McBee N, Saver J, Thompson RE, Martin N; ICES Investigators. ICES (Intraoperative Stereotactic Computed Tomography-Guided Endoscopic Surgery) for brain hemorrhage: a multicenter randomized controlled trial. *Stroke* 2016;47(11):2749-55.

Zhang D, **Papavassiliou E**. Spinal intradural arachnoid webs causing spinal cord compression with inconclusive preoperative imaging: A report of 3 cases and a review of the literature. *World Neurosurg* 2017;99:251-8.

Ophthalmology

Bouffard MA, Caplan LR, **Torun N**. Divergence palsy due to divalproex and oxcarbazepine. *Clin Neuropharmacol* 2017;40(3):154-5.

Bouffard MA, **Torun N**. The mystery of the locking eye. *JAMA Neurol* 2017;74(5):601-2.

Bouffard MA, Nathavitharana RR, Yassa DS, **Torun N**. Re-treatment with ethambutol after toxic optic neuropathy. *J Neuroophthalmol* 2017;37(1):40-2.

Jee D, Keum N, Kang S, **Arroyo JG**. Sleep and diabetic retinopathy. *Acta Ophthalmol* 2017;95(1):41-7.

Lefebvre DR, Mandeville JT, Yonekawa Y, **Arroyo JG, Torun N**, Freitag SK. A case series and review of bisphosphonate-associated orbital inflammation. *Ocul Immunol Inflamm* 2016;24(2):134-9.

Otolaryngology/Head and Neck Surgery

Banoub RG, Phillips KM, Hoehle LP, **Caradonna DS**, Gray ST, Sedaghat AR. Relationship between chronic rhinosinusitis exacerbation frequency and asthma control. *Laryngoscope* 2017; in press.

Campbell AP, Hoehle LP, Phillips KM, **Caradonna DS**, Gray ST, Sedaghat AR. Smoking: An independent risk factor for lost productivity in chronic rhinosinusitis. *Laryngoscope* 2017;127(8):1742-5.

Bibliography

Campbell AP, Phillips KM, Hoehle LP, Feng AL, Bergmark RW, **Caradonna DS**, Gray ST, Sedaghat AR. Depression symptoms and lost productivity in chronic rhinosinusitis. *Ann Allergy Asthma Immunol* 2017;118(3):286-9.

Campbell AP, Phillips KM, Hoehle LP, Gaudin RA, **Caradonna DS**, Gray ST, Sedaghat AR. Association between asthma and chronic rhinosinusitis severity in the context of asthma control. *Otolaryngol Head Neck Surg* 2017; in press.

Gaudin RA, Hoehle LP, Birkelbach MA, Phillips KM, Beule AG, **Caradonna DS**, Gray ST, Sedaghat AR. The association between allergic rhinitis control and sleep quality. *HNO* 2017; in press.

Gray ST, Hoehle LP, Phillips KM, **Caradonna DS**, Sedaghat AR. Patient-reported control of chronic rhinosinusitis symptoms is positively associated with general health-related quality of life. *Clin Otolaryngol* 2017; in press.

Hoehle LP, Phillips KM, Bergmark RW, **Caradonna DS**, Gray ST, Sedaghat AR. Symptoms of chronic rhinosinusitis differentially impact general health-related quality of life. *Rhinology* 2016;54(4):316-22.

Hoehle LP, Speth MM, Phillips KM, Gaudin RA, **Caradonna DS**, Gray ST, Sedaghat AR. Association between symptoms of allergic rhinitis with decreased general health-related quality of life. *Am J Rhinol Allergy* 2017;31(4):235-9.

Jalisi S, Rubin SJ, Wu KY, Kirke DN. Outcomes of head and neck cancer surgery in the geriatric population based on case volume at academic centers. *Laryngoscope* 2017;127(11):2539-2544.

Jamal BT, Grillone GA, **Jalisi S**. Chemoresponse Assay in Head and Neck Cancer Patients: A Three-Year Follow Up. *J Clin Diagn Res* 2017;11(5):XC01-XC03.

Kirke DN, Chitguppi C, Rubin SJ, Truong MT, **Jalisi S**. Adenoid cystic carcinoma of the base of tongue: A population-based study. *Am J Otolaryngol* 2017;38(3):279-284.

McDonough K, Crimlisk J, Nicholas P, Cabral H, Quinn EK, **Jalisi S**. Standardizing nurse training strategies to improve knowledge and self-efficacy with tracheostomy and laryngectomy care. *Appl Nurs Res* 2016;32:212-216.

Phillips KM, Hoehle LP, Bergmark RW, Campbell AP, **Caradonna DS**, Gray ST, Sedaghat AR. Association between nasal obstruction and risk of depression in chronic rhinosinusitis. *Otolaryngol Head Neck Surg* 2017;157(1):150-5.

Phillips KM, Hoehle LP, Bergmark RW, Campbell AP, **Caradonna DS**, Gray ST, Sedaghat AR. Chronic rhinosinusitis severity is associated with need for asthma-related systemic corticosteroids. *Rhinology* 2017;55(3):211-7.

Phillips KM, Hoehle LP, Bergmark RW, Campbell AP, **Caradonna DS**, Gray ST, Sedaghat AR. Chronic rhinosinusitis severity is associated with need for asthma-related systemic corticosteroids. *Rhinology* 2017; in press.

Phillips KM, Hoehle LP, Bergmark RW, **Caradonna DS**, Gray ST, Sedaghat AR. Acute exacerbations mediate quality of life impairment in chronic rhinosinusitis. *J Allergy Clin Immunol Pract* 2017;5(2):422-6.

Phillips KM, Hoehle L, Bergmark RW, **Caradonna DS**, Gray ST, Sedaghat AR. Reversal of smoking effects on chronic rhinosinusitis after smoking cessation. *Otolaryngol Head Neck Surg* 2017; in press.

Phillips KM, Hoehle LP, **Caradonna DS**, Gray ST, Sedaghat

AR. Association of severity of chronic rhinosinusitis with degree of comorbid asthma control. *Ann Allergy Asthma Immunol* 2016;117(6):651-4.

Rubin SJ, Cohen MB, Kirke DN, Qureshi MM, Truong MT, **Jalisi S**. Comparison of facility type outcomes for oral cavity cancer: Analysis of the national cancer database. *Laryngoscope* 2017;127(11):2551-2557.

Rubin SJ, Kirke DN, Ezzat WH, Truong MT, Salama AR, **Jalisi S**. Marital status as a predictor of survival in patients with human papilloma virus-positive oropharyngeal cancer. *Am J Otolaryngol* 2017;38(6):654-659.

Yamasaki A, Hoehle LP, Phillips KM, Feng AL, Campbell AP, **Caradonna DS**, Gray ST, Sedaghat AR. Association between systemic antibiotic and corticosteroid use for chronic rhinosinusitis and quality of life. *Laryngoscope* 2017; in press.

Plastic and Reconstructive Surgery

Alluri RK, Yin C, **Iorio ML**, Leland H, Mack WJ, Patel K. A critical appraisal of vascularized bone grafting for scaphoid nonunion. *J Wrist Surg* 2017;6(3):251-7.

Alluri RK, Yin C, **Iorio ML**, Leland H, Wong J, Patel K. Vascularized bone grafting in scaphoid nonunion: a review of patient-centered outcomes. *Hand (N Y)* 2017;12(2):127-34.

Becherer BE, Kamali P, Paul MA, Wu W, Curiel DA, Rakhorst HA, **Lee B**, **Lin SJ**, Kansal KJ. Prevalence of psychiatric comorbidities among women undergoing free tissue autologous breast reconstruction. *J Surg Oncol* 2017; in press.

Bhashyam AR, Harper CM, **Iorio ML**. Reversed palmaris longus muscle causing volar forearm pain and ulnar nerve paresthesia. *J Hand Surg Am* 2017;42(4):298.e1-298.e5.

Branford OA, Kamali P, Rohrich RJ, Song DH, Mallucci P, Liu DZ, Lang D, Sun K, Stubican M, **Lin SJ**. #PlasticSurgery. *Plast Reconstr Surg* 2016;138(6):1354-65.

Bucknor A, Chattha A, Ultee K, Wu W, Kamali P, Bletsis P, Chen A, **Lee BT**, Cronin C, **Lin SJ**. The financial impact and drivers of hospital charges in contralateral prophylactic mastectomy and reconstruction: A nationwide inpatient sample hospital analysis. *Breast Cancer Res Treat* 2017;165(2):301-10.

Chattha A, Bucknor A, Kamali P, Van Veldhuisen CL, Flecha-Hirsch R, Sharma R, Tobias AM, **Lee BT**, **Lin SJ**. Comparison of risk factors and complications in patients by stratified mastectomy weight: An institutional review of 1041 consecutive cases. *J Surg Oncol* 2017; in press.

Hughes CD, Urits I, **Fukudome E**, Shapiro FE. Safe anesthesia for outpatient cosmetic surgery. *Intern Med Rev* 2017; in press.

Irizarry D, **Lin SJ**. Plastic surgery. In: Jones DB, editor. *Pocket surgery*. Philadelphia: Wolters Kluwer; 2017 in press.

Kamali P, Curiel D, van Veldhuisen CL, Bucknor AEM, **Lee BT**, Rakhorst HA, **Lin SJ**. Trends in immediate breast reconstruction and early complication rates among older women: A big data analysis. *J Surg Oncol* 2017;115(7):870-7.

Kamali P, Lee M, Becherer BE, Wu W, Curiel D, Tran BNN, **Tobias AM**, **Lin SJ**, **Lee BT**. Medial row perforators are associated with higher rates of fat necrosis in bilateral DIEP flap breast

reconstruction. *Plast Reconstr Surg* 2017;140(1):19-24.

Kamali P, Lee M, **Lee BT**. Reply: Medial row perforators are associated with higher rates of fat necrosis in bilateral DIEP flap breast reconstruction #8232. *Plast Reconstr Surg* 2017; in press.

Kamali P, **Lin SJ**. Commentary on: Rates and predictors of readmission following body contouring procedures: an analysis of 5100 patients from the national surgical quality improvement program database. *Aesthet Surg J* 2017;37(8):927-9.

Kamali P, **Lin SJ**. Reply: The current role of three-dimensional printing in plastic surgery. *Plast Reconstr Surg* 2017;139(3):812e-3e.

Kamali P, Paul MA, Ibrahim AMS, Koolen PGL, Wu W, **Schermerhorn ML, Lee BT, Lin SJ**. National and regional differences in 32,248 postmastectomy autologous breast reconstruction using the Updated National Inpatient Survey. *Ann Plast Surg* 2017;78(6):717-22.

Kamali P, **Zettervall SL**, Wu W, Ibrahim AM, Medin C, Rakhorst HA, **Schermerhorn ML, Lee BT, Lin SJ**. Differences in the reporting of racial and socioeconomic disparities among three large national databases for breast reconstruction. *Plast Reconstr Surg* 2017;139(4):795-807.

Kazan R, Cyr S, Hemmerling TM, **Lin SJ**, Gilardino MS. The evolution of surgical simulation: the current state and future avenues for plastic surgery education. *Plast Reconstr Surg* 2017;139(2):533e-43e.

Koolen PGL, Li Z, Roussakis E, Paul MA, Ibrahim AMS, Matyal R, Huang T, Evans CL, **Lin SJ**. Oxygen-sensing paint-on bandage: Calibration of a novel approach in tissue perfusion assessment. *Plast Reconstr Surg* 2017;140(1):89-96.

Koolen PGL, Matos TR, Ibrahim AMS, Sun J, **Lee BT**, Frankenthaler RA, **Lin SJ**. Recurrence rates over 20 years in the treatment of malignant melanoma: Immediate versus delayed reconstruction. *Plast Reconstr Surg Glob Open* 2017;5(7):e1378.

Lee T, Patel N, Toskich BB, Fanzio PM, Cheng MH, **Lee BT, Singhal D**. High-volume hydrodissection for abdominally based free flaps: Preliminary results. *Microsurgery* 2017;37(4):307-11.

Lin SJ. Discussion: Consensus review of optimal perioperative care in breast reconstruction: Enhanced recovery after surgery (ERAS) society recommendations. *Plast Reconstr Surg* 2017;139(5):1072e-73e.

Lin SJ. Discussion: Crowdsourcing as a novel method to evaluate aesthetic outcomes of treatment for unilateral cleft lip. *Plast Reconstr Surg* 2016;138(4):875-6.

Lin SJ. Discussion: Patient-reported outcomes in weight loss and body contouring surgery: A cross-sectional analysis using the BODY-Q. *Plast Reconstr Surg* 2017;140(3):501-2.

Patel N, Pierson J, Lee T, Mast B, **Lee BT**, Estores I, **Singhal D**. Utilization and perception of integrative medicine among plastic surgery patients. *Ann Plast Surg* 2017;78(5):557-61.

Ricci JA, Crawford K, Ho OA, **Lee BT**, Patel KM, **Iorio ML**. Practical guidelines for venous thromboembolism prophylaxis in free tissue transfer. *Plast Reconstr Surg* 2016;138(5):1120-31.

Ricci JA, Epstein S, Momoh AO, **Lin SJ, Singhal D, Lee BT**. A meta-analysis of implant-based breast reconstruction and timing of adjuvant radiation therapy. *J Surg Res* 2017; in press.

Ricci JA, Kamali P, Becherer BE, Curiel D, Wu W, **Tobias AM, Lin SJ, Lee BT**. Umbilical necrosis rates after abdominal-based microsurgical breast reconstruction. *J Surg Res* 2017;215:257-63.

Ricci J, **Lin SJ**. Letter reply: Comparing the outcomes of different agents to treat vasospasm at microsurgical anastomosis during the papaverine shortage. *Plast Reconstr Surg* 2017;140(1):229e-231e.

Ricci JA, Vargas CR, Ho OA, **Lin SJ, Tobias AM, Lee BT**. Evaluating the use of tissue oximetry to decrease intensive unit monitoring for free flap breast reconstruction. *Ann Plast Surg* 2017;79(1):42-6.

Rodriguez MJ, Brown J, Giordano J, **Lin SJ**, Omenetto FG, Kaplan DL. Silk based bioinks for soft tissue reconstruction using 3-dimensional (3D) printing with *in vitro* and *in vivo* assessments. *Biomaterials* 2017;117:105-15.

Ruan QZ, Ricci JA, Silvestre J, Ho OA, **Lee BT**. Academic productivity of faculty associated with microsurgery fellowships. *Microsurgery* 2017;37(6):641-6.

Seth AK, **Iorio ML**. Super-thin and suprafascial anterolateral thigh perforator flaps for extremity reconstruction. *J Reconstr Microsurg* 2017;33(7):466-73.

Spiguel L, Shaw C, Katz A, Guo L, Chen HC, **Lee BT, Singhal D**. Fluorescein isothiocyanate: A novel application for lymphatic surgery. *Ann Plast Surg* 2017; 78(6S Suppl 5):S296-8.

Tas S, Colakoglu S, **Lee BT**. Nasal base retraction: A treatment algorithm. *Aesthet Surg J* 2017;37(6):640-53.

Taylor EM, **Iorio ML**. Surgeon-based 3D printing for microvascular bone flaps. *J Reconstr Microsurg* 2017;33(6):441-5.

Tran BNN, Fadayomi A, **Lin SJ**, Singhal D, **Lee BT**. Cost analysis of postmastectomy reconstruction: A comparison of two staged implant reconstruction using tissue expander and acellular dermal matrix with abdominal-based perforator free flaps. *J Surg Oncol* 2017;116(4):439-47.

Tran BNN, Singh M, **Lee BT**, Rudd R, **Singhal D**. Readability, complexity, and suitability analysis of online lymphedema resources. *J Surg Res* 2017;213:251-60.

van Paridon MW, Kamali P, Paul MA, Wu W, Ibrahim AMS, Kansal KJ, **Houlihan MJ, Morris DJ, Lee BT, Lin SJ, Sharma R**. Oncoplastic breast surgery: Achieving oncological and aesthetic outcomes. *J Surg Oncol* 2017;116(2):195-202.

Vargas CR, DePry J, **Lee BT**, Bordeaux JS. The readability of online patient information about Mohs micrographic surgery. *Dermatol Surg* 2016;42(10):1135-41.

Vargas CR, Koolen PG, Ho OA, **Tobias AM, Lin SJ, Lee BT**. Preoperative CT-angiography in autologous breast reconstruction. *Microsurgery* 2016;36(8):623-7.

Vargas CR, Ricci JA, Lee M, **Tobias AM**, Medalie DA, **Lee BT**. The accessibility, readability, and quality of online resources for gender affirming surgery. *J Surg Res* 2017;217:198-206.

Vosbikian MM, Harper CM, Byers A, Gutman A, Novack V, **Iorio ML**. The impact of safety regulations on the incidence of upper-extremity power saw injuries in the United States. *J Hand Surg Am* 2017;42(4):296.e1-296.e10.

Wada H, Vargas CR, Angelo J, Faulkner-Jones B, Paul MA, Ho OA, **Lee BT**, Frangioni JV. Accurate prediction of tissue viability at

Bibliography

postoperative day 7 using only two intraoperative subsecond near-infrared fluorescence images. *Plast Reconstr Surg* 2017;139(2):354-63.

Walley KC, Taylor EM, Anderson M, Lozano-Calderon S, **Iorio ML**. Reconstruction of quadriceps function with composite free tissue transfers following sarcoma resection. *J Surg Oncol* 2017;115(7):878-82.

Yang BW, **Iorio ML**, Day CS. Orthopaedic device approval through the premarket approval process: a financial feasibility analysis for a single center. *J Bone Joint Surg Am* 2017;99(6):e26.

Zhang K, Day C, **Iorio ML**. Concordance of patient and physician perceptions of care in an orthopedic clinic. *Orthopedics* 2017;40(4):242-6.

Podiatry

Bai S, Nagai M, Koerner SK, **Veves A**, **Sun L**. Structure-activity relationship study and discovery of indazole 3-carboxamides as calcium-release activated calcium channel blockers. *Bioorg Med Chem Lett* 2017;27(3):393-7.

Baltzis D, Dushay JR, Loader J, Wu J, Greenman RL, Roustit M, **Veves A**. Effect of linagliptin on vascular function: A randomized, placebo-controlled study. *J Clin Endocrinol Metab* 2016;101(11):4205-13.

Baltzis D, Roustit M, Grammatikopoulou MG, Katsaboukas D, Athanasiou V, Iakovou I, **Veves A**, Manes C, Trakatelli MC. Diabetic peripheral neuropathy as a predictor of asymptomatic myocardial ischemia in type 2 diabetes mellitus: A cross-sectional study. *Adv Ther* 2016;33(10):1840-7.

Chen SY, **Giurini JM**, Karchmer AW. Invasive systemic infection after hospital treatment for diabetic foot ulcer: Risk of occurrence and effect on survival. *Clin Infect Dis* 2017;64(3):326-34.

Lin YC, Wu J, Baltzis D, **Veves A**, Greenman R. MRI assessment of regional differences in phosphorus-31 metabolism and morphological abnormalities of the foot muscles in diabetes. *J Magn Reson Imaging* 2016;44(5):1132-42.

Veves A, **Giurini JM**, **Guzman RJ**, editors. *The diabetic foot: Medical and surgical management*, 4th edition. Switzerland; Springer International Publishing: 2017 in press.

Surgical Oncology

Ajmani GS, **James TA**, Kantor O, Wang CH, Yao KA. The impact of facility volume on rates of pathologic complete response to neoadjuvant chemotherapy used in breast cancer. *Ann Surg Oncol* 2017; in press.

Becherer BE, Kamali P, Paul MA, Wu W, Curiel DA, Rakhorst HA, **Lee B**, **Lin SJ**, **Kansal KJ**. Prevalence of psychiatric comorbidities among women undergoing free tissue autologous breast reconstruction. *J Surg Oncol* 2017; in press.

Belle JM, Vasilottos N, Nebesio TD, **James BC**. Pediatric toxic polycystic thyroid. *J Pediatr Endocrinol Metab* 2017;30(7):781-4.

Bychkovsky BL, Guo H, Sutton J, Spring L, Faig J, Dagogo-Jack I, Battelli C, **Houlihan MJ**, Yeh TC, Come SE, Lin NU. Use and yield of baseline imaging and laboratory testing in stage II breast cancer. *Oncologist* 2016;21(12):1495-1501.

Chattha A, Bucknor A, Kamali P, Van Veldhuisen CL, Flecha-Hirsch R, **Sharma R**, **Tobias AM**, **Lee BT**, **Lin SJ**. Comparison of risk factors and complications in patients by stratified mastectomy weight: An institutional review of 1041 consecutive cases. *J Surg Oncol* 2017; in press.

de Geus SW, **Eskander MF**, Bliss LA, **Kasumova GG**, Ng SC, **Callery MP**, **Tseng JF**. Neoadjuvant therapy versus upfront surgery for resected pancreatic adenocarcinoma: A nationwide propensity score matched analysis. *Surgery* 2017;161(3):592-601.

de Geus SW, Evans DB, Bliss LA, **Eskander MF**, Smith JK, Wolff RA, Mihsad RA, Weinstein MC, **Tseng JF**. Neoadjuvant therapy versus upfront surgical strategies in resectable pancreatic cancer: A Markov decision analysis. *Eur J Surg Oncol* 2016;42(10):1552-60.

Eskander MF, Bliss LA, McCarthy EP, de Geus SW, Chau Ng S, Nagle D, **Rodrigue JR**, **Tseng JF**. Massachusetts healthcare reform and trends in emergent colon resection. *Dis Colon Rectum* 2016;59(11):1063-72.

Eskander MF, de Geus SW, **Kasumova GG**, Ng SC, Al-Refaie W, Ayata G, **Tseng JF**. Evolution and impact of lymph node dissection during pancreaticoduodenectomy for pancreatic cancer. *Surgery* 2017;161(4):968-76.

Eskander MF, Schapira EF, Bliss LA, Burish NM, Tadikonda A, Ng SC, **Tseng JF**. Keeping it in the family: The impact of marital status and next of kin on cancer treatment and survival. *Am J Surg* 2016;212(4):691-9.

Gavrila A, **Hasselgren PO**, Glasgow A, Doyle AN, Lee AJ, Fox P, Gautam S, Hennessey JV, Kolodny GM, Cypess AM. Variable cold-induced brown adipose tissue response to thyroid hormone status. *Thyroid* 2017;27(1):1-10.

Hogg ME, Besselink MG, Clavien PA, Fingerhut A, Jeyarajah DR, Kooby DA, **Moser AJ**, Pitt HA, Varban OA, Vollmer CM, Zeh HJ 3rd, Hansen P; Minimally invasive pancreatic resection organizing committee. Training in minimally invasive pancreatic resections: A paradigm shift away from "see one, do one, teach one". *HPB (Oxford)* 2017;19(3):234-45.

James BC, Angelos P. Prophylactic vs. selective neck dissection in pediatric differentiated thyroid carcinoma. In: *Difficult decisions in endocrine surgery: An evidence-based approach*, 1st edition. Angelos P, Grogan RH, eds. Switzerland: Springer International Publishing; 2017 in press.

James BC, Jeon H, Kaplan EL, Angelos P, Grogan RH. Adrenal renal fusion: A case series and review of the literature. *World J Endocr Surg* 2017;9(2):61-4.

Kapoor T, Wrenn S, Callas P, **James TA**. Analysis of patient-detected breast cancer recurrence. *Breast Dis* 2017; in press.

Kasumova GG, Conway WC, **Tseng JF**. The role of venous and arterial resection in pancreatic cancer surgery. *Ann Surg Oncol* 2016; in press.

Kasumova GG, **Eskander MF**, de Geus SWL, Neto MM, **Tabatabaie O**, Ng SC, Mihsad RA, Mahadevan A, **Rodrigue JR**, **Tseng JF**. Regional variation in the treatment of pancreatic adenocarcinoma: Decreasing disparities with multimodality therapy. *Surgery* 2017; in press.

Kasumova GG, **Eskander MF**, **Kent TS**, Ng SC, **Moser AJ**, Ahmed M, Pleskow DK, **Callery MP**, **Tseng JF**. Hemorrhage after

pancreaticoduodenectomy: Does timing matter? HPB (Oxford). 2016;18(10):861-9.

Kasumova GG, Tabatabaie O, Eskander MF, Tadiakonda A, Ng SC, Tseng JF. National rise of primary pancreatic carcinoid tumors: Comparison to functional and nonfunctional pancreatic neuroendocrine tumors. *J Am Coll Surg* 2017;224(6):1057-64.

Linsk A, Mehta TS, Dialani V, Brook A, Chadashvili T, Houlihan MJ, Sharma R. Surgical upgrade rate of breast atypia to malignancy: An academic center's experience and validation of a predictive model. *Breast J* 2017; in press.

Mamtani A, Gonzalez JJ, Neo D, Slanetz PJ, Houlihan MJ, Herold CI, Recht A, Hacker MR, Sharma R. Early-stage breast cancer in the octogenarian: Tumor characteristics, treatment choices, and clinical outcomes. *Ann Surg Oncol* 2016;23(10):3371-8.

Mehrzad R, Nishino M, Nucera C, Dias-Santagata D, Hennessey JV, **Hasselgren PO.** Invasive follicular variant of papillary thyroid cancer harboring the NRAS mutation Q61K and presenting with bone metastasis—a case report. *Int J Surg Case Rep* 2017;38:180-4.

Mizrahi M, **Tseng JF, Wong D, Tung N, Eskander MF, Berzin TM, Pleskow DK, Sawhney MS.** Chronic pancreatitis-like change in BRCA2 mutation carriers. *Pancreas* 2017;46(5):679-83.

Patti JC, Ore AS, **Barrows C, Velanovich V, Moser AJ.** Value-based assessment of robotic pancreas and liver surgery. *Hepatobiliary Surg Nutr* 2017;6(4):246-57.

Sharma R, Shulman LN, James T. The future of quality improvement in breast cancer: Patient-reported outcomes. *Am J Med Qual* 2017;32(5):469-71.

Simpson RE, **James BC.** Pheochromocytoma, aldosteronoma, gastrinoma, insulinoma, somatostatinoma, vIPoma. In: *Clinical algorithms in general surgery: A practical guide.* Docimo S, Pauli EM, editors. Switzerland: Springer International Publishing; 2017 in press.

Tabatabaie O, Kasumova GG, Eskander MF, Critchlow JF, Tawa NE, Tseng JF. Totally implantable venous access devices: A review of complications and management strategies. *Am J Clin Oncol* 2017;40(1):94-105.

Tabatabaie O, Kasumova GG, Kent TS, Eskander MF, Fadayomi AB, Ng SC, Critchlow JF, Tawa NE, Tseng JF. Upper extremity deep venous thrombosis after port insertion: What are the risk factors? *Surgery* 2017;162(2):437-44.

van Paridon MW, Kamali P, Paul MA, Wu W, Ibrahim AMS, **Kansal KJ, Houlihan MJ, Morris DJ, Lee BT, Lin SJ, Sharma R.** Oncoplastic breast surgery: Achieving oncological and aesthetic outcomes. *J Surg Oncol* 2017;116(2):195-202.

Watkins AA, Kent TS, Gooding WE, Boggi U, Chalikhonda S, Kendrick ML, Walsh RM, Zeh HJ 3rd, Moser AJ. Multicenter outcomes of robotic reconstruction during the early learning curve for minimally-invasive pancreaticoduodenectomy. *HPB (Oxford)* 2017; in press.

Thoracic Surgery and Interventional Pulmonology

Assmann A, Vegh A, Ghasemi-Rad M, Bagherifard S, Cheng G, Sani ES, Ruiz-Esparza GU, Noshadi I, Lassaletta AD, **Gangadharan S, Tamayol A, Khademhosseini A, Annabi N.** A highly adhesive and naturally derived sealant. *Biomaterials* 2017;140:115-27.

Beqari J, Lembo A, **Critchlow J, Hamden A, Kent MS.** Pseudoachalasia secondary to thoracic aortic aneurysm. *Ann Thorac Surg* 2017;103(6):e517-18.

Buitrago DH, Wilson JL, Parikh M, Majid A, Gangadharan SP. Current concepts in severe adult tracheobronchomalacia: Evaluation and treatment. *J Thorac Dis* 2017;9(1):E57-E66.

Castillo-Angeles M, **Watkins AA, Acosta D, Frydman JL, Flier L, Garces-Descovich A, Cahalane MJ, Gangadharan SP, Atkins KM, Kent TS.** Mistreatment and the learning environment for medical students on general surgery clerkship rotations: What do key stakeholders think? *Am J Surg* 2017;213(2):307-12.

Expert Panel on Vascular Imaging and Interventional Radiology: Majdalany BS, Murrey DA Jr, Kapoor BS, Cain TR, Ganguli S, **Kent MS, Maldonado F, McBride JJ, Minocha J, Reis SP, Lorenz JM, Kalva SP.** ACR appropriateness criteria(®) Chylothorax treatment planning. *J Am Coll Radiol* 2017;14(5S):S118-26.

Heidinger BH, Anderson KR, Moriarty EM, Costa DB, **Gangadharan SP, VanderLaan PA, Bankier AA.** Size measurement and T-staging of lung adenocarcinomas manifesting as solid nodules ≤30 mm on CT: Radiology-pathology correlation. *Acad Radiol* 2017;24(7):851-9.

Heidinger BH, Anderson KR, Nemeč U, Costa DB, **Gangadharan SP, VanderLaan PA, Bankier AA.** Lung adenocarcinoma manifesting as pure ground-glass nodules: correlating CT size, volume, density, and roundness with histopathologic invasion and size. *J Thorac Oncol* 2017;12(8):1288-98.

Heidinger BH, Nemeč U, Anderson KR, Costa DB, **Gangadharan SP, VanderLaan PA, Bankier AA.** "Rounding" the size of pulmonary nodules: Impact of rounding methods on nodule management, as defined by the 2017 Fleischner Society Guidelines. *Acad Radiol* 2017; in press.

Kent M, Whyte R, Fleishman A, Tomich D, Forrow L, Rodrigue J. Public perceptions of overlapping surgery. *J Am Coll Surg* 2017;224(5):771-78.

Majid A, Alape D, Kheir F, Folch E, Ochoa S, Folch A, Gangadharan SP. Short-term use of uncovered self-expanding metallic airway stents for severe expiratory central airway collapse. *Respiration* 2016; 92(6):389-96.

Sheikine Y, Rangachari D, McDonald DC, Huberman MS, **Folch ES, VanderLaan PA, Costa DB.** EGFR testing in advanced non-small-cell lung cancer, a mini-review. *Clin Lung Cancer* 2016;17(6):483-92.

Watkins AA, Gondek SP, Lagisetty KH, Castillo-Angeles M, Gangadharan SP, Cahalane MJ, Kent TS. Weekly e-mailed teaching tips and reading material influence teaching among general surgery residents. *Am J Surg* 2017;213(1):195-201.

Wilson JL, Whyte RI, Gangadharan SP, Kent MS. Teamwork and communication skills in cardiothoracic surgery. *Ann Thorac Surg* 2017;103(4):1049-54.

Transplant Surgery

Butt Z, Dew MA, Liu Q, Simpson MA, Smith AR, Zee J, Gillespie BW, Abbey SE, Ladner DP, Weinrieb R, **Fisher RA, Hafliger S, Terrault N, Burton J, Sherker AH, DiMartini A.** Psychological outcomes of living liver donors from a multicenter prospective study: Results from the adult-to-adult living donor liver transplantation cohort study2 (A2ALL-2). *Am J Transplant* 2017;17(5):1267-77.

Bibliography

Dew MA, Butt Z, Liu Q, Simpson MA, Zee J, Ladner DP, Holtzman S, Smith AR, Pomfret EA, Merion RM, Gillespie BW, Sherker AH, **Fisher RA**, Olthoff KM, Burton JR Jr, Terrault NA, Fox AN, DiMartini AF. Prevalence and predictors of patient-reported long-term mental and physical health after donation in the Adult to Adult Living Donor Liver Transplantation Cohort Study (A2ALL). *Transplantation* 2017; in press.

DiMartini A, Dew MA, Liu Q, Simpson MA, Ladner DP, Smith AR, Zee J, Abbey S, Gillespie BW, Weinrieb R, Mandell MS, **Fisher RA**, Emond JC, Freise CE, Sherker AH, Butt Z. Social and financial outcomes of living liver donation: A prospective investigation within the adult-to-adult living donor liver transplantation cohort Study 2 (A2ALL-2). *Am J Transplant* 2017;17(4):1081-96.

Eskander MF, Bliss LA, McCarthy EP, de Geus SW, Chau Ng S, Nagle D, **Rodrigue JR**, **Tseng JF**. Massachusetts healthcare reform and trends in emergent colon resection. *Dis Colon Rectum* 2016;59(11):1063-72.

Fisher RA. Living donor liver transplantation: Eliminating the wait for death in end-stage liver disease? *Nat Rev Gastroenterol Hepatol* 2017;14(6):373-82.

Gomperts E, Belcher JD, **Otterbein LE**, Coates TD, Wood J, Skolnick BE, Levy H, Vercellotti GM. The role of carbon monoxide and heme oxygenase in the prevention of sickle cell disease vaso-occlusive crises. *Am J Hematol* 2017;92(6):569-82.

Itagaki K, **Riça I**, Zhang J, Gallo D, DePrato M, **Otterbein LE**, **Hauser CJ**. Intratracheal instillation of neutrophils rescues bacterial overgrowth initiated by trauma damage-associated molecular patterns. *J Trauma Acute Care Surg* 2017;82(5):853-60.

Kasiske BL, Asrani SK, Dew MA, Henderson ML, Henrich C, Humar A, Israni AK, Lentine KL, Matas AJ, Newell KA, LaPointe Rudow D, Massie AB, Snyder JJ, Taler SJ, Trotter JF, Waterman AD; Living Donor Collective participants including **Rodrigue JR**. The Living Donor Collective: A scientific registry for living donors. *Am J Transplant* 2017; in press.

Kasumova GG, **Eskander MF**, de Geus SWL, Neto MM, **Tabatabaie O**, Ng SC, Miksad RA, Mahadevan A, **Rodrigue JR**, **Tseng JF**. Regional variation in the treatment of pancreatic adenocarcinoma: Decreasing disparities with multimodality therapy. *Surgery* 2017;162(2):275-84.

Kent M, **Whyte R**, Fleishman A, Tomich D, Forrow L, **Rodrigue J**. Public perceptions of overlapping surgery. *J Am Coll Surg* 2017; in press.

Lee H, Zhang D, Wu J, **Otterbein LE**, Jin Y. Lung epithelial cell-derived microvesicles regulate macrophage migration via microRNA-17/221-induced Integrin $\beta(1)$ recycling. *J Immunol* 2017;199(4):1453-64.

Longhi MS, Vuerich M, Kalbasi A, Kenison JE, Yeste A, Csizmadia E, Vaughn B, Feldbrugge L, Mitsuhashi S, **Wegiel B**, **Otterbein L**, Moss A, Quintana FJ, Robson SC. Bilirubin suppresses Th17 immunity in colitis by upregulating CD39. *JCI Insight* 2017;2(9): e92791.

Mandelbrot DA, Fleishman A, **Rodrigue JR**, Norman SP, Samaniego M. Practices in the evaluation of potential kidney transplant recipients who are elderly: A survey of U.S. transplant centers. *Clin Transplant* 2017; in press.

Mandell MS, Smith AR, Dew MA, Gordon DB, Holtzman S, Howell T, DiMartini AF, Butt Z, Simpson MA, Ladner DP, Freise CE, McCluskey

SA, **Fisher RA**, Guarrera JV, Olthoff KM, Pomfret EA. Early postoperative pain and its predictors in the adult to adult living donor liver transplantation cohort study. *Transplantation* 2016;100(11):2362-71.

Rodrigue JR, Feranil M, Lang J, Fleishman A. Readability, content analysis, and racial/ethnic diversity of online living kidney donation information. *Clin Transplant* 2017;31(9).

Rodrigue JR, Tomich D, Fleishman A, Glazier AK. Vascularized composite allograft donation and transplantation: a survey of public attitudes in the United States. *Am J Transplant* 2017; in press.

Schallner N, Lieberum JL, Gallo D, LeBlanc RH 3rd, Fuller PM, Hanafy KA, **Otterbein LE**. Carbon monoxide preserves circadian rhythm to reduce the severity of subarachnoid hemorrhage in mice. *Stroke* 2017;48(9):2565-73.

Seth P, Csizmadia E, Hedblom A, Vuerich M, Xie H, Li M, Longhi MS, **Wegiel B**. Deletion of lactate dehydrogenase-A in myeloid cells triggers antitumor immunity. *Cancer Res* 2017;77(13):3632-43.

Wang Y, Hedblom A, Koerner SK, Li M, Jernigan FE, **Wegiel B**, **Sun L**. Novel synthetic chalcones induce apoptosis in the A549 non-small cell lung cancer cells harboring a KRAS mutation. *Bioorg Med Chem Lett* 2016;26(23):5703-6.

Urology

Berry DL, Hong F, Blonquist TM, Halpenny B, Filson CP, Master VA, Sanda MG, **Chang P**, Chien GW, Jones RA, Krupski TL, Wolpin S, Wilson L, Hayes JH, Trinh QD, Sokoloff M, Somayaji P. Decision support with the personal patient profile-prostate: A multicenter randomized trial. *J Urol* 2017; in press.

Chang P, Regan MM, Ferrer M, Guedea F, Patil D, Wei JT, Hembroff LA, Michalski JM, Saigal CS, Litwin MS, Hamstra DA, Kaplan ID, Ciezki JP, Klein EA, Kibel AS, Sandler HM, Dunn RL, Crociani CM, Sanda MG; PROST-QA Consortium. Relief of urinary symptom burden after primary prostate cancer treatment. *J Urol* 2017;197(2):376-84.

Gay HA, Sanda MG, Liu J, Wu N, Hamstra DA, Wei JT, Dunn RL, Klein EA, Sandler HM, Saigal CS, Litwin MS, Kuban DA, Hembroff L, Regan MM, **Chang P**; Prostate Cancer Outcomes and Satisfaction with Treatment Quality Assessment Consortium, Michalski JM. External beam radiation therapy or brachytherapy with or without short-course neoadjuvant androgen deprivation therapy: Results of a multicenter, prospective study of quality of life. *Int J Radiat Oncol Biol Phys* 2017;98(2):304-17.

Lee JY, Daignault-Newton S, Heath G, Scarlett S, Sanda MG, **Chang P**, Regan MM, Michalski JM, Sandler HM, Feng FY, Kuban DA, Zietman AL, Ciezki JP, Kaplan ID, Crociani C, McLaughlin WP, Mantz CA, Finkelstein SE, Suy S, Collins SP, Garin O, Ferrer M, Hamstra DA, Spratt DE. Multinational prospective study of patient-reported outcomes after prostate radiation therapy: Detailed assessment of rectal bleeding. *Int J Radiat Oncol Biol Phys* 2016;96(4):770-7.

Leow JJ, Meyer CP, Wang Y, Chang SL, Chung BI, Trinh QD, **Korets R**, Bhojani N. Contemporary trends in utilization and perioperative outcomes of percutaneous nephrolithotomy in the United States from 2003 to 2014. *J Endourol* 2017;31(8):742-50.

Lin DW, Newcomb LF, Brown MD, Sjoberg DD, Dong Y, Brooks JD, Carroll PR, Cooperberg M, Dash A, Ellis WJ, Fabrizio M, Gleave ME, Morgan TM, Nelson PS, Thompson IM, **Wagner AA**, Zheng Y;

Canary Prostate Active Surveillance Study Investigators. Evaluating the four Kallikrein Panel of the 4Kscore for prediction of high-grade prostate cancer in men in the Canary Prostate Active Surveillance Study. *Eur Urol* 2017;72(3):448-54.

Macleod LC, Ellis WJ, Newcomb LF, Zheng Y, Brooks JD, Carroll PR, Gleave ME, Lance RS, Nelson PS, Thompson IM Jr, **Wagner AA**, Wei JT, Lin DW. Timing of adverse prostate cancer reclassification on first surveillance biopsy: Results from the Canary Prostate Cancer Active Surveillance Study. *J Urol* 2017;197(4):1026-33.

Patel HD, Riffon MF, Joice GA, Johnson MH, **Chang P**, **Wagner AA**, McKiernan JM, Trock BJ, Allaf ME, Pierorazio PM. A prospective, comparative study of quality of life among patients with small renal masses choosing active surveillance and primary intervention. *J Urol* 2016;196(5):1356-62.

Uzosike AC, Patel HD, Alam R, Schwen ZR, Gupta M, Gorin MA, Johnson MH, Gausepohl H, Riffon MF, Trock BJ, Chang P, **Wagner AA**, McKiernan JM, Allaf ME, Pierorazio PM. Growth kinetics of small renal masses on active surveillance: Variability and results from the DISSRM Registry. *J Urol* 2017; in press.

Wagner AA, Cheng PJ, Carneiro A, Dovirak O, Khosla A, Taylor KN, Crociani CM, McAnally KC, Percy A, Dewey LE, Sanda MG, **Chang P**. Clinical use of expanded prostate cancer index composite for clinical practice to assess patient reported prostate cancer quality of life following robot-assisted radical prostatectomy. *J Urol* 2017;197(1):109-14.

Vascular and Endovascular Surgery

Bardia A, Sood A, Mahmood F, Orhurhu V, Mueller A, Montealegre-Gallegos M, Shnyder MR, Ultee KH, **Schermerhorn ML**, Matyal R. Combined epidural-general anesthesia vs general anesthesia alone for elective abdominal aortic aneurysm repair. *JAMA Surg* 2016;151(12):1116-23.

Beck AW, Sedrakyan A, Mao J, Venermo M, Faizer R, Debus S, Behrendt CA, Scali ST, Altreuther M, **Schermerhorn M**, Beiles B, Szeberin Z, Eldrup N, Danielsson G, Thomson I, Wigger PF, Björck M, Cronenwett JL, Mani K; International Consortium of Vascular Registries. Variations in abdominal aortic aneurysm care: A report from the international consortium of vascular registries. *Circulation* 2016; 134(24):1948-58.

Beqari J, Lembo A, **Critchlow J**, **Hamden A**, **Kent MS**. Pseudoachalasia secondary to thoracic aortic aneurysm. *Ann Thorac Surg* 2017;103(6):e517-18.

Bodewes TCF, Darling JD, Deery SE, O'Donnell TFX, Pothof AB, Shean KE, Moll FL, **Schermerhorn ML**. Patient selection and perioperative outcomes of bypass and endovascular intervention as first revascularization strategy for infrainguinal arterial disease. *J Vasc Surg* 2017; in press.

Bodewes TC, Johnson JM, Auster M, Huynh C, Muralidharan S, **Contreras M**, **LoGerfo FW**, **Pradhan-Nabzdyk L**. Intraluminal delivery of thrombospondin-2 small interfering RNA inhibits the vascular response to injury in a rat carotid balloon angioplasty model. *FASEB J* 2017;31(1):109-19.

Bodewes TCF, Pothof AB, Darling JD, Deery SE, Jones DW, **Soden PA**, Moll FL, **Schermerhorn ML**. Preoperative anemia associated with adverse outcomes after infrainguinal bypass surgery in patients with chronic limb-threatening ischemia. *J Vasc Surg* 2017; in press.

Bodewes TC, **Soden PA**, Ultee KH, **Zettervall SL**, Pothof AB, Deery SE, Moll FL, **Schermerhorn ML**. Risk factors for 30-day unplanned readmission following infrainguinal endovascular interventions. *J Vasc Surg* 2017;65(2):484-94.

Bodewes TCF, Ultee KHJ, **Soden PA**, **Zettervall SL**, Shean KE, Jones DW, Moll FL, **Schermerhorn ML**. Perioperative outcomes of infrainguinal bypass surgery in patients with and without prior revascularization. *J Vasc Surg* 2017;65(5):1354-65.

Buck DB, **Soden PA**, Deery SE, **Zettervall SL**, Ultee KHJ, Landon BE, O'Malley AJ, **Schermerhorn ML**. Comparison of endovascular stent grafts for abdominal aortic aneurysm repair in medicare beneficiaries. *Ann Vasc Surg* 2017; in press.

Chen J, Howell C, **Haller CA**, Patel MS, Ayala P, Moravec KA, Dai E, Liu L, Sotiri I, Aizenberg M, Aizenberg J, **Chaikof EL**. An immobilized liquid interface prevents device associated bacterial infection *in vivo*. *Biomaterials* 2017;113:80-92.

Columbo JA, **McCallum JC**, Goodney PP, Bower TC, **Schermerhorn ML**, Powell RJ, DeMartino RR. Multicenter experience of surgical explantation of carotid stents for recurrent stenosis. *Vasc Endovascular Surg* 2016; in press.

Darling JD, Bodewes TCF, Deery SE, **Guzman RJ**, **Wyers MC**, **Hamdan AD**, Verhagen HJ, **Schermerhorn ML**. Outcomes after first-time lower extremity revascularization for chronic limb-threatening ischemia between patients with and without diabetes. *J Vasc Surg* 2017; in press.

Darling JD, **McCallum JC**, **Soden PA**, **Guzman RJ**, **Wyers MC**, **Hamdan AD**, Verhagen HJ, **Schermerhorn ML**. Predictive ability of the society for vascular surgery wound, ischemia, and foot infection (WIFI) classification system after first-time lower extremity revascularizations. *J Vasc Surg* 2017;65(3):695-704.

Darling JD, **McCallum JC**, **Soden PA**, Hon JJ, **Guzman RJ**, **Wyers MC**, Verhagen HJ, **Schermerhorn ML**. Clinical results of single-vessel versus multiple-vessel infrapopliteal intervention. *J Vasc Surg* 2016;64(6):1675-81.

Darling JD, **McCallum JC**, **Soden PA**, Korepta L, **Guzman RJ**, **Wyers MC**, **Hamdan AD**, **Schermerhorn ML**. Results for primary bypass versus primary angioplasty/stent for lower extremity chronic limb-threatening ischemia. *J Vasc Surg* 2017;66(2):466-75.

Deery SE, Ergul EA, **Schermerhorn ML**, Siracuse JJ, Schanzer A, Goodney PP, Cambria RP, Patel VI; Vascular Study Group of New England. Aneurysm sac expansion is independently associated with late mortality in patients treated with endovascular aneurysm repair. *J Vasc Surg* 2017; in press.

Deery SE, O'Donnell TFX, Bodewes TCF, Dalebout BA, Pothof AB, Shean KE, Darling JD, **Schermerhorn ML**. Early reintervention after open and endovascular abdominal aortic aneurysm repair is associated with high mortality. *J Vasc Surg* 2017; in press.

Deery SE, **Schermerhorn ML**. Open versus endovascular abdominal aortic aneurysm repair in Medicare beneficiaries. *Surgery* 2017; in press.

Deery SE, **Schermerhorn ML**. Optimal vs feasible volume thresholds in vascular surgery. *JAMA Surg* 2017;152(8):766-7.

Deery SE, Shean KE, Wang GJ, Black JH 3rd, Upchurch GR Jr, Giles KA, Patel VI, **Schermerhorn ML**; Society for Vascular Surgery Vascular Quality Initiative. Female sex independently

Bibliography

predicts mortality after thoracic endovascular aortic repair for intact descending thoracic aortic aneurysms. *J Vasc Surg* 2017;66(1):2-8.

Deery SE, **Soden PA**, **Zettervall SL**, Shean KE, Bodewes TC, Pothof AB, Lo RC, **Schermerhorn ML**. Sex differences in mortality and morbidity following repair of intact abdominal aortic aneurysms. *J Vasc Surg* 2017;65(4):1006-13.

Jones DW, **Dansey K**, **Hamdan AD**. Lower extremity revascularization in end-stage renal disease. *Vasc Endovascular Surg* 2016;50(8):582-5.

Jones DW, **Schermerhorn ML**, Brooke BS, Conrad MF, Goodney PP, **Wyers MC**, Stone DH; Vascular Quality Initiative. Perioperative Clopidogrel is associated with increased bleeding and blood transfusion at the time of lower extremity bypass. *J Vasc Surg* 2017;65(6):1719-28.

Jones, DW and **Wyers, MC**. Lower extremity arterial reconstruction in patients with diabetes mellitus: principles of treatment. In: Veves A, Giurini JM, Guzman RJ, editors. *The diabetic foot: medical and surgical management*, 4th edition. Switzerland; Springer International Publishing: 2017 in press.

Kamali P, Paul MA, Ibrahim AMS, Koolen PGL, Wu W, **Schermerhorn ML**, **Lee BT**, **Lin SJ**. National and regional differences in 32,248 postmastectomy autologous breast reconstruction using the Updated National Inpatient Survey. *Ann Plast Surg* 2017;78(6):717-22.

Kamali P, **Zettervall SL**, Wu W, Ibrahim AM, Medin C, Rakhorst HA, **Schermerhorn ML**, **Lee BT**, **Lin SJ**. Differences in the reporting of racial and socioeconomic disparities among three large national databases for breast reconstruction. *Plast Reconstr Surg* 2017;139(4):795-807.

Klarin D, Lancaster RT, Ergul E, Bertges D, Goodney P, **Schermerhorn ML**, Cambria RP, Patel VI; Vascular Study Group of New England. Perioperative and long-term impact of chronic kidney disease on carotid artery interventions. *J Vasc Surg* 2016;64(5):1295-1302.

Lu K, Farber A, **Schermerhorn ML**, Patel VI, Kalish JA, Rybin D, Doros G, Siracuse JJ. The effect of ambulatory status on outcomes of percutaneous vascular interventions and lower extremity bypass for critical limb ischemia in the Vascular Quality Initiative. *J Vasc Surg* 2017;65(6):1706-12.

Martin M, **Wyers, MC**. Acute mesenteric ischemia. In: Sidawy AP, Perler BA, editors. *Rutherford's vascular surgery and endovascular therapy*, 9th edition. Philadelphia: Elsevier, Inc; 2017 in press.

Moll HP, Lee A, Peterson CR, Revuelta Cervantes J, Wojcik BM, Parulkar A, Mele A, **LoGerfo PJ**, Siracuse JJ, Csizmadia E, **da Silva CG**, **Ferran C**. A20 haploinsufficiency aggravates transplant arteriosclerosis in mouse vascular allografts: implications for clinical transplantation. *Transplantation* 2016;100(11):e106-16.

Morikis VA, Chase S, Wun T, **Chaikof EL**, Magnani JL, Simon SI. Selectin catch-bonds mechanotransduce integrin activation and neutrophil arrest on inflamed endothelium under shear flow. *Blood* 2017; in press.

Nabzdyk CS, **Pradhan-Nabzdyk L**, **LoGerfo FW**. RNAi therapy to the wall of arteries and veins: anatomical, physiologic, and pharmacological considerations. *J Transl Med* 2017;15(1):164.

O'Donnell TFX, Deery SE, Darling JD, Shean KE, Mittleman MA,

Yee GN, Dernbach MR, **Schermerhorn ML**. Adherence to lipid management guidelines is associated with lower mortality and major adverse limb events in patients undergoing revascularization for chronic limb-threatening ischemia. *J Vasc Surg* 2017;66(2):572-8.

O'Donnell TFX, Shean KE, Deery SE, Bodewes TCF, **Wyers MC**, O'Brien KL, Matyal R, **Schermerhorn ML**. A preoperative risk score for transfusion in infrarenal endovascular aneurysm repair to avoid type and cross. *J Vasc Surg* 2017; in press.

Patel MS, **Chaikof EL**. Disclosing industry relationships: A patient-centered approach. *JAMA Surg* 2016;151(10):895-6.

Patel MS, **Chaikof EL**. Ruptured aneurysm systems of care: A national imperative to improve clinical outcomes. *J Vasc Surg* 2017;65(3):589-90.

Patel MS, Miranda-Nieves D, Chen J, **Haller CA**, **Chaikof EL**. Targeting P-selectin glycoprotein ligand-1/P-selectin interactions as a novel therapy for metabolic syndrome. *Transl Res* 2017;183:1-13.

Pedigo SL, Guth CM, Hocking KM, Banathy A, Li FD, Cheung-Flynn J, Brophy CM, **Guzman RJ**, Komalavilas P. Calcification of human saphenous vein associated with endothelial dysfunction: a pilot histopathophysiological and demographical study. *Front Surg* 2017; in press.

Pothof AB, Bodewes TCF, O'Donnell TFX, Deery SE, Shean K, **Soden PA**, de Borst GJ, **Schermerhorn ML**. Preoperative anemia is associated with mortality after carotid endarterectomy in symptomatic patients. *J Vasc Surg* 2017; in press.

Pothof AB, **Soden PA**, Fokkema M, **Zettervall SL**, Deery SE, Bodewes TCF, de Borst GJ, **Schermerhorn ML**; Vascular Study Group of New England. The impact of contralateral carotid artery stenosis on outcomes after carotid endarterectomy. *J Vasc Surg* 2017; in press.

Raghuraman G, Hsiung J, Zuniga MC, Baughman BD, Hitchner E, **Guzman RJ**, Zhou W. Eotaxin augments calcification in vascular smooth muscle cells. *J Cell Biochem* 2017;118(3):647-54.

Schermerhorn ML, Jones DW. Management of descending thoracic aorta disease: evolving treatment paradigms in the TEVAR era. *Eur J Vasc Endovasc Surg* 2017;53(1):1-3.

Shean KE, **McCallum JC**, **Soden PA**, Deery SE, Schneider JR, Nolan BW, Rockman CB, **Schermerhorn ML**; Society for Vascular Surgery Vascular Quality Initiative. Regional variation in patient selection and treatment for carotid artery disease in the Vascular Quality Initiative. *J Vasc Surg* 2017;66(1):112-21.

Shean KE, **Soden PA**, **Schermerhorn ML**, **Zettervall SL**, Deery SE, Darling JD, **Hamdan A**, **LoGerfo FW**. Lifelong limb preservation: a patient-centered description of lower extremity arterial reconstruction outcomes. *J Vasc Surg* 2017; in press.

Siracuse JJ, Van Orden K, Kalish JA, Eslami MH, **Schermerhorn ML**, Patel VI, Rybin D, Farber A; Vascular Quality Initiative. Endovascular treatment of the common femoral artery in the Vascular Quality Initiative. *J Vasc Surg* 2017;65(4):1039-46.

Soden PA, **Schermerhorn ML**. Epidemiology of ruptured abdominal aortic aneurysm. In: *Ruptured abdominal aortic aneurysm: the definitive manual*. Starnes BW, Mehta M, Veith FJ, editors. Switzerland: Springer International Publishing; 2017. p. 15-48.

Soden PA, **Schermerhorn ML**. Reply. *J Vasc Surg* 2017;65(5):1549.

Soden PA, Zettervall SL, Curran T, Vouyouka AG, Goodney PP, Mills JL, Hallett JW Jr, Schermerhorn ML; Society for Vascular Surgery Vascular Quality Initiative. Regional variation in patient selection and treatment for lower extremity vascular disease in the vascular quality initiative. *J Vasc Surg* 2017;65(1):108-18.

Soden PA, Zettervall SL, Shean KE, Deery SE, Kalish JA, Healey CT, Kansal N, Schermerhorn ML; Vascular study group of new england (VSGNE). Effect of adjunct femoral endarterectomy in lower extremity bypass on perioperative and 1-year outcomes. *J Vasc Surg* 2017;65(3):711-19.

Soden PA, Zettervall SL, Shean KE, Vouyouka AG, Goodney PP, Mills JL, Hallett JW Jr, Schermerhorn ML; Society for Vascular Surgery Vascular Quality Initiative. Regional variation in outcomes for lower extremity vascular disease in the Vascular Quality Initiative. *J Vasc Surg* 2017;66(3):810-8.

Soden PA, Zettervall SL, Ultee KH, Darling JD, McCallum JC, Hamdan AD, Wyers MC, Schermerhorn ML. Patient selection and perioperative outcomes are similar between targeted and nontargeted hospitals (in the national surgical quality improvement program) for abdominal aortic aneurysm repair. *J Vasc Surg* 2017;65(2):362-71.

Soden PA, Zettervall SL, Ultee KH, Landon BE, O'Malley AJ, Goodney PP, DeMartino RR, Arya S, Schermerhorn ML; Society for Vascular Surgery Vascular Quality Initiative. Dual antiplatelet therapy is associated with prolonged survival after lower extremity revascularization. *J Vasc Surg* 2016;64(6):1633-44.

Stangenberg L, **Curran T, Shuja F, Rosenberg R, Mahmood F, Schermerhorn ML.** Development of a risk prediction model for transfusion in carotid endarterectomy and demonstration of cost-saving potential by avoidance of "type and screen". *J Vasc Surg* 2016;64(6):1711-18.

Tomee SM, Bastiaannet E, **Schermerhorn ML, Golledge J, Hamming JF, Lindeman JH.** The consequences of real life practice of early abdominal aortic aneurysm repair: a cost-benefit analysis. *Eur J Vasc Endovasc Surg* 2017;54(1):28-33.

Ultee KH, **Soden PA, Zettervall SL, McCallum JC, Siracuse JJ, Alef MJ, Verhagen HJ, Schermerhorn ML;** Vascular Study Group of New England. The perioperative effect of concomitant procedures during open infrarenal abdominal aortic aneurysm repair. *J Vasc Surg* 2016;64(4):934-40.

Ultee KH, **Zettervall SL, Soden PA, Buck DB, Deery SE, Shean KE, Verhagen HJM, Schermerhorn ML.** The impact of endovascular repair on management and outcome of ruptured thoracic aortic aneurysms. *J Vasc Surg* 2017;66(2):343-52.

Ultee KH, **Zettervall SL, Soden PA, Darling J, Bertges DJ, Verhagen HJ, Schermerhorn ML;** Vascular Study Group of New England. Incidence of and risk factors for bowel ischemia after abdominal aortic aneurysm repair. *J Vasc Surg* 2016;64(5):1384-91.

Ultee KH, **Zettervall SL, Soden PA, Darling J, Verhagen HJM, Schermerhorn ML.** Perioperative outcome of endovascular repair for complex abdominal aortic aneurysms. *J Vasc Surg* 2017;65(6):1567-75.

Veves A, Giurini JM, Guzman RJ, editors. The diabetic foot: medical and surgical management, 4th edition. Switzerland; Springer International Publishing: 2017 in press.

Wise ES, Wergin JE, Mace EH, Kallos JA, Muhlestein WE, Shelburne NJ, Hocking KM, Brophy CM, **Guzman RJ.** Upper extremity pulse pressure predicts amputation-free survival after lower extremity bypass. *Am Surg* 2017;83(7):804-11.

Zettervall SL, Buck DB, Soden PA, Cronenwett JL, Goodney PP, Eslami MH, Lee JT, Schermerhorn ML; Society for Vascular Surgery Vascular Quality Initiative. Regional variation exists in patient selection and treatment of abdominal aortic aneurysms. *J Vasc Surg* 2016;64(4):921-7.

Zettervall SL, Deery SE, Soden PA, Shean K, Siracuse JJ, Alef M, Patel VI, Schermerhorn ML; Vascular Study Group of New England. Editor's Choice – Renal complications after EVAR with suprarenal versus infrarenal fixation among all users and routine users. *Eur J Vasc Endovasc Surg* 2017;54(3):287-93.

Zettervall SL, Karthaus EG, Soden PA, Buck DB, Ultee KH, Schermerhorn ML, Wyers MC. Clinical presentation, management, follow-up, and outcomes of isolated celiac and superior mesenteric artery dissections. *J Vasc Surg* 2017;65(1):91-8.

Zettervall SL, Lo RC, Soden PA, Deery SE, Ultee KH, Pinto DS, Wyers MC, Schermerhorn ML. Trends in treatment and mortality for mesenteric ischemia in the United States from 2000 to 2012. *Ann Vasc Surg* 2017;42:111-9.

Zettervall SL, Marshall AP, Fleser P, Guzman RJ. Association of arterial calcification with chronic limb ischemia in patients with peripheral artery disease. *J Vasc Surg* 2017; in press.

Zettervall SL, Schermerhorn ML, Soden PA, McCallum JC, Shean KE, Deery SE, O'Malley AJ, Landon B. The effect of surgeon and hospital volume on mortality after open and endovascular repair of abdominal aortic aneurysms. *J Vasc Surg* 2017;65(3):626-34.

Zettervall SL, Soden PA, Buck DB, Cronenwett JL, Goodney PP, Eslami MH, Lee JT, Schermerhorn ML; Society for Vascular Surgery Vascular Quality Initiative. Significant regional variation exists in morbidity and mortality after repair of abdominal aortic aneurysm. *J Vasc Surg* 2017;65(5):1305-12.

Zettervall SL, Soden PA, Deery SE, Ultee K, Shean KE, Shuja F, Amdur RL, Schermerhorn ML. Comparison of renal complications between endografts with suprarenal and infrarenal fixation. *Eur J Vasc Endovasc Surg* 2017;54(1):5-11.

Zettervall SL, Soden PA, Shean KE, Deery SE, Ultee KH, Alef M, Siracuse JJ, Schermerhorn ML; Vascular Study Group of New England.. Early extubation reduces respiratory complications and hospital length of stay following repair of abdominal aortic aneurysms. *J Vasc Surg* 2017;65(1):58-64.

Zettervall SL, Soden PA, Ultee KH, Seldon C, Oh J, McGann K, Schermerhorn ML, Guzman RJ. Elevated serum phosphate levels are associated with decreased amputation-free survival after interventions for critical limb ischemia. *J Vasc Surg* 2017;65(2):431-7.

Zettervall SL, Ultee KH, Soden PA, Deery SE, Shean KE, Pothof AB, Wyers M, Schermerhorn ML. Predictors of renal dysfunction after endovascular and open repair of abdominal aortic aneurysms. *J Vasc Surg* 2017;65(4):991-6.

Zaiem F, Almasri J, Tello M, Prokop LJ, **Chaikof EL, Murad MH.** Surveillance after endovascular aortic repair. *J Vasc Surg* 2017; in press.



RESEARCH GROUP

Thomas Marandu, PhD

Charles Cook, MD

Associate Professor of Surgery

Chief, Acute Care Surgery, Trauma, and Surgical Critical Care

RESEARCH FOCUS

Most people are infected with multiple herpes family viruses. Unlike many viral infections, these viruses are not eradicated from the host, but become dormant in the host's tissues for their lifetime. During periods of immune compromise or stress, these viruses can reactivate. It is understood that herpes family viral reactivation is pathologic in immunocompromised people, such as transplant recipients or AIDS patients. My laboratory has been focused on defining the impact that these persistent viral infections have on immune competent hosts.

During the past 20 years, we and others have confirmed that these viruses can reactivate during critical illness. Of the family, cytomegalovirus (CMV) reactivation has been associated with worsened outcomes. My laboratory spent our early years of funding defining mechanisms by which CMV reactivation might be triggered using murine models to test our hypotheses. This transitioned to understanding the consequences of such reactivations; specifically how CMV reactivation might harm an immune competent host.

We identified the lungs as a potential target for CMV reactivation, and showed that reactivation is associated with lung injury during bacterial sepsis, something that we named CMV-ALI (cytomegalovirus associated acute lung injury). Clinical outcomes support this hypothesis, with roughly doubled durations of mechanical ventilation required for patients with CMV reactivation. Perhaps most importantly, our work showed that such reactivation events (and their attendant lung injury) can be prevented by antiviral prophylaxis. These results have been foundational to several clinical trials (two completed, one ongoing) that are beginning to corroborate these experimental observations.

Our current focus is to try to understand the mechanism of CMV-ALI. CMV infection/latency makes a lasting imprint in the immunity of its host, leaving CMV-latent hosts with exaggerated immune potential in their lungs. This means that when they encounter bacterial infections (like pneumonia or sepsis) they are more prone to inflammation and lung injury. We are currently evaluating different immune cell populations to understand their individual contributions to CMV-ALI. Our most recent work, done in collaboration with Drs. Carl Hauser, Michael Yaffe, Leo Otterbein, and the HALO group at BIDMC, suggests that neutrophils may play a pivotal role in these exaggerated immune responses.

Because we have a robust understanding of CMV biology, and have an animal model, we have been fortunate to develop numerous collaborations with colleagues in overlapping fields. We are currently supported for work with Dr. Antonio Chiocca's group at Brigham and Women's Hospital, studying the interactions between CMV and glioblastoma. Our current results have confirmed a contributory role of CMV to progression of this deadly brain tumor. More importantly, we are defining mechanistic pathways that should lead to novel therapies. We have also begun early collaborations with Dr. Richard Cummings at BIDMC to understand how CMV infection impacts cellular protein glycosylation.

ACCOMPLISHMENTS 2016-17

- Named Chair of Strategic Planning Committee for Surgical Infection Society

Invited Lectures:

- Cost and Consequences of Surgical Infections; 36th Annual Meeting Surgical Infection Society, May 18, 2016
- Impact of Latent Herpesviruses on Host Immunity; 14th Annual Advances in Inflammation Research, Alpert Medical School of Brown University, Providence RI, October 6, 2016
- Catheter associated blood stream infections: The quest for zero; American College of Surgeons Clinical Congress, San Diego CA, October 24, 2017
- Geriatric Injuries: Are rib fractures lethal in the elderly? Harvard Medical School Trauma and Critical Care Symposium, Boston, MA, November 21, 2017
- Surgical Infections: We need to start thinking differently; Department of Surgery Grand Rounds, VA Medical Center, Boston, MA, December 15, 2017

New Memberships:

- Boston Surgical Society
- New England Surgical Society

TEACHING, TRAINING, AND EDUCATION

Marion Griessl and Michael Gutknecht successfully completed their post-doctoral training in my laboratory in 2016 and 2017 and have returned to Germany. Thomas Marandu joined my laboratory from Tanzania to begin his postdoctoral studies in 2017.

SELECTED RESEARCH SUPPORT

NIH RO1 CA195532, Investigating the cytomegalovirus link to glioblastoma using a novel mouse model; NIH, 2015-2020; Co-Investigator (10% effort)

SELECTED PUBLICATIONS

Mansfield S, Dwivedi V, Byrd S, Trgovcich T, Griessl M, Gutknecht M, Cook CH. Bronchoalveolar lavage to detect cytomegalovirus infection, latency, and reactivation in immune competent hosts. *J Med Virol* 2016;88(8):1408-16.

Trgovcich T, Kincaid M, Thomas A, Griessl M, Zimmerman PD, Dwivedi V, Bergdall V, Klenerman P, Cook CH. Cytomegalovirus reinfections stimulate CD8 T-memory inflation. *PLOS One* 2016;11(11):e0167097

Griessl M, Gutknecht M, Co ok CH. Determination of suitable reference genes for RT-qPCR analysis of murine Cytomegalovirus in vivo and in vitro. *J Virol Methods* 2017;248:100-106.

Celestin AT, Odom SR, Angelidou K, Evans S, Coimbra R, Guidry CA, Cuschieri J, Banton KL, O'Neill PJ, Askari R, Namias N, Duane T, Dellinger EP, Sawyer R, Cook CH. Novel method suggests global superiority of short duration antibiotics for intra-abdominal infections. *Clin Infect Dis* 2017;65(9):1577-1579.

A complete list of publications begins on page 13.



Carl J. Hauser, MD

Lecturer on Surgery
Trauma Medical Director

RESEARCH FOCUS

The major basic science research focus of my research is clinical inflammation biology and the mechanisms and management of infection after injury and surgery. My lab is especially interested in the role of cellular “Danger” molecules, or “damage-associated molecular patterns” (aka “DAMPs” or “alarmins”) in inflammation. Our laboratory is a world leader in investigating the role of intracellular DAMPs derived from mitochondria. Our original work on this subject was published in *Nature* (March 4, 2010). It has been widely cited as a groundbreaking conceptual advance in sepsis and inflammation research, and has been cited more than 1,000 times. The known mitochondrial DAMPs include mitochondrial DNA, formyl peptides, and some of the mitochondrial lipids. Our recent work has shown that mitochondrial formyl peptides act as potent DAMPs. They circulate in plasma after injury where they activate innate immune cells while simultaneously causing heterologous suppression of cell-surface G-protein coupled receptors for critically important chemoattractants like chemokines and leukotrienes. Mitochondrial DNA is also a potent agonist that targets toll-like receptor 9 (TLR-9) and we have found that it is also a potent activator of neutrophil (PMN) extracellular traps (“NETs”). Signaling downstream from this receptor, however, may result in tolerance and so plays a critical role in suppression of immune function after injury.

Formyl peptides (FPs) derived from mitochondria are potent chemoattractants. As such, they are critically important activators of immune responses to damaged tissue, including phagocytic wound debridement and thus the initiation of healing. On the other hand, these molecules compete for the immune system’s “attention” in systemically injured patients. In work presented at the American Association for the Surgery of Trauma (AAST) we showed that innate responses to FPs released by injury render the host susceptible to infection by suppressing PMN surveillance of the lung after bacterial inoculation. In further work, we have now shown that only five of the 13 native mitochondrial FPs are active at the formyl peptide receptors. Having participated in the development of novel antagonists for the human and mouse formyl peptide receptors (FPRs) we are doing studies that use this information to create tools for diagnosis and therapeutic intervention.

Our current work, therefore, centers on modulating inflammation in a way that balances the need for inflammation after injury as an initiator of tissue repair and the susceptibility to infection that systemic inflammation incurs. Molecular aspects of these problems that we study (and which participants can become expert in) include neutrophil signaling, chemokine biology (intracellular calcium flux signaling), the regulation of endothelial permeability in SIRS, and the study of neutrophil NETs. Current investigations and collaborations with external organizations include studies investigating formyl peptide DAMPs in the plasma of trauma and septic patients as well as patients with cancer. We are also studying small peptides that inhibit the formyl peptide receptor family. Current collaborations within the institution include work with my longtime colleague Kiyoshi Itagaki, PhD, and the labs of Leo Otterbein, PhD, and Wolfgang Junger, PhD.

Last year, our work on these critical innate immune mechanisms became the foundation of a large Department of Defense focused project award. This programmatic award addresses the role of DAMPs in creating susceptibility of wounded war-fighters to infection. Our multi-PI grant includes work with the laboratories of Leo Otterbein, PhD, Michael Yaffe, MD, PhD, Simon Robson, MD, PhD, James Lederer, PhD, and Danny Talmor, MD. All these are powerhouse on the Longwood campus and have grouped together as the Harvard-Longwood (“HALO”) consortium for translational biology. This collaborative program uses computational biology to address the interactive rolls of DAMPs like formyl peptides, mitochondrial DNA, heme, carbon monoxide, purine metabolites (ATP and adenosine), reactive oxygen intermediates, complement, with the changing physical-chemical environment of the lung over time to result in altered innate immune cellular phenotypes. These are then permissive of healthcare-acquired pneumonia.

RESEARCH GROUP

Kiyoshi Itagaki, PhD
Barbora Vlkova, PhD
Quanzhi Zhang, MD

ACCOMPLISHMENTS 2016-17

- Served as Medical Director of Trauma Services, BIDMC
- Achieved re-verification of BIDMC as an ACS Level 1 Trauma Center
- Founded the Harvard Longwood (HALO) consortium for translational inflammation biology
- Distinguished Service Medal for contributions to Military Medicine by the Armed Forces of Columbia
- Elected Founding Councilor for Clinical Studies, International Association for the Study of Danger Signaling

Visiting Professorships and Invited Presentations:

- Novartis Institute of Biomedical Research Seminars in Basic Science, Danger Signaling After Tissue Injury, Cambridge, MA
- Plenary lecture, Mitochondrial DAMPs and inflammation, American Transplant Society, Frontiers in Inflammation Relevant to Transplantation
- Plenary lecture, The biology of surgical site infections, the Surgical Infection Society, Palm Beach, FL
- Plenary presentation, Application of exogenous PMN to the airway rescues bacterial overgrowth initiated by trauma DAMPs, The American Association for the Surgery of Trauma, Waikoloa, HI
- Invited lecture, Crush injury: Mitochondria matter, The Society of Critical Care Medicine, Critical Care Congress, Honolulu, HI
- Presidential address, Ownership, The Western Trauma Association, Snowbird, UT
- AAST Webinar, Danger signaling: An important new principle in trauma and surgical injury
- Plenary presentation, A subset of five human mitochondrial formyl peptides mimic bacterial peptides and functionally deactivate human neutrophils (PMN), Western Trauma Association, Whistler, BC
- Scott R. Petersen Distinguished Lectureship, Ownership, St. Joseph's Hospital and Medical Center, Phoenix, AZ
- The molecular biology of trauma, X Congreso Internacional de Cirugia Y Trauma Vascular, Hospital Militar Central, Universidad Militar Nueva Granada, Bogota, Columbia
- Management of trauma to the femoral vessels, X Congreso Internacional de Cirugia Y Trauma Vascular, Hospital Militar Central, Universidad Militar Nueva Granada, Bogota, Columbia
- Missed retroperitoneal vascular trauma in the age of damage control surgery, X Congreso Internacional de Cirugia Y Trauma Vascular. Hospital Militar Central, Universidad Militar Nueva Granada, Bogota, Columbia
- Keynote presentation, The role of DAMPs in human injury, International Association for the Study of Danger Signaling, Guanajuato, Mexico
- Keynote lecture, The role of danger molecules in susceptibility to infection and therapeutic opportunities, Symposium on DAMP-mediated remote organ failure and immunosuppression in the acutely ill patient: Where Trauma meets Sepsis, Faculté de Médecine, Strasbourg, France
- Keynote lecture: DAMPs and PAMPs and why they matter in critical intra-abdominal injury/illness, The Abdominal Compartment Society, Banff, Alberta, Canada
- The global impact of abdominal sepsis on human health, The Abdominal Compartment Society, Banff, Alberta, Canada
- Future advances in modulating the inflammatory response in the peritoneal cavity: What will be needed? The Abdominal Compartment Society, Banff, Alberta, Canada
- Activation of clinical inflammation by mitochondrial DAMPs, Queen Mary Hospital Trauma Science Colloquium, London, England

SELECTED PUBLICATIONS

Itagaki K, Riça I, Zhang J, Gallo D, DePrato M, Otterbein LE, Hauser CJ. Intratracheal instillation of neutrophils rescues bacterial overgrowth initiated by trauma damage-associated molecular patterns. *J Trauma Acute Care Surg* 2017;82(5):853-860.

Atefi G, Aisiku O, Shapiro N, Hauser CJ, Dalle Lucca J, Flaumenhaft R, Tsokos GC. Complement activation in trauma patients alters platelet function. *Shock* 2016;46(3 Suppl 1):83-8.

Sandler N, Kaczmarek E, Itagaki K, Zheng Y, Otterbein L, Khabbaz K, Liu D, Senthilnathan V, Gruen RL, Hauser CJ. Mitochondrial DAMPs are released during cardiopulmonary bypass surgery and are associated with postoperative atrial fibrillation. *Heart Lung Circ* 2018;27(1):122-129.

Coimbra R, Kozar RA, Smith JW, Zarzaur BL, Hauser CJ, Moore FA, Bailey JA, Valadka A, Jurkovich GJ, Jenkins DH, Davis KA, Price MA, Maier RV. The Coalition for National Trauma Research (CNTR) supports the call for a national trauma research action plan. *J Trauma Acute Care Surg* 2017;82(3):637-645.

Barrett CD, Celestin A, Eskander MF, Fish E, Glass CC, Gospodinov G, Gupta A, Hauser CJ. Surgeon performed ultrasound in predicting wound infections: No collection, no infection. *J Trauma Acute Care Surg* 2016;80(2):229-36.

TEACHING, TRAINING, AND EDUCATION

I am involved in teaching trainees at all levels, including Harvard Medical School students, General Surgery residents, and fellows in our accredited Surgical Critical Care Fellowship Program. In addition, I participate in the Department of Surgery's Clinical Research Program, serving as a mentor to residents conducting clinical research projects. I helped develop the curriculum for our Surgical Critical Care Fellowship Program.

SELECTED RESEARCH SUPPORT

DAMP-mediated innate immune failure and pneumonia after Trauma; Department of Defense Focused Program Award, 2016-2021; PI: Carl J. Hauser, MD

Harvard Trauma Inflammation T32 Training Program in Trauma, Burn, and Peri-operative Injury; NIH, 2013-2018; Co-Director: Carl J. Hauser, MD (PI: Wolfgang Junger, PhD)

HBI-002 to treat traumatic injury; NIH, 2017-2019 (PI: Stephen Gomperts, MD, PhD, MGH)



Wolfgang G. Junger, PhD

Professor of Surgery

RESEARCH FOCUS

Immune cells release cellular ATP that fuels inside-out signaling mechanisms that regulate the activation and functions of neutrophils and T lymphocytes. Under normal circumstances, the released ATP regulates chemotaxis and proliferation of immune cells through autocrine feedback mechanisms that involve ATP and adenosine receptors. These purinergic signaling mechanisms regulate calcium influx and other downstream signaling pathways that are required for proper function of neutrophils and T lymphocytes. However, severe injuries, burns, and infections can cause the release of ATP from inflamed and damaged tissues. This systemic ATP interferes with the autocrine purinergic signaling mechanisms that regulate immune cell responses. This results in immune dysfunction that causes clinical complications such as multiple organ failure, immunosuppression, and sepsis. The focus of this laboratory has been to define the cellular and molecular mechanisms that lead to these complications.

Our work has revealed a complex network of metabolic pathways that regulate ATP release and the purinergic signaling mechanisms that control immune cell functions. This network involves mitochondria that produce the ATP that fuels purinergic signaling. Thus, mitochondria are the link between the metabolic and calcium signaling events and the purinergic signaling mechanisms that regulate immune cell functions. We found that mitochondrial function in T cells is reduced in critical care patients and that impaired mitochondrial ATP production is directly correlated with the severity of sepsis. Our studies suggest that pharmacological targeting of purinergic signaling is a promising new approach to restore immune competence in critical care and trauma patients.

RESEARCH GROUP

Mona Arbab, MD

Yi Bao, PhD

Mahtab Fakhari, MD

Carola Ledderose, PhD

Yutaka Kondo, MD, PhD

Xiaou Li, MD

Christian Slubowski, PhD

Koichiro Sueyoshi, MD, PhD

ACCOMPLISHMENTS 2016-2017

- Ad hoc reviewer for scientific journals including *Nature*, *Science*, *Nature Reviews*, *Nature Medicine*, *Nature Biotechnology*, *Nature Communications*, *Nature Medicine*, *Science Signaling*, *PLoS ONE*, *EMBO Journal*, *Shock*, *Critical Care Medicine*, *Purinergic Signalling*, *Journal of Clinical Investigations*, *Journal of Leukocyte Biology*, *FASEB Journal*, and many more
- Reviewer of grant proposals submitted to National Institutes of Health, the Swiss National Research Foundation, the French National Research Agency, Israeli National Research Foundation, Austrian National Research Foundation, and Belgium National Research Foundation, Wellcome Trust, and others
- Faculty mentor for underrepresented minority medical students; Harvard Medical School, Boston
- Invited plenary session speaker at the Conference on Shock Wave Therapy in Vienna, Austria; invited plenary speaker at the CD38 & CD157 Brainstorming Meeting in Mantua, Italy. Visiting Professor Brown University, Providence, Rhode Island
- Editorial Board member of the journal *Shock: Injury, Inflammation*, and *Sepsis: Laboratory and Clinical Approaches*; Associate Editor of *Purinergic Signalling*

TEACHING, TRAINING, AND EDUCATION

- Advisor and career counseling of Yi Bao, PhD, and Carola Ledderose, PhD
- Thesis advisor of medical students from the Paracelsus Medical University, Salzburg, Austria
- Program Director of Harvard Trauma Inflammation Training Program
- Thesis advisor of master students from the Fachhochschule Technikum, Vienna, Austria
- Faculty mentor of T32 fellows enrolled in the Harvard Trauma Inflammation Training Program

SELECTED RESEARCH SUPPORT

Neutrophil activation and trauma; NIH, 1999-2017; PI: Wolfgang Junger, PhD

Autocrine regulation of neutrophil chemotaxis; NIH, 2009-2019; PI: Wolfgang Junger, PhD

Administrative supplement for neutrophil activation and trauma grant; NIH, 2013-2016; PI: Wolfgang Junger, PhD

Regulation of T cell signaling in trauma; NIH, 2013-2018; PI: Wolfgang Junger, PhD

Harvard Trauma Inflammation Training Program; NIH, 2013-2018; PD: Wolfgang Junger, PhD

Chronic subdural hematoma and inflammation; Eleanor and Miles Shore Fellowship Program; 2014-2016; Co-Investigator: Wolfgang Junger, PhD (PI: Martina Stippler, MD)

SELECTED PUBLICATIONS

Li X, Kondo Y, Bao Y, Staudenmaier L, Lee A, Zhang J, Ledderose C, Junger WG. Systemic adenosine triphosphate impairs neutrophil chemotaxis and host defense in sepsis. *Crit Care Med* 2017;45(1):e97-e104.

Ledderose C, Bao Y, Kondo Y, Fakhari M, Slubowski C, Zhang J, Junger WG. Purinergic signaling and the immune response in sepsis: A review. *Clin Ther* 2016;38(5):1054-65.

Ledderose C, Woehrl T, Ledderose S, Strasser K, Seist R, Bao Y, Zhang J, Junger WG. Cutting off the power: Inhibition of leukemia cell growth by pausing basal ATP release and P2X receptor signaling? *Purinergic Signal* 2016;12(3):439-51.

Gupta PK, Godec J, Wolski D, Adland E, Yates K, Pauken KE, Cosgrove C, Ledderose C, Junger WG, Robson SC, Wherry EJ, Alter G, Goulder PJ, Klenerman P, Sharpe AH, Lauer GM, Haining WN. CD39 expression identifies terminally exhausted CD8+ T cells. *PLoS Pathog* 2015;11(10):e1005177.

Bao Y, Ledderose C, Graf AF, Brix B, Birsak T, Lee A, Zhang J, Junger WG. mTOR and differential activation of mitochondria orchestrate neutrophil chemotaxis. *J Cell Biol* 2015;210(7):1153-64.

Ledderose C, Bao Y, Ledderose S, Woehrl T, Heinisch M, Yip L, Zhang J, Robson SC, Shapiro NI, Junger WG. Mitochondrial dysfunction, depleted purinergic signaling, and defective T cell vigilance and immune defense. *J Infect Dis* 2016;213(3):456-64.

A complete list of publications begins on page 13.



Michael B. Yaffe, MD, PhD

David H. Koch Professor of Biology and Biological Engineering,
Massachusetts Institute of Technology

RESEARCH GROUP

Christopher Barrett, MD
Molly Bird
Pau Creixell Morera, PhD
Thomas Dietzel
Vasilena Gocheva, PhD
Ingred Goretti Rica, PhD
Robert Grant, PhD
Erika Handly
Yuliana Hernandez
Mun Kyung Hwang, PhD
Brian Joughin, PhD
Yi Wen Kong, PhD
Alex Kruswick
Fred Chiu-Lai Lam, PhD
Daniel Lim, PhD
Tatiana Netterfield
Jesse Patterson, PhD
Ganapathy Sriram, PhD
Lucia Suarez Lopez, PhD
Bert van de Kooij, PhD
Shohreh Varmeh, PhD

Dr. Yaffe also has a joint appointment
in Surgical Oncology at BIDMC.

RESEARCH FOCUS

The goal of our research is to understand how cells respond to stress and injury at the molecular level, and how this response can be therapeutically manipulated to improve the care of patients with trauma, critical illness or cancer. We study specific signaling pathways in the cell that respond to stress, DNA damage, and inflammatory cytokines, and use experimental and computational tools to understand and how these pathways are biochemically wired, and how the outputs of these pathways are integrated at the molecular and systems level to control the subsequent fate of the stressed and damaged cells. We are particularly interested in cross-talk between (1) stress, inflammation and immune function after trauma, (2) stress, inflammation, innate immune function and cancer, and (3) targeting stress, DNA damage, and cell cycle control pathways for cancer treatment. Our lab has a longstanding interest in inventing new technologies to address these questions including novel proteomic methods, high-throughput signaling assays and peptide library screens, RNAi screens using high-content imaging, and novel computational/bioinformatics methods, together with more traditional techniques from cell biology, physical biochemistry, structural biology, and mouse genetics.

Signaling pathways and networks that control the DNA damage response, cell cycle progression and cancer

When cells encounter stress or injury such as DNA damage, they activate complex signaling networks that regulate their ability to recover, repair the damage, and return to a homeostatic equilibrium. These networks must integrate a wide variety of signals from inside and outside the cell, transduced through protein kinase and lipid signaling pathways, to ultimately control cell cycle arrest or progression, coordinately regulate specific patterns of gene expression, and/or initiate senescence or cell death. Mutations in, or dysfunction of, protein kinase signaling pathways that normally respond to DNA damage, for example, play critical roles in tumor development and progression, while intentional targeting of these pathways can enhance the ability of commonly used DNA-damaging chemotherapy and radiation to cure cancer. We have been attacking this research area along two fronts: 1) characterizing the molecular details of the DNA damage response with a focus on protein kinases, phospho-binding domains, RNA-binding proteins, and epigenetic modulation of chromatin at the site of damage, and 2) examining whether cross-talk between various signaling pathways and the DNA damage-response can be pharmacologically manipulated to enhance the response of tumors to DNA damaging agents alone, or in combination with immunotherapy.

We showed, for example, that p53-defective tumor cells become dependent on signaling through the stress-activated p38-MK2 pathway to resist killing by chemotherapy, and have now created a variety of standard and novel conditional MK2 knock-out mice, as well as nanoparticles delivering MK2-targeted RNAi and CRISPR, to target this pathway *in vivo* in several cancer models. We are continuing to explore the roles of the MK2 pathway in a variety of cancer-relevant phenotypes, as well as performing CRISPR-based screens to look for new modifiers of the DNA damage response that can be therapeutically targeted. This work has led to a new focus on the role of RNA-binding proteins as critical integrators of stress and DNA damage response pathways in the cell. Finally, we discovered the phenomenon of 'dynamic network re-wiring,' in which tumor cell treatment with a specific schedule of signaling pathway inhibitors and DNA-damaging chemotherapy can be used to dramatically enhance cell killing in a subset of triple-negative breast cancer and non-small cell lung cancer. We are now trialing this approach in human PDX models of TNBC, in collaboration with Dr. Gerburg Wulf (Hematology-Oncology, BIDMC), as well as extending that work into colon, head and neck, and prostate cancer models.

Signaling pathways and networks that control cytokine responses and inflammation

Misregulation of cytokine feedback loops, along with inappropriate activation of the blood clotting cascade causes dysregulation of cell signaling pathways in innate immune cells (neutrophils and macrophages), resulting in tissue damage and multiple organ failure following trauma or sepsis. Our research is focused on understanding the role of the p38-MK2 pathway in cytokine control and innate immune function, and on cross-talk between cytokines, clotting factors, and neutrophil NADPH oxidase-derived ROS in tissue damage, coagulopathy, and inflammation, using biochemistry, cell biology, and mouse knock-out/knock-in models. We recently discovered a particularly important link between abnormal blood clotting and the complement pathway cytokine C5a which causes excessive production of extracellular ROS and organ damage by neutrophils after traumatic injury.

ACCOMPLISHMENTS 2016-2017

- Chief Scientific Advisor and Academic Editor, *Science Signaling*
- One of eight investigators nationally to win the Revolutionizing Innovative Visionary Environmental Health Research (RIVER) award from the NIH

TEACHING, TRAINING, AND EDUCATION

I am heavily involved in teaching at the undergraduate, graduate, and medical school level. I teach 7.05 (Undergraduate Biochemistry) and 7.10 (Physical Chemistry of Biomolecular Systems) at MIT, as well as 7.61 (Signaling and Cell Biology), a graduate-level overview course. I also teach extensively on critical care topics to ICU residents and fellows. Every two years I teach an EMBL-sponsored Signaling in Cancer course in Spetses, Greece.

SELECTED RESEARCH SUPPORT

Protein kinase signaling in the genotoxic stress response; NIH, 2017-2025; PI: Michael Yaffe, MD, PhD

Modeling human phosphorylation networks through kinome-wide profiling; NIH, 2013-2018; Co-PIs: Benjamin Turk, PhD, and Michael Yaffe, MD, PhD

Analysis and Characterization of Trauma-Induced Coagulopathy, Project 9: The Role and Mechanisms of Trauma-Induced Endothelial Injury and inflammation that Results in Coagulopathy and End-Organ Damage. NIH, 2013-2019; Co-PIs: Michael Yaffe, MD, PhD, Brian Zuckerbraun MD, Mitchell Cohen MD

DAMP-Mediated Innate Immune Failure After Trauma; DoD, 2015-2020; Co-PIs: Carl Hauser MD, Leo Otterbein PhD, James Lederer PhD, Daniel Talmor MD, Simon Robson MD PhD, Michael Yaffe MD, PhD

SELECTED PUBLICATIONS

Barrett CD, Hsu AT, Ellson CD, Miyazawa BY, Kong YW, Greenwood JD, Sanjeev Dhara S, Neal MD, Sperry JL, Park MS, Cohen MJ, Zuckerbraun BS, Yaffe MB. Blood clotting and traumatic injury with shock mediates complement-dependent neutrophil priming for extracellular ROS, ROS-dependent organ injury and coagulopathy. *Clin Exp Immunology* 2018 (online, in press).

Suarez-Lopez L, Sriram G, Kong YW, Morandell S, Merrick KA, Hernandez Y, Haigis KM, Yaffe MB. MK2 contributes to tumor progression by promoting M2 macrophage polarization and tumor angiogenesis. *Proc Natl Acad Sci U S A* 2018;115(18):E4236-E4244.

Alkan O, Schoeberl B, Shah M, Koshkaryev A, Heinemann T, Drummond DC, Yaffe MB, Raue A. Modeling chemotherapy-induced stress to identify rational combination therapies in the DNA damage response pathway. *Science Signal* 2018;11(540).

Dreaden EC, Kong YW, Quadir MA, Correa S, Suárez-López L, Barberio AE, Hwang MK, Shi AC, Oberlton B, Gallagher PN, Shopsowitz KE, Elias KM, Yaffe MB, Hammond PT. RNA-peptide nanoplexes drug DNA damage pathways in high-grade serous ovarian tumors. *Bioeng Transl Med* 2018; 3(1):26-36.

Barrett CD, Moore HB, Banerjee A, Sillman CC, Moore EE, Yaffe MB. Human neutrophil elastase mediates fibrinolysis shutdown through competitive degradation of plasminogen and generation of angiotensin. *J Trauma Acute Care Surg* 2017; 83(6):1053-1061.

Xiao H, Qi R, Li T, Awuah SG, Zheng Y, Wei W, Kang X, Song H, Wang Y, Yu Y, Bird MA, Jing X, Yaffe MB, Birrer MJ, Ghoroghchian PP. Maximizing synergistic activity when combining RNAi and platinum-based anticancer agents. *J Am Chem Soc* 2017;139(8):3033-3044.

Yaffe MB, Gough NR. Leveraging signaling research to understand and treat disease. *Sci Signal* 2016;9(421).

A complete list of publications begins on page 13.

Kamal R. Khabbaz, MD

David S. Ginsburg Associate Professor of Surgery
Chief, Cardiac Surgery



RESEARCH GROUP

Louis Chu, MD

David Liu, MD

Feroze-ud-Den Mahmood, MD

RESEARCH FOCUS

The Valve Research Group primarily investigates the dynamic behavior of heart valves in both normal and pathologic states. Heart valves are complex 3-dimensional (3D) structures that undergo dynamic changes during the cardiac cycle. Investigating this behavior is of critical importance in understanding the pathophysiology of and devising management strategies for valvular disease.

Together with Dr. Feroze Mahmood and a multidisciplinary Valve Research Group, normal and abnormal size, shape, and geometric parameters pertaining to the mitral, tricuspid, and aortic valves are being researched. In addition, we are studying the impact different surgical interventions (e.g., aortic valve replacement and mitral annuloplasty) have on native valve function and surrounding anatomy. To accomplish this, we analyze 3D echocardiographic data using commercially available software, including Philips Qlab and TomTec Image Arena. These software programs enable us to dynamically track and measure anatomical changes in a clinically feasible fashion.

We are currently in the process of extending similar analyses to normal and pathologic tricuspid valves, leading to a more robust understanding of tricuspid valve behavior. Investigations are also underway to investigate the in vivo effects of different annuloplasty devices on dynamic valve motion and geometry. These data and analyses hold significant potential in furthering the evidence base for valve repair strategies and surgical decision-making toward achieving the best outcomes.

The multidisciplinary Valve Research Group is involved with multiple national and international universities, engaged in devising new methods of interrogating valvular structures using 3D echocardiography. We are continuing our collaboration with Cardiology and Vascular and Endovascular Surgery on multiple projects including clinical trials, which include the following:

Multi-Center Experience with the Rapid Deployment EDWARDS INTUITY Valve System For Aortic Valve ReplaceMent (TRANSFORM Trial, Protocol Number 2011-02): The purpose of this clinical investigation is to assess the safety and effectiveness of the investigational EDWARDS INTUITY Valve System in subjects with aortic stenosis or stenosis-insufficiency requiring replacement of the native aortic valve.

Clinical trial of the on-X valve using low dose anticoagulation: The purpose of this study is to define the lowest level of required antithrombotic therapy for mitral or aortic valve replacement using the On-X Valve.

Medtronic Core Valve U.S. Pivotal Trial – Extreme Risk Patients; Medtronic CoreValve® U.S. Pivotal Trial – High Risk Surgical Patients; Medtronic CoreValve® U.S. Continued Access Study; Medtronic CoreValve® U.S. Expanded Use Study; Medtronic CoreValve® SURTAVI Trial: The purpose of this study is to determine the safety and efficacy of the Medtronic CoreValve® System in the treatment of symptomatic severe aortic stenosis in high-risk and very high-risk subjects who need aortic valve replacement.

Early Feasibility Study of the CardiAQ™ Transcatheter Mitral Valve (TMV) System with Transseptal Delivery System for the Treatment of Moderate to Severe Mitral Regurgitation
REPRISE III: REpositionable Percutaneous Replacement of Stenotic Aortic Valve through Implantation of Lotus™ Valve System-Randomized Clinical Evaluation

Evaluation of Xience versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization

ACCOMPLISHMENTS 2016-2017

Several studies are in progress. Studies completed so far have shown promising results. The results of one study demonstrate that left-ventricular outflow tract area is significantly underestimated by two-dimensional (2D) measurements when compared with 3D data. This underestimation of the LVOT area with 2D echocardiography potentially overestimates the degree of aortic stenosis (AS). Such errors in assessing disease severity can have important clinical consequences vis-à-vis the decision to operate vs. not operate.

In another study, we report that the implantation of prosthetic valves in the aortic position is associated with changes in dynamic mitral annular geometry. Earlier, our understanding of the effects of aortic valve replacement was limited to geometric analyses of mitral annular conformation at a single point in the cardiac cycle (end-systole).

We have also successfully demonstrated the use of 3D echocardiography in analyzing mitral valve geometry in patients with functional mitral valve regurgitation (FMR). Previously, the understanding of annular dynamics in FMR was largely limited to information derived from animal models.

The Valve Research Group has been recognized and granted the status of hospital "core laboratory" for 3D printing establishing a state-of-the-art 3D printing laboratory. Additionally multiple echocardiography simulators serve as a dedicated simulation laboratory.

TEACHING, TRAINING, AND EDUCATION

As Program Director of the BIDMC Cardiothoracic Surgery Residency Program, I have trained 21 cardiothoracic surgical fellows. Three have gone on to become Chairman or Chief of Cardiothoracic Surgery at their respective institutions; one has become Director of Minimally Invasive Surgery. This training includes weekly seminars, direct operative supervision, teaching cardiac surgery techniques, innovations in percutaneous valve mitral valve repair, and new aortic valve deployment techniques.

I also teach BIDMC General Surgery residents (PGY-2, PGY-3) in cardiac surgery techniques, and continue to teach a course on echocardiography at Harvard Medical School. In addition, I teach third- and fourth-year HMS students rotating on cardiothoracic surgery and an elective in thoracic and cardiovascular surgery for fourth-year HMS students.

ABSTRACTS, POSTERS, AND EXHIBITS

Multi-Center Experience with the Rapid Deployment EDWARDS INTUITY Valve System For Aortic Valve Replacement (TRANSFORM Trial, Protocol Number 2011-02); Edwards Lifesciences; 2014-2024; PI: Kamal Khabbaz MD (Co-Investigator: David Liu MD)

Cardiac Surgery Retrospective Review; Departmental Funding 2010-2020; PI: Kamal Khabbaz MD (Co-Investigators: David Liu MD, Louis Chu, MD)

SELECTED PUBLICATIONS

Mahmood F, Matyal R, Mahmood F, Sheu RD, Feng R, Khabbaz KR. Intraoperative echocardiographic assessment of prosthetic valves: A practical approach. *J Cardiothorac Vasc Anesth* 2018;32(2):823-837.

Hai T, Amador Y, Mahmood F, Jeganathan J, Khamooshian A, Knio ZO, Matyal R, Nicoara A, Liu DC, Senthilnathan V, Khabbaz KR. Changes in tricuspid annular geometry in patients with functional tricuspid regurgitation. *J Cardiothorac Vasc Anesth* 2017;31(6):2106-2111.

Khamooshian A, Amador Y, Hai T, Jeganathan J, Saraf M, Mahmood E, Matyal R, Khabbaz KR, Mariani M, Mahmood FJ. Dynamic three-dimensional geometry of the aortic valve apparatus: A feasibility study. *J Cardiothorac Vasc Anesth* 2017;31(4):1290-1300.

Jeganathan J, Saraf R, Mahmood F, Pal A, Bhasin MK, Huang T, Mittel A, Knio Z, Simons R, Khabbaz K, Senthilnathan V, Liu D, Sellke F, Matyal R. Mitochondrial dysfunction in atrial tissue of patients developing postoperative atrial fibrillation. *Ann Thorac Surg* 2017;104(5):1547-1555.

Dearani JA, Gold M, Leibovich BC, Ericsson KA, Khabbaz KR, Foley TA, Julsrud PR, Matsumoto JM, Daly RC. The role of imaging, deliberate practice, structure, and improvisation in approaching surgical perfection. *J Thorac Cardiovasc Surg* 2017;154(4):1329-1336.

Sandler N, Kaczmarek E, Itagaki K, Zheng Y, Otterbein L, Khabbaz K, Liu D, Senthilnathan V, Gruen RL, Hauser C. Mitochondrial DAMPs are released during cardiopulmonary bypass surgery and are associated with postoperative atrial fibrillation. *J Heart Lung Circ* 2018;27(1):122-129.

A complete list of publications begins on page 13.



Vitaliy Y. Poylin, MD

Assistant Professor of Surgery
Director, Rectal Cancer Program

RESEARCH FOCUS

A major focus of my research has been on improving care for patients with Inflammatory Bowel Disease (IBD) and evaluating outcomes after colon and rectal surgery, especially minimally invasive colorectal surgery. In close collaboration with colleagues from IBD Gastroenterology and Acute Care Surgery, as well as colon and rectal surgeons from other Harvard institutions, we currently are involved in a number of projects evaluating outcomes after Ileal Pouch Anal Anastomosis (IPAA) surgery, the effects of new biologically active medications on IBD surgery outcomes, and decision making in IBD surgery. Recently I completed an outcome study of a novel technique in creating low anastomosis in IPAA surgery and examined outcomes of surgery in older patients with Ulcerative Colitis.

Current projects include:

- Decision making in IBD surgery
- Effect of Clostridium Difficile infection on outcomes of IPAA surgery
- Effects of new biologically active medications on outcomes of IBD surgery
- Effects of non-related surgery on IBD outcomes

RESEARCH GROUP

Jose Cataneo, MD

Jonathan Pastrana Del Valle, MD

ACCOMPLISHMENTS 2016-2017

- Named a *Boston* magazine top doctor
- Member of Clinical Guidelines Committee for the American Society of Colon and Rectal Surgeons, working on guidelines for surgery for ulcerative colitis, rectal cancer, and lower gastrointestinal bleeding
- Elected into the Academy of Medical Educators at BIDMC
- Completed the Physician Leadership Development Course BIDMC

Invited Presentations

- Closed incision negative pressure wound therapy is associated with decreased surgical site infection in high-risk colorectal surgery laparotomy wounds; American Society of Colon and Rectal Surgeons Annual Meeting, Plenary Session, 2017
- Mortality is a rare event following elective and non-elective surgery for ulcerative colitis; Winner of the Young Investigator Award; Digestive Disease Week, 2017
- Surgery for ulcerative colitis in geriatric patients is safe without increased risks compared to younger patients; Digestive Disease Week, 2017
- Despite prophylaxis, venous thromboembolism is not rare following elective and non-elective surgery for ulcerative colitis; Digestive Disease Week, 2017
- Oral exams and beyond; Invited speaker; American Society of Colon and Rectal Surgeons Annual Meeting, 2017

TEACHING, TRAINING, AND EDUCATION

This year I participated in Harvard combined courses on colorectal surgery for primary care physicians and surgeons. I have recently given lectures at Harvard Medical School on topics including anal fissures, managing common anal complaints, and technical tips and tricks in colorectal surgery.

Additionally, I participate in resident and medical student training in colorectal surgery, and I mentor residents interested in colon and rectal surgery. I also give lectures to GI and oncology fellows on common anorectal conditions, inflammatory bowel disease, and surgical approaches to rectal cancer.

SELECTED PUBLICATIONS

Poylin, V, Curran, T, Alvarez, D, Nagle, D, Cataldo, T. Primary vs. delayed perineal proctectomy? There is no free lunch. *Int J Colorectal Dis.* 2017; 32 (8):1207-1212.

Poylin, V, Mowschenson, P, Nagle, D, Cataldo, T., Rectal Eversion Technique: A method to achieve very low rectal transection and anastomosis with particular value in laparoscopic cases. *Dis Colon Rectum.* 2017;60 (12):1329-1331.

Tillou, J, Nagle, D, Poylin, V, Cataldo, T. The impact of surgeon choices on costs associated with uncomplicated minimally invasive colectomy: You are not as important as you think. *Gastroenterology Report.* In Press.

Poylin, V, Kunitake, H. Complications after anorectal surgery. *Clin Colon Rectal Surg.* 2016;29 (1):14-21.

Tillou, J., Poylin, V. Functional disorders: slow transit constipation. *Clin Colon Rectal Surg.* 2017;30 (1):76-86.

Feuerstein, J, Alosilla, M, Curran, T, Falchuk, K, Poylin, V. Mortality is a rare event following elective and non-elective surgery for ulcerative colitis. *Digestive Disease and Science.* In Press.

A complete list of publications begins on page 13.

Miguel Alonso-Alonso, MD, PhD

Assistant Professor of Surgery

Director, Laboratory of Bariatric and Nutritional Neuroscience



RESEARCH GROUP

- Gabrielle Giacona
- Greta Magerowski, BA
- Sean Manton, BS
- Nicole Milani
- Helen Mizrach
- Jorge Hevia Orozco, MD PhD
- Laura Patriarca, BS

RESEARCH FOCUS

In our laboratory we study eating behavior, nutrition and obesity in human subjects. We are particularly interested in complex regulatory aspects that go beyond homeostasis and the hypothalamus. It is now established that the interplay between brain regions related to reward processing and those that support complex aspects of cognition, such as executive functions, play a critical role in human eating behavior and obesity. This emerging neuro-cognitive model can help identify new targets to accelerate the development of preventive and therapeutic strategies for obesity. Our research combines nutrition, psychology and clinical measures with cutting-edge noninvasive cognitive neuroscience tools, such as computerized testing, functional neuroimaging and neurotechnologies. Our laboratory has two main goals. First, we want to understand the neurocognitive basis of human nutrition, eating behavior and obesity. Second, we want to develop innovative applications and tools derived from this research for quantitative assessment, diagnostics, and therapeutics. Ongoing research includes:

Development of new methodologies to study the neurocognitive basis of human eating behavior

The study of human eating behavior has typically relied on self-report measures and the use of restricted experimental settings that do not capture the complexity of food choices and the situational component that we face when confronted with food. We are developing a methodological platform to simultaneously monitor and evaluate neural, cognitive, and behavioral measures during a meal conducted in a semi-naturalistic setting. This method integrates electroencephalography and portable eye-tracking together with behavioral and nutritional assessments. Potential applications include precision phenotyping of individuals and early evaluation of interventions. Additionally, we have developed a programmable computerized meal table with capabilities to sense and display information during the course of a meal. This novel tool fills a gap in the field as it allows experimental manipulation of the meal with an unprecedented level of possibilities. In addition to meal-related methodologies, we have also developed computerized tests to assess cognitive domains related to food. These tasks are being used by local, national, and international research teams.

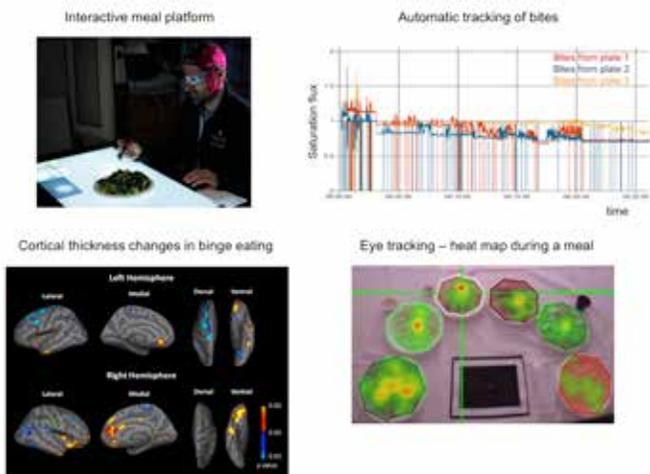
Application of noninvasive neuromodulation for obesity therapeutics

We continue to conduct research studies examining the use of transcranial direct current stimulation (tDCS) in patients with obesity. Following the report of weight loss with anodal tDCS over the left

prefrontal cortex (Gluck, Alonso-Alonso et al. Obesity 2015) we have continued working in the same direction to try to replicate and extend the findings. Interest for the use of tDCS in obesity has grown substantially in the past two years and, as a result, we have established a network of international research collaborations in this area to conduct clinical trials to accelerate and scale data collection. Ongoing studies are exploring new targets, such as the role of prefronto-cerebellar connections in appetite, the effects of lateral occipital region in food-specific attention, and genetic influences in the response to tDCS.

Look AHEAD Extension trial

I am a Co-Investigator of the NIH-NIDDK Look AHEAD Extension trial, responsible for the BIDMC portion of the Boston site. The primary aims of this trial are to test legacy effects of the intervention on increased lifespan and reduced health care costs, while the secondary aim is to determine its effect on key dimensions of healthy aging.



▲ FIGURE 1: Our research integrates an innovative computerized meal platform with brain imaging and portable eye-tracking to study human eating behavior.

ACCOMPLISHMENTS 2016-2017

During this period I have continued to serve as a member of the Boston Nutrition Obesity Research Center (BNORC), formerly being part of the Executive Committee, and the Harvard Nutrition and Obesity Research Center (NORCH).

Editorial Roles

I have been an ad hoc reviewer for a number of top journals in the field, including *American Journal of Psychiatry*, *American Journal of Clinical Nutrition*, *Neuropsychopharmacology*, *Appetite*, and *Brain Stimulation* and an Associate Editor of *Frontiers in Eating Behavior*.

Invited Presentations

I have been invited to give talks in a growing number of venues and institutions:

On bites, bytes and brains: new technologies to study and manipulate human eating behavior; Longwood Nutrition Seminar, Division of Nutrition, Harvard Medical School, Boston, MA, 2017

Prospects for neuromodulation in obesity; NYC Neuromodulation Conference, New York, NY 2017

New methodologies to study and manipulate human eating behavior; Basque Culinary Center, San Sebastian, Spain, 2017

Mens sana in corpore sano: recent advances in obesity and the brain; Pronokal Scientific Symposium, Valencia, Spain, 2017

Reprogramming brain and meals: applications in obesity; Jlabs Umass Lowell, Lowell, MA (Johnson & Johnson Innovation), Lowell, MA, 2017

Neurocognitive basis of obesity and prospects for the use of neuromodulation with tDCS; Graduate Program in Medical Sciences, LabEEL, UERJ, Rio de Janeiro, Brazil, 2017

Neurocognitive basis of obesity and prospects for the use of neuromodulation with tDCS; Taipei Medical University Hospital, Taipei City, Taiwan, 2017

"Making laboratory meals great again": new approaches to study human eating behavior and neurocognition. Monday Nutrition Seminars. Department of Nutrition, Harvard T. H. Chan School of Public Health. Boston, MA, 2017

Subliminal impact of basic tastes for decision making on food selections; International Congress of Nutrition IUNS, Buenos Aires, Argentina, 2017

TEACHING, TRAINING, AND EDUCATION

Teaching, mentoring and training are important activities of the Laboratory. Approximately 30% of my time involves supervision of students, fellows, and laboratory members in areas of nutrition, eating behavior, obesity and the brain. After the successful HMS Division of Nutrition Symposium, "Your brain can help you eat better" in 2011, and, more recently, Hacking Eating Tracking in 2015, our laboratory has attracted more attention and we are very often contacted for internship and fellowship opportunities. During 2016-2017, we hosted national and international visiting scholars for specific training in the use of tDCS in obesity: Jeffrey Liou, MD (Taiwan), Priscila Giacomo Fassini, PhD (Brazil), Chi Tang, MD (Boston University Medical Center), and Jorge Hevia Orozco, MD, PhD (Mexico).

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SELECTED RESEARCH SUPPORT

Bashir S, Vernet M, Najib U, Perez J, Alonso-Alonso M, Knobel M, Yoo WK, Edwards D, Pascual-Leone A. Enhanced motor function and its neurophysiological correlates after navigated low-frequency repetitive transcranial magnetic stimulation over the contralesional motor cortex in stroke. *Restor Neurol Neurosci* 2016;34(4):677-89.

Patriarca L, Magerowski G, Alonso-Alonso M. Functional neuroimaging in obesity. *Curr Opin Endocrinol Diabetes Obes* 2017;24(3):260-5.

Amo C, De Santiago L, Zarza Lucíañez D, León Alonso-Cortés JM, Alonso-Alonso M, Barea R, Boquete L. Induced gamma band activity from EEG as a possible index of training-related brain plasticity in motor tasks. *PLoS One* 2017;12(10):e0186008.

Heinitz S, Reinhardt M, Piaggi P, Weise CM, Diaz E, Stinson EJ, Venti C, Votruba SB, Wassermann EM, Alonso-Alonso M, Krakoff J, Gluck ME. Neuromodulation directed at the prefrontal cortex of subjects with obesity reduces snack food intake and hunger in a randomized trial. *Am J Clin Nutr* 2017;106(6):1347-1357.

Bikson M, Paneri B, Mourdoukoutas A, Esmailpour Z, Badran BW, Azzam R, Adair D, Datta A, Fang XH, Wingeier B, Chao D, Alonso-Alonso M, Lee K, Knotkova H, Woods AJ, Hagedorn D, Jeffery D, Giordano J, Tyler WJ. Limited output transcranial electrical stimulation (LOTES-2017): Engineering principles, regulatory statutes, and industry standards for wellness, over-the-counter, or prescription devices with low risk. *Brain Stimul* 2018;11(1):134-157.

ABSTRACTS, POSTERS, AND EXHIBITS

Action for Health in Diabetes Extension Study Research Project; NIH, 2016-2021; Co-investigator: Miguel Alonso-Alonso, MD, PhD (PI: David Nathan, MD, Massachusetts General Hospital)

Effects of a nutritional shake on brain and cognitive function; Nutrient Foods, LLC, 2015-2017; PI: Miguel Alonso-Alonso, MD, PhD

Feihe Nutrition Laboratory; Feihe International LLC, 2015-2019; Collaborator: Miguel Alonso-Alonso, MD, PhD (PI: Elliot Chaikof, MD PhD, BIDMC)

A complete list of publications begins on page 13.



Mark P. Callery, MD, FACS

Professor of Surgery
Chief, General Surgery

RESEARCH FOCUS

Clinical outcomes research in pancreaticobiliary surgery

Our group's work focuses on outcomes research in high-acuity pancreaticobiliary surgery. Fueled by a robust clinical practice that focuses on treatment of pancreatic malignancies, cystic lesions, pancreatitis, and complex biliary conditions in a multidisciplinary setting, we perform more than 200 major pancreaticobiliary operations per year.

A prospective database of more than 4,000 operations and 750 pancreatic resections has been developed and maintained from this practice, providing the substrate for our investigations. Areas of emphasis are the development and critical analysis of clinical pathways and other systems initiatives for optimal patient care. Separate investigations are centered on technical and perioperative management aspects of surgical care for diseases of the pancreas and biliary tree. We have also explored the impact of surgical complications associated with pancreatic operations, especially the Whipple procedure. We continue to assess and develop metrics for quality assessment in high acuity surgery especially as aligned with quality of life measures and risk mitigation strategies. Additional recent efforts have included investigations into readmission after pancreatectomy with goals of understanding how and why they occur, and when and when not readmissions can be avoided.

Our original description of the Fistula Risk Score (FRS) for pancreatectomy has been embraced worldwide for daily clinical use. As part of a national and international pancreatectomy research consortium, we have participated in its validation nationally and internationally, and proud of its validation at many high-volume pancreatic surgery centers across the USA. Our consortium also has evaluated the FRS in terms of economic impact, quality and detailed manners of risk mitigation.

Other outcomes studies over the last year have involved the investigation of the relationship between pancreatectomy for cancer, complications, and initiation/completion of adjuvant therapy, and the analysis of outcomes for patients undergoing palliative surgery in the setting of pancreatic cancer. Work is also ongoing to develop, employ, and evaluate a patient-education tool to provide additional and improved information to patients upon discharge after pancreatectomy. The effectiveness of this tool will be evaluated via patient-satisfaction surveys and readmission rate/cause assessment.

ACCOMPLISHMENTS 2016-2017

- Elected President of the Boston Surgical Society, 2017
- Elected President of the Americas Hepato-Pancreato-Biliary Association (AHPBA) Foundation, 2017
- Invited Professor, World Pancreas Forum in Bern, Switzerland, 2017
- Gastrointestinal Surgery Advisory Council, American Board of Surgery, 2016-2017
- Editor, *HPB*
- Invited Faculty, SAGES Leadership Development and Health Care Policy Program
- Treasurer, Executive Committee, Society for Surgery of the Alimentary Tract, 2016
- Nominated for a Harvard Medical School Excellence in Mentoring Award, 2017

TEACHING, TRAINING, AND EDUCATION

I have taught medical students, residents, and fellow physicians in many settings for over 20 years. I was a founding faculty advisor for Harvard Medical School's John Warren Surgical Society for students interested in surgical careers. For my longstanding efforts as a teacher to Harvard Medical School students, in 2005 I was awarded the George W. Starkey Award for Excellence in Teaching, which is given annually to a faculty member by third-year HMS students. More recently, I was honored to be nominated by HMS students to receive the S. Robert Stone Award for Excellence in Teaching, which is presented annually to a member of the BIDMC faculty for outstanding achievement in the teaching of medical students. I continue to serve on the Harvard Medical School Committee on Admissions. In 2017, I was nominated for a Harvard Medical School Excellence in Mentoring Award.

SELECTED PUBLICATIONS

Kasumova GG, Eskander MF, Kent TS, Ng SC, Moser AJ, Ahmed M, Pleskow DK, Callery MP, Tseng JF. Hemorrhage after pancreaticoduodenectomy: does timing matter? *HPB* 2016;18(10):861-869.

McMillan MT, Ecker BL, Behrman SW, Callery MP, Christein JD, Drebin JA, Fraker DL, Kent TS, Lee MK, Roses RE, Sprys MH, Vollmer CM Jr. Externalized stents for pancreato-duodenectomy provide value only in high-risk scenarios. *J Gastrointest Surg* 2016;20(12):2052-2062.

McMillan MT, Soi S, Asbun HJ, Ball CG, Bassi C, Beane JD, Behrman SW, Berger AC, Bloomston M, Callery MP, Christein JD, Dixon E, Drebin JA, Castillo CF, Fisher WE, Fong ZV, House MG, Hughes SJ, Kent TS, Kunstman JW, Malleo G, Miller BC, Salem RR, Soares K, Valero V, Wolfgang CL, Vollmer CM Jr. Risk-adjusted outcomes of clinically relevant pancreatic fistula following pancreatoduodenectomy: a model for performance evaluation. *Ann Surg* 2016;264(2):344-52.

de Geus SW, Eskander MF, Bliss LA, Kasumova GG, Ng SC, Callery MP, Tseng JF. Neoadjuvant therapy versus upfront surgery for resected pancreatic adenocarcinoma: a nationwide propensity score matched analysis. *Surgery* 2017;161(3):592-601.

Gouma DJ, Callery MP. Bile duct injury: examining results of early repair by the index surgeon. *HPB (Oxford)* 2017;19(1):1-2.

McMillan MT, Allegrini V, Asbun HJ, Ball CG, Bassi C, Beane JD, Behrman SW, Berger AC, Bloomston M, Callery MP, Christein JD, Dickson E, Dixon E, Drebin JA, Fernandez-Del Castillo C, Fisher WE, Fong ZV, Haverick E, Hollis RH, House MG, Hughes SJ, Jamieson NB, Kent TS, Kowalsky SJ, Kunstman JW, Malleo G, McElhany AL, Salem RR, Soares KC, Sprys MH, Valero V 3rd, Watkins AA, Wolfgang CL, Zureikat AH, Vollmer CM Jr. Incorporation of procedure-specific risk into the ACS-NSQIP surgical risk calculator improves the prediction of morbidity and mortality after pancreatoduodenectomy *Ann Surg* 2017;265(5):978-86.

Susan J. Hagen, PhD

Associate Professor of Surgery
Associate Vice-Chair for Research



RESEARCH FOCUS

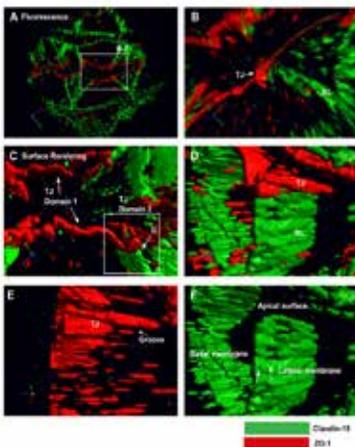
The focus of my laboratory is to understand how barrier dysfunction facilitates gastric cancer development during *Helicobacter pylori* infection. We approach our work by studying the details of gastric barrier function in general, and its disruption during infection and cancer development using genetic, advanced microscopy, and genomic approaches. Our aims have two important goals: one is to understand basic science principles and the other is translational.

Although the stomach expresses a specific subset of claudin molecules, which are proteins that confer barrier properties to epithelial cells at the tight junction, it highly expresses one particular claudin, claudin-18 (*CLDN18*). *CLDN18* is a cation-specific tight junction protein that is transcriptionally down-regulated in *H. pylori* infection in mice as well as in human patients with gastric cancer. Because *CLDN18* protein and its gene, *CLDN18*, are attenuated in disease, we made *CLDN18* knockout mice to study its role in mucosal barrier function in general and in gastric cancer pathogenesis in particular. Our recent work demonstrates that *CLDN18*: 1) is not tight junction associated but is rather a basolateral membrane protein (Figure 1). This work was done using super-resolution microscopy techniques by Dr. Ang; 2) is an important signaling molecule that regulates gastric homeostasis; and 3) is a potent tumor suppressor in the stomach. We recently demonstrated that knockout of *CLDN18* promotes rapid gastric cancer development. Due to these results, we created two gastric cell-specific conditional knockout mouse lines to genetically dissect the role of *CLDN18* in gastric tumorigenesis. We complement the animal studies with in vitro work using primary cultured gastric epithelial cells that contain nearly pure parietal or chief cells, or gastric organoids. We have work in progress to evaluate the role of cytokines in down-regulation of *CLDN18* using the reductionist models, with the hypothesis that interleukin-1beta down-regulates *CLDN18*, leading to gastric cancer development (Figure 2). With collaborators, we also use human pathology samples from gastritis through gastric cancer to evaluate gene-expression patterns for novel biomarkers related to *CLDN18* that may inform patient management, drive biomarker development for early screening, and/or uncover therapeutic opportunities for novel drug development targeting gastric cancer.

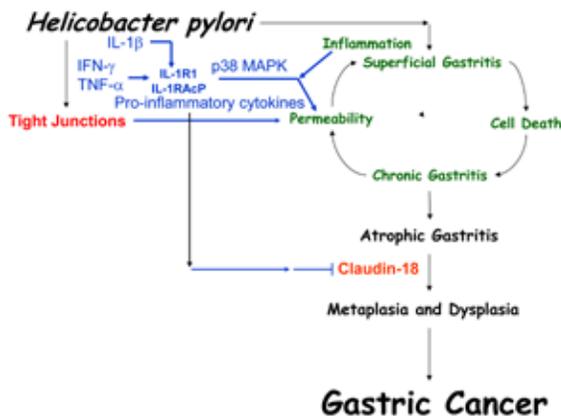
A second project in the lab involves a close collaboration with Dr. David Cohen, Chief of Gastroenterology and Hepatology at Weil Cornell in New York, to study the role of thioesterase superfamily member 1 (Them1) in hepatic steatosis/NAFLD. We became involved with this project due to our expertise in microscopy, specifically in correlative light (LM) and electron (EM) microscopy. Using adipocytes in culture, we have shown that Them1 associates with glycogen. As metabolism is stimulated, PKC activation via a distinct pathway changes the localization of Them1/glycogen. We are currently working to understand the physiological consequences of the Them1/glycogen interaction and rearrangement after stimulation. For this project, we have been using the new High Pressure Freezer, transfecting cells and expressing EGFP for confocal (LM) and APEXII for EM, and have been using the biotin-labeling technique with APEXII to determine *in vivo* binding partners for Them1.

RESEARCH GROUP

- Lay-Hong Ang, PhD
- Tyler Caron, DVM
- Aniket Gad, MS
- Salih Karahan
- Yue Li, PhD
- Lena Liu
- Kathleen Scott, DVM
- Kyle Smith
- Suzanne White



▲ FIGURE 1: *CLDN18* is not tight junction associated, but is rather a basolateral membrane protein.



◀ FIGURE 2: We are evaluating the role of cytokines in down-regulation of *CLDN18* using the reductionist models, with the hypothesis that interleukin-1beta down-regulates *CLDN18*, leading to gastric cancer development.

Individual Accomplishments

Yue Li and I served as mentors for Avi Goyal, a high school student from Chicago, who was in the Research Science Institute's (RSI) summer research program at MIT. The program ran from June 27-August 3, 2017. Avi worked in the laboratory on the Them1 project.

I served as a mentor for Salih Karahan, a 3rd year medical student from Turkey. Mr. Karahan was in the laboratory June-August 2017 and worked on the gastric cancer project.

I sat on the GMPB study section for 3 grant review sessions in 2016.

Yue Li was awarded a prestigious travel award by the Biophysical Society to attend Experimental Biology 2017. This award included a weekend professional development workshop prior to the meeting.

Yue Li was accepted to attend the Mount Desert Island Biological Labs course for GI Fellows, "Origins and Frontiers of Hepatobiliary and Gastrointestinal Physiology," in September 2017. Attendance was awarded competitively to a small number of applicants.

Invited Presentations (selected)

"Tight Junctions and Gastric Cancer: Three Critical Concepts." BK21 PLUS Project for Bioactive Nutrition 2016 Visiting Professor, Department of Food & Nutrition, College of Human Ecology, Yonsei University, Korea, 2016

"Tight Junctions and Gastric Cancer: Three Critical Concepts". Department of Pharmacology, College of Medicine, Yonsei University, Korea, 2016

TEACHING, TRAINING, AND EDUCATION

In addition to teaching students, technicians, and post-doctoral fellows in the research laboratory, I taught investigators to use the electron microscope and to do electron microscopy (EM) tomography in the EM facility at BIDMC.

Resident Courses

Module Leader in 2016 and 2017 for the Comparative Physiology Course at Mount Desert Island Biological Laboratory. Approximately 12 medical/surgical residents rotated through the module, "Gastric Acid Secretion," during the one-week course.

GI Fellows Courses

Module Leader in 2017 for a Physiology Course at Mount Desert Island Biological Laboratory. Approximately 12 GI fellows or PhD research fellows rotated through the module, "Gastric Acid Secretion," during the one-week course.

SELECTED RESEARCH SUPPORT

Gastric Cancer Research Fund; 2015-ongoing; PI: Susan J. Hagen, PhD

Them1-mediated metabolic regulation and pathogenic role in NAFLD; NIH, 2015-2020; Multi-PI R01: David E. Cohen, MD, PhD, Weill Cornell Medical College; Susan J. Hagen, PhD; Eric A. Ortlund, PhD, Emory University

Biology of alimentary epithelia in health and disease; NIH, 2015-2020; Microscopy and Histopathology Core B PI: Susan J. Hagen, PhD (PI: Wayne Lencer, MD, Boston Children's Hospital)

Biomedical research training for veterinary scientists; NIH, 2013-2018; Academic Mentor: Susan J. Hagen, PhD (PI: James G. Fox, DVM, MIT)

Live-cell LSM 880 confocal microscope; BIDMC Capital Investment Award, 2017

Palmer CJ, Bruckner RJ, Paulo JA, Kazak L, Long JZ, Mina AI, Deng Z, LeClair KB, Hall JA, Hong S, Zushin P-JH, Smith KL, Gygi SP, Hagen SJ, Cohen DE, Banks AS. Cdkal1, a type 2 diabetes susceptibility gene, regulates mitochondrial function in adipose tissue. *Mol Metab* 2017;6(10):1212-25.

Hagen SJ. Non-canonical functions of claudin proteins: beyond the regulation of cell-cell adhesions. *Tissue Barriers* 2017;5(2):e1327839.

Desai A, Alves-Bezerra M, Li Y, Ozdemir C, Bare CJ, Li Y, Hagen SJ, Cohen DE. Regulation of fatty acid trafficking in liver by thioesterase superfamily member 1 and contribution to hepatic steatosis in mice. *J Lipid Res* 2017; in press.



Daniel B. Jones, MD, MS, FACS, FASMBS

Professor of Surgery

Vice Chair, Surgery (Technology and Innovation)

Chief, Division of Bariatric and Minimally Invasive Surgery

Co-Director, Carl J. Shapiro Simulation and Skills Center

RESEARCH GROUP

George Blackburn, MD, PhD
 Dale Bond, MD
 Caroline Cao, PhD
 Suvranu De, PhD
 Jody Dushay, MD
 Yu Fang, PhD
 Emily Fitzpatrick, MD
 David Fobert
 Cullen, Jackson, PHD
 Stephanie Jones, MD
 Michael McBride, RN
 Brian Nguyen, MD
 Jaisa Olasky, MD
 Kate Otto, RD
 Caroline Park, MD
 Ganesh Sankaranarayanan, PhD
 Mandeep Sawhney, MD, MPH
 Steven Schwaitzberg, MD
 Darren Tavernelli, RN
 Linda Trainor, RN
 Christina Wee, MD, MPH



FIGURE 1:
 The Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) developed the Fundamental Use of Surgical Energy (FUSE) program to meet the need for increased education and training in the principles and properties of operating electrosurgical instruments safely.

RESEARCH FOCUS

My education-based research has established a technical skills laboratory validating new teaching tools and instituting curriculums for medical students, residents and surgeons in practice. Using group video trainers, we demonstrated for the first time in Surgery that intense skills training improved operative performance. Computer trainers which provided immediate feedback further improved trainees' ability to perform a laparoscopic cholecystectomy. Other simulators included novel models for laparoscopic hernia repair, common bile duct exploration, and ultrasound-guided breast biopsy. Studies demonstrated error with sleep deprivation among post-call surgical residents. Furthermore, programs for medical students suggest the benefit from early exposure to simulation.

Simulation/Education There are six ongoing R01 NIH-funded collaborative projects among the Center for Modeling, Simulation and Imaging in Medicine (CeMSIM), Rensselaer Polytechnic Institute (RPI), the Carl J. Shapiro Simulation and Skills Center, Beth Israel Deaconess Medical Center (BIDMC), and Tufts University:

Virtual Basic Laparoscopic Skills Trainer (VBLaST) is a virtual reality trainer that replicates the FLS tasks for skills training. In this project, a specialized interface with haptic feedback was to replicate the FLS box for the VBLaST. Validation studies are conducted at the Carl J. Shapiro Simulation and Skills Center.

Virtual Natural Orifice Transluminal Endoscopic Surgery (VR-NOTES) simulator provides a training and testing platform for both transgastric and transvaginal NOTES cholecystectomy. Currently the VR-NOTES simulator has virtual organ models through which a fly-through simulation can be done along the predetermined path for a transgastric approach. A haptic interface with a realistic flexible endoscope is being developed to interact with the VR-NOTES simulator.

Generation (Gen) 2 Cognitive Simulator seeks to create a Star Trek hallodeck experience by creating an environment as close to real surgery as possible, including the operating room environment, devices, avatars, and room noises, making the training very realistic.

Virtual Electrosurgery Trainer (VEST) is an ongoing project that includes basic modules to teach ways to avoid patient injury during an electrosurgery procedure. The VEST can simulate insulation failure, capacitive and direct coupling. An interface with two ports for trocar and tool placement whose motion are captured by optical and gyroscope sensors was built to interface the VEST for testing.

Virtual Airway Simulation Trainer (VAST) develops a simulator to teach difficult airway as might be encountered in an obese patient. Criticothroidotomy is also taught.

Virtual Endoluminal Surgery Simulator (VESS) is used to teach advanced therapeutic endoscopy for the treatment of colorectal cancer.

Other funding from the CRICO-RMF has supported our project, FUSE: Catalysts and barriers to implementation and quality initiative in the OR. We studied the adoption of the SAGES Fundamental Use of Surgical Energy in an online educational curriculum.

Bariatric Surgery My research also focuses on the clinical outcomes. In collaboration with Christina Wee, MD, MPH (Department of Medicine, BIDMC) we have a large database from which we have published this year on the following topics: expectations for weight loss and willingness to accept risk, quality of life among obese patients, obesity-related stigmata and functional status, patient factors associated with undergoing laparoscopic adjustable gastric banding vs Roux-en-Y gastric bypass, and high-risk alcohol use after weight loss surgery. This research is funded by the NIH.

In collaboration with Brown University we are funded by the NIH to better understand how we can use technology to help our bariatric surgery patients with lifestyle changes. In addition, I am PI for an NIH study, Ecological momentary assessment of behavioral and psychosocial predictors of weight loss following bariatric surgery.

ACCOMPLISHMENTS 2016-2017

- President, Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)
- Trustee-at-Large, Society for Surgery of the Alimentary Tract (SSAT)
- Past President, Association for Surgical Education (ASE)
- Chair, Essentials Task Force, www.Essentials.ASMBS.org

Invited Presentations

Visiting Professor, University of Nebraska, "Safer Surgery," Omaha, Nebraska, 2016

"Safer Surgery in Bariatric Surgery," University of Vermont Mackay-Page Lectureship, Burlington, VT, 2016

Visiting Professor, OHSU, "Team based operative care: in bariatric surgery," Portland, OR, 2016

"Heritage of Societies - SAGES," 38th Annual Meeting of the Korean Society of Endoscopic & Laparoscopic Surgeons (KSELS), Seoul, Korea, 2016

"Patient Safety", 8th International Conference of Metabolic and Bariatric Surgery, Stare Jablonki, Poland, 2016

"Who decides medical necessity: the third party payer, the docs or a judge?" International Surgery Group (ISG), Edinburgh, Scotland, 2106

Sigman Visiting Professor, "The simulation center as the hub for research and innovation." Montreal, Canada, 2016

"Advancing safety and improving outcomes with MBSAQIP accreditation of bariatric centers in the United States." 15th World Congress of Endoscopic Surgery, Suzhou, China, 2016

TEACHING, TRAINING, AND EDUCATION

- ASE/ACS Skills-based Simulation Curriculum for Medical School Years 1-3; Released national curriculum for medical students using educational theory and assessment metrics
- Fundamental Use of Surgical Energy (FUSE). International curriculum and certification to advance OR safety
- Essentials. Multidisciplinary curriculum to management of bariatric surgery patient
- SAGES MASTERS program. Curriculum for deliberate, learning after fellowshi
- Co-Director, Carl J. Shapiro Simulation and Skills Center, BIDMC
- HMS Longitudinal Bariatric Experience
- Site Director; OR CRICO Team Training with Simulation
- Course Director, BIDMC Surgery Grand Rounds, weekly CME lecture series

The Theodore Drapanas Memorial Lectureship, "Safer surgery with simulation," University at Buffalo, Buffalo, NY, 2017

"Management of biliary tract after gastric bypass: choledocholithiasis and biliary dyskinesia." SAGES, Houston, TX, 2017

"Update on bariatric surgery." 77th Scientific Session, American Diabetes Association, San Diego, CA, 2017

"Deliberate lifelong learning using simulators, simulation and the internet." The Korean Society of Laparoscopic and Endoscopic Surgeons (KSELS), Busan, Korea, 2017

Recognition and Awards

- Baylor Hospital Visiting Professor, Dallas, Texas
- University of Nebraska Visiting Professor, Omaha, Nebraska
- Mackay-Page Lectureship Guest of Honor to the University of Vermont
- Oregon Health Sciences University Visiting Professor, Portland, OR
- 12th Harvey H. Sigman Lecture in Medical Education, McGill University, Jewish General Hospital, Montreal, Canada
- American Society for Metabolic and Bariatric Surgery, The Edward Mason Service of Distinction Medal
- Best Doctors in America; Top Doctors, Boston magazine, US News & World Report; America's Top Surgeons, Consumers Research Council of America

Editorial Roles

Editorial Board: *Surgical Endoscopy*, *Bariatric Times*, *UpToDate*, and *Surgery for Obesity and Related Disorders*

SELECTED PUBLICATIONS

Jones DB, Sung R, Weinberg C, Korelitz T, Andrews A. Three dimensional modeling may improve surgical education and clinical practice. *Surg Innov*, 23(2):189-195, 2016.

Robinson TN, Olasky J, Young P, Feldman LS, Fuchshuber PR, Jones SB, Madani A, Brunt LM, Mikami D, Jackson GP, Mischna J, Schweitzberg S, Jones DB. Fundamental use of surgical energy (FUSE) certification: validation and predictors of success. *Surg Endosc*, 30:916-924, 2016.

Telem DA, Majid SF, Powers K, Demaria E, Morton J, Jones DB. Assessing national provision of care: variability in bariatric clinical care pathways *Surg Obes Relat Dis*, 13:281-286, 2017.

Schweitzberg SD, Dorozhkin V, Sankaranarayanan G, Matthes K, Jones DB, De S. Natural orifice transluminal endoscopic surgery (NOTES): emerging trends and specifications for a virtual reality simulator, *Surg Endosc* 30:190-198, 2016.

Wee CC, Davis RB, Jones DB, Apovian CA, Chiodi S, Huskey KW, Hamel MB. Sex, race, and quality factors most important to patients' well-being among those seeking bariatric surgery, *Obesity Surgery*, 26: 1308-1316, 2016.

SELECTED RESEARCH SUPPORT

Ecological momentary assessment of behavioral and psychological predictors of weight loss following bariatric surgery; NIH, 2015-2017; PI: Daniel Jones, MD, MS

Development and validation of virtual endoluminal surgery simulator (VESS) for the treatment of colorectal cancer; NIH, 2016-2021; PI: Suvranu De, PHD

Development and validation of a virtual basic laparoscopic skill trainer (VBLAST); NIH, 2009-2017; PI: Daniel Jones, MD, MS

Developing physics-based virtual simulation technology for natural orifice transluminal endoscopic surgery; NIH, 2009-2017; PI: Daniel Jones, MD, MS

Development and validation of a virtual electrosurgical skill trainer (VEST); NIH, 2011-2017; PI: Daniel Jones, MD, MS

Physically realistic virtual surgery; NIH, 2011-2017; PI: Daniel Jones, MD, MS

Virtual Airway Simulation Trainer (VAST) NIH, 2014-2018; PI: Stephanie Jones, MD



Tara S. Kent, MD, MS

Associate Professor of Surgery

Vice Chair for Education

Program Director, General Surgery Residency

RESEARCH FOCUS

Research in pancreaticobiliary surgery

Our group's work focuses on patient-centered outcomes research in pancreaticobiliary surgery. Fueled by a robust clinical practice that focuses on treatment of pancreatic malignancies, cystic lesions, pancreatitis, and complex biliary conditions in a multidisciplinary setting, we perform more than 200 major pancreaticobiliary operations per year.

A prospective database of more than 4,000 operations and 750 pancreatic resections has been developed and maintained from this practice, providing the substrate for our investigations. In addition, we have utilized national large databases as well. Areas of emphasis are investigation into the transition from inpatient to post-discharge care, readmission rates, and prediction of post-discharge needs. Based on earlier work, we developed a discharge informational tool for patients and we are currently evaluating its utility after pancreatectomy.

Recent efforts have focused on investigation of the means by which patients process information about their pancreatic cancer diagnosis and treatment options, with a goal of improving patient understanding of, and contribution to, their care. We have assessed the readability, accuracy, and suitability of available online information on pancreatic cancer, the communication between the care team and patients and families, and the use of health literacy assessments. We are now investigating the relationship between designated language and time to definitive treatment. We are currently developing a process to assess health literacy and cultural expectations in patients with new pancreas cancer diagnoses, in order to evaluate the impact of these factors on patient progression to care.

Surgical education research

Our surgical education research effort includes the study of factors influencing in-training exam scores, including the impact of a modified style of curriculum delivery. Other recent efforts have included: a study of resident confidence after completion of an intern-level practical skills curriculum, and the development of a structured face-to-face clinical assessment for interns. In addition, with support from a Shapiro Institute grant, we developed and evaluated a curriculum on the learning environment and mistreatment. Currently, we are working to modify this curriculum for the faculty. Additionally, we are involved in the development of a multicenter study of the impact of a curriculum on cultural dexterity, for which NIH funding is pending.

RESEARCH GROUP

Courtney Barrows, MD
Rodrigo Calvillo-Ortiz, MD
Manuel Castillo-Angeles, MD, MPH
Tovy Kamine, MD
Kristin E. Raven, MD
Alessandra Storino, MD, MS
Ammara A. Watkins, MD

ACCOMPLISHMENTS 2016-2017

- Chair, Americas Hepato-Pancreato-Biliary Association (AHPBA) Education and Training Committee, as of 2016
- Certificate, Applied Biostatistics, Harvard Catalyst: Harvard Clinical and Translational Science Center, 2017
- Editorial Board member, Journal of Surgical Education, as of 2017
- Promoted to Associate Professor of Surgery, 2017

TEACHING, TRAINING, AND EDUCATION

- I continue as Program Director of the General Surgery Residency, a position I have held since September 2012. I administer the training of our 45 categorical and 11 preliminary trainees
- As Vice Chair for Education (since 2014), I oversee the department's educational programs at the student, resident, and fellow levels
- I serve on the Entrustable Professional Activities (EPA) Working group, representing the Americas Hepato-Pancreato-Biliary Association (AHPBA) on this Fellowship Council-based group, developing EPAs as standards for fellowship-level training

SELECTED RESEARCH SUPPORT

Affinity Research Collaborative (ARC) of the Harvard Departments of Surgery, 2015-16 Mitigating disparities through enhancing surgeons' ability to provide culturally relevant care; Co-investigator (PI: Adil Haider, MD, MPH, Brigham and Women's Hospital)

Risk assessment and reduction in pancreatic surgery; Contributing member (PI: Jennifer Tseng, MD, MPH, Boston University School of Medicine)

Reducing resident mistreatment and improving the learning environment for medical students on general surgery clerkship rotations; Carl J. Shapiro Institute of Education and Research (2015-16), BIDMC; PI: Tara S. Kent, MD, MS

SELECTED PUBLICATIONS

Watkins AA, Bliss LA, Cameron DB, Tseng JF, Kent TS. Deconstructing the "July effect" in operative outcomes: a national study. *J Gastrointest Surg* 2016;20(5):1012-9.

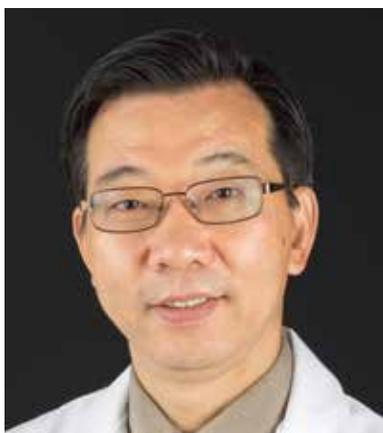
Storino A, Castillo-Angeles M, Watkins AA, Vargas C, Mancias JD, Bullock A, Demirjian A, Moser AJ, Kent TS. Assessing the accuracy and readability of online health information for patients with pancreatic cancer. *JAMA Surg*. 2016; 151(9):831-7.

Castillo-Angeles M, Watkins AA, Acosta D, Frydman JL, Flier L, Garces-Descovich A, Cahalane MJ, Gangadharan SP, Atkins KM, Kent TS. Mistreatment and the learning environment for medical students on general surgery clerkship rotations: what do key stakeholders think? *Am J Surg* 2017;213(2):307-312.

Changoor NR, Udyavar NR, Morris MA, Torain M, Mullen JT, Kent TS, Smink DS, Green A, Haider AH. Surgeons' perceptions toward providing care for diverse patients: the need for cultural dexterity training. *Ann Surg* 2017 [epub ahead of print].

Acosta D, Castillo-Angeles M, Garces-Descovich A, Watkins AA, Gupta A, Critchlow JF, Kent TS. Surgical practical skills learning curriculum: implementation and interns' confidence perceptions. *J Surg Ed* 2018;75(2):263-270.

A complete list of publications begins on page 13.



Jin-Rong Zhou, PhD

Associate Professor of Surgery
Director, Nutrition/Metabolism Laboratory

RESEARCH FOCUS

The long-term goal of my research is to define efficacious and safe nutritional and bioactive regimens for the prevention and therapy of cancer and other metabolic disorders. My laboratory has focused on evaluating the efficacy and safety of several bioactive natural compounds on the growth, progression, and metastasis of certain types of cancer in both *in vitro* and *in vivo* model systems, and investigating the mechanisms of action of these bioactive components. Since cancer stem cells are recognized to be responsible for drug resistance and metastasis of cancer, our special effort has been in identifying bioactive components for targeting cancer stem cells. Additionally, we have investigated the effects of bioactive components on blood glucose management, alleviation of chronic kidney disease, and prevention of autism. In the past year, my laboratory has focused on the following projects.

RESEARCH GROUP

Hamid Abdolmaleky, MD
Reza Alam, MD
Lixia He, PhD
Sheng Yin, PhD

Tanshinones as potent anti-cancer and anti-cancer stem cell agents by targeting Aurora A and B kinases

Our studies have shown that tanshinones, which include cryptotanshinone (CT), tanshinone I (T1), and tanshinone IIA (T2A), have potent anti-proliferation and anti-cancer stem cell (CSC) self-renewal activities against several types of cancer cell lines. Further investigations showed that, among these tanshinones, T1 had the most potent activities and inhibited the growth of prostate tumors and lung tumors in animal models, with minimal side effects. Further mechanism studies demonstrated that downregulation of Aurora A and B kinases was an important mechanism shared by all three tanshinones. To further improve the anti-cancer activities of bioactive agents with additive and/or synergistic combination, our studies showed that the combination between CT and T1 or T2A had synergistic effect against prostate cancer in part via downregulation of aurora kinases, whereas the combination of T1 and T2A had an antagonistic effect associated with upregulation of aurora kinases. Our other studies also showed that T1 and resveratrol combination had a synergistic effect on inhibiting prostate cancer, in part via downregulation expression of aurora A and c-myc in a combined manner. We are in the processing to verify the efficacy of these synergistic combination regimens in clinically relevant animal models of cancer.

Bioactive components delay the development and progression of chronic kidney injury by inhibiting inflammation

We have also studied the effects of bioactive components, activated lactic acid (ALA), and a soy germ extract (SGE), on chronic kidney disease *in vitro* and *in vivo*. Both ALA and SGE showed anti-inflammatory and oxidative stress-suppressing activities in kidney cell models *in vitro*. Further *in vivo* study also showed the preventive efficacy of ALA or SGE on an adenine-induced chronic kidney injury animal model by inhibiting inflammation and reducing toxicity in the kidney that was associated with modulating inflammation biomarkers in blood and kidney samples. Additionally, these bioactive components had minimal side effect *in vivo*, supporting that these bioactive components may warrant further investigation for potential clinical application.

Anti-inflammatory effect of bioactive components for prevention of autism

In this research project, we have successfully established the iPSC-differentiated neuronal and astrocytic cell models for identifying active components and for mechanism studies. Our studies showed that autistic iPSC-derived astrocytes had significantly increased inflammation levels, compared with that of the normal controls. Using this novel cell model, we have identified several candidate bioactive agents that showed potent anti-inflammation activities in astrocytes. We are in the process of further verifying the *in vivo* efficacy to elucidate mechanisms of action of bioactive agents.

ACCOMPLISHMENTS 2016-2017

Grant Review Activities

- Review panel, Key Programs, National Science Foundation of China, 2017
- Review panel, General Research Fund, Research Grant Council, Hong Kong, 2017
- Ad hoc member, SEP-3 for Provocative Questions, NCI/NIH, 2017
- Review panel, Function and Efficacy of Nutrients Review Panel of National Institute of Food and Agriculture (NIFA), US Department of Agriculture (USDA), 2017

Editorial Services

- Ad hoc manuscript reviewer: eight scientific journals
- Editorial board member: *Health; Digital Chinese Medicine; Journal of Genetic, Molecular and Cellular Biology; Journal of Disease and Global Health; Single Cell Biology; World Journal of Clinical Oncology; International J. Tropical Disease & Health*
- Editor: *Frontiers in Biosciences*
- Editor-in-Chief: *Nutrition and Metabolic Insights* (2012-present), *Journal of Health Sciences* (2013-present)

Invited Presentations

- Precision Medicine: Challenges and Opportunities; Jiangsu Oncology Medical Quality Control Center Annual Meeting/Cancer Chemotherapy Conference, Nanjing, China, 2016
- Soybeans for prevention of breast cancer: epidemiological associations and experimental evidence; 1st ICC Asia-Pacific Grains Conference, May 21-24, 2017, Xiamen, China, 2017

TEACHING, TRAINING, AND EDUCATION

I have been training post-doctoral fellows on a daily basis for the past year. In addition, I served as the co-supervisor of graduate students and thesis defense committee member at the Nanjing University of Chinese Medicine, China, and at the Institute of Food Science Research, Spain.

- Nutritional strategies to delay metastatic recurrence in cancer survivors; 13th China Nutrition Science Congress, Beijing, China, 2017
- Nutrition and Cancer Prevention; Center for Agro-Products Processing, Institute of Food Science and Technology, Chinese Agricultural Academy of Sciences, Beijing, China, 2017
- Target on cancer stem cells by natural bioactive components against metastatic recurrence; Food Safety and Technology Research Centre, Department of Applied Biology and Chemical Technology, The Hong Kong Polytechnic University, Hong Kong, China, 2017
- Soybeans for prevention and therapy of breast cancer: beneficial or harmful?; Specialty Committee of Breast Diseases of World Federation of Chinese Medicine Societies Annual Meeting, Shanghai, China, 2017

Others

- Chair, Diet & Cancer Research Interest Group, American Society of Nutrition, 2017
- Co-Chair, Diet and Cancer: Molecular and Cellular Targets Section, Experimental Biology Annual Meeting, Chicago, IL, 2017
- Chair, Nutrition and Chronic Diseases Section, 13th China Nutrition Science Congress, Beijing, China, 2017
- Member, Organizing Committee, 3rd World Congress on Cancer and Prevention Methods, Barcelona, Spain, 2017
- Vice Chairperson, The 1st Board of Specialty Committee of Breast Diseases, World Federation of Chinese Medicine Societies
- Distinguished Medical Expert, Jiangsu Provincial Commission of Health and Family Planning, China, 2016-2018

SELECTED PUBLICATIONS

Wang S, Shen P, Zhou J, Lu Y. Diet phytochemicals and cutaneous carcinoma chemoprevention: A review. *Pharmacology Research* 2017;119:327-46.

del Castillo MD, Iriando-DeHond A, Martinez-Saez N, Fernandez-Gomez B, Iriando-DeHond M, Zhou J-R. Applications of recovered compounds in food products. In *Handbook of Coffee Processing By-Products: Sustainable Applications*. Edited by C. Galanakis, Elsevier, 2017; Chapter 6, pp 171-194.

Alam R, Abdolmaleky HM, Zhou J-R. Microbiome, inflammation, epigenetic alterations, and mental diseases. *Am J Med Genet B Neuropsychiatr Genet* 2017;174: 651-60.

SELECTED RESEARCH SUPPORT

Maternal anti-inflammatory diet for prevention of autism in offspring; Allen Foundation, 2015-2017; PI: Jin-Rong Zhou, PhD

Effects of bioactive agents on prevention of chronic kidney disease; Nichimo Biotics Co. and Lifetrade Co., Japan, 2015-2018; PI: Jin-Rong Zhou, PhD

Effects of Epimedium flavonoids extract (EFE) on osteoporosis and breast cancer; Kanion Pharmaceutical Co., China, 2017-2020; PI: Jin-Rong Zhou, PhD

Nutraceuticals for diabetes management: Efficacy evaluation and mechanism elucidation; Feihe Nutrition Laboratory, BIDMC, 2016-2018; PI: George Blackburn, MD, PhD/Elliot Chaikof, MD, PhD (Co-Investigator: Jin-Rong Zhou, PhD)

A complete list of publications begins on page 13.



Richard D. Cummings, PhD

Professor of Surgery

Vice Chair, Basic and Translational Research

Director, National Center for Functional Glycomics

Director, Harvard Medical School Center for Glycoscience

RESEARCH FOCUS

A key quest of my research during the past 35 years has been to understand the structure and function of glycoconjugates in cell adhesion and signaling, studying the molecular and biochemical functions of surface and secreted glycoproteins in normal biological processes and disease. We study the molecular nature and specificity of protein-glycan interactions and their roles in biology, and how glycans are recognized by glycan-binding proteins (GBPs). My laboratory has been instrumental in developing new technologies in glycoscience, discovering novel functions of glycans in immune recognition and modulation, viral (influenza), parasitic (helminth) and bacterial infections, cell adhesion, selectin biology and leukocyte trafficking, new enzymes and molecular chaperones that regulate protein glycosylation, and educating students in the field of glycoscience.

Early work in our laboratory established the identities and specificities of many glycosyltransferases and glycan-binding proteins and plant lectins. In our translational studies, we are exploring glycoimmunology, and the roles of adaptive and innate immune responses to pathogens, as well as human diseases that are both heritable and acquired, and which involve altered glycosylation. We have developed novel techniques in the field for glycan analysis and for exploring the structure/function relationships of glycans, using genetic/molecular approaches, biophysical and biochemical strategies, and multiple glycan microarray and glycan bead strategies. We are also developing semi-synthetic methods for making glycoconjugates and for isolating, characterizing, and derivatizing glycans. Such technologies are revolutionary and are growing at a rapid pace; thus, I expect such microarray (and flow cytometry-based arrays) to be a major contributor to the field of glycoscience going forward.

I hold numerous patents in the field of glycoscience. My laboratory is the headquarters of the National Center for Functional Glycomics (NCFG), of which I am the Director, and the Protein-Glycan Interaction Resource of the Consortium for Functional Glycomics (CFG), of which I am the Chair, and offers glycan microarray services to hundreds of laboratories worldwide. We also have a strong effort in promoting and developing bioinformatics and databases related to glycoscience. My laboratory and the NCFG moved to Harvard Medical School (HMS) and Beth Israel Deaconess Medical Center (BIDMC) in the fall of 2015, where

I have founded and was appointed Director of the new Harvard Medical School Center for Glycoscience. My research goals are centered on identifying the structures, functions and biosynthesis of complex glycoconjugates in a variety of normal and pathologic biological processes.

Glycoprotein Interactions Regulate Platelet, Endothelial Cell, Leukocyte, and Metastatic Tumor Cell Adhesion and Trafficking

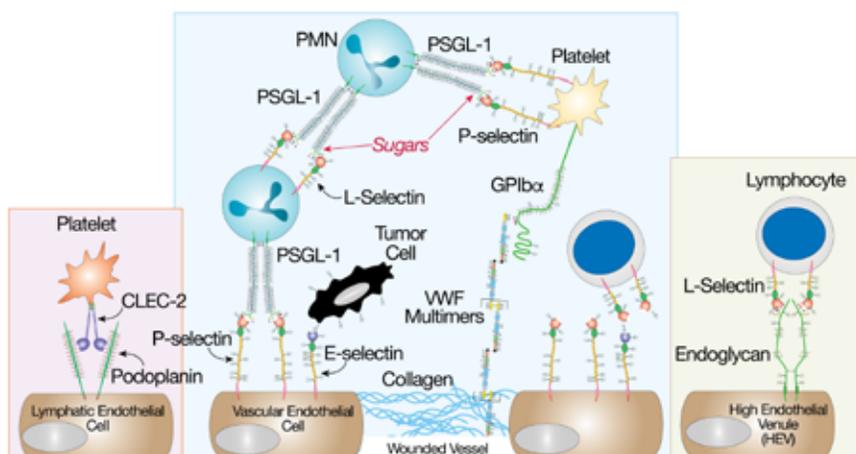


FIGURE 1: Glycoprotein interactions regulate platelet, endothelial cell, leukocyte, and metastatic tumor cell adhesion and trafficking.

RED BOX: Platelet interactions with lymphatic endothelial cells

BLUE BOX: Polymorphonuclear (PMN) leukocytes interacting with vascular endothelial cells, and other PMNs; Tumor cells interact with vascular endothelial cells; Platelet and VWF interactions at wound sites; Lymphocyte interactions with vascular endothelial cells

YELLOW BOX: Lymphocyte interactions with high endothelial venules

RESEARCH GROUP

- Lauren Byrd-Leotis, PhD
- Deniz Eris, PhD
- Chao Gao, PhD
- Melinda Hanes, PhD
- Jamie Heimburg-Molinaro, PhD
- Nan Jia, PhD
- Sylvain Lehoux, PhD
- Yasuyuki Matsumoto, PhD
- Tanya McKittrick, PhD
- Akul Mehta, PhD
- Kathryn A. Stackhouse, MD
- Kathrin Stavenhagen, PhD
- Xiaodong Sun, PhD
- Mohui Wei, PhD
- Junwei Zeng, PhD

ACCOMPLISHMENTS 2016-2017

- Director, National Center for Functional Glycomics (NCFG), 2015-Present
- Highlight and interview by Elizabeth Cooney, HMS News, "Sweet Spot" 2016
- Interview by Vivien Marx, "Metabolism: sweeter paths in glycoscience", in *Nature Methods* 2017;14(7):667.
- Invited Speaker, Tufts University School of Medical, Boston, MA, 2016
- Invited Speaker, Oklahoma Medical Research Foundation, Oklahoma City, OK, 2016
- Invited Keynote Lecturer, EMBO Workshop, Nice, France, 2016
- Presenter Opening Session, 2016 Society for Glycobiology Annual Meeting, New Orleans, LA, 2016
- Appointed Professor of Surgery, 2017
- Appointed Member, Scientific Advisory Board, Institute for Protein Innovation, HMS, 2017
- CCR Investigator, NCI Chemical Biology Laboratory, 2017
- Appointed Associate Editor – *Science Advances*, 2017
- Invited Speaker, Abbott Nutrition Internal Science Meeting, Columbus, OH, 2017
- Invited Grand Rounds Lecturer, Department of Surgery, BIDMC, 2017
- Duke University, Department of Biochemistry, Durham, NC, 2017
- University of Georgia and CCRC, Atlanta, GA, 2017
- Invited Speaker, Gordon Research Conference, Glycobiology 2017, Ventura, CA, 2017
- Invited Speaker, ASBMB Annual Meeting, Experimental Biology 2017, Chicago, IL, 2017
- Invited Presenter, BioMedical Seminar, Drexel University, Philadelphia, PA, 2017
- Invited Presenter, Alliance of Glycobiologists for Detection of Cancer, Steering Committee Meeting, Bethesda, MD, 2017
- Invited Presenter, NIH & FDA Glycoscience Research Day, Bethesda, MD, 2017
- Invited Speaker, 12th Jenner Glycobiology and Medicine Symposium, Dubrovnik, Croatia, 2017
- Invited Speaker, ESPGHAN Annual Meeting, Abbott Sponsored Symposium, Prague, Czech Republic, 2017
- Invited Presenter, 2017 Gordon Research Conference on Carbohydrates, Mount Snow, VT, 2017
- Invited Speaker, CEIRS Network Annual Meeting, Emory University, Atlanta, GA, 2017
- Invited Speaker, Siamab Therapeutics, Newton, MA, 2017
- Scientific Advisory Board Meeting, Gates Foundation, Ragon Institute, Cambridge, MA, 2017
- Invited Speaker, 24th International Symposium on Glycoconjugates, Jeju Island, Korea, 2017
- Invited Speaker, Center for Immunology and Inflammatory Disease, Massachusetts General Hospital, Charlestown, MA, 2017
- "Compositions and uses of lectins"- Patent #9,572,864B2, R.D. Cummings, Sean R. Stowell, Connie Arthur; Emory University, 2017
- "Compositions and Methods for Functional Glycomics"- Patent #9,772,337, R.D. Cummings, David F. Smith, Xuezheng Song; Emory University, 2017

TEACHING, TRAINING, AND EDUCATION

In 2017, I was inducted into the BIDMC Academy of Medical Educators.

I mentored three doctoral students, two of whom completed their degrees. In 2016, Alexander Noll received his PhD from Emory University with a thesis entitled "Human Milk Glycan Interactions with Glycan-Binding Proteins of the Gastrointestinal Tract." He published three original peer-reviewed publications and has a

comprehensive review ready for submission. In 2017, Matthew Kudelka received his PhD from Emory University with a thesis entitled "Cosmc is an X-linked inflammatory bowel disease risk gene that spatially regulates gut microbiota and contributes to sex-specific risk." He published three original peer-reviewed publications and three reviews. Chris Cutler remains under my direction for his PhD work at BIDMC, granted from Emory University.

SELECTED PUBLICATIONS

Kudelka MR, Hinrichs B, Darby T, Moreno CS, Nishio H, Cutler CE, Wang J, Wu H, Zeng J, Wang Y, Ju T, Stowell SR, Nusrat A, Jones RM, Neish AS, Cummings RD. Cosmc is an X-linked Inflammatory Bowel Disease Risk Gene that Spatially Regulates Gut Microbiota and Contributes to Sex-specific Risk. *Proc Natl Acad Sci USA* 2016;113(51):14787-14792.

Schneider C, Wicki S, Graeter S, Timcheva TM, Keller CW, Quast I, Leontyev D, Djoumierska-Alexieva IK, Käsermann F, Jakob SM, Dimitrova PA, Branch DR, Cummings RD, Lünemann JD, Kaufmann T, Simon HU, von Gunten S. IVIG regulates the survival of human but not mouse neutrophils. *Sci Rep* 2017;7(1):1296.

Laan LC, Williams AR, Stavenhagen K, Giera M, Kooij G, Vlasakov I, Kalay H, Kringel H, Nejsum P, Thamsborg SM, Wuhrer M, Dijkstra CD, Cummings RD, van Die I. The whipworm (*Trichuris suis*) secretes prostaglandin E2 to suppress proinflammatory properties in human dendritic cells. *FASEB J*, 2017;31(2):719-731.

Hanes MS, Moremen KW, Cummings RD. Biochemical characterization of functional domains of the chaperone Cosmc. *PLoS One*, 2017;12(6): e0180242.

Varki A, Cummings RD, Esko J. *Essentials of Glycobiology – 3rd Edition*. Cold Spring Harbor Laboratory Press Inc., Boston, 2017. [Note that Cummings is the illustrator for all figures in all editions of *Essentials of Glycobiology*.]

SELECTED RESEARCH SUPPORT

National Center for Functional Glycomics; NIH/NIGMS, 2013-2018; PI: Richard D. Cummings, PhD

Modulation of inflammatory responses by helminth glycans; NIH/NIGMS, 2013-2018; PI: Richard D. Cummings, PhD

Smart Anti-Glycan Reagents to Generate the Human Glycome Atlas; NIH/NCI, 2015-2018; MPI: Richard D. Cummings, PhD (Co-PI: Ray Mernaugh, PhD, Vanderbilt University)

Discovery Platform of Mycobacterium tuberculosis Glycans; Gates Foundation, 2016-2018; PI: Richard D. Cummings, PhD

Human Milk Glycan Research; Abbott Laboratories Contract, 2015-2018; PI: Richard D. Cummings, PhD

Lijun Sun, PhD

Associate Professor of Surgery
Director, Center for Drug Discovery and Translational Research



RESEARCH GROUP

Jea Eun Cheong, PhD
Finith Jernigan, PhD
Steffi Knoener, PhD

RESEARCH FOCUS

The Center for Drug Discovery and Translational Research, which I direct, provides a platform and expertise in medicinal chemistry to promote bench-to-bedside translation. My laboratory has studied the optimal integration of molecular simulations into the generation of bioactive molecules. In collaboration with investigators at Harvard Medical School, we have applied this research methodology for the discovery of novel inhibitors of the protein-protein interaction (PPI) between interleukin (IL)-18 and its receptor (collaborator: Dr. Leena Pradhan-Nabzdyk, BIDMC), the lipogenic enzyme ATP-citrate lyase (ACL) (collaborator: Dr. Vikas Sukhatme, BIDMC), the CDC-like kinase (CLK) in highly aggressive cancers (collaborator: Dr. Bruce Zetter, Boston Children's Hospital), the cell cycle modulators as cytotoxic agents in drug resistant cancer cells (collaborator: Dr. Barbara Wegiel, BIDMC), the mast cell degranulation (collaborator: Dr. Aristidis Veves, BIDMC), the indoleamine/tryptophan dioxygenase (IDO/TDO), as well as the arylhydrocarbon receptor (AhR) (collaborator: Dr. Elliot Chaikof, BIDMC).

IL-18 plays a significant role in driving the inflammatory processes responsible for the development of intimal hyperplasia (IH). Via molecular simulation and *in silico* screening, we recently identified small molecule compounds that inhibit IL-18 signaling with low micromolar potency. Preliminary data suggest the small molecules elicit IL-18 antagonistic activity by inhibiting the PPI between IL-18 and its receptor. We are actively engaged in the characterization and improvement of the novel inhibitors.

Overly activated mast cells are implicated in the pathology of a number of diseases, including diabetic neuropathy and diabetic foot ulcer. Mast cell activation and the release of a spectrum of proinflammatory mediators are controlled by calcium channels. We have synthesized a new class of calcium channel blockers that effectively inhibit channel function and mast cell degranulation. We have demonstrated efficacy in mouse models of diabetic wound healing and diabetic peripheral neuropathy.

In the ACL project, we showed that ACL inhibitors reduced the population of the cancer stem-like cells (CSC) in a lung cancer cell line (A549) and an engineered breast cell line. The ACL inhibitors also inhibited the tumorigenesis in 3D *in vitro* tumorsphere assays. Research by others has recently showed a role of ACL in directing the polarization of the M2 phenotype macrophages that in the tumor microenvironment promote cancer immune escape. Our hypothesis is that inhibition of ACL might offer a unique approach to eradicate cancer cells by simultaneously reducing CSC and immune suppression in tumors. We are currently characterizing novel ATP-competitive ACL inhibitors that interrupt the rate-limiting step of the enzymatic reaction.

IDO and TDO are promising drug targets in immuno-oncology. Via *in silico* screen of compound library, we have identified IDO or TDO selective inhibitors that belong to different chemical scaffolds from all the reported inhibitors. The *in vitro* activity of the initial screening hits in biochemical assays is improved by conducting lead optimization studies.

CLKs are a class of kinases that regulate the alternative splicing of messenger RNA and are considered attractive drug targets for cancer as well as neurodegenerative disorders. We have discovered a class of benzimidazoles as highly selectively CLK inhibitors that inhibited cancer growth *in vitro* and *in vivo*. Structure-activity relationship study is currently one focus of our research.

ACCOMPLISHMENTS 2016-2017

We have successfully established a number of collaborative research programs that are supported by extramural funding provided by a federal agency or by other sources. Our research has started to bear fruit in a number of dimensions. In addition to the discovery and dissemination of new knowledge (including eight peer-reviewed publications), one major objective of our center is to promote technological and therapeutic innovations that address highly unmet patients needs. One of the technologies invented in our laboratory was licensed by a venture capital firm, which formed the cornerstone platform technology in a biotech startup focusing on the discovery and development of novel anticancer and anti-inflammatory therapies. Further, we are in active discussions for multiple funding or licensing opportunities to advance our innovations toward improving patient care. Thus far, we have filed four U.S. provisional patent applications, and have planned to submit multiple additional applications, based on the inventions from our center:

- Substance P, Mast Cell Degranulation Inhibitors and Peripheral Neuropathy. Application # 62/162,972
- Chalcone Compounds. Application # 62/245,725
- Compounds for treating proliferative diseases. Application # 62/261,240
- Mast-Cell Modulators and uses thereof. Application # 62/278,722

In addition to regularly presenting our research in national and international conferences, I was also an invited speaker/chair in a number of drug discovery conferences, including: 12th Annual Drug Discovery Chemistry in San Diego, CA, 2017, and 14th Annual Mastering Medicinal Chemistry Conference in Boston, MA, 2017 (Session Chair). We have published invited editorial and review article (*Trends in Pharmacol Sci by Cell Press*) in cancer immunotherapy. I also served as a reviewer for the journal *Eur J Med Chem*.

TEACHING, TRAINING, AND EDUCATION

I have been committed to the training of next-generation scientists who are passionate about translational biomedical research. My laboratory has welcomed visiting scholars from medical centers and industrial research institutes to work side by side with research fellows. In addition, we also provided internship opportunities for high school graduates who would enter colleges for higher education in basic and biological science. On numerous occasions, I have provided technical expertise to research fellows from collaborators' laboratories, guided their study designs, and made impactful influence in their scientific development and professional careers. I am inspired by the success of the talented fellows and motivated to transform the center to become a platform of excellence for training and biomedical innovation.

SELECTED RESEARCH SUPPORT

Development of Small Molecule Inhibitors of IL-18 to Prevent Intimal Hyperplasia; NIH, 2016-2018; Co-PI Lijun Sun, PhD (Contact PI: Leena Pradhan- Nabzdyk, PhD)

Targeting activated mast cells in diabetic foot ulcers; Joslin DRC F&P Award, 2015-2016; PI: Lijun Sun, PhD

Facile synthesis of glycosulfopeptides and related bioconjugates; NIH, 2015-2019; Co-Investigator: Lijun Sun, PhD (PI: Elliot Chaikof, MD, PhD)

PSGL-1 glycopeptide mimetic for treatment of metabolic syndrome; NIH, 2016-2020; Co-Investigator: Lijun Sun, PhD (PI: Elliot Chaikof, MD, PhD)

SELECTED PUBLICATIONS

Wang Y, Hedblom A, Koerner SK, Li M, Jernigan FE, Wegiel B, Sun L. Novel synthetic chalcones induce apoptosis in the A549 non-small cell lung cancer cells harboring a KRAS mutation. *Bioorg Med Chem Lett* 2016;26(23):5703-5706.

Koerner SK, Hanai J, Bai S, Jernigan FE, Oki M, Komaba C, Shuto E, Sukhatme VP, Sun L. Design and synthesis of emodin derivatives as novel inhibitors of ATP-citrate lyase. *Eur J Med Chem* 2017;126:920-928.

Jernigan FE, Hanai J, Sukhatme VP, Sun L. Discovery of furan carboxylate derivatives as novel inhibitors of ATP-citrate lyase via virtual high-throughput screening. *Bioorg Med Chem Lett* 2017;27(4):929-935.

Jernigan FE, Sun L. In silico discovery and therapeutic potential of IDO1 and TDO2 inhibitors. *Future Med Chem* 2017;9(12):1309-1311.

Cheong JE, Zaffagni M, Chung, I, Xu Y, Wang Y, Jernigan FE, Zetter BR, Sun L. Synthesis and anticancer activity of novel water soluble benzimidazole carbamates. *Eur J Med Chem* 2017;in press (DOI: 10.1016/j.ejmech.2017.11.037).

Cheong JE, Sun L. Targeting IDO1/TDO2-KYN-AhR pathway for cancer immunotherapy - challenges and opportunities. *Trends Pharmacol Sci* 2017;in press (DOI: 10.1016/j.tips.2017.11.007).

A complete list of publications begins on page 13.



Jeffrey Arle, MD, PhD

Associate Professor of Surgery
Associate Chief, Neurosurgery

RESEARCH FOCUS

Our research efforts have focused on computational modeling of neural stimulation and circuitry related to devices and therapies used in neuromodulation. These therapies include deep brain stimulation (DBS), spinal cord stimulation (SCS), vagus nerve stimulation (VNS), motor cortex stimulation (MCS), and other related aspects of neural processing. Modeling has included circuitry models of the basal ganglia in Parkinson's disease and the DBS electrode in a discrete solution, M1 and S1 regions of cortex with cortico-thalamic processing, three-dimensional modeling of the activating function and fibers of passage, and patterns of stimulation and power in tremor control.

More recently, we have focused on mechanisms of action to treat chronic pain using high frequency and burst type spinal cord stimulation as well as work showing how computational models of neural circuitry can be used to help streamline new drug development in major depressive disorder. We have also worked on a new analysis of theoretical changes in information processing in axons of passage through regions using deep brain stimulation in Parkinson's disease and other disorders. Our work has been presented this past year at the International Neuromodulation Society meeting in Edinburgh, Scotland, the Neuromodulation Society of New Zealand and Australia in Adelaide, Australia, the International Society of Intraoperative Neurophysiology in Seoul, South Korea, the North American Neuromodulation Society meeting in Las Vegas, NV, and the Spine Intervention Society meeting in San Francisco, CA.

In these recent efforts, we have further developed and refined our hypothesis on how high frequency stimulation systems modulate axons, both in suppressing or blocking them as well as in stimulating them. We continue to examine the fundamental mechanisms of neuromodulation therapies, an area of rapidly developing technology and innovation. This work has also been, and continues to be, generously funded by the Sydney Family Foundation in addition to internal funding through the Beth Israel Deaconess Medical Center Department of Surgery.

RESEARCH GROUP

Kristen Carlson
LZ Mei, MS
Jay Shils, PhD

ACCOMPLISHMENTS 2016-2017

Organizational and Academic Work

- Appointed Co-chair of the Research and Scientific Policy Committee for the International Neuromodulation Society
- Appointed Board Member of the International Society of Intraoperative Neurophysiology
- Continued as a member of the North American Neuromodulation Society (NANS) Policy and Advocacy Committee
- Appointed as member of the Epilepsy Foundation of New England Patient Advisory Board
- Continued as Associate Editor at *Neurosurgery*
- Appointed Associate Editor at *Neuromodulation*

Invited Presentations and Meetings

- International Neuromodulation Society meeting, Edinburgh, Scotland, 2017
- Neuromodulation Society of New Zealand and Australia, Adelaide, Australia, 2017
- International Society of Intraoperative Neurophysiology, Seoul, South Korea, 2017
- North American Neuromodulation Society meeting, Las Vegas, NV, 2017
- Spine Intervention Society meeting, San Francisco, CA, 2017

SELECTED RESEARCH SUPPORT

The Sydney Family Foundation

SELECTED PUBLICATIONS

Lytton WW, Arle J, Bobashev G, Ji S, Klassen TL, Marmarelis VZ, Schwaber J, Sherif MA, Sanger TD. Multiscale modeling in the clinic: Diseases of the brain and nervous system. *Brain Inform* 2017;4(4):219-230.

Arle JE and Carlson KW. The use of dynamic computational models of neural circuitry to streamline new drug development. *Drug Discovery Today* 2016;19:69-75.

Deer TR, Lamer TJ, Pope JE, Falowski SM, Provenzano DA, Slavin K, Golovac S, Arle J, Rosenow JM, Williams K, McRoberts P, Narouze S, Eldabe S, Lad SP, De Andrés JA, Buchser E, Rigoard P, Levy RM, Simpson B, Mekhail N. The Neurostimulation Appropriateness Consensus Committee (NACC) safety guidelines for the reduction of severe neurological injury. *Neuromodulation* 2017;20(1):15-30.

Arle JE, Carlson KW, Mei L. Investigation of mechanisms of vagus nerve stimulation for seizure using finite element modeling. *Epilepsy Res* 2016;126:109-18.

Arle JE, Mei L, Carlson KW, Shils JL. High-frequency stimulation of dorsal column axons: Potential underlying mechanism of paresthesia-free neuropathic pain relief. *Neuromodulation* 2016;19(4):385-97.

Arle JE, Mei LZ, Carlson KW and Shils JL. Theoretical effect of DBS on axonal fibers of passage: Firing rates, entropy, and information content. *Stereo Funct Neurosurg* 2018;96(1):1-12.

A complete list of publications begins on page 13.



Christopher S. Ogilvy, MD

Professor of Neurosurgery

Director, Brain Aneurysm Institute

Ajith Thomas, MD

Associate Professor of Neurosurgery

Co-Director, Brain Aneurysm Institute

RESEARCH FOCUS

Clinical Research

Flow Diverter Technology The Brain Aneurysm Institute has been at the forefront of introducing cutting edge technology, such as flow diverters and the new ATLAS stent. We have accumulated one of the largest experiences with flow diverter technology in the world and have been able to add substantially to understanding of the safety and efficacy of this device. Our publications in peer reviewed literature, which number about 25 this past year, are a reflection of this growing practice.

Anticoagulation regimens For endovascular techniques, we have investigated the type of anticoagulation needed to enhance the safety of device delivery. We examined data from our own institution as well as a number of collaborative multi-institutional studies in an attempt to refine the antiplatelet agent regimens and radiographic follow-up for these individuals. We have documented that almost 30% of patients who are non-responders to Clopidogrel warrant treatment with Ticagrelor. By altering these patients' antiplatelet regimen, stroke rates can be reduced dramatically when using intravascular flow diversion.

Management of Dural AV Fistulas We have developed significant expertise in the management of both cranial and spinal dural AV fistulas. As part of this effort, we have introduced a new classification system for cavernous carotid fistulas based on venous drainage to guide treatment and prognosis.

Subarachnoid hemorrhage We have also hypothesized that anti-angiogenic factors, such as soluble Fms-like tyrosine kinase-1 and soluble transforming growth factor co-receptor endoglin, are important contributors to the pathophysiology of delayed cerebral ischemia. Analysis of CSF from subarachnoid hemorrhage patients seems to confirm this hypothesis. The findings were published in *World Neurosurgery*.

Aneurysm Recanalization Stratification Scale We have developed the Aneurysm Recanalization Stratification Scale, which uses accessible predictors including aneurysm-specific factors (size, rupture, and intraluminal thrombosis) and treatment-related features (treatment modality and immediate angiographic result) to predict retreatment risk after endovascular therapy.

Technological and Other Scientific Innovations

In collaboration with Conor Walsh, PhD, at the Harvard School of Engineering and Applied Sciences (SEAS), Dr. Thomas designed a hand-held, portable cranial drilling device that can be used with any diameter drill bit to create holes in the skull without endangering underlying brain tissue. The drill will make it safer for neurosurgeons to penetrate the skull for smaller probes such as intracranial pressure monitors. It will allow healthcare professionals in allied specialties, such as trauma surgery, to place intracranial monitors safely. This project received the 2011 Excellence in Medical Device Design Award from SEAS.

Basic Science

In the laboratory, in collaboration with Christiane Ferran, MD, PhD, Dr. Thomas has been exploring the hypothesis that some of the limitations surrounding neural stem cell

RESEARCH GROUP

Abdulrhaman Alturki, MD
 Luis Ascanio-Cortez, MD
 Kohei Chida, MD
 Alejandro Enrlquez-Marulanda, MD
 Christoph Griessenauer, MD
 Raghav Gupta
 Kimberly Kicielinski, MD
 Georgios Maragos, MD
 Justin Moore, MD, PhD
 Rouzbeh Motiei-Langroudi, MD
 Mohamed Salem, MD

transplantation can be overcome by the addition of periventricular endothelial cells (PvEC) from the embryonic brain. This novel concept is the outgrowth of several recent studies in the area of angiogenesis and neurogenesis, where it is postulated that PvECs migrate in the embryonic brain in a similar manner to neurons, and have a reciprocal relationship in the development of neuronal networks and the vasculature that supports them. Dr. Thomas' project involves characterizing the molecular interactions between neural precursor cells and embryonic derived mouse brain periventricular endothelial cells to show enhanced bidirectional effects on neurogenesis and vasculogenesis. This understanding will inform the optimal conditions for transplanting an appropriate combination of these cells within a mouse focal ischemia model. Publications have resulted from this collaboration, with more in the process.

ACCOMPLISHMENTS 2016-2017

- 2016 Excellence in Clinical Research Mentorship, Department of Surgery (Dr. Ogilvy)
- 2017 Physician Champion Award, The Brain Aneurysm Foundation (Dr. Ogilvy)
- Appointed Associate Member of the Broad Institute (Dr. Thomas)

TEACHING, TRAINING, AND EDUCATION

- J.G. Galbraith Lecture, The University of Alabama at Birmingham Department of Neurosurgery (Dr. Ogilvy)
- BIDMC Site Director, combined BIDMC/Boston Medical Center Neurosurgical Residency Program (Dr. Thomas)
- Fellowship Director, Endovascular and Operative Neurovascular Fellowship, BIDMC (Dr. Thomas)

SELECTED RESEARCH SUPPORT

Griessenauer CJ, Chua M, Hanafy K, Tachie Y, Chen A, LeBlanc R, Patel A, Salem M, Karumanchi A, Ogilvy CS, Thomas A. Anti-angiogenic factor soluble fms-like Tyrosine Kinase-1 (sFlt-1) identifies patients at risk for severe cerebral vasospasm the first day after aneurysmal subarachnoid hemorrhage. Congress of Neurological Surgeons Meeting, Boston MA, 2017 (poster)

Phan K, Dmytriw A, Griessenauer CJ, Moore J, Ogilvy CS, Thomas A. Endovascular thrombectomy alone versus combined intravenous thrombolysis and thrombectomy: A systematic review and Meta-analysis. Congress of Neurological Surgeons Meeting, Boston, MA, 2017 (poster)

Schmalz P, Sneh G, Alturki A, Stapleton CJ, Thomas A, Ogilvy CS. Outcome of combined endovascular and surgical treatment of unruptured anterior communicating artery aneurysm: Changing indications for intervention in the modern era. Congress of Neurological Surgeons Meeting, Boston, MA, 2017 (poster)

Adeeb N, Ogilvy CS, Hussain S, Hakeem S, Moore J, Foreman P, Dmytriw A, Gupta R, Limbucci N, Mangiafico S, Kumar A, Michelozzi C, Zhang Y, Pereira V, Matouk C, Harrigan M, Siddiqui A, Levy E, Renieri L, Marotta T, Cognard C, Thomas A. Incidence of branch occlusion and ischemic complications following pipeline embolization of posterior circulation aneurysm. Congress of Neurological Surgeons Meeting, Boston, MA, 2017 (poster)

Motiei-Langroudi R, Stippler M, Alturki A, Griessenauer E, Kasper E, Arle J, Alterman R, Ogilvy CS, Thomas A. Factors predicting the need for surgery of the opposite side after unilateral evacuation of bilateral chronic subdural hematomas. Congress of Neurological Surgeons Meeting, Boston, MA, 2017 (poster)

SELECTED PUBLICATIONS

Adeeb N, Griessenauer CJ, Foreman PM, Moore JM, Shallwani H, Motiei-Langroudi R, Alturki A, Siddiqui AH, Levy EI, Harrigan MR, Ogilvy CS, Thomas AJ. Use of platelet function testing before pipeline embolization device placement: A multicenter cohort study. *Stroke* 2017;48(5):1322-1330.

Griessenauer J, Adeeb N, Foreman PM, Gupta R, Patel AS, Moore J, Abud TG, Thomas AJ, Ogilvy CS, Baccin CE. Impact of coil packing density and coiling technique on occlusion rates for aneurysms treated with stent-assisted coil embolization. *World Neurosurg* 2016;94:157-166.

Griessenauer CJ, Ogilvy CS, Foreman PM, Chua MH, Harrigan MR, He L, Fusco MR, Mocco JD, Stapleton CJ, Patel AB, Sonig A, Siddiqui AH, Thomas AJ. Pipeline embolization device for small intracranial aneurysms: Evaluation of safety and efficacy in a multicenter cohort. *Neurosurgery* 2017;80(4):579-587.

Gupta R, Moore JM, Adeeb N, Griessenauer CJ, Patel AS, Chua MH, Thomas AJ, Ogilvy CS. Clinical presentation, progression, and treatment outcomes of moyamoya disease in the elderly. *Acta Neurochir (Wien)* 2016;158(12):2409-2414.

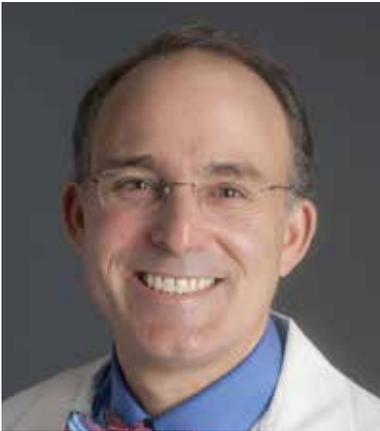
Gupta R, Moore JM, Griessenauer CJ, Adeeb N, Patel AS, Youn R, Poliskey K, Thomas AJ, Ogilvy CS. Assessment of dual-antiplatelet regimen for pipeline embolization device placement: A survey of major academic neurovascular centers in the United States. *World Neurosurg* 2016;96:285-292.

Ogilvy CS, Motiei-Langroudi R, Ghorbani M, Griessenauer CJ, Alturki AY, Thomas AJ. Flow diverters as useful adjunct to traditional endovascular techniques in treatment of direct carotid-cavernous fistulas. *World Neurosurg* 2017;105:812-817.

A complete list of publications begins on page 13.

Jorge G. Arroyo, MD, MPH

Associate Professor of Ophthalmology



RESEARCH GROUP

Yousef Aldairy, MD
 Mohamed Elmasry, MD
 Efen Gonzalez, MD
 Mark Kuperwasser, MD
 Michael Lewen, MD
 Alex Pisig, MD
 Steven Reinecke, MD
 Peng Sun, MD
 Rachel Tandias

RESEARCH FOCUS

Our research focuses on the efficacy and outcomes of novel ophthalmologic surgical techniques, treatment options and imaging for vitreomacular traction, development of an ophthalmic tissue repository, and predictive measures for visual and anatomical success following treatment for retinal diseases.

Surgical Techniques

Endoscopic visualization of the peripheral retina and ciliary body is a valuable tool in vitreoretinal surgery. We are currently conducting two retrospective case series to evaluate the use of endoscopy in (1) ciliary body membrane peeling for patients with ocular hypotony and (2) pars plana vitrectomy with retinectomy for complex retinal detachments complicated by severe proliferative vitreoretinopathy. Our data suggest that while use of the endoscope increases surgical duration, endoscopic vitreoretinal visualization aids in therapeutic and preventative maneuvers, and limits the use of additional intraoperative supplies.

Hypotony is a relatively common postoperative complication for which treatment, either by pharmacologic or surgical means, remains challenging. Our preliminary data suggest that endoscopy-assisted ciliary body membrane peeling has favorable effects in increasing intraocular pressure and stabilizing visual acuity in eyes with chronic hypotony after surgical retinal detachment repair. We have also identified several factors that are correlated with favorable visual and anatomical prognosis following ciliary body membrane peeling.

Vitreomacular Traction: Treatment and Imaging Analysis

Vitreomacular traction (VMT) results when abnormally strong vitreomacular adhesions (VMA) between the vitreous and retina cause tugging of the retina as the vitreous contracts, resulting in distortion of the neurosensory retina, which can lead to vision loss. We conducted a retrospective case series to compare all available treatment options for patients diagnosed with VMT. We also performed a meta-analysis of published literature to assess the rate of VMT resolution among patients who received one of three options: a control injection of saline, intravitreal ocriplasmin (IVO), or pneumatic vitreolysis (PV, the intravitreal injection of an expansile gas with intermittent face down positioning). Our case series confirmed that pars plana vitrectomy has the highest efficacy in treating VMT, as compared with the other nonsurgical options. Both our case series and meta-analysis showed that PV had a higher rate of VMT resolution compared with IVO at Day 28 post-treatment.

We also published a case report describing a patient with resistant VMT successfully treated with an intravitreal injection of a lower dose of ocriplasmin and a residual intravitreal gas bubble from pneumatic vitreolysis. Our report showed the efficacy of combining the mechanical forces of PV with the enzymatic fibrinolytic activity available in a lower dose of ocriplasmin to treat resistant VMT cases, non-invasively.

We have also conducted a study to investigate the value of imaging via spectral-domain optical coherence tomography (SD-OCT) in predicting changes in acuity following successful treatment for VMT. Our results show that recovery of the cone outer segment tips (COST) line and inner segment/outer segment (IS/OS) line defects as observed by SD-OCT is positively correlated with visual acuity improvement after successful VMT treatment.

Presentations

In May 2017, our research team attended the annual meeting for the Association for Research in Vision and Ophthalmology (ARVO) in Baltimore. We presented our work on endoscopy-assisted retinectomy for complex retinal detachments as well as our findings regarding the capacity of SD-OCT to predict visual outcomes following surgery for VMT. In 2017, I also presented our findings on macular hole formation following pneumatic vitreolysis for vitreomacular traction at the Retina Society and the Macula Society.

Ongoing Projects

Consistent with our interest in studying novel treatments for vitreomacular traction (VMT), we are currently investigating the efficacy of pneumatic vitreolysis (PV) for symptomatic VMT in eyes with and without macular holes. In our current case series, we have found that PV successfully released VMT in all eyes with early or full thickness macular holes (FTMH). However, MH closure was not achieved in any eyes with full thickness MH following PV alone. Our preliminary analysis suggests that foveal thinning is a risk factor for the development of FTMH and that PV alone may be ineffective in treating cases of VMT associated with FTMH.

We have continued to utilize our database of nearly 20 years of clinical and surgical data from the BIDMC retina service to compare treatments and study outcomes and predictive factors for various retinal conditions. We are currently conducting a retrospective comparison of outcomes following different types of retinal detachment repair, including pars plana vitrectomy, scleral buckle with and without vitrectomy, and pneumatic retinopathy. We are also examining long-term visual and anatomical outcomes of choroidal detachment repair in a small case series. In addition, we are investigating the association between the condition of the posterior vitreous, classified as one of five stages, and postoperative measures following vitrectomy for ocular complications associated with diabetes.

TEACHING, TRAINING, AND EDUCATION

I have continued to train rotating residents, fellows, and medical school students from around the world in clinical, surgical, and research settings. We have welcomed several new members to our Retina Service and clinical research team, including ocular oncology specialist Dr. Efrén Gonzalez, BIDMC-Lahey Hospital surgical fellows Dr. Steven Reinecke and Dr. Michael Lewen, and BIDMC-Joslin Diabetes Center medical retina fellows Dr. Yousef Aldairy, Dr. Mohamed Elmasry, and Dr. Alex Pisig. Dr. Peng Sun of the First Hospital of China Medical University in Shenyang is completing a 2-year International Retina Research Fellowship with our department. We are working with four Boston University Master's students conducting their clinical research theses with our group. Rachel Tandias is our current clinical research assistant.

SELECTED RESEARCH SUPPORT

Tandias R, Sun P, Arroyo JG. Outcomes of Relaxing Retinotomy for Rhegmatogenous Retinal Detachment with Proliferative Vitreoretinopathy. Poster presented at the annual meeting of the Association for Research in Vision and Ophthalmology (ARVO), Baltimore, MD, 2017.

Sun P, Tandias R, Yu G, Arroyo JG. Correlation between macular features in spectral-domain optical coherence tomography images and visual outcome after vitreomacular traction surgery. Poster presented at the annual meeting of the Association for Research in Vision and Ophthalmology (ARVO), Baltimore, MD, 2017.

Yu G, Sun P, Van Zyl T, Tandias R, Arroyo JG. Bilateral Central Retinal Vein Occlusions in a Young Patient with a History of Eosinophilic Pneumonia and Thalamic Stroke. Retin Cases Brief Rep 2016;Dec 29:Epub ahead of print.

Arroyo JG, Yu G, Tandias R, Wagley S. Pneumo-Enzymatic Vitreolysis for Resistant Vitreomacular Traction. Ann Clin Case Rep 2016;1(1104):1-2.

Yu G, Duguay J, Marra KV, Gautam S, Le Guern G, Begum S, Sharifzadeh A, Arroyo JG. Efficacy and safety of treatment options for vitreomacular traction: A Case Series and Meta-Analysis. Retina 2016 Jul;36(7):1260-70.

Chang JS, Marra K, Flynn HW Jr, Berrocal AM, Arroyo JG. Scleral Buckling in the Treatment of Retinal Detachment Due to Retinal Dialysis. Ophthalmic Surg Lasers Imaging Retina 2016 Apr 1;47(4):336-40.

Marra KV, Wagley S, Kuperwaser MC, Campo R, Arroyo JG. Care of Older Adults: Role of Primary Care Physicians in the Treatment of Cataracts and Macular Degeneration. J Am Geriatr Soc 2016 Feb;64(2):369-77.

Nurhan Torun, MD

Chief of Ophthalmology

Assistant Professor of Ophthalmology



RESEARCH GROUP

Marc A. Bouffard, MD

Edsel Ing, MD

RESEARCH FOCUS

My research in 2016-2017 focused on investigating newer non-invasive tests for giant cell arteritis (GCA). GCA is the most common vasculitis of the elderly and causes irreversible blindness in up to 20 percent of patients. GCA can be a diagnostic conundrum when it presents in an atypical or occult fashion. There is no highly specific biomarker for GCA to date. Blood tests for inflammation have limited sensitivity, and "seronegative" GCA can occur in up to 4 percent of patients. The 1990 American College of Rheumatology (ACR) classification criteria for GCA are not diagnostic criteria. Although TABx is an invasive and time-consuming test, most authorities feel that it remains the gold standard for the diagnosis of GCA.

Although the most common complication of GCA is visual loss, most clinical prediction algorithms for GCA do not incorporate an ocular blood flow measurement. Possible methods to assess reduction in blood flow in GCA include fluorescein angiography, oculoplethysmography, dynamic contour tonometry, and OCT angiography. Delayed choroidal filling greater than 20 seconds on fluorescein angiography is suggestive but not specific for GCA. In patients with GCA, Dr. Thomas Bosley (Johns Hopkins University) showed there is reduced ocular pulse amplitude with his pneumo-oculoplethysmography (OPG) technique. OPG is a cumbersome technique that is rarely performed nowadays.

Pascal Dynamic contour tonometry was popularized for glaucoma over the last decade. Dynamic contour tonometry (DCT) provides a digital readout of intraocular pressure as well as an estimation of the ocular pulse amplitude (OPA). The OPA is the difference in intraocular pressure during the cardiac cycle, and represents the pulsatile wave front produced by the varying amount of choroidal blood flow between systole and diastole. The DCT painlessly estimates the OPA and ocular blood flow in 7 seconds. In collaboration with a group at the University of Toronto, we hypothesized that the DCT OPA would be reduced in patients with positive TABx compared with negative TABx. All patients undergoing TABx for suspected GCA were included in this prospective, multicenter study. On univariate logistic regression, only the average ocular pulse amplitude and platelet count showed a statistically significant difference between the biopsy groups. Age, CRP, biopsy length, and jaw claudication did not show a statistically significant difference on univariate logistic regression. We found OPA to be inversely related to the risk of GCA and to be a statistically significant predictor of positive TABx; we concluded that it can be incorporated as part of a prediction rule for GCA (Figure 1).

In addition, our project "Oculomotor Assessment as a Potential Biomarker for Huntington's Disease," for which I am collaborating with Dr. Wasim Malik (Massachusetts General Hospital) and Dr. Samuel Frank (BIDMC), was funded by the Huntington's Disease Society of America. The major goals of this project are to develop a novel eye-movement based paradigm for assessment, diagnosis and progression monitoring of Huntington's disease (HD), using a convenient and portable eye-tracking system, and to develop a novel quantitative biomarker for early diagnosis of HD, leading to better detection, improved clinical management, and therapy development for this disease.

FIGURE 1: Box plots of our a priori predictor variables comparing negative and positive biopsy groups

ACCOMPLISHMENTS 2016-2017

- I was selected for the Physician Leadership Program at BIDMC for 2017-2018.
- In July 2017, I was invited to Waterville, Maine, to give the following four one-hour talks at the Lancaster Course, one of the largest ophthalmology review courses given to national and international ophthalmologists and residents. I was asked to deliver the same talks again in July 2018:
 - Pearls and Pitfalls of Neuro-ophthalmic Examination
 - Neuro-ophthalmic Emergencies
 - Central Processing Disorders of Vision
 - Ocular Myasthenia and Extraocular Myopathies
- I was the primary thesis advisor to Anh-Dao Cheng (former Boston University MSc candidate, currently enrolled in Boston University Medical School) for her MSc Thesis: Optic Nerve Atrophy: How Sensitive is MRI Determined Optic Nerve Size Compared to Optical Coherence Tomography (OCT)?
- I accepted an invitation to give a talk on Electrophysiological testing in Neuro-ophthalmology at the New England Ophthalmological Society Meeting in June 2018.
- I was invited to give Thorndike lecture series talk to internal medicine residents at BIDMC on Ophthalmic Emergencies in September 2017.
- I was the guest speaker at Parkinson's Disease Baby Boomer Support Group in June 2017 and discussed vision related problems in Parkinson's Disease.

TEACHING, TRAINING, AND EDUCATION

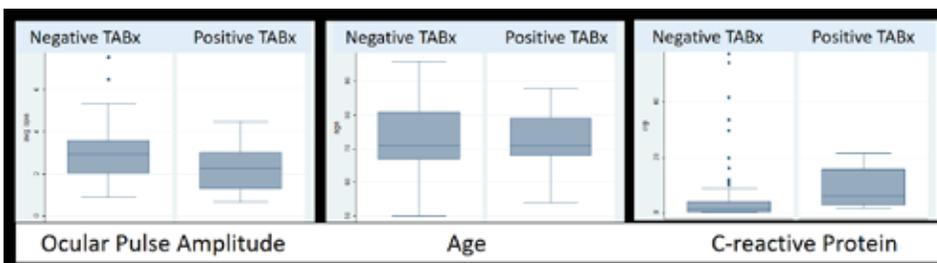
I am involved in didactic and bedside teaching of residents. I developed a curriculum of 12 core neuro-ophthalmology lectures that I delivered each year to neurology residents at BIDMC. I supervise ophthalmology residents in my comprehensive ophthalmology clinics and while doing on-call duty. I am actively involved in surgical teaching of ophthalmology residents as well.

I am also one of the instructors teaching the Core Medicine Ophthalmology Course to Harvard Medical School students in the Longwood Medical Area; this involves 8 to 10 two-hour lectures each year.

Since 2015, I have been one of the Neuro-ophthalmology Fellowship Preceptors for the Harvard Neuro-ophthalmology Fellowship

SELECTED RESEARCH SUPPORT

Oculomotor Assessment as a Potential Biomarker for Huntington's Disease; Huntington's Disease Society of America, 2016-2018; Co-investigators: Nurhan Torun, MD and Samuel Frank, MD (PI: Wasim Q. Malik, PhD)



SELECTED PUBLICATIONS

- Gaier ED, Torun N. The enigma of NAION: An update for the comprehensive ophthalmologist. *Curr Opin Ophthalmol* 2016;27(6):498-504.
- Bouffard MA, Nathavitharana R, Yassa D, Torun N. Retreatment with ethambutol after toxic optic neuropathy. *J Neuroophthalmol* 2017;37(1):40-42.
- Bouffard MA, Torun N. Divergence Palsy due to Divalproex and Oxcarbazepine. *Clin Neuropharmacol* 2017;40(3):154-155.
- Bouffard MA, Cornblath W, Rizzo III JF, Lee MS, DeLott LB, Eggenberger E, Torun N. Transient Monocular Vision Loss Upon Awakening: A Benign Amaurosis Phenomenon. *J Neuroophthalmol* 2017;37(2):122-125.
- Ravindran K, Schmalz P, Torun N, Ronthal M, Chang YM, Thomas AJ. Angiographic Findings in the Tolosa-Hunt Syndrome and Resolution after Corticosteroid Treatment. *Neuroophthalmology* 2017;42(3):159-163.
- Ing E, Pagnoux C, Tyndel F, Sundaram A, Hershenfeld S, Ranalli P, Chow S, Le T, Lutchman C, Rutherford S, Lam K, Bedi H, Torun N. Lower dynamic contour tonometry ocular pulse amplitude is associated with biopsy-proven giant cell arteritis. *Can J Ophthalmol* 2018;53(3):215-221.

A complete list of publications begins on page 13.



Scharukh Jalisi, MD, MA, FACS

Chief, Otolaryngology/Head and Neck Surgeon

RESEARCH FOCUS

I joined BIDMC in 2017 with my main focus of research being outcomes in head and neck cancer, economic impact of head and neck surgical oncology, and clinical trials pertaining to head and neck cancer. At present the group is working on establishing a core clinical research program. With increasing patient volume we are also working on offering clinical trials through the division.

ACCOMPLISHMENTS 2016-2017

- Appointed Chief of Otolaryngology/Head and Neck Surgery at BIDMC in 2017 (Dr. Jalisi)
- Appointed to the Scientific Review Committee of the 2020 International Head and Neck Conference scheduled in Chicago (Dr. Jalisi)
- Invited to speak about outcomes in head and neck surgical oncology at the University of Arizona, and the University of California at Irvine (Dr. Jalisi)
- Lectured on microvascular reconstruction and cranial base surgery at Louisiana State University, New Orleans (Dr. Jalisi)
- Invited to speak about cranial base surgery at Tulane University (Dr. Jalisi)
- Invited to speak about outcomes in head and neck surgical oncology and disparities in head and neck oncologic management at the ENT Society meeting in London, England (Dr. Jalisi)
- Presented Core Curriculum in Primary Care: Laryngologic Emergencies at Beth Israel Deaconess Hospital–Needham (Dr. Mallur)
- Presented Harvard Otolaryngology Update: Management of Benign Laryngeal Lesions (Dr. Mallur)
- Participated in invitation-only round table group, Advances and Controversies in Laryngology (Dr. Mallur)

RESEARCH GROUP

David Caradonna, MD
Pavan Mallur, MD

TEACHING, TRAINING, AND EDUCATION

- I was director of the head and neck surgical oncology and microvascular fellowship at Boston Medical Center, and intend to start a fellowship program at BIDMC
- I am providing head and neck surgical oncology training to the Combined Harvard Otolaryngology residents
- I taught second-year Harvard Medical School students during their Otolaryngology Elective
- I provide Head and Neck Surgery training for PGY 3 General Surgery residents at BIDMC
- I established the Head and Neck Nursing Education Program at BIDMC

SELECTED PUBLICATIONS

Jalisi S, Rubin SJ, Wu KY, Kirke DN. Outcomes of head and neck cancer surgery in the geriatric population based on case volume at academic centers. *Laryngoscope* 2017;127(11):2539-2544.

Rubin SJ, Cohen MB, Kirke DN, Qureshi MM, Truong MT, Jalisi S. Comparison of facility type outcomes for oral cavity cancer: Analysis of the national cancer database. *Laryngoscope* 2017;127(11):2551-2557.

Jamal BT, Grillone GA, Jalisi S. Chemoresponse Assay in Head and Neck Cancer Patients: A Three-Year Follow Up. *J Clin Diagn Res* 2017;11(5):XC01-XC03.

McDonough K, Crimlisk J, Nicholas P, Cabral H, Quinn EK, Jalisi S. Standardizing nurse training strategies to improve knowledge and self-efficacy with tracheostomy and laryngectomy care. *Appl Nurs Res* 2016;32:212-216.

Kirke DN, Chitguppi C, Rubin SJ, Truong MT, Jalisi S. Adenoid cystic carcinoma of the base of tongue: A population-based study. *Am J Otolaryngol* 2017;38(3):279-284.

Rubin SJ, Kirke DN, Ezzat WH, Truong MT, Salama AR, Jalisi S. Marital status as a predictor of survival in patients with human papilloma virus-positive oropharyngeal cancer. *Am J Otolaryngol* 2017;38(6):654-659.

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Bernard T. Lee, MD, MBA, MPH

Professor of Surgery

Chief, Plastic and Reconstructive Surgery

Co-Director, Peter Jay Sharp Program in Aesthetic and Reconstructive Breast Surgery

RESEARCH GROUP

Justin Cohen, MD, MHS
Andres Doval, MD
Sherise Epstein, MD
Andreas Lamelas, MD
Joseph Ricci, MD
Qing Ruan, MD
Bao Ngoc Tran, MD



▲ FIGURE 1: Vascular pedicle of a hemifacial flap model prior to face transplantation

RESEARCH FOCUS

Over the last several years, my basic science research has focused on near infrared imaging (NIR) technologies to identify perfusion characteristics of flaps in reconstructive surgery. In collaboration with Dr. John V. Frangioni (BIDMC), we are using two imaging modalities: Fluorescence-Assisted Resection and Exploration (FLARE) system and Spatial Frequency Domain Imaging (SFDI). We have successfully translated this technology from large animal models to first-in-human clinical trials.

Moreover, by virtue of our results using these technologies and with the collaboration of Dr. Hak Soo Choi (Massachusetts General Hospital), we want to advance in the knowledge of vascularized composite allotransplantation (VCA) by combining immunohistochemically techniques with our well-developed NIR technologies in order to detect early signs of graft rejection. We are working to develop small and large animal protocols to start our research in this field for reconstructive surgery.

Finally, our clinical research group is examining outcomes and patient satisfaction after breast cancer and reconstructive surgery. Using a large institutional database at BIDMC, as well as national databases from the ACS-NSQIP, we have been able to explore risk factors that lead to complications. In addition, we have been able to understand the relationships between type of reconstruction and patient satisfaction. Most recently, we have been examining patient access, health literacy, and readability of online resources for plastic surgery as well as metrics related with plastic surgeons academic output.

Near infrared imaging systems

Our most recent studies have focused on using the FLARE system to examine perfusion and thrombosis in microsurgery. Using a fluorophore such as indocyanine green, we can identify areas of occlusion and thrombosis within the vasculature. This enables us to resect and repair vessels and identify reestablished perfusion with the FLARE system. This allows assessment of real-time perfusion characteristics and image guidance during surgery. We also are examining near infrared imaging using different fluorophores in transplant rejection models.

In a separate face transplantation model, we are using SFDI to identify perfusion characteristics by targeting tissue constituents (such as hemoglobin). Through the use of this imaging system, we can examine oxygenation of our face transplantation models over a large field of view. In conjunction with surface profilometry, we can provide gradient maps of three-dimensionally complex reconstructive flaps with a single capture snapshot for guidance in the operating room and during surgery. We have successfully translated this technology for use in a clinical trial in patients undergoing breast reconstruction.

Patient access and health literacy in plastic and reconstructive surgery

Our clinical outcomes research team has extensively examined the area of health literacy and patient access. The AMA and NIH guidelines are for patient-directed health literature to be written at a sixth grade level. Unfortunately, most patient resources are well above this level. Our group has examined online patient resources and their readability for patients not only in the English-speaking population but also in the Spanish-speaking population. Finally, our group is also designing new patient materials at appropriate reading levels to evaluate their use in patient education.

ACCOMPLISHMENTS 2016-2017

I am currently the Chief of the Division of Plastic and Reconstructive Surgery at BIDMC. I serve on multiple national committees at the American Society of Plastic Surgeons (In-Service Examination, Scientific Program and Instructional Course, Health Policy, and Healthcare Delivery Committees), American Society for Reconstructive Microsurgery (Treasurer-Elect, Finance, and Future Growth Committees), and American Association of Plastic Surgeons (Program Committee). I am also the co-chair of the performance measures work group on autologous breast reconstruction for the American Society of Plastic Surgeons.

Our research team has been awarded the Commission on Cancer Best Paper Award at the Massachusetts Chapter of the American College of Surgeons meeting, Best Overall Manuscript Award at the Association for Academic Surgery meeting, Joseph E. Murray Best Resident Presentation Award at the New England Society of Plastic and Reconstructive Surgeons meeting, and Best Resident Presentation Award in Breast Reconstruction at the American Society of Plastic Surgeons meeting.

I am currently the Editor-in-Chief of the *Journal of Reconstructive Microsurgery* and serve on the editorial boards of *Annals of Plastic Surgery*, *Journal of Plastic, Reconstructive, & Aesthetic Surgery*, and *ePlasty*. I am also an editor of a two-volume textbook on reconstructive surgery, *Encyclopedia of Flaps*.

TEACHING, TRAINING, AND EDUCATION

I have been training medical students, general surgery and plastic surgery residents, clinical fellows, and research fellows for over a decade. We have had multiple students from Harvard Medical School (HMS) as well as international students working on our research team. I serve as the course director for the plastic surgery medical student clerkship at BIDMC, as a mentor in the Holmes Society, and as a mentor for medical students and residents applying to plastic surgery residency programs. I was awarded the Young Mentor Award by HMS in 2012, Harvard Plastic Surgery Residency Teaching Award in 2013, and BIDMC Department of Surgery Clinical Research Mentorship Award in 2017.

Invited Presentations

- Medial row perforators are associated with higher rates of fat necrosis in bilateral DIEP breast reconstruction, Academic Surgical Congress meeting
- The impact of timing of radiation in implant based breast reconstruction: A systematic review, Academic Surgical Congress meeting
- Health literacy in surgery: Breast cancer and reconstruction, Department of Surgery Grand Rounds, American Society of Plastic Surgeons/Plastic Surgery Foundation (ASPS/PSF) Visiting Professor and Lecturer, University of Missouri-Columbia
- Improving outcomes in breast reconstruction, Plastic Surgery Division Rounds, ASPS/PSF Visiting Professor and Lecturer, University of Colorado
- What's trending at the *Journal of Reconstructive Microsurgery* and an Introduction to the journal publication process, World Society for Reconstructive Microsurgery Meeting; Seoul, Korea
- Work related musculoskeletal disorders among plastic surgeons: A systematic review, World Society for Reconstructive Microsurgery Meeting; Seoul, Korea
- DIEP flaps in women with abdominal scars: A comparison of complication rates between different abdominal incisions; American Society for Reconstructive Microsurgery
- Does hormone therapy use increase perioperative complications in abdominal based microsurgical breast reconstruction? American Association of Plastic and Reconstructive Surgery

SELECTED PUBLICATIONS

Lee BT, Agarwal JP, Ascherman JA, Caterson SA, Gray DD, Hollenbeck ST, Khan SA, Loeding L, Mahabir RC, Miller AS, Perdakis G, Schwartz JS, Sieling BA, Thoma A, Wolfman J, Wright JL. Evidence-based clinical practice guideline: autologous breast reconstruction with DIEP or pedicled TRAM abdominal flaps. *Plast Reconstr Surg* 2017;140:651-664e.

Wada H, Vargas C, Angelo J, Faulkner-Jones B, Paul MA, Ho O, Lee BT, Frangioni JV. Accurate prediction of tissue viability at post-operative day 7 using only 2 intraoperative sub-second near-infrared fluorescence images. *Plast Reconstr Surg* 2017; 139(2):354-363.

Ricci JA, Vargas CR, Ho OA, Lin SJ, Tobias AM, Lee BT. Evaluating the use of tissue oximetry to decrease intensive unit monitoring for free flap breast reconstruction. *Ann Plast Surg* 2017;79:42-46.

Epstein S, Sparer EH, Tran BN, Ruan QZ, Dennerlein JT, Singhal D, Lee BT. Prevalence of work-related musculoskeletal disorders among surgeons and interventionalists: a meta-analysis. *JAMA Surg* 2018;153(2):e174947.

Tran BN, Fadayomi A, Lin SJ, Singhal D, Lee BT. Cost analysis of postmastectomy reconstruction: a comparison of two-staged implant reconstruction using tissue expander and acellular dermal matrix with abdominal based perforator free flaps. *J Surg Oncol* 2017;116:439-447.

Ricci JA, Kamali P, Becherer BE, Curiel D, Wu W, Tobias AM, Lin SJ, Lee BT. Umbilical necrosis rates after abdominal based microsurgical breast reconstruction. *J Surg Res* 2017;215:257-263.

SELECTED RESEARCH SUPPORT

Real-time flap viability monitoring during facial transplantation using SFDI; NIH, 2013-2018; PIs: John V. Frangioni, MD, PhD, and Bernard T. Lee, MD, MBA, MPH

Intraoperative near-infrared fluorescence imaging; NIH, 2010-2015; Co-Investigator: Bernard T. Lee, MD, MBA, MPH (PI: John V. Frangioni, MD, PhD)

A complete list of publications begins on page 13.



Samuel J. Lin, MD

Associate Professor of Surgery

Program Director, BIDMC/Harvard Medical School Plastic Surgery
Residency

RESEARCH FOCUS

Over the past year, my focus continues to be both basic and clinical research across a spectrum of disciplines in plastic and reconstructive surgery. These are collaborative projects utilizing the expertise and experiences of scientists, engineers, and clinicians. Our main collaborators include: Massachusetts Institute of Technology (MIT), Tufts University, Massachusetts General Hospital/Wellman Center for Photomedicine, and Boston Children's Hospital.

RESEARCH GROUP

Austin D. Chen
Sabine A. Egeler, MD
Anna Rose Johnson, BA, MPH
Masoud Malyar, MD
Abbas Peymani, MD

Electrochemical activation and inhibition of neuromuscular systems with modulation of ion concentrations using ion-selective membranes

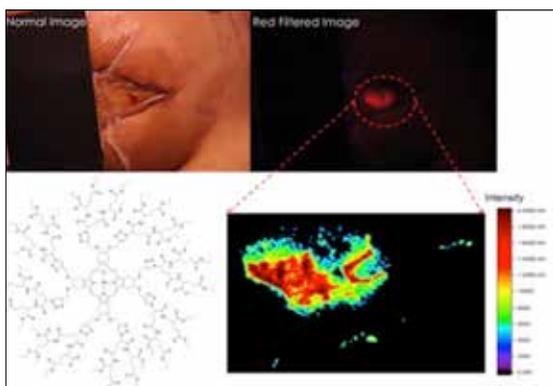
This project is a collaborative effort with MIT since 2008. Our pilot data was published in *Nature Materials* on October 2011. The primary focus of our work is the development of an electrochemical nerve stimulation and blocking method via local modulation of ion concentrations at the peripheral nerve surface using a microelectromechanical systems (MEMS) device. Our goal is to fabricate innovative neuroprosthetic devices that can reduce the threshold for nerve stimulation to aid in paralysis/paresis and/or block nerve firing to reduce pain for conditions such as facial nerve paralysis, chronic pain, and nerve dysfunction syndromes.

Use of silk-based orthopedic devices to modulate healing

This project is a collaborative effort with scientists and engineers at Tufts University in which we are developing degradable silk protein-based orthopedic devices (screws and plates). Our pilot data was published in *Nature Communications* on March 2014. These devices may be able to provide immediate surgical stabilization for orthopedic repair, promote active repair, and reduce infections by releasing therapeutics, and also be fully degrading, avoiding the need for future surgeries for removal.

Use of novel oxygen-sensing paint-on liquid bandage for tissue oxygenation monitoring

This project is a collaborative effort with the Wellman Center for Photomedicine/Massachusetts General Hospital in which we are developing a novel oxygen-sensing paint-on liquid bandage (see Figure 1) for use in perioperative tissue oxygenation monitoring following microvascular free tissue reconstruction. Our pilot animal model data was published in *Plastic and Reconstructive Surgery* on July 2017, and we have since conducted a first in-human trial. This technology may be able to address limitations of the gold standard in tissue oxygenation monitoring. It has potential to improve flap failure rates by providing timely and accurate data to guide decision-making.



▲ FIGURE 1: A novel oxygen-sensing paint-on liquid bandage is being tested for use in perioperative tissue oxygenation monitoring.

3D printing in plastic surgery

We have been also focused on other applications of 3D printing, e.g. 3D printed surgical tools for use in plastic surgery either through customized implants or surgical planning. Potential applications in regards to our other basic science research include the use of 3D printing for production of silk screws and plates.

Outcomes research in plastic surgery

We also have an active clinical research group examining outcomes, techniques, and patient satisfaction following reconstructive and aesthetic plastic surgery procedures, including the head and neck, breast, and abdominal areas. Using large institutional databases at BIDMC, as well as national databases from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP), Healthcare Cost and Utilization Project (HCUP), we have been able to explore risk factors that lead to complications, trends over time, healthcare disparities, and cost analysis.

ACCOMPLISHMENTS 2016-2017

- Over the last year, I have been focused upon the continued development of medical devices that derive from our research in electrical stimulation and neural blocking, bioresorbable devices, and oxygen-sensing paint-on liquid bandage.
- I served as a grant reviewer of the Netherlands Organization for Scientific Research, ZonMW, and Small Business, National Institutes of Health, Musculoskeletal Oral and Skin Sciences (NIH/MOSS).
- I continued writing plastic and reconstructive surgery books, atlases, and books chapters, with recent projects in the past year being:
 - 1) Lee M, Lin SJ. Scapular/Parascapular Cutaneous Flaps. In: Butler C, Hanasono M, editors. Handbook of Reconstructive Flaps. Submitted August 2016.
 - 2) Xu G, Hwang P, Lin SJ. Rhinoplasty. In Orgill D, editor. Scientific American Plastic Surgery. Submitted August 2016.
 - 3) Irizarry D, Lin SJ. Plastic Surgery. In Jones D, editor, Pocket Surgery. In press, July 2017.
- My editorial activities include continuing to serve as Academic Editor of Public Library of Science (*PLoS One*), Associate Editor of *Plastic and Reconstructive Surgery*, and Associate Editor of *Plastic and Reconstructive Surgery-Global Open*. I was recently selected to serve as Section Editor for the *Outcomes Section in Plastic and Reconstructive Surgery*.
- I also continued as ad hoc reviewer for: *Plastic and Reconstructive Surgery*, *Annals of Plastic Surgery*, *The Laryngoscope*, *Microsurgery*, *Journal of Neurology*, *Neurosurgery*, and *Psychiatry, Head and Neck*, *International Journal of Surgery Case Reports*, and the *International Journal of Surgery*.
- I was also an invited speaker at a number of regional, national, and international meetings.

Awards

- 2016; Nomination, Daniel D Federer Teaching Award (Harvard Medical School)
- 2016; MCACS Annual Meeting Commission on Cancer Best Manuscript Award
- 2017; Association of Surgeons in Training/Otolaryngology Trainees Manuscript (ASiT/AOT) Award
- 2017; Association of Surgeons in Training/Plastic Surgery Trainees Association Manuscript (ASiT/PLASTA) Prize
- 2017; Joseph E. Murray Manuscript Award Recipient, New England Society of Plastic Surgeons
- 2017; Best International Collaboration – Bronze, Plastic and Reconstructive Surgery-Global Open

TEACHING, TRAINING, AND EDUCATION

I have been training medical students, general surgery, and plastic surgery residents, clinical and research fellows for the past 10 years at BIDMC. Currently, I serve as the Program Director of the BIDMC/Harvard Medical School Plastic Surgery Residency Program. In this role, I oversee the medical education and experience of residents who rotate on plastic surgery, organizing a microsurgery lab for the residents and presenting on a range of topics for didactics. I am also the co-director of the Aesthetic and Reconstructive Plastic Surgery Fellowship. In addition to my work with fellows and residents, I help mentor medical students from Harvard Medical School (HMS) and other U.S. and international medical schools.

SELECTED PUBLICATIONS

- Branford O, Kamali P, Rohrich RJ, Song DH, Mallucci P, Liu DZ, Lang D, Sun K, Stubican M, Lin SJ. #PlasticSurgery. *Plast Reconstr Surg* 2016;138(6):1354-1365.
- Li C, Hotz B, Ling S, Guo J, Haas DS, Marelli B, Omenetto F, Lin SJ, Kaplan DL. Regenerated silk materials for functionalized silk orthopedic devices by mimicking natural processing. *Biomaterials* 2016;110:24-33.
- Rodriguez MJ, Brown J, Giordano J, Lin SJ, Omenetto FG, Kaplan DL. Silk based bioinks for soft tissue reconstruction using 3-dimensional (3D) printing with in vitro and in vivo assessments. *Biomaterials* 2017;117:105-115.
- Koolen P, Li Z, Roussakis E, Ibrahim A, Matyal R, Huang T, Evans CL, Lin SJ. Oxygen Sensing Paint-On Bandage: Calibration of a Novel Approach in Tissue Perfusion Assessment. *Plast Reconstr Surg* 2017;140(1):89-96.
- van Veldhuisen CL, Kamali P, Wu W, Becherer BE, Sinno HH, Ashraf AA, Ibrahim AMS, Tobias A, Lee BT, Lin SJ. Prospective, Double-Blind Evaluation of Umbilicoplasty Techniques Using Conventional and Crowdsourcing Methods. *Plast Reconstr Surg*. 2017;140(6):1151-1162.
- Chattha A, Bucknor A, Chen AD, Lee BT, Lin SJ. Indocyanine Green Angiography Use in Breast Reconstruction: A National Analysis of Outcomes and Cost in 110,320 Patients. *Plast Reconstr Surg* 2018;141(4):825-832.

SELECTED RESEARCH SUPPORT

Degradable Orthopedic Hardware; NIH/NIAMS, 2015-2020; Co-PI: Samuel J. Lin, MD

Medical 3D Printing; Defense Logistics Agency and Triton Systems, Inc., SBIR Phase 1, 2016-2017; Expert Consultant: Samuel J. Lin, MD

Severe Trauma Female Simulation Training System; Defense Health Program and Triton Systems, Inc., SBIR Phase 1, 2016-2017; Expert Consultant: Samuel J. Lin, MD

Lateral Canthotomy and Cantholysis Training System; Defense Health Program (DHP) and Triton Systems, Inc., SBIR Phase 1 and 2, 2017-2019; Expert Consultant: Samuel J. Lin, MD

A complete list of publications begins on page 13.

Dhruv Singhal, MD

Assistant Professor of Surgery
Director of Lymphatic Surgery



RESEARCH GROUP

Andres Doval, MD
Sherise Epstein, MPH
Aaron Fleishman, MPH
Anna Rose Johnson, MPH
Leo Magrini, BS
Claire Rosenwasser, MS
Qing Ruan, MD
Bao Tran, MD

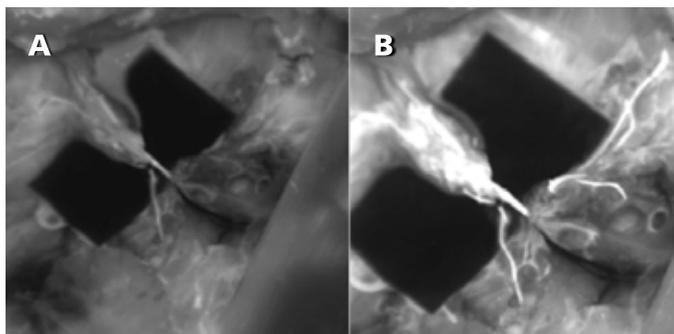
RESEARCH FOCUS

Over the last several years, my clinical and basic science research has primarily been focused on the surgical prevention and treatment of lymphedema. In addition, our clinical research group has recently been studying (1) the potential applications of integrative medicine in the care of the plastic surgery patient and (2) the impact of ergonomics on a surgeon's well-being.

Surgical Prevention and Treatment of Lymphedema

Over the past year, in the midst of building a comprehensive clinical program in the surgical management of lymphedema, our group has worked in parallel to construct a complementary research program. Working closely with the FIRST team, we developed a robust quality improvement database that is capable of tracking patients and their outcomes longitudinally. Similarly, we have launched a unique biorepository that now houses healthy and diseased lymphatic tissue. Working closely with Dr. Timothy Padera at the Steele Laboratories at Massachusetts General Hospital (MGH), we are developing protocols for further tissue investigation.

In the laboratory, we have worked to develop the first animal model to investigate the physiology of preventing lymphedema surgically at the time of lymphadenectomy. Specifically, working in collaboration with Dr. Hak Soo Choi, Gordon Center for Imaging at MGH, we are utilizing unique lymphatic specific dyes to report real-time changes in lymphatic flow from an extremity. In doing so, we have demonstrated a 47% increase in lymphatic flow out of an extremity if a surgical lymphatic bypass is performed at the time of the lymphadenectomy.



▲ (A) FLARE image of a lymphaticovenous bypass in the swine groin prior to hind limb lymphatic injection with fluorophore. (B) Post injection image demonstrating free passage of dye from lymphatic channels into the venous system. Note that the exposure time (400 ms) was the same in images A and B.

Integrative Medicine and Plastic Surgery

Our clinical outcomes team has previously demonstrated that a high percentage of patients presenting to plastic surgery clinics have already demonstrated an interest and utilized integrative or complementary techniques within one year of presentation to our service. More recently, in collaboration with Dr. Gloria Yeh, Director of Research at the Cheng-Tsui Integrated Health Center at BIDMC, we have been evaluating which natural products and mind-body techniques demonstrate high level evidence for efficacy in the peri-operative management of the plastic surgery patient. Most recently, working in collaboration with Dr. Yeh and Dr. Weidong Lu at the

Zakim Center for Integrative Therapies at the Dana Farber Cancer Institute, we have been awarded a Pilot Grant from the Osher Institute to prospectively study the biologic changes of acupuncture on patients with breast cancer-related lymphedema. We began enrolling patients in March, 2018.

Surgical Ergonomics

Over the past year, our clinical research team, in collaboration with Dr. Jack Dennerlein at the Harvard T.H. Chan School of Public Health, has studied and published on the significantly higher rate of work related musculoskeletal disorders in surgeons compared to the general population. We simultaneously evaluated the current state of ergonomic education provided to residents in surgical training, highlighting the need for the development of a more robust educational model.

ACCOMPLISHMENTS 2016-2017

I am currently the Director of Lymphatic Surgery at BIDMC. This past year I served on the Program Committee and Young Microsurgeon's Committee for the American Society of Reconstructive Microsurgery.

In the fall of 2017, alongside Dr. Sumner Slavin, I co-chaired the first Lymphedema Symposium at the BIDMC (www.harvardlymphaticsurgery.org). The meeting was a tremendous success, with over 230 participants who traveled from around the world to attend. The two-day event included a separate pathway for clinicians and patients. The highlight for the entire event was a panel of patients that presented on their experience of undergoing lymphatic surgery at BIDMC.

I received a 2017 Boston Red Sox Medical All-Star Award for our team's role in treating lymphedema patients in New England.

I am an ad hoc reviewer for: *Plastic and Reconstructive Surgery*, *Annals of Plastic Surgery*, *Journal of Reconstructive Microsurgery*, and *the International Microsurgery Journal*.

Invited Presentations

Dyes and lymphatic surgery, American Society for Reconstructive Microsurgeons, 2017

Early results in preventing lymphedema: A potential paradigm shift for lymphatic surgery, Academic Surgical Congress, 2017

Integrative medicine in plastic surgery: A systematic review of our literature, Society of Asian Academic Surgeons, 2017

Craniofacial neurofibromatosis – Guidelines for management, 30th World Congress of the International College for Maxillofacial Surgery, 2017

Fluorescein isothiocyanate: A novel application for intra-operative lymphatic imaging, 26th World Congress of Lymphology, 2017

A novel animal model for the surgical prevention of lymphedema: The power of molecular imaging, 26th World Congress of Lymphology, 2017

Early results in preventing lymphedema: A potential paradigm shift in lymphatic surgery, 26th World Congress of Lymphology, 2017

Referrals of plastic surgery patients to integrative medicine centers: A review of resource utility, Society of Asian Academic Surgeons, 2017

Early results in preventing lymphedema: A potential paradigm shift in lymphatic surgery, New England Society and Plastic and Reconstructive Surgery, 2017

Large animal model of modified lymphatic microsurgical preventative healing approach (LYMPHA), New England Society and Plastic and Reconstructive Surgery, 2017

SELECTED PUBLICATIONS

Patel N, Pierson J, Lee T, Mast B, Estores I, Singhal D. Utilization and perception of integrative medicine among plastic surgery patients. *Ann Plast Surg* 2017; 78(5):557-561.

Tran BN, Singh M, Lee BT, Rudd R, Singhal D. Readability, complexity, and suitability of online lymphedema resources. *J Surg Res* 2017; 213:251-260.

Spiguel L, Shaw C, Katz A, Guo L, Chen HC, Lee BT, Singhal D. Fluorescein isothiocyanate: A novel application for lymphatic surgery. *Ann Plast Surgery* 2017;78(6S Suppl5):S296-S298.

Epstein S, Tran BN, Capone AC, Ruan QZ, Lee BT, Singhal D. Work-related musculoskeletal disorders among plastic surgeons: A systematic review. *J Reconstr Microsurg* 2017 In press.

Hahamoff M, Gupta N, Munoz D, Lee BT, Clevenger P, Shaw C, Spiguel L, Singhal D. Lymphedema surveillance for breast cancer patients reveal the promise of surgical prevention. *J Surg Res* 2018; In press.

Epstein S, Tran BN, Capone AC, Ruan QZ, Fukudome EY, Ricci JA, Testa MA, Dennerlein JT, Lee BT, Singhal D. The current states of surgical ergonomics education in U.S. surgical training: A survey study. *Ann Surg* 2018, In press.

TEACHING, TRAINING, AND EDUCATION

I have been training medical students, general surgery and plastic surgery residents, clinical fellows, and research fellows for the past 5 years.

SELECTED RESEARCH SUPPORT

Acupuncture for breast cancer related lymphedema; Osher Center for Integrative Medicine, 2018-2019; PI: Dhruv Singhal, MD (Co-investigators: Gloria Yeh, MD, MPH, Weidong Lu, PhD)

A complete list of publications begins on page 13.

Aristidis Veves, MD, DSc

Rongxiang Xu, MD, Professor of Surgery in the Field of Regenerative Medicine
Director of the BIDMC Rongxiang Xu, MD, Center for Regenerative Therapeutics



RESEARCH GROUP

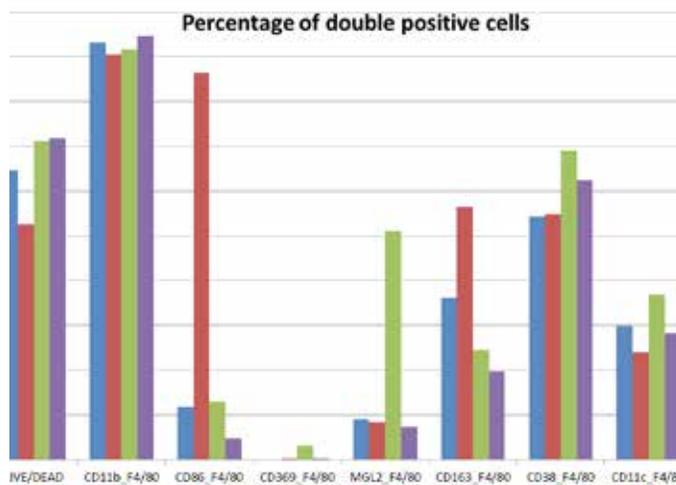
Licia Aduane
Vanessa Camacho
Konstantinos Kounas, MD
Antonio Lobao
George Theocharidis, PhD
Peng Wang, MD

RESEARCH FOCUS

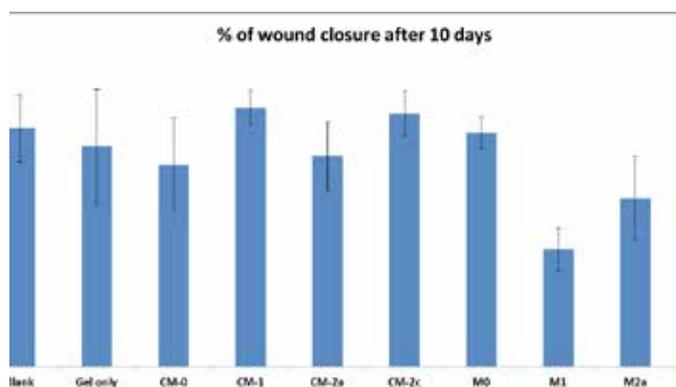
I am mainly involved in 'bench to bedside' research. My main research field is diabetes and its complications, with the main emphasis on wound healing and cardiovascular disease. Approximately 90 percent of my effort is dedicated to research, 5 percent for teaching and an additional 5 percent for administrative and other relevant professional activities.

Translational research is a major part of my research activities. My work mainly focuses on the interaction between neuropathy and microvascular disease in the development of diabetic foot ulceration and the subsequent impairment of wound healing. This work has been supported by the NIH and nonprofit organizations. I collaborate with investigators from various departments at BIDMC, and investigators from other institutions, such as Brigham and Women's Hospital, to conduct additional translational research.

I conduct investigator-initiated research studies that examine the effects of various FDA-approved medications on cardiovascular function. These studies, although funded by industry, have been conceived, designed, and executed by my unit and focus on possible new mechanisms through which these medications exert their beneficial effects. I have also served as the lead investigator and lead author in industry sponsored multicenter trials that investigated the efficacy of new therapeutic interventions for the management of diabetic foot ulceration.



▲ FIGURE 1: Flow cytometry analysis of primary mouse macrophages after 24 hours inside the bandages



◀ FIGURE 2: Wound healing analysis of mice with bandages covering their wounds

I also run my own basic research laboratory that mainly explores the findings of this translational research and tries to identify mechanisms underlying the observed results. My laboratory works closely with other laboratories in BIDMC and is funded by NIH grants. I also collaborate with Dr. David Mooney's laboratory at the Wyss Institute and Harvard Engineering School and Dr. Jonathan Garlick's at Tufts Medical School. The main aim of our collaboration is the development of new wound-healing products. This collaboration has resulted in NIH funding of our grant applications.

The results of my research have been published in prestigious medical journals, including *Lancet*, *Diabetes*, and *Circulation*. My work, according to Google Scholar as of December 2017, has resulted in more than 17,200 citations an h-index of 67 and i10-index of 149.

I have also been the Director of the Rongxiang Xu, MD, Center for Regenerative Therapeutics since its establishment in December 2015. The center was established after a generous donation from the National Rongxiang Xu Foundation and its mission is to further advance the treatment of patients throughout the world with chronic wounds, burns, and other conditions resulting from a failure of tissue repair and regeneration. As part of its mission, the Center provides resources for the conduction of collaborative bench-to-bedside research with investigators worldwide, as well as the education of physicians and scientists internationally.

ACCOMPLISHMENTS 2016-2017

A major aim of our work this year was to confirm the ability of monocytes polarized to M1 and M2 *in vitro*, to impact healing of neuropathic wounds in diabetic animals when introduced to the wound site, and to determine the propensity of naïve monocytes derived from T1DM and T2DM to polarize to the M1 phenotype at the wound site.

A method was first developed to allow for the production of an off-the-shelf product that could be manufactured in terms of hundreds of bandages within the span of a few days. Once we had established our method for the production of bandages, RAW 264.7 murine macrophages were used to test the feasibility of these bandages as a delivery vehicle. We next optimized the isolation *in vitro* expansion and polarization of primary mouse monocytes. Next, we investigated whether the primary cells could be loaded and polarized into the bandages (see Figure 1).

Finally, in our first pilot *in vivo* experiment, bandages loaded with cells were used to cover dorsal wounds in wild-type C57BL/6 mice. The wound closure calculations from the experiment show a clear effect of the macrophages in wound healing, especially the M1 phenotype (see Figure 2). We are currently in the process of analyzing all the histology data and are planning for a larger scale experiment with higher number of mice and using the diabetic db/db model.

In other research, we are testing the ability of biomaterials that sequentially release factors to first recruit and then direct the M2 phenotype to enhance healing in diabetic, neuropathic rodent wounds.

In the final year of the grant, we plan to complete the remaining animal experiments that will provide all necessary data that will allow us to prove or reject our primary hypothesis regarding the role of M2 macrophages. In addition, we will investigate whether our biomaterials can successfully improve impaired diabetic wound healing.

TEACHING, TRAINING, AND EDUCATION

My teaching responsibilities include participation in the training of podiatry residents, supervision of the fellows and junior faculty in my laboratory, and participation in mentorship committees of junior faculty members from other units. I am also involved in educational activities of the Center for Education at BIDMC, which provides guidance to candidates for NIH K-series awards. Finally, I participated as series editor, book editor or co-editor and author in numerous textbooks. One of these textbooks (Diabetes and Cardiovascular Disease) has been already translated to the Italian language and another one (Diabetic Foot) to the Greek language.

SELECTED RESEARCH SUPPORT

Obstructive sleep apnea increases cardiovascular risk in type 2 diabetes; NIH, 2011-2017; Co-PI/Contact PI: Aristidis Veves, PhD, DSc

Role of Macrophages in Impaired Wound Healing in Diabetes; NIH, 2015-2018; Co-PI/Contact PI: Aristidis Veves, MD, DSc

Skin inflammatory phenotypes as biomarkers of myocardial and vascular remodeling; NIH, 2016-2021; Co-PI/Contact PI: Aristidis Veves, MD, DSc

Single cell transcriptome sequencing of diabetic foot skin; Diacomp 2017-2018; PI: Aristidis Veves, MD, DSc

SELECTED PUBLICATIONS

Bai S, Nagai M, Koerner SK, Veves A, Sun L. Structure-activity relationship study and discovery of indazole 3-carboxamides as calcium-release activated calcium channel blockers. *Bioorganic & Medicinal Chemistry Letters* 2017;27(3):393-397.

Tellechea A, Pradhan-Nabzdyk L, LoGerfo FW, Veves A. Neuropeptides, Inflammation, and Diabetic Wound Healing – lessons from experimental models and human subjects. In: Veves A, Giurini JM, Guzman RJ (Eds). *The Diabetic Foot: Medical and Surgical Management (Fourth Edition)*. Totowa, NJ: Humana Press; In Press.

Zheng Y, Shu B, Fu J, Kafanas A, Veves A. Structural and Functional Changes in Skin of the Diabetic Foot. In: Veves A, Giurini JM, Guzman RJ (Eds). *The Diabetic Foot: Medical and Surgical Management (Fourth Edition)*. Totowa, NJ: Humana Press; In Press.

Roustit M, Loader J, Baltzis B, Zhao W, Veves A. Microvascular changes in the diabetic foot. In: Veves A, Giurini JM, Guzman RJ (Eds). *The Diabetic Foot: Medical and Surgical Management (Fourth Edition)*. Totowa, NJ: Humana Press; In Press.

Loader J, Roustit M, Baltzis B, Veves A. Vascular Dysfunction, Inflammation, and Exercise in Diabetes. In: Reusch JEB, Regensteiner JC, Stewart K, Veves A (Eds). *Diabetes and Exercise (Second Edition)*. Totowa, NJ: Humana Press; 2017, pp 137-150.

Reusch JEB, Regensteiner JC, Stewart K, Veves A. *Diabetes and Exercise (Second Edition)*. Totowa, NJ: Humana Press; October 2017.

Veves A, Giurini JM, Guzman RJ. *The Diabetic Foot: Medical and Surgical Management (Fourth Edition)*. Totowa, NJ: Humana Press; January 2018.

A complete list of publications begins on page 13.



RESEARCH FOCUS

My research is focused on clinical studies related to endocrine surgery. Recent studies involved different aspects of the follicular variant of papillary thyroid cancer (FVPTC). In one project, we determined the relationship between follicular adenoma and FVPTC and found that increasing numbers of tumors diagnosed as FVPTC were accompanied by a simultaneous decrease in cases signed out as follicular adenoma. The study, published in *Surgery* (2016;159:1396-1406), suggests that patients with tumors diagnosed as FVPTC may sometimes be subjected to unnecessarily extensive surgical treatment and radioiodine treatment.

In another project, the influence of thyroid hormones on cervical brown adipose tissue (BAT) was examined. The study is important because BAT activation by thyroid hormones may protect from obesity, insulin resistance/diabetes, and the metabolic syndrome. The study was a feasibility investigation to determine the possibility of using BAT obtained during neck surgery (thyroidectomy or parathyroidectomy) to examine the regulation of BAT activity and was published in *THYROID* (2016;27:1-10).

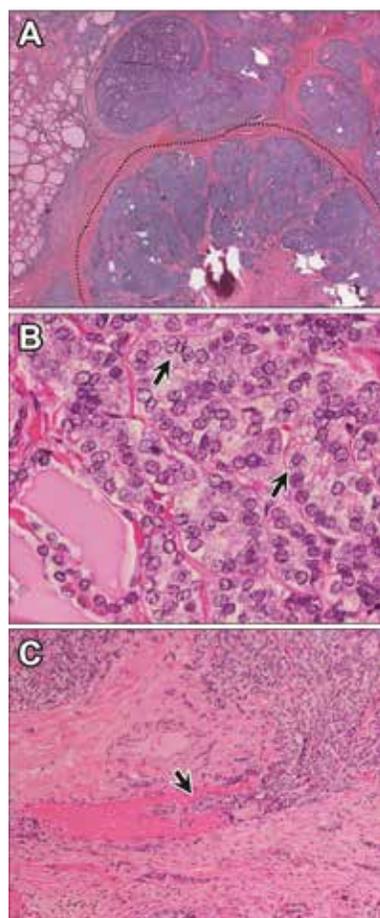
We are presently performing studies testing whether certain features of “suspicious for cancer” cytology combined with features of preoperative thyroid ultrasound may make it possible to differentiate between invasive FVPTC and Non-Invasive Follicular Thyroid Neoplasm with Papillary-Like Nuclear Features (NIFTP). This would make it possible to recommend less aggressive surgery in many patients with cytology being “suspicious for cancer.”

Although NIFTP can be managed as a non-malignant tumor, invasive FVPTC continues to be considered a malignant tumor. We recently performed genetic analysis of an invasive FVPTC in a patient with an aggressive variant of invasive FVPTC. A 47-year-old man presented with a metastasis to his right iliac bone as the initial manifestation of a 1.6 cm invasive FVPTC (Figures 1 and 2).

The patient underwent total thyroidectomy but despite additional aggressive treatment, the disease progressed, resulting in the patient’s demise. Next-generation sequencing of the primary tumor using a pan-cancer targeted mutation and gene fusion panel revealed *NRAS* Q61K mutation and no other oncogenic alterations, suggesting that an isolated *RAS* mutation in invasive FVPTC may be associated with aggressive clinical behavior, challenging the prevailing concept that thyroid neoplasms with isolated *RAS* mutations are associated with favorable clinical behavior. The patient was reported in *Int J Surg Case Rep* (2017;38:1-5).

A study was recently initiated to determine the role of different preoperative imaging tests (ultrasound, Sestamibi scanning, and four-dimensional CT, 4D-CT) in patients with primary hyperparathyroidism. In particular, we will investigate the results of 4D-CT, a novel modality of preoperative imaging in patients with hyperparathyroidism.

Ongoing studies are based on a prospective database in the Section of Endocrine Surgery that has been active for about 15 years and contains information from more than 6,000 patients.



▲ FIGURE 2: Histological appearance of a tumor with invasive FVPTC: A) Infiltrative growth of cancer into the surrounding thyroid parenchyma; B) Nuclear features characteristic of papillary cancer but follicular architecture; C) Vascular invasion



▲ FIGURE 1: Abdominal/pelvic CT in a patient presenting with right hip pain caused by bony metastasis from an invasive FVPTC

Administrative responsibilities and Committees

- Vice Chair, Research
- Director, Section of Endocrine Surgery
- Chair, Department of Surgery Appointment-Reappointment-Promotion Committee (through June 2017)

Recruitment of an additional member of the Section of Endocrine Surgery

Benjamin James, MD, was recently recruited to the Section of Endocrine Surgery. Dr. James performed a Fellowship in Endocrine Surgery at the University of Chicago followed by a Fellowship in Research in Endocrine Surgery at the same institution. After completing these fellowships, he joined the faculty of the Department of Surgery at Indiana University, Indianapolis, where he built a thriving practice in endocrine surgery. He is a welcome addition to the Section of Endocrine Surgery at BIDMC and brings novel and innovative surgical approaches to the treatment of thyroid, parathyroid, and adrenal disorders.

Editorial roles

- Associate Editor: *Metabolism*
- Editorial Board: *Nutrition; International Journal of Interferon, Cytokines, and Mediator Research*
- Ad hoc reviewer: Multiple journals, including *American Journal of Physiology, Annals of Surgery, British Journal of Surgery, Endocrinology, Journal of Surgical Research, World Journal of Surgery, Critical Care Medicine*

Other

Creation of a *Surgical History Group* in the Department of Surgery (together with Dr. Sidney Levitsky). The following activities took place during 2017:

- Study visit to the Warren Anatomical Museum, Harvard Medical School
- Surgical Grand Rounds by Dr. Peter Kopp: "*From First Successful Thyroidectomy to the Nobel Prize in Physiology and Medicine: The Legacy of Theodor Kocher (1841-1917)*"
- Lecture by Frederick Millham, MD: "*Did a Surgeon Lose the U.S. Civil War? The Wounding and Death of General Thomas J (Stonewall) Jackson*"

TEACHING, TRAINING, AND EDUCATION

Surgery Grand Rounds

May 24, 2017: "*Current Best Practices in the Management of Thyroid Nodules*"

Student Teaching (preceptor groups, HMS students)

- July – September, 2016
- October – December, 2016
- January – March, 2017
- April – June, 2017

Mehrzad R, Nishino M, Connolly J, Wang H, Mowschenson P, Hasselgren PO. The relationship between the follicular variant of papillary thyroid cancer and follicular adenomas. *Surgery* 2016;159:1396-13406.

Gavrila A, Hasselgren PO, Glasgow A, Doyle AN, Lee AJ, Fox P, Gautam S, Hennessey J, Kolodny G, Cypess AM. Variable cold-induced brown adipose tissue response to thyroid hormone status. *Thyroid* 2016;27:1-10.

Mehrzad R, Nishino M, Nucera C, Dias-Santagata D, Hennessey JV, Hasselgren PO. Invasive follicular variant of papillary thyroid cancer harboring the NRAS mutation Q61K and presenting with bone metastasis – A case report. *Int J Surg Case Rep* 2017;38:1-5.

Hasselgren PO, Cannon JW, Fischer JE. Perioperative management: Practical principles, molecular basis of risk, and future directions. Chapter 2. In Fischer JE (ed). *Mastery of Surgery*, 7th edition, 2017.

Benjamin C. James, MD, MS

Assistant Professor of Surgery
Section Chief, Endocrine Surgery
Associate Surgery Clerkship Director, BIDMC



RESEARCH GROUP

Courtney Barrows, MD
Janeil Belle, MD
Ryan Graham, BS
David Haggstrom, MD
Lava Timsina, PhD

RESEARCH FOCUS

Over the past several decades there has been a substantial increase in the diagnosis and treatment of differentiated thyroid cancer. This rise has largely been attributed to increased detection of nonaggressive and nonlethal thyroid cancers. It has been suggested that this rise has resulted in an epidemic of overtreatment of thyroid cancer. My research has focused on population-level analysis of thyroid cancer incidence and the clinical and economic implications of this rapid rise.

Effect of healthcare expansion on the treatment of thyroid cancer

In 2006, the Commonwealth of Massachusetts passed a health care reform law which expanded health insurance for government-subsidized, self-pay, and uninsured individuals in the state. I hypothesized that as a result of healthcare expansion, there would be an increase in the rate of thyroidectomy for thyroid cancer related to increased access to care. To evaluate this hypothesis, we used data from the State Inpatient Databases (SID) for Massachusetts and six control states. Using difference-in-difference models, we were able to show a startling 26 percent increase in the treatment of thyroid cancer as a direct result of this healthcare reform. These results were published this year in *JAMA Surgery* (2017;152(8):734-740) and was widely cited in *Medscape*, *Science Newsline*, and *Ecancer*, among others.

Economic impact of a diagnosis of thyroid cancer

Cancer care expenditure in the United States continues to rise yearly and is projected to surpass \$150 billion by 2020. Although thyroid cancer has a generally high survival rate, it is associated with a potential long term financial and psychological impact, which has not previously been rigorously studied. We aimed to evaluate the comparative prevalence of financial and psychological hardship among U.S. thyroid cancer and non-thyroid cancer survivors. In an ongoing evaluation using the Agency for Healthcare Research and Quality Medical Expenditure Panel Survey (MEPS), we have found that thyroid cancer survivors experience a significantly higher level of both material and psychological financial hardship compared to non-thyroid cancer survivors. These findings suggest that financial hardship may be under-recognized in the medical community and warrants further investigation into the etiology behind the financial burden associated with a diagnosis of thyroid cancer.

Treatment patterns in thyroid cancer

Over the past 15 years, there has been a growing body of literature suggesting a rising incidence of thyroid cancer without a rise in mortality. As a result, there has been a shift in guidelines to offer less aggressive surgical intervention. These recommendations have come as multiple studies have shown that patients with thyroid cancer may have a similar prognosis when undergoing less aggressive surgical intervention such as thyroid lobectomy. Our group hypothesized that despite evidence of equivalent survival with less aggressive treatment, patients are still undergoing aggressive surgeries for the treatment of thyroid cancer regardless of the size of the cancer. We are currently evaluating these treatment patterns and have shown in preliminary research that the trends in treatment patterns over the past 15 years, have not changed.

ACCOMPLISHMENTS 2016-2017

- Elected to the Editorial Board of the Journal of Surgical Research
- Elected to the Program Committee for the Academic Surgical Congress
- Appointed Associate Surgery Clerkship Director, BIDMC

Invited Presentations

- An update in international trends in incidence rates of thyroid cancer from 1973-2007, Academic Surgical Congress
- Surgical outcomes in pediatric Graves' disease, Academic Surgical Congress
- An estimate of economic and psychological hardship among thyroid cancer survivors, American College of Surgeons
- 25 years of therapy for papillary thyroid cancer, American Thyroid Association

TEACHING, TRAINING, AND EDUCATION

I have developed an endocrine surgery teaching series for residents rotating on the endocrine surgery service. This series has been developed to prepare residents for both the written and oral general surgery boards. As a result of my dedication to education, I was given a teaching award in 2016. I have also taken on a teaching role in the Department of Surgery at BIDMC as the associate clerkship director for Harvard Medical School students.

SELECTED PUBLICATIONS

Applewhite MK, James BC, Aschebrook-Kilfoy B, Kaplan EL, Angelos P, Grogan RH. Quality of life in thyroid cancer is similar to that of other cancers with worse survival. *World Journal of Surgery* 2016;40(3):551-61.

James BC, Cipriani N, Aschebrook-Kilfoy B, Kaplan EL, Angelos P, Grogan RH. Incidence and survival trends of rare malignancies of the thyroid, parathyroid, adrenal, and endocrine pancreas. *Annals of Surgical Oncology* 2016;23(2):424-33.

White MG, James BC, Nocon C, Nagar S, Kaplan E, Angelos P, Grogan RH. One-hour PTH after thyroidectomy predicts symptomatic hypocalcemia. *Journal of Surgical Research* 2016;201(2):473-79.

Jafari A, Campbell D, Campbell BH, Nono H, Sisenda T, Makaya D, James BC, Cordes SR. Humanitarian thyroid surgery in elderly Kenya: Analysis of short and long-term outcomes. *Otolaryngology Head and Neck Surg* 2017;156(3):464-471.

Loehrer AP, Murthy SS, Song Z, Lubitz CC, James BC. Association of insurance expansion with surgical management of thyroid cancer. *JAMA Surgery* 2017;152(8):734-740.

Kaplan EL, James BC, Grogan RH, George W. Crile, MD: Prolific Surgeon, Experimentalist, and Patriot. In Pasiaka JL, Lee J. eds. *Surgical Endocrinopathies: Clinical Management and the Founding Fathers*. Springer 2016.



Ted A. James, MD, MHCM, FACS

Associate Professor of Surgery
Chief, Breast Surgical Oncology
Co-Director, BreastCare Center
Vice Chair, Academic Affairs

RESEARCH FOCUS

Our breast cancer surgery outcomes research program is focused on assessing the effectiveness, quality, and value of specific care practices and interventions in the surgical management of breast cancer. The goal is to derive best practices, determine optimal processes, and improve quality of care in the management of patients with breast cancer. The program integrates health services research, including the use of large internal and national cancer databases, to critically appraise clinical results and patient reported outcomes.

Outcomes include traditional clinical metrics in breast cancer (e.g. survival, complications, local recurrence), as well as patient well-being, satisfaction, functional status, and impact on the healthcare system. The results then “translate” into practice and policy by working with clinicians, professional societies, patients, payers, and purchasers of healthcare.

Outcomes research seeks to understand the end results of particular health care practices and interventions. By linking the care people get to the outcomes they experience, outcomes research has become the key to developing better ways to monitor and improve the quality of care.

RESEARCH GROUP

Amulya Alapati, MD
Sayuri P Jinadasa, MD
Leo Magrini
Luis Riba, MD
Teresa Russell
Promise Ukandu

ACCOMPLISHMENTS 2016-2017

- National Cancer Database research awards
- Invited podium presentations at multiple national surgical research meetings
- Peer-reviewed publications in surgical journals

TEACHING, TRAINING, AND EDUCATION

- Our research fellow completed a Master of Science in Epidemiology Degree Program, a 42.5 credit program with the goal of training clinicians with the quantitative skills needed for a clinical research career. Research training is provided through a series of required and elective courses. In addition, students in this program are required to complete a research thesis under the joint supervision of a local research advisor and a member of the faculty of the Department of Epidemiology at the Harvard School of Public Health.
- Our research team receives formal mentoring in the areas of clinical outcomes research, quantitative and qualitative methods, designing high-level observational studies, assessing validity, working with clinical registries, managing and analyzing large datasets, mixed methods research, implementation science, manuscript preparation, grant writing skills, and academic career development.
- Our Clinical Scholarship Program pairs all first-year categorical general surgery residents with a faculty research mentor who guides the residents throughout the year as they acquire the skills to develop and implement a clinical research project. The objectives of the Clinical Scholarship Program are to provide residents with a robust foundation for scholarship early in their training, increase their academic productivity, and enhance their opportunities to compete for national grants.

SELECTED RESEARCH SUPPORT

Translating research into practice: A regional collaborative to reduce disparities in breast cancer care. NIH; 2017-2022. Collaborating PI: Ted James

SELECTED PUBLICATIONS

Riba LA, Gruner RA, Fleishman A, James TA. Surgical risk factors for the delayed initiation of adjuvant chemotherapy in breast cancer. *Ann Surg Oncol* 2018;25(7):1904-1911.

Kantor O, Sipsy LM, Yao K, James TA. A predictive model for axillary node pathologic complete response after neoadjuvant chemotherapy for breast cancer. *Ann Surg Oncol* 2018;25(5):1304-1311.

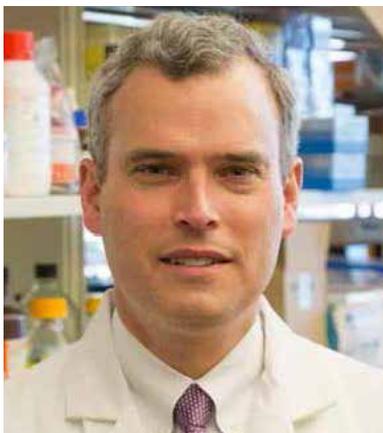
Trentham-Dietz A, Ergun MA, Alagoz O, Stout NK, Gangnon RE, Hampton JM, Dittus K, James TA, Vacek PM, Herschorn SD, Burnside ES, Tosteson ANA, Weaver DL, Sprague BL. Comparative effectiveness of incorporating a hypothetical DCIS prognostic marker into breast cancer screening. *Breast Cancer Res Treat* 2018 Feb;168(1):229-239.

Kapoor T, Wrenn S, Callas P, James TA. Analysis of patient-detected breast cancer recurrence. *Breast Dis* 2017;37(2):77-82.

Ajmani GS, James TA, Kantor O, Wang CH, Yao KA. The impact of facility volume on rates of pathologic complete response to neoadjuvant chemotherapy used in breast cancer. *Ann Surg Oncol* 2017;24(11):3157-3166.

James TA. The impact of financial barriers on access to quality care in breast cancer. *Bulletin of the American College of Surgeons* 2017;102(10):72.

A complete list of publications begins on page 13.



A. James Moser, MD

Associate Professor of Surgery
Co-Director, BIDMC Pancreas and Liver Institute
Co-Director, BIDMC Pancreatic Cancer Research program

RESEARCH FOCUS

Dr. Moser is a leader in complex, advanced surgical oncology including minimally-invasive surgery of the pancreas and liver and vascular resection for borderline resectable tumors. He is Co-Director of the multidisciplinary Pancreas and Liver Institute with Michael Curry, M.D., Director of Liver Transplantation and Chief of Hepatology, and Manuel Hidalgo, MD, PhD, Clinical Director of the BIDMC Cancer Center and Chief of Hematology/Oncology.

The Pancreas and Liver Institute combines BIDMC's key strengths in advanced endoscopy with advanced minimally-invasive and robotic surgery, integrated patient-centered multidisciplinary care for pancreas and liver diseases, and leadership of innovative clinical trials within the Dana-Farber/Harvard Cancer Center. He also co-leads BIDMC's Pancreatic Cancer Research Program with Dr. Hidalgo. Current areas of primary interest include: minimally-invasive cancer surgery; biomarker development and computational biology approaches to precision medicine for pancreatic diseases, and particularly pancreatic cancer.

Dr. Moser is currently principal investigator for Project Survival™, a multisite collaborative research effort to develop early prognostic and therapeutic biomarkers for pancreatic cancer. His current research group includes five research fellows, including a Fulbright scholar and two fellows pursuing their master's degrees at the Harvard School of Public Health. The team is supported by a large community of grateful patients and families funding patient-centered care for pancreatic cancer through the Alliance of Families Fighting Pancreatic Cancer. Dr. Moser has been published more than 100 times and is an active participant in multiple national and international societies, including the American Surgical Association.

RESEARCH GROUP

- William E. Gooding, MS
- Wendy Hori, RN
- Sjors Klompmaker, MD
- Robert Najarian, MD
- Ana Sofia Ore, MD
- Katie Stackhouse, MD
- Wald Van der Vliet, MD
- Monica Solis Velasco, MD
- Koen Verhoulen, MD

ACCOMPLISHMENTS 2016-2017

- Elected to the American Surgical Association
- Co-established and direct (with Manuel Hidalgo, MD, PhD) the Pancreatic Cancer Research Program within the BIDMC Cancer Research Institute (CRI).
- Launched BIDMC Department of Surgery Pancreatic Disease Registry and Biorepository Core Facility
- First annual observance of World Pancreatic Cancer Day at the BIDMC Pancreas and Liver Institute and Cancer Center on behalf of pancreatic cancer survivors, their families, and clinical and translational researchers tackling this deadly disease
- Surgical-services wide analysis of factors contributing to intraoperative flow disruptions affecting the hepatobiliary (HPB) surgery and assessment of Quality Assurance/ Performance Improvement (QA/PI) processes to improve efficiency

TEACHING, TRAINING, AND EDUCATION

- Alliance of Families Fighting Pancreatic Cancer Translational Research Fellowship Award: Mentored translational research training grant to prepare the next generation of surgeon-scientists to tackle the challenges of curing pancreatic cancer
- Fox-25 Boston Television interview with Drs. A. James Moser and Senthil Muthuswamy: "New research leading to new treatments- patient-derived organoids"
- Weekly CME-approved multidisciplinary pancreatobiliary management conference

SELECTED RESEARCH SUPPORT

Project Survival: Multisite identification and validation of prognostic biomarkers for pancreatic cancer detection and treatment; Berg Pharma, 2015-2022; PI: A. James Moser, MD; Co-PI: Manuel Hidalgo, MD PhD; Co-I: Robert Najarian, MD, and Senthil Muthuswamy, PhD

Phase II study of pancreatic enzyme replacement therapy (Zenpep) on completion rates of adjuvant therapy among subjects with resected pancreatic ductal adenocarcinoma; Allergan Inc., 2016-2019; PI: A. James Moser, MD; Co-PI: Bruno Bockorny, MD

Dendritic cell-cancer cell fusion vaccines for PDAC treatment; Jimmy V Foundation, 2018-2021; PI: Manuel Hidalgo, MD PhD; Co-PIs: David Avigan, MD; A. James Moser, MD; Senthil Muthuswamy, PhD; Mandeep Sawhney, MD

A scalable blood-based pancreatic cancer test for high-risk screening; 2017-2018; PI: David S. Freedman PhD; Co-PI: Bruno Bockorny, MD; Co-I: A. James Moser, MD

SELECTED PUBLICATIONS

Klompmaaker S, van Zoggel D, Watkins AA, Eskander MF, Tseng JF, Besselink MG, Moser AJ. Nationwide evaluation of patient selection for minimally-invasive distal pancreatectomy using ACS-NSQIP. *Ann Surg* 2017;266(6):1055-1061.

Watkins AA, Kent TS, Gooding WE, Boggi U, Chalikonda S, Kendrick ML, Walsh RM, Zeh HJ III, Moser AJ. Multicenter outcomes of robotic reconstruction during the early learning curve for minimally-invasive pancreaticoduodenectomy. *HPB (Oxford)* 2018;20(2):155-165.

Hogg ME, Besselink MG, Clavien PA, Fingerhut A, Jeyarajah DR, Kooby DA, Moser AJ, Pitt HA, Varban OA, Vollmer CM, Zeh HJ 3rd, Hansen P; Minimally Invasive Pancreatic Resection Organizing Committee. Training in Minimally Invasive Pancreatic Resections: a paradigm shift away from "See one, Do one, Teach one". *HPB (Oxford)* 2017;19(3):234-245.

Patti JC, Ore AS, Barrows C, Velanovich V, Moser AJ. Value-based assessment of robotic pancreas and liver surgery. *Hepatobiliary Surg Nutr* 2017;6(4):246-257.

Vergauwen MAT, Perillo M, Garces-Des-covich A, Barrows CE, Moser AJ, Mortelé KJ. Radiologic evaluation of patients undergoing the modified Appleby procedure for locally advanced pancreatic neoplasms: A case series. *Abdom Radiol (NY)* 2018;43(2):467-475.

Barrows C, Ore AS, Solis-Velasco M, Moser AJ. "Minimally-Invasive Transduodenal Ampullary Resection." In: *Minimally Invasive Surgery of the Pancreas*. Boggi U Ed. Milan, Italy. Springer-Verlag Italia 2017, p. 131-139.

A complete list of publications begins on page 13.

Ranjna Sharma, MD

Assistant Professor of Surgery



RESEARCH FOCUS

CLINICAL RESEARCH

Outcomes of breast cancer treatment in the high risk octogenarian patient population

This study is a retrospective review evaluating treatment outcomes in patients aged 80-89 who were diagnosed with early-stage, high-risk breast cancer between the years of 2000-2010. The high risk cohort was defined as patients with triple negative disease, Her2+ tumors, and/or Grade 3 tumors.

Clinical treatments and outcomes of patients with Phyllodes tumors of the breast: a modern case series

This is a retrospective study looking at our institutional experience with this patient population to better understand management patterns and propose treatment plans for patients with this diagnosis in the future. We will evaluate each patient's margins of resection, use of adjuvant radiation therapy, and rates of local and distant recurrence.

Analysis of delayed hormonal therapy and its impact on morbidity and mortality in women with breast cancer

In this study, the National Cancer Database will be used to study patients with ER+ breast cancer and the initiation time point of adjuvant endocrine therapy to determine reasons for delay in initiation of endocrine therapy and if the time of initiation has an impact on survival.

Can pre-operative axillary imaging predict nodal disease burden at the time of axillary lymph node dissection in patients with locally advanced breast cancer?

This study is a retrospective review of breast cancer patients from a single institution's tumor registry over a 10-year time period. We are evaluating pre-operative axillary imaging with ultrasound and/or MRI to assess disease burden in axillary lymph nodes and correlate these findings with the amount of disease at the time of axillary lymph node dissection in patients with biopsy-proven axillary disease.

TRANSLATIONAL RESEARCH

Intraoperative real-time breast cancer margin assessment with nonlinear microscopy

We have developed a protocol using Acridine Orange dye with nonlinear microscopy for intra-operative evaluation of surgical margins in oncologic resection specimens. This study is currently in the pre-clinical phase.

Genomic analysis of risk factors for local recurrence after wide local excision for DCIS of the breast

In this study, tissue specimens of patients diagnosed with ductal carcinoma in situ (DCIS) are undergoing genomic analysis to assist in determining risk of disease recurrence. This genomic data will be coupled with clinicopathologic features to better understand risk of disease recurrence.

ACCOMPLISHMENTS 2016-2017

- Promotion to Assistant Professor of Surgery
- Director of Breast Surgery, BID-Needham
- Co-Director of BreastCare Center BID-Needham
- Certificate in Applied Biostatistics, Harvard Medical School (HMS)
- Fellow, American College of Surgeons
- Member, DFCI/HCC SRC-3/IRB-D
- Member, BIDMC Cancer Committee
- Medical Chart Reviewer for Quality Assurance, BIDMC Cancer Committee Tumor Registry
- Course Director, Multidisciplinary Breast Tumor Board
- Selected to Society of Surgical Oncology Committee membership: Constitution and Bylaws Committee, Continuing Medical Education Committee
- Selected to ACS Massachusetts Chapter Young Fellows/Residents Committee

TEACHING, TRAINING, AND EDUCATION

- Patient-Doctor II Course: Lifestyles of a Surgeon
- HMS/BIDMC Pre-Internship Surgical Boot Camp: Taught fourth-year Harvard Medical School students fine-needle aspiration, core biopsy, and incision and drainage techniques
- HMS General Surgery Clerkship Tutorial leader
- Clinical Scholarship Program projects:
 - Clinical treatments and outcomes of patients with Phyllodes tumors of the breast: a modern case series; Gabrielle Cervoni, MD, general surgery resident
 - Analysis of delayed hormonal therapy and its impact on morbidity and mortality in women with breast cancer; Nicole Moraco, MD, general surgery resident
- MIT Student Introduction to Surgery Program
- Boston University Shadowing Program

SELECTED PUBLICATIONS

Manders JB, Kuerer HM, Smith BD, McCluskey C, Farrar WB, Frazier TG, Li L, Leonard CE, Carter DL, Chawla S, Medeiros LE, Guenther JM, Castellini LE, Buchholz DJ, Mamounas EP, Wapnir IL, Horst KC, Chagpar A, Evans SB, Riker AI, Vali FS, Solin LJ, Jablon L, Recht A, Sharma R, Lu R, Sing AP, Hwang ES, White J; Study investigators and study participants. Clinical utility of the 12-gene DCIS Score Assay: Impact on radiotherapy recommendations for patients with ductal carcinoma in situ. *Ann Surg Oncol* 2017;24(3):660-668.

Linsk A, Mehta T, Dialani V, Chadashvilli T, Houlihan MJ, Johnson NB, Brook A, Sharma R. Surgical upgrade rate of breast atypia to malignancy: An academic center's experience and validation of a predictive model. *Breast J* 2018;24(2):115-119.

Van Paridon MW, Paul MA, Kamali P, Ibrahim AMS, Kansal KJ, Houlihan MJ, Morris DJ, Lee BT, Lin S, Sharma R. Oncoplastic breast surgery: Achieving oncological and aesthetic outcomes. *J Surg Oncol* 2017; 116 (2):195-202.

Mele A, Mehta P, Brook A, Recht A, Slanetz PJ, Sharma R. Breast conserving surgery alone for ductal carcinoma in situ: Factors associated with increased risk of local recurrence. *Ann Surg Oncol* 2017;24 (5):1221-1226.

Sharma R, Shulman LN, James T. The future of quality improvement in breast cancer: Patient-reported Outcomes. *Am J Med Qual*. 2017;32(5):469-47.

Mamtani A, Gonzalez JJ, Neo D, Friedman R, Recht A, Hacker MR, Sharma R. Treatment strategies in octogenarians with early-stage high-risk breast cancer. *Ann Surg Oncol*. 2018;25(6):1495-1501.

A complete list of publications begins on page 13.



Sidharta P. Gangadharan, MD

Associate Professor of Surgery
Chief, Thoracic Surgery and Interventional Pulmonology

RESEARCH FOCUS

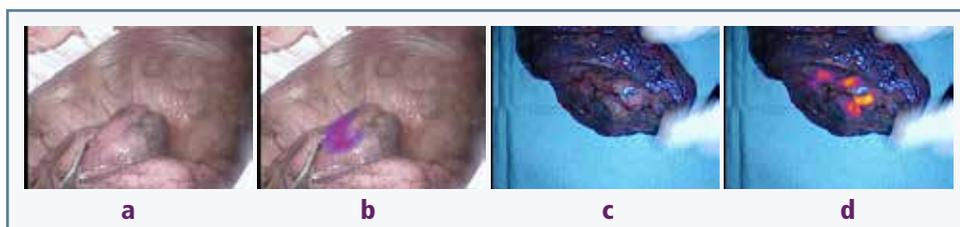
I perform clinical outcomes research that spans the range of thoracic diseases, but with a particular interest in tracheobronchomalacia (TBM). To date, our department maintains the largest TBM registry in the United States, which has enabled us to develop current guidelines and analyze outcomes for medical, endoscopic, and surgical therapy. Through this analysis, we hope to delineate best care practices through refined patient selection methods and improved medical, endoscopic, and surgical techniques. In the last year, we have partnered with the laboratory of Richard Cummings, PhD, to expand the scope of our research to include examination of the pathogenesis of this entity—specifically the potential role of glycan-binding proteins involved in immune regulation and TBM. A better understanding of this pathway and its relation to TBM could potentially lead to the development of novel therapies.

Additionally, we are currently evaluating the acoustical features of cough and respiratory sounds in patients with symptomatic, severe, diffuse TBM. By recording these features, we hope to define a unique acoustic signature and eventually investigate its diagnostic utility.

I have been investigating novel methods of staging lung cancer utilizing near-infrared imaging technology. I am the site PI for the “A Phase 2, Single dose, Open-Label, Exploratory Study to Investigate the Safety and Efficacy of OTL38 Injection for Intraoperative Imaging of Folate Receptor Positive Lung Nodules.” Patients enrolled in the study are administered a single dose of OTL38, a folate analog ligand conjugated with an indole cyanine-like green dye. During their procedure as indicated by standard of care, an imaging system equipped with near-infrared technology is used to aid in malignancy detection. We were the first in this study to enroll and plan to continue through 2018.

RESEARCH GROUP

Daniel Buitrago, MD
Oliver Chow, MD
Michael Kent, MD
Mark Maxfield, MD
Ben Scott, MD
Rani Singh, PhD
Richard Whyte, MD
Jennifer Wilson, MD
Jenny Yu, MD



▲ *In vivo* evaluation of a pulmonary nodule: (a) without endoscopic imaging system; (b) detection of pulmonary nodule using endoscopic imaging system in a patient infused with OTL-38 prior to procedure; (c) back table analysis of excised pulmonary nodule without imaging system; and (d) analysis of the same nodule utilizing imaging system in near- infrared imaging model.

ACCOMPLISHMENTS 2016-2017

- The significance and management of excessive dynamic airway collapse: A pro/con debate, American College of Chest Physicians (CHEST) Annual Conference, Toronto, ON, 2017
- Parenchymal-sparing approaches to lung metastases, Invited speaker and tumor board panelist, World Congress of Interventional Oncology annual meeting, Boston, MA, 2017
- Technical aspects of tracheobronchoplasty for tracheobronchomalacia, Invited operative training session, NYU Langone Medical Center, New York, NY, 2017
- What's new for TBM 2017, Guest speaker, Tri-State Thoracic Society, Egg Harbor, WI, 2017
- Complex airway surgery: Tracheobronchoplasty, Grand Rounds, Department of Anesthesia, Brigham and Women's Hospital, 2017
- Advanced open esophageal and tracheal procedures, Course director, Society of Thoracic Surgeons Annual Meeting, STS University Course, Houston, TX, 2017
- Finding the right job and transitioning to practice, Course director, Society of Thoracic Surgeons Annual Meeting, Residents Symposium, Houston, TX, 2017
- Outstanding Filipino-American Physician Award, Philippine Medical Association of New England, 2017
- GK 50 Honoree, List of Boston's 50 Most Influential People of Color in Healthcare & Life Sciences, Calette Phillips Communications, Neighborhood Health Plan and Partners Healthcare, 2017
- Boston's Top Doctors, Thoracic and Cardiac Surgery, Castle Connolly and Boston Magazine, 2016 and 2017
- While participating in the EMPROVE and LIBERATE Trials, the Interventional Pulmonary team identified a subgroup of patients for which endobronchial lung volume reduction by way of intrabronchial valves (IBVs) was not an option due to incomplete interlobar fissures. In 2016-2017, in collaboration with Spiration, Inc., we successfully showed complete targeted lobar collapse through a minimally invasive surgical stapling technique to complete interlobar fissures followed by IBV placement in both ex-vivo and live animal models. In 2018, we plan to transition this research to a pivotal human clinical trial in hopes of helping patients who would otherwise not be candidates for such treatment.

TEACHING, TRAINING, AND EDUCATION

I have been involved in education administration for the Department of Surgery as the Program Director for Cardiothoracic Surgery and as an Assistant Program Director for the General Surgery Residency Program. From a teaching perspective, I deliver regular didactic sessions and simulation sessions for residents. On a national level, I present didactic lectures and hands-on training courses on complex tracheal diseases and surgical treatments.

ABSTRACTS, POSTERS, AND EXHIBITS

Alape D, Kheir F, Gangadharan S, Parikh M, Wilson J, Chee A, Majid A. Stent trial for expiratory central airway collapse: Does the type of stent really matter? CHEST Conference, Toronto, ON, 2017

Whyte RI, Beqari J, Ritzer L, Wilson JL, Gangadharan SP, Majid A, Kent MS. Should thoracic surgeons be doing EBUS and other advanced bronchoscopic cases? Western Thoracic Surgical Association, Colorado Springs, CO, 2017

Buitrago D, Majid A, Alape D, Wilson J, Parikh M, Kent M, Gangadharan S. Single-center experience of tracheobronchoplasty for tracheobronchomalacia: Perioperative outcomes. Thirtieth Annual Meeting of the General Thoracic Surgical Club, Clearwater Beach, FL, 2017

SELECTED PUBLICATIONS

Castillo-Angeles M, Watkins AA, Acosta D, Frydman JL, Flier L, Garces-Descovich A, Cahalane MJ, Gangadharan SP, Atkins KM, Kent TS. Mistreatment and the learning environment for medical students on general surgery clerkship rotations: What do key stakeholders think? *Am J Surg* 2017;213(2):307-312.

Heidinger BH, Anderson KR, Moriarty EM, Costa DB, Gangadharan SP, VanderLaan PA, Bankier AA. Size measurement and T-staging of lung adenocarcinomas manifesting as solid nodules ≤ 30 mm on CT: Radiology-Pathology correlation. *Acad Radiol* 2017;24(7):851-859.

Wilson JL, Whyte RI, Gangadharan SP, Kent MS. Teamwork and communication skills in cardiothoracic surgery. *Ann Thorac Surg* 2017;103(4):1049-1054.

Heidinger BH, Anderson KR, Nemeč U, Costa DB, Gangadharan SP, VanderLaan PA, Bankier AA. Lung adenocarcinoma manifesting as pure ground-glass nodules: Correlating CT size, volume, density, and roundness with histopathologic invasion and size. *J Thorac Oncol* 2017;12(8):1288-1298.

Heidinger BH, Nemeč U, Anderson KR, Costa DB, Gangadharan SP, VanderLaan PA, Bankier AA. "Rounding" the size of pulmonary nodules: Impact of rounding methods on nodule management, as defined by the 2017 Fleischner Society Guidelines. *Acad Radiol* 2017;24(11):1422-1427.

Assmann A, Vegh A, Ghasemi-Rad M, Bagherifard S, Cheng G, Sani ES, Ruiz-Esparza GU, Noshadi I, Lassaletta AD, Gangadharan S, Tamayol A, Khademhosseini A, Annabi N. A highly adhesive and naturally derived sealant. *Biomaterials* 2017;140:115-127.

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Adnan Majid, MD

Associate Professor of Medicine
Chief, Section of Interventional Pulmonology

RESEARCH GROUP

Daniel Alape, MD
Alex Chee, MD
Andres de Lima, MD
Sebastian Fernandez- Bussy, MD
Erik Folch, MD, MSc
Christian Ghattas, MD
Van Holden, MD
Fayez Kheir, MD
Timothy LeClair, MD
Mathieu Marcoux, MD
Mihir Parikh, MD
Estefania Rivera, MD
Melibea Sierra, MD
Rani Singh, PhD

RESEARCH FOCUS

Our research is clinical in nature and aims at improving care for patients with lung, airway and pleural disorders. Our research areas include:

Emphysema

Prospective, Randomized, Controlled Multicenter Clinical Study to Evaluate the Safety and Effectiveness of the IBV® Valve System for the Single Lobe Treatment of Severe Emphysema (EMPROVE). We are evaluating the improvement of lung function after treatment with the IBV® Valve System compared to medical management. Benefits of the IBV to patients may include:

- Reduction in lung volume
- Improvement in pulmonary function and quality of life

Lung Function Improvement after Bronchoscopic Lung Volume Reduction with Pulmonx Endobronchial Valves (EBV) Used in Treatment of Emphysema (LIBERATE). This is a phase 3, multi-center, prospective, randomized, controlled study with EBV treatment. Benefits to patients may include:

- Improvement in lung function
- Increased exercise tolerance

Prolonged air leaks

Safety and Effectiveness of the Spiration Valve System in Air Leaks, Valves against Standard Therapy (VAST). We are evaluating the treatment with the Spiration Valve System (SVS) as compared to standard chest tube drainage management and other standard-of-care interventions in this multicenter, prospective, randomized, controlled study. Benefits to the patients may include:

- Reduction in air leak resolution time and overall hospital stay

Lung cancer diagnostics

Evaluation of the Archimedes™ System for Transparenchymal Nodules Access 2 (EAST 2). The purpose of this study is to continue evaluating the safety and performance of an updated version of the LungPoint System (called the Archimedes™ System) for aiding the physician in guiding endoscopic tools to

pulmonary nodule(s) located more distally in parenchymal tissue. Benefits of this system may include:

- Higher yield rate than existing bronchoscopic biopsy modalities
- Patient access to a minimally invasive bronchoscopic approach to the diagnosis of lung cancer

A Multi-Center Trial of the ProLung Test™ (Transthoracic Bioconductance Measurement) as an Adjunct to CT Chest Scans for the Risk Stratification of Patients with Pulmonary Lesions Suspicious for Lung Cancer. This study aims to demonstrate the safety and efficacy of the ProLung Test in the risk stratification of patients with pulmonary lesions identified by CT that are suspicious for lung cancer.

Tracheobronchomalacia

Our division maintains the largest tracheobronchomalacia (TBM) registry in the United States, which has enabled us to develop current guidelines for medical, endoscopic, and surgical therapy.

Airway Stents for Excessive Dynamic Airway Collapse: A Randomized Trial. This study is a prospective, randomized clinical trial to determine the role of airway stenting and to identify patients with excessive dynamic airway collapse (EDAC) who may benefit from surgical correction or repair.

Malignant pleural effusions

A Pivotal Multi-Center, Randomized, Controlled, Single Blinded Study Comparing the Silver Nitrate-Coated Indwelling Pleural Catheter (SNCIPC) to the Uncoated PleurX® Pleural Catheter for the Management of Symptomatic, Recurrent, Malignant Pleural Effusions (SWIFT). The purpose for the protocol is to perform a prospective, multicenter, randomized, controlled clinical trial to examine the clinical utility and efficacy of indwelling pleural catheter material on pleurodesis in the treatment of symptomatic, recurrent malignant pleural effusions, comparing silver-nitrate coated vs uncoated (standard-of-care device) pleural catheters.

ACCOMPLISHMENTS 2016-2017

- Dr. Fayed Kheir was recently awarded the 2016-2017 American Association of Bronchology and Interventional Pulmonology (AABIP) Research Award. I am one of the mentors on this project, entitled "Fibrinolytic Therapy versus Medical Thoracoscopy for Treatment of Pleural Infection." This trial is a prospective, randomized clinical trial to compare two currently accepted standard-of-care treatment strategies for the management of pleural infections in adults. This proposal was selected as the best among several high-quality submissions sent to the AABIP Award Committee.
- While participating in the EMPROVE and LIBERATE Trials, we identified a subgroup of patients for which endobronchial lung volume reduction by way of intrabronchial valves (IBVs) was not an option due to incomplete interlobar fissures. In 2016-2017, in collaboration with Dr. Sidhu Gangadharan and Spiration, Inc., we successfully showed complete targeted lobar collapse through a minimally invasive surgical stapling technique to complete interlobar fissures followed by IBV placement in both ex-vivo and live animal models. In 2018, we plan to transition this research to a pivotal human clinical trial in hopes of helping patients who would otherwise not be candidates for such treatment.

TEACHING, TRAINING, AND EDUCATION

The Interventional Pulmonary (IP) Fellowship Program at BIDMC started in 2000 and merged with the Massachusetts General Hospital (MGH) IP fellowship in 2012 to create the Combined BIDMC-MGH IP Fellowship Program, of which I am the director. Our fellowship is one of the largest in the nation. Each year we accept three physicians into the competitive one-year program. Over the last 17 years, 31 fellows have graduated from the program and moved on to develop successful programs around the United States.

We also offer a variety of educational activities for trainees and faculty at BIDMC and around the world, including our annual "Introduction to Interventional Pulmonology" course.

Invited Presentations

- Management of Hemoptysis Workshop; American Thoracic Society: Post Graduate Course, Washington, DC, 2017
- Role of Bronchoscopy in Asthma Diagnosis; Clinica Alemana, Universidad del Desarrollo, Santiago, Chile, 2017
- Bronchial Thermoplasty: Choosing the Right Patient; Clinica Alemana, Universidad del Desarrollo, Santiago, Chile, 2017
- EBUS-TBNA: Indications, diagnostic yield, complications; Peruvian Association of Bronchology and Interventional Pulmonology, Lima, Peru, 2017
- EBUS: Other Applications; Peruvian Association for Bronchology and Interventional Pulmonology, Lima, Peru, 2017
- Live EBUS Case at Maison de Sante; Peruvian Association for Bronchology and Interventional Pulmonology, Lima, Peru, 2017
- New Diagnostic Techniques in Lung Cancer; V Bienal de Neumologia, Seville, Spain, 2017

ABSTRACTS, POSTERS, AND EXHIBITS

Alape D, Kheir F, Gangadharan S, Parikh M, Wilson J, Chee A, Majid A. Stent trial for expiratory central airway collapse: Does the type of stent really matter? CHEST Conference, Toronto, ON, 2017

Sierra M, Fernandez-Bussy S, Mehta H, Kheir F, Barry M, Jantz M, Chee A, Parikh M, Majid A. Bronchial thermoplasty in severe uncontrolled asthma with different phenotypes. CHEST Conference, Toronto, ON, 2017

De Lima A, Kheir F, Fernandez-Bussy S, Parikh M, Chee A, Majid A. Tunneled pleural catheters for the treatment of patients with pleural infection and a non-expandable lung: A single-center case series. CHEST Conference, Toronto, ON, 2017

Ghattas C, Kheir F, Gesthalter Y, Parikh M, Chee A, Sierra M, Majid A. Sonographic features of lymph nodes during endobronchial ultrasound guided transbronchial needle aspiration in comparison with mediastinoscopy. CHEST Conference, Toronto, ON, 2017

Rivera E, Kheir F, Chee A, Parikh M, Fernandez-Bussy S, Majid A. Volumetric analysis of pleural effusions: a quantitative comparison between Chest CT and thoracentesis drainage. CHEST Conference, Toronto, ON, 2017

SELECTED PUBLICATIONS

Fernández-Bussy S, Labarca G, Caviedes I, Mehta HJ, Jantz M, Majid A. Endoscopic lung volume reduction in advanced pulmonary emphysema: initial experience in Chile. *Rev Med Chil* 2017;145(5):667-672.

Kheir F, Rivera E, Majid A. An adolescent with dyspnea and cough: A case of congenital tracheal stenosis. *Am J Respir Crit Care Med* 2017;196(7):e30-e31.

Majid A, Kheir F, Chung J, Alape D, Husta B, Oh S, Folch E. Covered balloon-expanding stents in airway stenosis. *J Bronchology Interv Pulmonol* 2017;24(2):174-177.

Fernandez-Bussy S, Labarca G, Majid A. In reply: Biodegradable stent for vanishing bronchus syndrome after lung transplantation. *J Heart Lung Transplant* 2017;36(5):592.

Buitrago DH, Wilson JL, Parikh M, Majid A, Gangadharan SP. Current concepts in severe adult tracheobronchomalacia: Evaluation and treatment. *J Thorac Dis* 2017;9(1):E57-E66.

Majid A, Ochoa S, Chatterji S, Fernandez-Bussy S, Kheir F, Rivera E, Cheng G, Folch E. Safety and efficacy of tissue plasminogen activator and DNase for complicated pleural effusions secondary to abdominal pathology. *Ann Am Thorac Soc* 2017;14(3):342-346.

A complete list of publications begins on page 13.



Mihir S. Parikh, MD

Instructor in Medicine

Director of Interventional Pulmonology at BID–Milton

RESEARCH GROUP

Jason Beattie, MD
Andres DeLima, MD
Van Holden, MD
Carlos Sisniega, MD
Morgan Soffler, MD
Juan Pablo Uribe Becerra, MD

RESEARCH FOCUS

My research aims to better understand the way we train learners in medical procedures and the metrics we use to confirm mastery of these skills. As medical training evolves from volume-based metrics to competency-based assessments, I want to find more accurate and more efficient techniques to teach medical procedures in the context of the myriad pressures facing our learners during their packed training schedules. To that end, I am conducting a number of clinical trials aimed at improving procedural education for pulmonary and critical care medicine fellows. I am also running several quality improvement studies investigating ways to improve outcomes in commonly performed pleural procedures.

ACCOMPLISHMENTS 2016-2017

- Joined medical staff of BIDMC and BID–Milton
- Named Instructor in Medicine at Harvard Medical School
- Named Director of Interventional Pulmonology at BID–Milton
- Named Program Director of Endobronchial Ultrasound Fellowship at BIDMC
- Ran annual bootcamp course in Bronchoscopy and Pulmonary Procedures Course at BIDMC
- Invited speaker at regional medical center grand rounds (including MetroWest Hospital, BID–Milton, and BIDMC)
- Invited speaker at CME course in Principles of Critical Care Medicine course
- Multiple published manuscripts and conference presentations (see next page)

TEACHING, TRAINING, AND EDUCATION

I am one of the core training faculty for the Interventional Pulmonology Fellowship Program at BIDMC. I serve as Program Director for the Endobronchial Ultrasound Fellowship Program at BIDMC and I also serve on the Program Evaluation Committee for the Combined MGH/BIDMC Pulmonary and Critical Care Medicine Fellowship Program. I also run our annual bootcamp course in Bronchoscopy and Pulmonary Procedures attended by in-coming pulmonary and critical care medicine fellows throughout the northeastern U.S. I also teach pulmonary pathophysiology to medical students in Harvard's HST program.

ABSTRACTS, POSTERS, AND EXHIBITS

Rivera E, Holden V, Parikh M. Characteristics of indwelling pleural catheter related infections. International Conference of the American Thoracic Society, Dallas, TX, 2018

DeLima A, Ghattas C, Parikh M. Impact of a one-day introductory course to pulmonary and pleural procedures. International Conference of the American Thoracic Society, Dallas, TX, 2018

Holden V, Chee A, Parikh M, Majid A. Safety and efficacy of a new fully covered self-expandable metallic airway stent. International Conference of the American Thoracic Society, Dallas, TX, 2018

Rivera E, Kheir F, Husta B, Chee A, Parikh M, Majid A. Fluid infusion through chest tube to facilitate pleural procedures. CHEST Annual Meeting, Toronto, ON, 2017

De Lima A, Kheir F, Fernandez-Bussy S, Parikh M, Chee A, Majid A. Tunneled pleural catheters for the treatment of patients with pleural infection and a non-expandable lung: A single-center case series. CHEST Annual Meeting, Toronto, ON, 2017.

SELECTED PUBLICATIONS

Buitrago DH, Wilson JL, Parikh M, Majid A, Gangadharan S. Current concepts in severe adult tracheobronchomalacia: Evaluation and treatment. *J Thorac Dis* 2017;9(1):E57-E66.

Parikh M, Krishna G. "Endobronchial Ultrasound," in Orloff LA, Ed., *Head and Neck Ultrasonography*. San Diego: Plural Publishing, 2017, pp. 273-283.

Parikh M, Wilson J, Majid A, Gangadharan S. Airway stenting in tracheobronchomalacia. *Journal of Visualized Surgery* 2017;22(3): 172.

Kheir F, Cheng G, Rivera E, Folch A, Folch E, Fernandez-Bussy S, Keyes C, Parikh M, Channick C, Chee A, Majid A. Concurrent versus sequential intrapleural instillation of tissue plasminogen activator and deoxyribonuclease for pleural infection. *Journal of Bronchology and Interventional Pulmonology* 2018;25(2):125-131.

Buitrago D, Majid A, Alape D, Wilson J, Parikh M, Kent M, Gangadharan S. Single-center experience of tracheobronchoplasty for severe tracheobronchomalacia: Clinical practice patterns and perioperative outcomes. *Ann Thorac Surg* 2017; In press.

VanderLaan P, Rangachari D, Majid A, Parikh M, Gangadharan S, Kent M, Huberman M, Kobayashi S, Costa D. Tumor biomarker testing in non-small cell lung cancer: A decade of change. *Lung Cancer* 2018;116:90-95.

Buitrago D, Gangadharan S, Majid A, Kent MS, Alape D, Wilson JL, Parikh M, Kim DH. Frailty characteristics predict respiratory failure in patients undergoing tracheobronchoplasty. *Ann Thorac Surg* 2018;106(3):836-841.



Jennifer L. Wilson, MD

Instructor in Surgery

RESEARCH GROUP

Alexander Bankier, MD
Alex Chee, MD
Sidhu P. Gangadharan, MD
Michael S. Kent, MD
Adnan Majid, MD
Mihir Parikh, MD
James R. Rodrigue, PhD
Paul Vanderlaan, MD
Richard I. Whyte, MD

RESEARCH FOCUS

My research has focused largely on clinical outcomes in the following areas:

Complex Airway Disease

This high volume program at BIDMC allows us to encounter a large number of patients with adult tracheobronchomalacia. As part of our collaboration with interventional pulmonology, we continue to build on an existing database so that we can learn more about the etiology, natural disease process with and without intervention, and surgical outcomes—and increase the recognition of this rare disease. We are currently working on developing and validating a quality of life questionnaire for adult tracheobronchomalacia so that we can better follow our patients' outcomes in the future.

Lung Cancer

I am part of several collaborative groups with Alexander Bankier, MD (Chief, Cardiothoracic Imaging Section of Radiology) and Paul Vanderlaan, MD (Director of Thoracic Pathology). Our collaborative projects have included radiology-pathology-surgical correlates of squamous cell lung cancer as well as lung cancers with specific pathologic findings such as visceral pleural invasion. In addition, we are exploring inter-observer agreement among pathologists for frozen section on lung cancer adenocarcinoma subtypes.

Lung Cancer Screening

I have recently joined the Department of Public Health Lung Cancer Screening Work Group in order to learn more about how we can collaborate to combat lung cancer screening disparities. There are many opportunities for focus groups, pilot implementation projects, hospital level, state level, and national level interventions that could help us better understand and mitigate lung cancer screening disparities.

Other research interests include:

- Quality improvement and cost effectiveness
 - Reducing cost in the OR for VATS lobectomy cases with immediate charge feedback and charge labeling
- Resident and fellow education
- Mediastinal diseases

Invited Presentations:

- Update on Lung Cancer Screening; Surgical Grand Rounds, Mount Auburn Hospital, Cambridge, MA
- Thoracic Surgery: Current Practices and Future Directions; Medicine Grand Rounds, Cambridge Health Alliance, Cambridge, MA
- Training Fellows in Robotic Surgery; American Association for Thoracic Surgeons annual meeting in Boston, MA

Invited Instructor:

- Advanced Open Esophageal and Tracheal Procedures; Society of Thoracic Surgeons Annual Meeting, Houston, TX
- Chest Tube Primer; BIDMC Critical Care fellow presentation
- Disorders of the Mediastinum: Thymic Lesions; JCTSE TSRA Core Curriculum presentation for BIDMC cardiothoracic residents and fellows
- Disorders of the Pleura; JCTSE TSRA Core Curriculum presentation for BIDMC cardiothoracic residents and fellows
- Neoplasms of the Lung; JCTSE TSRA Core Curriculum presentation for BIDMC cardiothoracic residents and fellows
- Benign Lung Conditions; JCTSE TSRA Core Curriculum presentation for BIDMC cardiothoracic residents and fellows

Other Accomplishments:

- Completed the Summer Program in Clinical Effectiveness at the Harvard T.H. Chan School of Public Health, Boston, MA
- Lead a quality improvement project at BIDMC: Thoracic surgery patient education pamphlet creation
- Completed the American Board of Thoracic Surgeons full board certification
- Started a thoracic tumor board at Cambridge Health Alliance, Cambridge, MA
- Joined the Department of Public Health Lung Cancer Screening Work Group

TEACHING, TRAINING, AND EDUCATION

Weekly thoracic surgery resident and fellow preoperative conference is held in order to help residents make the leap from trainee to surgeon. At this conference, residents present all upcoming cases and key points are highlighted in an open teaching environment that focuses on board preparation for the rotating residents and cardiothoracic fellows, as well as real world clinical decision making. Furthermore, having medical students, residents, and fellows in the operating room allows for constant level appropriate teaching such as live anatomy review, basic and complex surgical techniques, and perioperative management of patients. The aim of our program is to create independent and clinically competent surgeons who recognize the importance of treating the patient and their disease.

ABSTRACTS, POSTERS, AND EXHIBITS

Whyte RI, Beqari J, Ritzer L, Wilson JL, Gangadharan SP, Majid A, Kent MS. Should thoracic surgeons be doing EBUS and other advanced bronchoscopic cases? Western Thoracic Surgical Association meeting, Colorado Springs, CO, 2017 (Abstract, Dr. Whyte)

Buitrago DH, Wilson JL, Alape D, Parikh M, Majid A, Gangadharan SP. Perioperative outcomes in 161 consecutive patients undergoing tracheobronchoplasty for severe diffuse tracheobronchomalacia. General Thoracic Journal Club, Clearwater, FL, 2017 (Abstract, Dr. Buitrago)

Maxfield, MW, Buitrago DH, Wilson JL, Parikh M, Majid A, Gangadharan SP. Re-do Tracheobronchoplasty for Recurrent Trcheobronchomalacia. General Thoracic Journal Club, Clearwater, FL, 2017 (Poster, Dr. Maxfield)

Wilson JL, Whyte RI, Gangadharan SP, Kent MS. Teamwork and communication skills in cardiothoracic surgery. *Ann Thorac Surg* 2017;103(4):1049-1054.

Buitrago DH, Wilson JL, Parikh M, Majid A, Gangadharan SP. Current concepts in severe adult tracheobronchomalacia: Evaluation and treatment. *J Thorac Dis* 2017;9(1):E57-E66.

Wilson JL and Whyte RI. The management of primary chest wall tumors. *Current Surgery Therapy 12th Edition* 2017;867-871.

Feczko A, McKeown E, Wilson JL, Louie BE, Aye RW, Gorden JA, Vallieres E, Farivar AS. Assessing survival and grading the severity of complications in octogenarians undergoing pulmonary lobectomy. *Canad Resp Jour* 2017;6294895.

Robert A. Fisher, MD, FACS

Professor of Surgery
Chief, Transplantation



RESEARCH GROUP

Giuseppe Pettinato, PhD
Melissa Thompson

RESEARCH FOCUS

I took the lead in the NIH-funded multicenter “A2ALL” (Adult to Adult Living Donor Liver Transplant) prospective study. Of the original nine PIs in participating centers in the United States, I was one of only six of them to hold the U01 for both five-year complete grant periods, including the three-year extension. This study has become the landmark trial for living-donor liver transplant in this country since its inception in 2001 and completion on August 31, 2014, with the receipt of over \$8 million in NIH and private funding over the years. In early 2016 we received approval from UNOS to reinstate the living donor liver transplant program at BIDMC, and since then four successful adult LDLTs have been performed, with three more scheduled for 2018.

In addition to the A2ALL NIH multicenter trial, I was awarded NIH funding for spinoff studies looking at genomics and proteomics of hepatitis-C-associated cirrhosis and hepatocellular carcinoma (HCC), which produced landmark results and publications describing profiles of patients with hepatitis-C who develop HCC and which patients will have a high risk of recurrence after transplantation.

Success in both scientific research and clinical hepatocyte transplantation since 1991 has led to my strong involvement in the field of cell transplantation, with frequent invitations to chair or moderate sessions at national and international meetings of organ transplant and cell transplant societies. I have been formally appointed to the Editorial Boards of *Liver Transplantation*, *Cell Transplantation*, and *Cell R4 Journal*. I am also an ad hoc reviewer of many journals in the field and abstract reviewer for the American Transplant Congress, International Liver Transplantation Society, The Transplantation Society, and the International Cancer Association. I am also honored to serve as President of the Cell Transplant and Regenerative Medicine Society (September 2017-September 2019).

Melissa Thompson, BS, Cell Transplant Specialist, is my Research Program Manager for all laboratory operations. We are the center at BIDMC for hepatocyte and stem cell transplant, with continuation of my FDA IND in hepatocyte transplantation which started in Richmond. Giuseppe Pettinato, PhD, Instructor in Surgery, is the Director of my Stem Cell Lab. BIDMC has an American Society of Transplant Surgeons (ASTS)-accredited Kidney Fellowship Program and my expectation is to reinstate our ASTS-accredited Liver Fellowship Program, eventually extending that to an ASTS-accredited Pancreas Program, and finally an accredited Hepatobiliary Surgery Program combined with the Hepatobiliary Surgery Group here at BIDMC after the Lahey merger practice legalities are completed.

- President of the Cell Transplant and Regenerative Medicine Society
- Serve on Board of Directors for the American Foundation for Donation and Transplantation
- Member of the editorial boards for *Liver Transplantation*, *Liver Disease Review Letters*, *Medscape*, *LL Transplantation Editorial Advisory Board*, *Transplantation Proceedings*, *World Journal of Transplantation*, and *Cell R4 Journal*

Invited Presentations

- Tissue engineering and biomaterials for regenerative medicine; 9th World Congress of Regenerative Medicine and Stem Cell, Seoul, South Korea, 2016
- Challenges in clinical translation with hepatocytes; Center for Drug Safety and Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Workshop on Novel Biotechnology in Liver Diseases, Shanghai, China, 2017
- Differentiation of hiPSC into hepatocyte-like clusters; Center for Drug Safety and Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Workshop on Novel Biotechnology in Liver Diseases, Shanghai, China, 2017
- Challenges in clinical translation with hepatocytes; Canadian Society of Transplantation/ Cell Transplant and Regenerative Medicine Society Joint Scientific Meeting; Halifax, Nova Scotia, 2017

TEACHING, TRAINING, AND EDUCATION

It has been my privilege to nurture students, residents, fellows, undergraduates and research students by teaching and challenging them on the floor, in clinic, in the OR, and in my research lab. Some of my trainees have gone on to illustrious careers of their own, and at least two are now department chairs.

Since my arrival at BIDMC in the fall of 2014, I have given invited talks and in-services to multiple departments in the hospital, especially in the clinical area of live donor liver transplantation, including two daylong multidisciplinary Mock Drills to teach the processes and procedures involved in this difficult surgery to peers, nurses and OR staff. I have also been an invited speaker at regional conferences including the Nurses' Conference at the New England Organ Bank, and courses such as the HMS course "Advances in Gastroenterology."

SELECTED RESEARCH SUPPORT

Advancing Renal Transplant Efficacy and Safety Outcomes with Everolimus-based regimen (TRANSFORM); Novartis Pharmaceuticals, 2015-2017; Co-PI: Robert A. Fisher, MD

Allogenic Hepatocyte Transplant for Chronic Liver Failure Support, with Y-90 HCC Rx to Increase Hepatocyte Nidation; FDA, 2010-present; PI: Robert A. Fisher, MD

Pettinato G, Ramanathan R, Fisher RA, Mangino MJ, Zhang N, Wen X. Scalable differentiation of human iPSCs in a multicellular spheroid-based 3D culture into hepatocyte-like cells through direct Wnt/ -catenin pathway inhibition. *Sci Rep* 2016;6:32888.

Butt Z, Dew MA, Liu Q, Simpson MA, Smith AR, Zee J, Gillespie BW, Abbey SE, Ladner DP, Weinrieb R, Fisher RA, Hafliger S, Terrault N, Burton J, Sherker AH, Di Martini A. Psychological outcomes of living liver donors from a multi-center, prospective study: Results from the adult to adult living donor liver transplantation cohort study (A2ALL). *Am J Transplant* 2017;17(5):1267-1277.

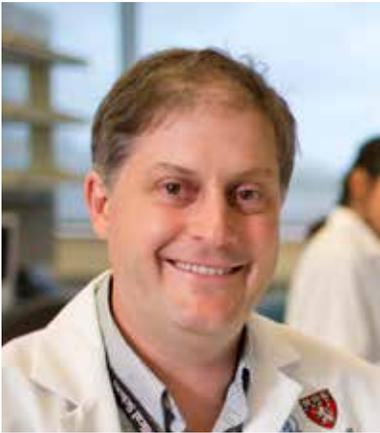
DiMartini A, Dew MA, Liu Q, Simpson MA, Ladner DP, Smith AR, Zee J, Abbey S, Gillespie BW, Weinrieb R, Mandell MS, Fisher RA, Emond JC, Freise CE, Sherker AH, Butt Z. Social and financial outcomes of living liver donation: a prospective investigation within the Adult-to-Adult Living Liver Cohort Study-2 (A2ALL-2). *Am J Transplant* 2017;17(4):1081-1096.

Fisher RA. Living donor liver transplantation: eliminating the wait for death in end-stage liver disease? *Nat Rev Gastroenterol Hepatol* 2017;14(6):373-82.

Dew MA, Butt Z, Liu Q, Simpson MA, Zee J, Ladner DP, Holtzman S, Smith AR, Pomfret EA, Merion RM, Gillespie BW, Sherker AH, Fisher RA, Olthoff KM, Burton JR Jr, Terrault NA, Fox AN, DiMartini AF. Prevalence and predictors of patient-reported long-term mental and physical health after donation in the Adult to Adult Living Donor Liver Transplantation Cohort Study (A2ALL). *Transplantation* 2018;102(1):105-118.

Leo E. Otterbein, PhD

Professor of Surgery



RESEARCH FOCUS

Inhaled carbon monoxide (CO) is in numerous FDA phase trials, based in large part from the research that has arisen from my laboratory over the past decade. We continue to maintain a focus on the innate immune response and defense mechanisms in models of trauma, infection, ischemia reperfusion injury, and regenerative responses to tissue damage. The foundation of our work lies in the study of protective genes and in particular those that degrade heme and include heme oxygenase-1 (HO-1) and biliverdin reductase (BVR). Both of these genes are intimately involved in the stress response and function in large part by generating CO and bilirubin as endogenous products. We have expanded our research program to include collaborative projects on cancer, neurology and more recently exercise physiology. Each of these complement and advance our understanding of the acute stress response and the roles of HO-1/CO as they relate to immunologic and pathophysiological responses. Ultimately, we are interested in translational research to provide solutions towards alleviating human suffering.

Role of Heme in Trauma and Infection

This year we reinforced collaborative efforts in models of trauma and the impact on susceptibility to pneumonia. As Co-Director of a 6-project CDMRP Department of Defense focused research award (\$10M) awarded in 2017, we are seeking to provide deliverables to benefit the injured warfighter. As PI of one project our approach is to define how heme influences recovery from trauma and susceptibility to bacterial infection. The research involves interactive studies with Carl Hauser, MD (BIDMC, Surgery), Jim Lederer, PhD (BWH, Surgery), Daniel Talmor (BIDMC,

Anesthesiology), Simon Robson (BIDMC, Medicine), and Michael Yaffe, MD, PhD (MIT). Our data in sepsis models shows that HO-1 derived CO acts directly on bacteria, coercing them to generate ATP, which activates local immune cells including macrophages and neutrophils and initiates a full immune response to clear bacteria through an inflammasome-mediated mechanism of action. Additionally HO-1/CO promote liver regeneration after a crush injury.

Neuroprotection with HO-1 and the Role of the Circadian Clock

We maintain an active collaboration with Khalid Hanafy, MD, PhD, (BIDMC, Neurology) in the study of hemorrhagic stroke, where we find that glia-expressed HO-1 is critical in resolution of injury and impacts neurotransmission as it relates to memory. Inhaled CO enhances recovery, reduces inflammation and cell death, and improves cognitive function. The mechanism involves the ability of CO to boost phagocytosis of erythrocytes. Recently we reported in *Stroke* the circadian rhythm of HO-1 in the brain and demonstrate that HO-1/CO promote recovery from hemorrhagic stroke in part by modulation of central clock genes including Period and NPAS2 among others. We are actively collaborating with the labs of Dr. Hanafy (BIDMC, Neurology) and Dr. Eng Lo (MGH, Radiology) in a multi-PI approach in conjunction with pharma to develop CO as a treatment strategy for hemorrhagic stroke.

Given the above salutary effects of CO in the brain, we submitted a proposal to the National Football League (NFL) and were selected as part of a multi-institutional program grant (\$18M) to evaluate the effects of CO to alleviate brain injury simulating that which would occur as a result of multiple mild concussions that occur during football games. Together with Dr. Ping Lu (BIDMC, Medicine), and Dr. Patrick Fuller (BIDMC, Neurology) we will test over the next five years the ability of CO to limit injury and promote recovery in preclinical models of concussion. Exciting preliminary data in mice demonstrate the remarkable role of HO-1 in brain homeostasis.

Carbon Monoxide and Kidney Transplant

We are funded with Phase 2 NIH SBIR (\$1.5M) to study an exciting and innovative oral CO solution in rat and pig models of kidney transplant in collaboration with Hillhurst Biopharmaceuticals. These studies are ongoing, but complement and expand on those we reported on with inhaled CO, which showed a benefit to reduce delayed graft function and triggered the first human trial. The oral formulation is simple and is being applied to multiple model systems including TBI and trauma. Proof of principal has been demonstrated and the CO formulation is now being prepared for human testing.

HO-1 in Cancer

In collaboration and funded by Agios Pharmaceuticals, we are interested in the role of macrophages in tumor growth testing the hypothesis that the phenotype of the macrophage regulates its ability to direct Tcell function. Using our regulated HO-1 null mice, we find that blockade of HO-1 significantly reduces tumor growth.

RESEARCH GROUP

Eva Cszmadia, MS
 Mahtab Faktari, MD
 David Gallo
 James Harbison
 Ghee Lee, MS
 Shazhad Shaefi, MD
 Rodrigo Souza, PhD
 Janick Weber

Relationship Between the Microbiome, Glycome, and Tissue Damage

It has been known that the intestinal microbiome is important in numerous immune regulatory functions and that HO-1/CO can influence the intestinal flora in models of acute inflammation. Additionally, preliminary data show that injury leads to a change in serum N-glycosylation. This finding is part of a new collaborative project with Richard Cummings (BIDMC, Surgery) and Carl Hauser (BIDMC, Surgery), to integrate glycobiology and microbiome modulation in response to injury comparing human and murine samples.

HO-1 and Exercise Metabolism

A new project in the laboratory, we are interested in how physical exercise influence HO-1 expression and can contribute to offering protection in models described above. Preliminary findings suggest that exercise metabolism is influenced by heme catabolism and the generation of CO.

ACCOMPLISHMENTS 2016-2017

We continue to be one of the leaders in the area of heme metabolism and the stress response, providing mechanistic insight into the role of HO-1 and its bioactive products carbon monoxide and the bile pigments. Our publications continue to provide important contributions toward therapeutic use of these molecules in the clinic, which guided more than 10 ongoing clinical trials with CO. We consider ourselves a team with excellent technical skills combined with creative and innovative approaches to research design, always with translation to human disease in our sites.

Invited Presentations

- 10th International Conference on Heme Oxygenases, Seoul, South Korea
- University California San Diego/ Scripps Institute of Oceanography
- World Conference on Microcirculation, Vancouver, CA
- American Chemical Society, New Orleans, LA
- Gasotransmitters and Medicine, Atlanta, GA
- Oral Carbon Monoxide, Hillhurst Pharma, Tucson, AZ
- Virtual IACUC Scenario's, PRIM&R and IACUC Conference, Boston, MA

Other Accomplishments

- Chair of the BIDMC Institutional Animal Care and Use Committee
- BIDMC Site Miner for the Center for Integration of Medicine and Innovative Technology (CIMIT)
- BIDMC representative for the Boston Biomedical Innovations Center (B-BIC), Technology Assessment and Development Group
- Continue in my 15th consecutive year as an NIH study section member for K01, K08, K02, K99, and loan repayment, grant applications
- Served as grant reviewer for the Wellcome Trust, United Kingdom Medical Research Council, Israel Science Foundation, Yale University Pepper awards, New Zealand Research Foundation, and Pasteur Institute among others

TEACHING, TRAINING, AND EDUCATION

I continue to participate in the training of graduate students, post-doctoral fellows, surgical residents, and junior faculty in basic research, grant proposals, and career guidance. I was a preceptor for the Trauma T32 training grant 2017/18 and am currently mentoring a K08 and AHA applications. As the BIDMC CIMIT site miner and as a member of the B-BIC Technology Assessment and Development Group, I mentor and provide specialized expertise in entrepreneurial start-up ventures for innovative technologies. In addition to the science, I also advise on grant submissions, potential commercialization of ideas, interactions with the Technology Ventures Offices, and various accelerator and venture opportunities.

SELECTED RESEARCH SUPPORT

DAMP-mediated innate immune failure and pneumonia after trauma; DoD, 2016-2021; Co-Director: Leo Otterbein, PhD

Harvard Trauma Inflammation Training Program; NIH T32 Training Grant, 2013-2019; Preceptor: Leo Otterbein, PhD (Director: Carl Junger, PhD)

HBI-002 to treat delayed graft function after transplant; NIH, 2016-2019; PI: Leo Otterbein, PhD

Immunomodulatory effects of bilirubin are mediated through the aryl hydrocarbon receptor, O₂ and purinergic pathways; NIH, 2017-2022; Co-Investigator: Leo Otterbein, PhD (PI: Maria Longhi, MD, PhD)

Heme Oxygenase-1 (HO-1) and tumor growth; Agios Pharmaceuticals, 2017-2019; PI: Leo Otterbein, PhD

HBI-002 to treat traumatic injury; NIH, 2017-2019; Academic Site PI: Leo Otterbein, PhD (PI: Stephen Gomperts, MD, PhD, MGH)

SELECTED PUBLICATIONS

Nemeth Z, Csizmadia E, Vikstrom L, Bisht K, Feiz, A, Otterbein S, Zuckerbraun B, Costa DB, Pandolfi PP, Fillinger J, Döme B, Otterbein LE, Wegiel B. Alterations of tumor microenvironment by carbon monoxide impedes lung cancer growth. *Oncotarget* 2016;26:23919-32.

Chan MC, Ziegler O, Liu L, Rowe GC, Das S, Otterbein LE, Arany Z. Heme oxygenase and carbon monoxide protect from muscular dystrophy. *Skeletal Muscle* 2016;28:41.

Itagaki K, Riça I, Zhang J, Gallo D, DePrato M, Otterbein LE, Hauser CJ. Intratracheal instillation neutrophils rescues bacterial overgrowth initiated by trauma damage-associated molecular patterns. *J. Trauma Acute Care Surg* 2017;82: 853-860.

Sandler N, Kaczmarek E, Itagaki K, Zheng Y, Otterbein L, Khabbaz K, Liu D, Senthilnathan V, Gruen RL, Hauser CJ. Mitochondrial DAMPs are released during cardiopulmonary bypass surgery and are associated with postoperative atrial fibrillation. *Heart Lung Circ* 2018;27(1):122-129.

Longhi MS, Vuerich M, Kalbasi A, Kenison JE, Yeste A, Csizmadia E, Vaughn B, Feldbrugge L, Mitsuhashi S, Wegiel B, Otterbein L, Moss A, Quintana FJ, Robson SC. Bilirubin suppresses Th17 immunity in colitis by upregulating CD39. *JCI Insight* 2017;2(9).

Lee H, Zhang D, Wu J, Otterbein LE, Jin Y. Lung epithelial cell-derived microvesicles regulate macrophage migration via MicroRNA-17/221-induced integrin β 1 recycling. *J. Immunol* 2017;199:1453-1464.

Schallner N., Lieberum J-L, Gallo D, LeBlanc RH, Fuller PM, Hanafy, KA, Otterbein, LE. Carbon monoxide preserves circadian rhythm to reduce the severity of subarachnoid hemorrhage in mice. *Stroke* 2017;48: 2565-2573.

James R. Rodrigue, PhD

Professor

Vice Chair for Clinical Research



RESEARCH GROUP

Alind Amedi
Jasmine Austrie
Michaela Carroll
Charles D'Alessandro
Sarah Duncan
Mario Feranil
Aaron Fleishman, MPH
Lean Magrini
Claire Rosenwasser
Stephanie Ward

RESEARCH FOCUS

Our research seeks to answer two central questions:

“How can we reduce the gap between the number of people who need organ transplants and the availability of organs for transplantation?”

In recent years, the number of deceased organ donors has remained flat and the number of living donors has declined. In the meantime, the number of people waiting for a lifesaving organ transplant continues to rise, with over 120,000 people currently on the national transplant waiting list. Together with colleagues at BIDMC, the New England Donor Services, and several transplant programs around the country, we are developing and evaluating novel strategies to increase the rates of both living and deceased donation. These strategies address individual and systematic barriers we have identified through earlier research that are associated with lower organ donation rates.

“How can we reduce persistent race and income disparities in transplantation?”

Some minorities and low-income patients, relative to white patients and those with more financial resources, experience more kidney transplant access barriers, are more likely to have initiated dialysis at time of transplant referral, wait longer for a deceased donor transplant, are less likely to receive a live donor kidney transplant, have higher mortality rates on the waiting list, and have less optimal transplant outcomes. Since the proportion of patients on the kidney transplant waiting list is increasing for racial/ethnic minorities (while declining for whites), the shortage of deceased donor kidneys is likely to exacerbate these transplant disparities in the years ahead. We are conducting studies to better understand the precise cause of these disparities, to evaluate novel strategies for mitigating these disparities, and to examine the impact of policy changes on these disparities.

The success of our research program is due largely to the collaborative partnerships we have with federal and state governments, organ procurement organizations, and researchers from diverse professional backgrounds, including behavioral and medical sciences, public health, surgery, bioethics, nursing, and health services.

ACCOMPLISHMENTS 2016-2017

We received NIH funding to evaluate strategies to reduce racial and income disparities in live donor kidney transplantation, another Health Resources and Services Administration (HRSA) grant to evaluate a novel program to increase favorable attitudes toward vascularized composite allotransplantation and donation among military veterans, and a Patient-Centered Outcomes Research Institute (PCORI) contract to further evaluate the effectiveness of a home-based intervention to reduce racial disparity in kidney transplantation.

I co-authored several manuscripts examining outcomes in living kidney donors and the disparity-reducing benefits of the novel Transplant House Calls intervention. I accepted invitations to present our work at the European Society of Transplantation in Barcelona, and at several U.S. transplant programs, including the University of Wisconsin and Medical University of South Carolina.

I developed and implemented the FIRST Program (www.bidmcFIRST.com), a robust clinical research platform in the Department of Surgery upon which clinical research can be cultivated, nourished, and expanded.

Other recent accomplishments include:

- Continued service on NIH Study Section (Behavioral Medicine)
- Invited Participant for the Consensus Conference to Decrease Kidney Discards, sponsored by the National Kidney Foundation
- Selected to serve on two committees (Living Donor, Vascularized Composite Allograft) of the Organ Procurement and Transplantation Network
- Appointed to the Living Donor Committee of the American Society of Transplant Surgeons
- Appointed Associate Editor of Clinical Transplantation
- Inducted as a Fellow into the American Society of Transplantation
- Received the Clinician of Distinction Award from the American Society of Transplantation

TEACHING, TRAINING, AND EDUCATION

I continue to provide training and mentorship to post-doctoral fellows and research assistants. Other activities include:

- Director of the department's Clinical Scholarship Program, providing first-year residents with mentored clinical research experience
- Director of the Facilitating Innovative Research & Surgical Trials (FIRST) Program in the Department of Surgery, a clinical research platform providing guidance and mentorship to faculty, fellows, and residents
- Chair of the Department of Surgery Appointment, Re-appointments, and Promotions Committee

SELECTED RESEARCH SUPPORT

House calls and decision support: Increasing access to live donor transplantation; NIH, 2012-2017; PI: James Rodrigue, PhD

Increasing donor designation rates in teenagers: Effectiveness of a driver's education intervention; HRSA, 2014-2017; PI: James Rodrigue, PhD

Kidney paired donation: A randomized trial to increase knowledge and reduce perceived barriers; HRSA, 2015-2018; PI: James Rodrigue, PhD

House calls and peer mentorship: Increasing access to live donor transplantation; PCORI, 2017-2021; PI: James Rodrigue, PhD

Increasing VCA donation knowledge, attitudes, willingness, and designations in veterans; HRSA, 2017-2020; PI: James Rodrigue, PhD

Living donor wage reimbursement trial; NIH, 2017-2022; PI: James Rodrigue, PhD

SELECTED PUBLICATIONS

Rodrigue JR, Fleishman A. Health insurance trends in United States living kidney donors (2004-2015). *Am J Transplant* 2016;16:3504-3511.

Rodrigue JR, Tomich D, Fleishman A, Glazier AK. Vascularized Composite Allograft (VCA) donation and transplantation: a survey of public attitudes in the United States. *Am J Transplant* 2017; 17: 2687-95.

Friedman Ross L, Rodrigue JR, Veatch RM. Ethical and logistical issues raised by the Advanced Donation Program "pay it forward" scheme. *J Med Philos* 2017; 42:518-36.

Rodrigue JR, Paek M, Schold JD, Pavlakis M, Mandelbrot DA. Predictors and moderators of educational interventions to increase the likelihood of potential living donors for black patients awaiting kidney transplantation. *J Racial Ethn Health Disparities*; In press.

Rodrigue JR, Luskin R, Nelson H, Glazier A, Henderson G, Delmonico FL. Measuring critical care providers attitudes and knowledge about controlled donation and circulatory death. *Prog Transplant* 2018;28(2):142-150.

Rodrigue JR, Feranil M, Lang J, Fleishman A. Readability, content analysis, and racial/ethnic diversity of online living kidney donation information. *Clin Transplant* 2017;e13039.

A complete list of publications begins on page 13.

Barbara Wegiel, PhD, DSc

Associate Professor of Surgery



RESEARCH GROUP

Giacomo Canesin, PhD
Reeham Choudhury
Eva Csizmadia, MSc
Andreas Hedblom, PhD
Seyed Mahdi Hejazi, PharmD, MSc

RESEARCH FOCUS

My research focuses on how the metabolites such as heme or bile pigments regulate innate inflammatory responses during organ injury and carcinogenesis. This work has implications for understanding novel targets and potential therapeutics for treatment of cancer and beyond. Working with others at BIDMC, I am developing anti-cancer molecules that target cell cycle progression and the tumor microenvironment.

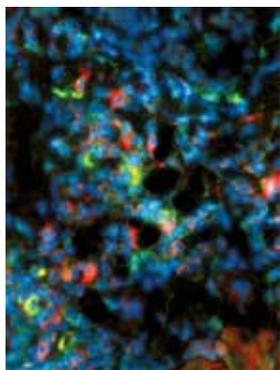
Specifically, my laboratory dissects the roles of innate immune cells (i.e., myeloid cells) in stress responses. My interest lies in regulatory mechanisms related to the heme biology and other immunometabolic genes (i.e., LDH-A) in tumor evolution and cancer therapy. The metabolic pathway of heme degradation is a critical regulator of inflammation and tumor growth. Much of my efforts have been directed towards understanding how the enzymes involved in heme degradation (biliverdin reductase/BVR and heme oxygenase-1/HO-1) and the products (carbon monoxide, biliverdin/bilirubin, iron) control metabolism and gene regulation in both immune and cancer cells.

ACCOMPLISHMENTS 2016-2017

- Cover of July 2017 issue of *Cancer Research* (Seth P, Csizmadia E, Hedblom A, Vuerich M, Xie H, Li M, Longhi MS, Wegiel B. Deletion of lactate dehydrogenase-A in myeloid cells triggers antitumor immunity. *Cancer Res* 2017;77(13)3632-3643.)
- Ad-hoc Reviewer of Polish National Academy grants, NIH, Harvard Catalyst
- Member of American Heart Association, American Association for Cancer Research, BIDMC Cancer Research Institute and DF/HCC
- Honorary Lecturer in Molecular Oncology, Aston University, UK

TEACHING, TRAINING, AND EDUCATION

During the last two years, I have been a supervisor for three post-doctoral fellows, two summer students and one intern. I am involved in teaching experimental design, molecular and biochemical techniques, data acquisition and analysis, as well as manuscript preparation.



- ◀ The cover of *Cancer Research* in July 2017, to accompany the paper, "Deletion of Lactate Dehydrogenase-A in Myeloid Cells Triggers Antitumor Immunity." The paper describes research which suggests that lactic acid, expressed by macrophages, is a major contributor to the suppression of T cells in the tumor microenvironment. Not only does this research add to the understanding of how immunosuppression encourages tumor growth, but it also suggests new targets for treatment.

SELECTED RESEARCH SUPPORT

Role of biliverdin reductase during sterile inflammation in the liver; NIH, 2016-2020; PI: Barbara Wegiel, PhD, MSc

Fibroids and endometriosis program; BIDMC Chief Academic Office funds, 2016-2019; PI: Barbara Wegiel, PhD, MSc

SELECTED PUBLICATIONS

Nemeth Z, Li M, Seth P, Csizmadia E, Dome B, Johansson M, Persson J, Otterbein LE, Wegiel B. Heme oxygenase-1 in macrophages controls prostate cancer progression. *Oncotarget* 2015;6(32):33675-88.

Nemeth Z, Csizmadia E, Vikstrom L, Li M, Bisht K, Feizi A, Otterbein S, Zuckerbraun B, Costa D, Pandolfi PP, Fillinger J, Döme B, Otterbein LE, Wegiel B. Alterations of tumor microenvironment by carbon monoxide impedes lung cancer growth. *Oncotarget* 2016;7(17):23919-32.

Wegiel B, Wang Y, Li M, Jernigan F, Sun L. Novel indolyl-chalcones target stathmin to induce cancer cell death. *Cell Cycle* 2016;15(9):1288-94.

Wang Y, Hedblom, Koerner SF, Li M, Jernigan FE, Wegiel B, Sun L. Novel synthetic chalcones induce apoptosis in the A549 non-small cell lung cancer cells harboring a KRAS mutation. *Bioorg Med Chem Lett* 2016;26(23):5703-5706.

Seth P, Csizmadia E, Hedblom A, Vuerich M, Xie H, Li M, Longhi MS, Wegiel B. Deletion of lactate dehydrogenase-A in myeloid cells triggers antitumor immunity. *Cancer Res* 2017;77(13)3632-3643.)

Peter Chang, MD, MPH

Assistant Professor of Surgery
 Director, BIDMC Prostate Cancer Center
 Director, BID–Milton Robotic Surgery Program



RESEARCH FOCUS

My research focus is in urologic cancer, and is highly collaborative in nature, most importantly within BIDMC, but also with outside institutions. I work very closely with Andrew Wagner, MD, and together we co-lead the Urology research team and share research personnel. Our team’s research in kidney and bladder cancer are described in Dr. Wagner’s report. As Director of the BIDMC Prostate Cancer Center, I will describe my research efforts to optimize quality-of-life in prostate cancer patients.

RESEARCH GROUP

- Catrina M. Crociani, MPH
- Sara Hyde
- Kyle McAnally
- Adrian Waisman, MD
- Andrew Wagner, MD

Prostate cancer

Quality-of-life assessment in prostate cancer patients

At BIDMC, we are committed to giving every patient with prostate cancer a chance to have the best quality of life possible. Unfortunately, prostate cancer treatment can cause significant side effects, and doctors tend to underestimate how bad these are, potentially leaving patients with long-lasting quality of life problems. My research focuses on accurate and objective measurement of prostate cancer quality of life using patient-reported outcome questionnaires. I developed a new questionnaire called “EPIC for Clinical Practice (EPIC-CP),” designed to be used by clinicians rather than researchers (Chang P et al, J Urol Sep 2011). I recently showed that EPIC-CP can allow a doctor to estimate the chances of a patient recovering sexual function after prostate cancer surgery (Chipman et al, J Urol Mar 2014). Due to its development here at BIDMC, our institution is at the forefront in using EPIC-CP as part of prostate cancer care. Dr. Wagner and I recently published our results

on the “real-world” use of EPIC-CP in post-surgery patients in the *Journal of Urology* (Wagner AA et al, J Urol Jan 2017). As a next step, I hope to show how using EPIC-CP can improve the practitioner work-flow and improve patient outcomes.

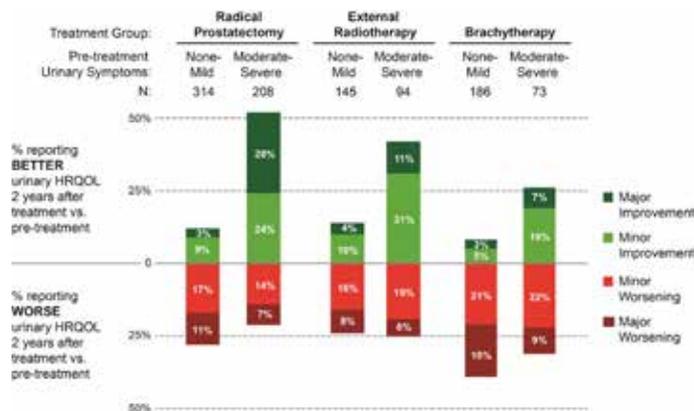
Quality-of-life outcomes after prostate cancer treatment

I am also interested in finding out what problems patients have after different treatments (surgery, external radiation, radioactive seed implants), and determining whether we can use this information to better guide patients toward optimal treatments. I am the Co-overall Principal Investigator of the PROST-QA study; this is a prospective, multicenter, longitudinal study that has the most complete and rigorous collection of prostate cancer quality-of-life data in the world. I recently published the results of a study showing that a subset of patients have improvement in their quality of life after prostate cancer treatment, specifically radical prostatectomy (Chang P et al, J Urol Feb 2017).

Helping prostate cancer patients make treatment decisions

Unlike other cancers, in which options may be limited after initial diagnosis, prostate cancer patients face a seemingly impossible task of choosing among several treatment options. Working with Donna Berry, PhD, RN (Dana-Farber Cancer Institute), I serve as BIDMC site-responsible Principal Investigator for an NIH R01-funded randomized trial called Personal Patient Profile – Prostate (P3P). This unique study investigates the effectiveness of a web-based interactive program that gathers patient characteristics, quality-of-life (using EPIC-CP), personal preferences, and priorities, and uses this information to customize videos that counsel patients on how to discuss these issues with their doctor. We recently published our results in the *Journal of Urology* (Berry et al, J Urol Jul 2017).

Figure 1: Ordinal Change in Overall Urinary Bother from Pre-Treatment to 2 Years Post-Treatment in the PROST-QA Cohort



▲ FIGURE 1: Prostate cancer urinary quality of life tends to improve after treatment with radical prostatectomy for men with pre-existing lower urinary tract symptoms.

ACCOMPLISHMENTS 2016-2017

Funding from the Martin and Diane Trust Career Development Chair in Surgery helped me to complete two research studies on prostate cancer quality of life, both of which resulted in primary author publications in the *Journal of Urology* in 2017.

My leadership of the PROST-QA cohort allowed securing of additional funding from the Movember Foundation to help support further prostate cancer research.

TEACHING, TRAINING, AND EDUCATION

As a proud prior graduate of the Harvard Longwood Program in Urology and the BIDMC Minimally Invasive Urologic Oncology fellowship, I now have the privilege of being the co-director of the fellowship, training the next generation of residents and last year's fellow, Marc Manganiello, MD.

I was selected to be a faculty member for the 17th Biennial Jerome P. Richie Harvard Urologic Oncology Course, a two-day CME course that takes place every other year.

SELECTED RESEARCH SUPPORT

Prostate active surveillance study; Canary Foundation, 2013-ongoing; Co-investigator: Peter Chang, MD, MPH (PI: Daniel Lin, MD)

True Nth International; Movember Foundation, 2017-2019; PI: Peter Chang, MD, MPH

SELECTED PUBLICATIONS

Wagner AA, Cheng PJ, Carneiro A, Dovirak O, Khosla A, Taylor KN, Crociani CM, McAnally KC, Percy A, Dewey LE, Sanda MG, Chang P. Clinical use of EPIC for clinical practice (EPIC-CP) to assess patient-reported prostate cancer quality of life following robot-assisted radical prostatectomy. *JUrol* 2017; 197(1):109-114.

Chang P, Regan MM, Ferrer M, Guedea F, Patil D, Wei JT, Hembroff LA, Michalski JM, Saigal CS, Litwin MS, Hamstra DA, Kaplan ID, Ciezki JP, Klein EA, Kibel AS, Sandler HM, Dunn RL, Crociani CM, Sanda MG, PROST-QA Consortium. Relief of urinary symptom burden after primary prostate cancer treatment. *J Urol* 2017; 197(2): 376-384.

Danzig MR, Ghandour RA, Chang P, Wagner AA, Pierorazio PM, Allaf ME, McKiernan JM. Active surveillance is superior to radical nephrectomy and equivalent to partial nephrectomy for preserving renal function in patients with small renal masses: Results from the DISSRM registry. *Urol Oncol* 2017;35(3):116.

Gay HA, Sanda MG, Liu J, Wu N, Hamstra DA, Wei JT, Dunn RL, Kelin EA, Sandler HM, Saigal CS, Litwin MS, Kuban DA, Hembroff L, Regan MM, Chang P, Prostate Cancer Outcomes and Satisfaction with Treatment Quality Assessment Consortium, Michalski JM. External beam radiation therapy or brachytherapy with or without short-course neoadjuvant androgen deprivation therapy: Results of a multicenter, prospective study of quality of life. *Int J Radiat Oncol Biol Phys* 2017;98(2):304-317.

Berry DL, Hong F, Blonquist TM, Halpenny B, Filson CP, Master VA, Sanda MG, Chang P, Chien GW, Jones RA, Krupski TL, Wolpin S, Wilson L, Hayes JH, Trinh QD, Sokoloff M, Somayaji P. Decision support with the personal patient profile-prostate: A multi-center randomized trial. *J Urol* 2018;199(1):89-97.

Taplin ME, Montgomery B, Xie W, Zhang Z, Bubley G, Lin D, Preston M, Trinh QD, Chang P, Wagner A, Mostaghel E, Kantoff P, Nelson P, Kibel A. Post prostatectomy outcomes of patients with high risk prostate cancer treated with neoadjuvant androgen blockade. *Prostate Cancer Prostatic Dis* 2017 [Epub ahead of print].

A complete list of publications begins on page 13.

**RESEARCH GROUP**

Peter Steinberg, MD

Ruslan Korets, MD

Assistant Professor of Surgery

Director, Urology Training Program

RESEARCH FOCUS**Clinical Outcomes in Surgical Treatment of Nephrolithiasis**

My research focuses on nephrolithiasis with an emphasis on assessing patterns of care and outcomes in patients undergoing minimally invasive treatment of kidney stone disease. Our research team works closely with colleagues within BIDMC as well as with collaborators at outside institutions. Our group has recently examined perioperative outcomes and costs associated with percutaneous nephrolithotomy (a minimally invasive percutaneous surgical procedure), when surgical teams involve single specialty and multi-specialty surgical teams (Speed et al, *J Endourol* Nov 2017). Additionally, we examined factors affecting radiation exposure from fluoroscopic imaging used for percutaneous renal access during lithotripsy. We are also developing a prospective endourologic database that will examine stone characteristics of patients treated at our center.

Surgical Education

I have initiated a multi-institutional study assessing a novel online platform to enhance resident education called myTIPreport. This platform is utilized to provide real-time feedback to trainees after each surgical procedure. The evaluations are performed using a Zwisch model to improve the quality and quantity of feedback delivered to surgical trainees. The aim is to encourage dialogue between faculty and trainees, allowing directed and meaningful feedback to be given to residents after each surgical case. The findings from the pilot study were presented at the New England Section of the American Urological Association 2017 Annual Meeting. As a next step, I hope to assess the effect of this teaching platform on surgical skill acquisition.

ACCOMPLISHMENTS 2016-2017

During the past year, I assumed the role of director of urologic education at BIDMC and now oversee academic and clinical programs for training the future generation of urology residents and medical students during their urology elective.

During the most recent meeting of the New England Section of the American Urologic Association, I was invited as a panelist to discuss Appropriate Uses of SWL, URS, and PCNL. At that meeting, I was honored to be elected as a representative to the New England Section of American Urologic Association Judicial and Ethics Committee.

TEACHING, TRAINING, AND EDUCATION

Teaching and surgical education are important aspects of my career and practice. I have been involved in several educational initiatives utilizing technology to enhance surgical education. I have contributed to the Robotic Surgery Curriculum, which has been implemented across several of the Harvard Medical School-affiliated teaching hospitals. This curriculum incorporates robotic simulator exercises, as well as one-on-one video review of performed surgeries to help familiarize residents with surgical anatomy and the procedural steps of robotic urologic procedures they will master during training.

During the past year, I served as faculty for the Stone Institute, a Hands-On Training Program for urology residents attending the American Urological Association Annual Meeting. This one-day course consisted of didactic and hands-on sessions aimed at improving surgical aptitude in percutaneous and endoscopic techniques, and attracted over 40 residents from across the country.

Additionally, I was elected to the BIDMC Academy of Medical Educators and continue to broaden my role in surgical education.

ABSTRACTS, POSTERS, AND EXHIBITS

Manganiello M, Haleblian G, Canes D, Chang P, Wagner A, Korets R. Multi-institutional pilot evaluation of an online feedback platform for surgical skill acquisition. New England Section of American Urological Association Annual Meeting, Montreal, CA; 2017 (abstract)

Bose, S, Bearely P, Latini J, Korets R. Radiation exposure during percutaneous nephrolithotomy: A comparative analysis of single specialty versus multi-specialty procedures. New England Section of American Urological Association Annual Meeting, Montreal, CA; 2017 (abstract)

Speed J, Wang Y, Leow J, McClintock T, Bhojani N, Trinh Q, Chang S, Korets R. Percutaneous renal access by urologist vs radiologist: Trends and perioperative outcomes in PCNL. New England Section of American Urological Association Annual Meeting, Montreal, CA; 2017 (abstract)

Speed J, Cole A, Latini J, McClintock T, Wang Y, Chang S, Korets R. The effect of marital status on post-operative outcomes after PCNL. New England Section of American Urological Association Annual Meeting, Montreal, CA; 2017 (abstract)

Reese S, McClintock R, Krasnow R, Mossanen M, Chang S, Korets R. Prophylactic antibiotic utilization patterns and postoperative infectious complications following percutaneous nephrolithotomy. World Congress of Endourology, Vancouver, CA; 2017 (abstract)

SELECTED PUBLICATIONS

Leow JJ, Leow JJ, Meyer CP, Wang Y, Chang S, Chung BI, Trinh QD, Korets R, Bhojani N. Contemporary trends in utilization and perioperative outcomes of percutaneous nephrolithotomy in the United States from 2003 to 2014. *J Endourol* 2017; 31(8):742-50.

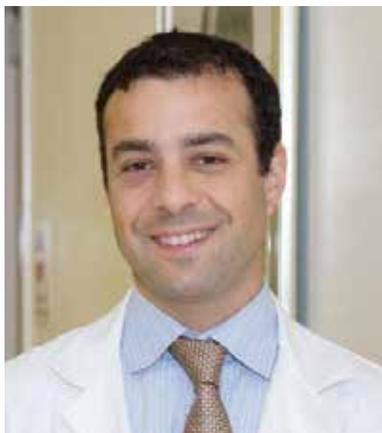
Speed JM, Wang Y, Leow JJ, Bhojani N, Trinh QD, Chang SL, Korets R. The effect of physician specialty obtaining access for percutaneous nephrolithotomy on perioperative costs and outcomes. *J Endourol* 2017; 31(11):1152-56.

Andrew A. Wagner, MD

Associate Professor of Surgery

Director, Minimally Invasive Urologic Surgery

Director, Minimally Invasive Urologic Surgery Fellowship Program



RESEARCH FOCUS

Kidney cancer

Our group is interested in evaluating recovery trends (as measured by prospectively collecting patient reported quality of life data) after kidney surgery. Using this data we are able to provide detailed recovery expectations for these patients. We also aim to define the costs of kidney surgery, including hospital costs and societal costs — by incorporating patient-reported data about leave from work, salary lost, and family leave. We were the first group to evaluate societal costs of kidney surgery in the period following hospital discharge. This work was first presented at the New England AUA meeting in 2015, and has been accepted for publication in the *Canadian Journal of Urology* in 2018.

Our team has helped refine robotic surgery for kidney cancer; however we are also interested in non-operative approaches to small renal masses. Together with researchers from Johns Hopkins University and Columbia University, we are a main contributor to the DISSRM trial (Delayed Intervention and Surveillance for Small Renal Masses). This is a multicenter prospective study evaluating the role of surveillance and surgery of small kidney tumors over time. We have studied quality of life in these patients, evaluated changes in kidney function over time, evaluated tumor growth characteristics, and developed a scoring system to help clinicians during the decision-making process.

RESEARCH GROUP

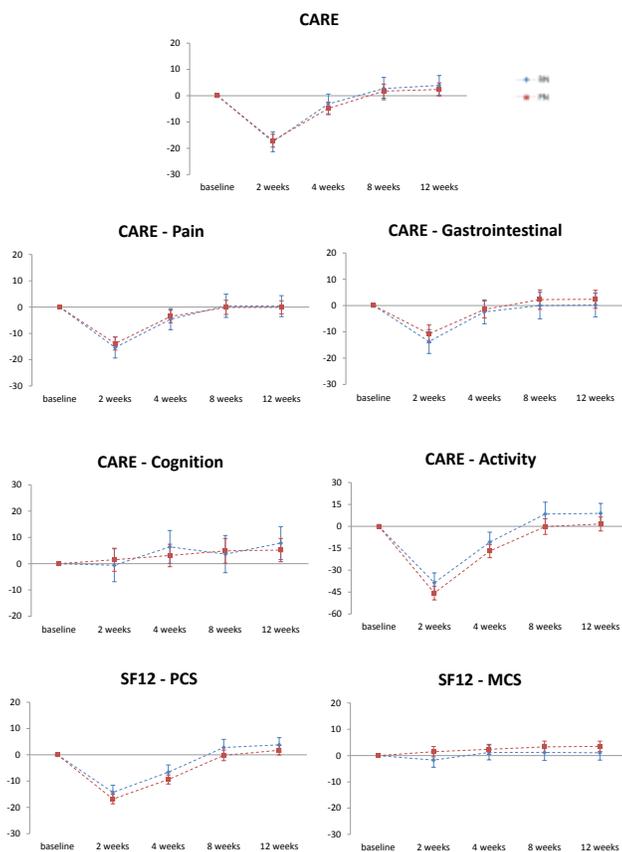
- Peter Chang, MD, MPH
- Joan Delto, MD
- Catrina Crociani, MPH
- Kyle McAnally
- Sarah Hyde
- Jialin Mao, MPH
- Adrien Waisman, MD

Prostate cancer

For over a decade, BIDMC has been a leader in evaluating quality of life for prostate cancer patients. Our group developed the EPIC-CP, a short form quality of life instrument used by clinicians worldwide to evaluate prostate cancer patients. Updates from this work were recently published in the *Journal of Urology* in 2017. Our group is also the area's leader in active surveillance for low risk prostate cancer. We are the only Northeast member of the Canary Prostate Cancer Active Surveillance Study (Canary-PASS). This is the largest prospective multicenter study of active surveillance for prostate cancer, with over 1,700 patients enrolled. We are collecting clinical data and biologic samples from patients in an effort to identify important biomarkers that could distinguish which patients have more aggressive prostate cancer from those with indolent disease. Recently we have looked at the timing of cancer progression, use of a four-kallikrein panel for prediction of prostate cancer progression, and evaluated a genomic index in cancer progression.

Bladder cancer

We are the first urology team in Boston to regularly perform radical cystectomy and urinary diversion completely robotically. We are gathering prospective data with a focus on clinical outcomes and validated quality of life. We also recently joined the IRCC (International Radical Cystectomy Consortium) for radical cystectomy, a large (50 center) database project aimed at evaluating trends in cystectomy treatment over time. This work was also presented at the 2015 New England AUA meeting, and will be presented as a podium presentation at the 2018 AUA meeting in San Francisco.



▲ FIGURE 1: Patient-reported quality of life changes after minimally invasive partial and radical nephrectomy as measured by the Convalescence and Recovery Evaluation (CARE) and the Short-Form 12 (SF-12).

ACCOMPLISHMENTS 2016-2017

- We published the first prospective evaluation of quality of life after robotic prostatectomy using the EPIC-CP short-form instrument
- We've enrolled over 175 patients on the prospective prostate cancer active surveillance study (Canary-PASS)
- We published the first known evaluation of quality of life outcomes following laparoscopic adrenalectomy
- We trained our 5th Minimally Invasive Urology Fellow, Marc Mangianello, MD and our fellowship became officially endowed by our grateful patients

TEACHING, TRAINING, AND EDUCATION

In addition to training our urology residents, in July 2010, we launched a Minimally Invasive Urologic Surgery Fellowship Program. Our fellowship was recently endowed by our grateful patients and is now the Esta and Robert Epstein Fellowship in Minimally Invasive Urologic Surgery. This fellowship is a unique training opportunity in New England, allowing fellows exposure to several hundred major laparoscopic and robotic surgery cases per year as well as exposure to our research program.

SELECTED RESEARCH SUPPORT

Canary Prostate Cancer Active Surveillance Study (PASS); Canary Foundation, 2010-present; BIDMC Site PI: Andrew A. Wagner, MD

SELECTED PUBLICATIONS

Wagner AA, Cheng PJ, Carneiro A, Dovirak O, Khosla A, Taylor KN, Crociani CM, McAnally KC, Percy A, Dewey LE, Sanda MG, Chang P. Clinical use of expanded prostate cancer index composite for clinical practice to assess patient-reported prostate cancer quality of life following robot-assisted radical prostatectomy. *J Urol* 2017;197:109-14.

Althaus AB, Dovirak O, Chang P, Taylor KN, O'Halloran TD, Wagner AA. Aspirin and clopidogrel during robotic partial nephrectomy, is it safe? *Can J Urol* 2015;22(2):7984-9.

Dovirak O, Chang P, Mao J, Taylor K, Wagner AA. How to quantify recovery after laparoscopic adrenalectomy: an assessment of patient-reported health-related quality of life. *Surg Laparosc Endosc Percutan Tech* 2016;26(4):290-4.

Uzosike AC, Patel HD, Alam R, Schwen ZR, Gupta M, Gorin MA, Johnson MH, Gausepohl H, Riffon MF, Trock BJ, Chang P, Wagner AA, McKiernan JM, Allaf ME, Pierorazio PM. Growth kinetics of small renal masses on active surveillance: Variability and results from the DISSRM registry. *J Urol* 2017;[Epub ahead of print].

Macleod LC, Ellis WJ, Newcomb LF, Zheng Y, Brooks JD, Carroll PR, Gleave ME, Lance RS, Nelson PS, Thompson IM Jr, Wagner AA, Wei JT, Lin DW. Timing of adverse prostate cancer reclassification on first surveillance biopsy: Results from the Canary Prostate Cancer Active Surveillance Study. *J Urol* 2017;197:1026-33.

Lin DW, Newcomb LF, Brown MD, Sjoberg DD, Dong Y, Brooks JD, Carroll PR, Cooperberg M, Dash A, Ellis WJ, Fabrizio M, Gleave ME, Morgan TM, Nelson PS, Thompson IM, Wagner AA, Zheng Y; Canary Prostate Active Surveillance Study Investigators. Evaluating the four kallikrein panel of the 4Kscore for prediction of high-grade prostate cancer in men in the Canary Prostate Active Surveillance Study. *Eur Urol* 2017;72(3):448-454.



Elliot L. Chaikof, MD, PhD

Johnson and Johnson Professor of Surgery
Chair, Department of Surgery
Surgeon-in-Chief

RESEARCH FOCUS

Our laboratory (chaikoflab.org) is focused on the discovery of new drugs and the development of tissue engineered organs based upon the principles of chemistry, biomolecular engineering, and 3-D fabrication technologies. Ongoing research is directed at the following areas.

Drug discovery

Identification of new drugs to inhibit inflammation and thrombosis

Selectins play an important role in the recruitment of leukocytes to inflamed tissue. We are currently synthesizing compounds to block inflammatory responses that contribute to deep venous thrombosis, atherosclerosis, metabolic syndrome, inflammatory bowel disease, and cancer metastasis.

Biomaterials science

Design of anti-thrombogenic surfaces

The development of artificial organs remains limited by the propensity of all synthetic surfaces to induce thrombus formation despite systemic anticoagulation. Current studies are designing surfaces that present molecules that resist clotting and whose bioactive surfaces can be 'regenerated' in situ to extend and improve the clinical performance of blood contacting devices, such as vascular grafts, heart valves, left ventricular devices, and implantable artificial lungs and kidneys.

Tissue engineering and regenerative medicine

Engineering blood vessels

Synthetic blood vessel substitutes for cardiac or vascular surgery do not exist. Ongoing efforts in our group seek to design new synthetic collagen and elastin analogues and to assemble them along with vascular wall cells derived from stem cells to engineer a living artery.

Vascular biology

Targeted therapies to promote vascular wall healing

Restenosis remains a major cause of failure after angioplasty and stenting for treatment of lower extremity peripheral arterial disease. New approaches are being developed that target thrombotic and inflammatory events at the site of vessel wall injury through antibody directed targeting of activated platelets.

RESEARCH GROUP

- Jiaxuan Chen, PhD
- Erbin Dai, MD
- Carolyn A. Haller, PhD
- Oki Ham, PhD
- Liyong Liu, MD
- Appi Reddy Mandhapati, PhD
- David Miranda Nieves
- Simon Park, PhD
- Diane (Dayoung) Park, PhD
- Walter Weaver, PhD
- Daniel Wong, MD



▲ Members of Dr. Chaikof's laboratory

◀ Daniel Wong, MD

ACCOMPLISHMENTS 2016-2017

Through established collaborations with David Liu, PhD (Chemistry, Harvard University/Broad Institute), and Jian Liu, PhD (Chemistry, University of North Carolina), we have expanded our efforts directed at identifying and harnessing biologically inspired designs to limit blood clotting on artificial surfaces. Additional collaborations have supported ongoing drug discovery efforts including those with Richard Cummings, PhD, Vice Chair of Translational Research in the Department of Surgery and Director, Harvard Medical School (HMS) Center for Glycoscience, and Robert Woods, PhD, Professor of Computational Chemistry, Complex Carbohydrate Research Center, University of Georgia, as well as with Lijun Sun, PhD, Associate Professor of Surgery at HMS and Director of the Center for Drug Discovery in the Department of Surgery. Tissue engineering programs represent collaborations with Chad Cowan, PhD in Cardiology, BIDMC, Axel Guenther, PhD, Professor of Mechanical Engineering at the University of Toronto, and Jennifer Lewis, PhD, Professor of Biologically Inspired Engineering in the Harvard School of Engineering. The development of a new generation of infection-resistant biomaterials represents a collaboration with Joanna Aizenberg, PhD, Professor of Materials Science in the Harvard School of Engineering.

Elected Vice-Chair for Section 01 in the National Academy of Medicine (Physical Sciences, Mathematical Sciences, Computer/Information Sciences, Biomedical Engineering, Engineering Sciences)

Co-Chair, Mapping the Human Glycome in Health and Disease, Radcliffe Institute for Advanced Studies

Member, Convening on the Physician Scientist Workforce, National Institutes of Health

TEACHING, TRAINING, AND EDUCATION

Harvard-MIT HST PhD candidate David Miranda Nieves received a National Defense Science and Engineering Graduate Fellowship to support his PhD studies

Postdoctoral fellow Perla Ayala, PhD, was appointed Assistant Professor, Department Bioengineering, California State University - Long Beach

Postdoctoral fellow E. Vickie Dydek, PhD, joined the scientific staff of MIT Lincoln Laboratory

Postdoctoral fellow Jennifer Gagner, PhD, joined the scientific staff of IDEXX

Postdoctoral fellow Stephanie Grainger, PhD, joined the scientific staff of Infraredx

Postdoctoral fellow Donny Hanjaya-Putra, PhD, appointed Assistant Professor, Department of Chemical Engineering, University of Notre Dame

Postdoctoral fellow Jessie Jeon, PhD, was appointed Assistant Professor, Department of Mechanical Engineering, Korea Advanced Institute of Science & Technology (KAIST)

Postdoctoral fellow Venkat Krishnamurthy, PhD, joined the scientific staff of AstraZeneca Pharmaceuticals

Postdoctoral fellow Madhukar Patel, MD, Surgical Resident, Massachusetts General Hospital, received 2015 American College of Surgeons Resident Research Award and NIH Postdoctoral Fellowship Award

Postdoctoral fellow Daniel Wong, MD, Surgical Resident, BIDMC, received 2017 American College of Surgeons Resident Research Award and NIH Postdoctoral Fellowship Award

SELECTED RESEARCH SUPPORT

In situ regeneration of bioactive surfaces: Rechargeable anti-thrombogenic films; NIH, 2013-2017; PI: Elliot L. Chaikof, MD, PhD

Facile synthesis of glycosulfopeptides and related bioconjugates; NIH, 2015-2019; PI: Elliot L. Chaikof, MD, PhD

A PSGL-1 glycopeptide mimetic for treatment of venous thromboembolism; NIH, 2015-2019; PI: Elliot L. Chaikof, MD, PhD

A PSGL-1 glycopeptide mimetic for treatment of metabolic syndrome, NIH, 2016-2021; PI: Elliot L. Chaikof, MD, PhD

SELECTED PUBLICATIONS

Dorr BM, Ham O, An C, Chaikof EL, Liu DR. Reprogramming the specificity of sortase enzymes by directed evolution. *Proc Natl Acad Sci USA* 2014; 111:13343-13348.

Angsana J, Chen J, Smith S, Xiao J, Wen J, Liu L, Haller CA, Chaikof EL. Syndecan-1 modulates the motility and resolution responses of macrophages. *Arteriosclerosis Thromb Vasc Biol* 2015; 35:332-40.

Kim W, Haller CA, Dai E, Wang X, Hagemeyer CE, Liu DR, Peter K, Chaikof EL. Targeted anti-thrombotic protein micelles. *Angew Chem Int Ed* 2015;54:1461-5.

Krishnamurthy VR, Sardar MYR, Yu Y, Song X, Haller CA, Dai E, Wang X, Hanjaya-Putra D, Sun L, Morikis V, Simon SI, Woods R, Cummings RD, Chaikof EL. Glycopeptide analogues of PSGL-1 inhibit P-selectin in vitro and in vivo. *Nature Communications* 2015; 6: 6387.

Patsch C, Challet-Meylan L, Thoma EC, Urlich E, Heckel T, Zon LI, Chaikof EL, Gerszten RE, Graf M, Iacone R, Cowan CA. Generation of vascular endothelial and smooth muscle cells from human pluripotent stem cells. *Nature Cell Biology* 2015; 17(8):994-1003.

Ham HO, Qu Z, Haller CA, Dorr BM, Dai E, Kim W, Liu DR, Chaikof EL. In situ regeneration of bioactive coatings enabled by an evolved *Staphylococcus aureus* sortase A. *Nature Communications* 2016; 7:11140.

Angsana J, Chen J, Liu L, Haller CA, Chaikof EL. Efferocytosis as a regulator of macrophage chemokine receptor expression and polarization. *European J Immunology* 2016; 46:1592-1599.

Chen J, Howell C, Haller CA, Patel MS, Ayala P, Moravec KA, Dai E, Liying L, Sotiri I, Aizenberg M, Aizenberg J, Chaikof EL. An immobilized liquid interface prevents device associated bacterial infection in vivo. *Biomaterials* 2017; 113:80-92.

A complete list of publications begins on page 13.

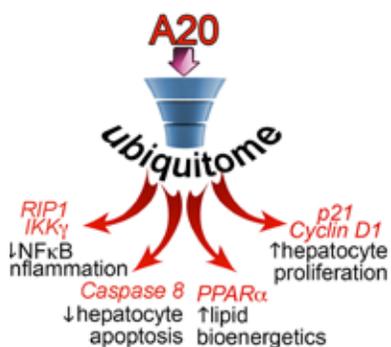


RESEARCH GROUP

Erin Driscoll
 Kevin Elkhoury
 Cleide Gonçalves da Silva, PhD
 Philip LoGerfo
 Erin McIntosh, MD
 Marianna Pavlyha
 Jesus Revuelta-Cervantes, PhD



▲ Dr. Ferran (center) with two members of her laboratory, Dr. Gonçalves da Silva, Instructor in Surgery at HMS (left), and Dr. Revuelta-Cervantes, a post-doctoral fellow.



▲ A20, or the molecular basis for the Prometheus Myth

RESEARCH FOCUS

My laboratory focuses on:

- Defining the molecular signature of what “return to homeostasis” entails in the face of injury, whether inflammatory, immune, infectious, metabolic, or mechanical
- Identifying the culprits that hinder “return to homeostasis,” and thus result in pathology
- Validating signature molecules in animal models of human disease for potential clinical translation as diagnostic, prognostic, and therapeutic tools

This line of research was triggered by our seminal discovery that up-regulation of the ubiquitin-editing protein A20 or the anti-apoptotic Bcl member, A1, in endothelial cells in response to inflammatory stimuli, serves a general “protective” function by shutting down inflammation through inhibition of the transcription factor NF- κ B (JBC 1996;271:18068). Subsequent studies confirmed A20 as one of humans’ most potent and ubiquitous physiologic anti-inflammatory molecules. A20 not only goes to the NF- κ B heart of inflammation, but also beyond to control IFN gamma and alpha/beta signaling, and modulate cell survival and proliferation, with return to homeostasis as the ultimate goal. We established the therapeutic benefits of A20-based therapies in a number of animal models of human diseases that share inflammation as a central pathogenic component, mainly in the three fields listed below.

Vascular diseases

Our data qualifies a potent “atheroprotective” and novel anti-angiogenic function of A20 in animal models of:

- Neointimal hyperplasia post-balloon angioplasty
- Transplant arteriosclerosis, the main cause of failure of vascularized allografts
- Accelerated atherosclerosis of diabetes
- Vein graft and prosthetic arterial graft failure
- Proliferative retinopathies, namely retinopathy of prematurity and diabetic retinopathy

Liver regeneration and repair

We have also extensively established a potent “hepatoprotective” role for A20 in the liver, stemming from combined anti-inflammatory, anti-apoptotic, and pro-proliferative functions of A20 in hepatocytes. Accordingly, A20-based therapies protect mice from lethality in models of acute chemically-induced toxic hepatitis, lethal radical hepatectomy where 90% of the liver is resected, prolonged warm liver ischemia, and orthotopic liver transplantation using marginal livers.

Additionally, we uncovered an unsuspected phenotype in A20 heterozygous mice, whereby a benign 2/3 hepatectomy causes a staggering 50% lethality. These data have important clinical implications. Indeed, single nucleotide polymorphisms that negatively impact A20 expression and/or function should be recognized in order to gauge safety of extensive liver resections for donation or tumor.

We also recently discovered that A20 regulates lipid metabolism in a way that improves fatty liver disease in a mouse model of human non-alcoholic fatty liver disease.

Current pre-translational studies in pigs using clinically safe viral vectors to specifically induce A20 expression in the liver are very promising and prelude clinical implementation.

Treatment of diabetes

Islet Transplantation: A20 retained its anti-apoptotic and anti-inflammatory functions in β -cells, thus was an ideal candidate to genetically engineer islet grafts for the treatment of diabetes.

Insulin Alternatives: Recently, we uncovered a novel anti-diabetic function of A20, whereby hepatic overexpression of A20 in a mouse model of type I diabetes restored glycemic control in an insulin independent manner. We are characterizing the molecular basis of this novel function of A20 and exploring its potential use as an anti-diabetic therapy in both type I and type II diabetes.

Administrative

- Member of the Promotion, Appointment, and Reappointment Committee, Harvard Medical School (HMS)
- Member of the Committee for Senior appointment (COSA), BIDMC
- Member of the Promotion and reappointment Committee, Department of Surgery, BIDMC
- Member of the search committee for Scientific Director of the Transplant Center, Massachusetts General Hospital, HMS
- Member of the search committee for Chief of Urology, BIDMC, HMS
- Member of the search committee for Chief Academic Officer, BIDMC
- Member of the executive committee of the Center for Vascular Biology Research, BIDMC

Scientific review board

- Reviewer for the NIH ZEB-OSR-C (O1) study section Multiscale Modeling (MSM) Program
- Reviewer for the NIH Surgery Anesthesia Traumatology (SAT) study section
- Reviewer for the Fund for Scientific Research-FNRS, Brussels, Belgium
- Reviewer for the Swiss National Science Foundation, Zurich, Switzerland

Invited presentations and visiting professorships

- "What returns to vascular homeostasis entails," Lebanese American University, Beirut, Lebanon
- "Novel technologies to revolutionize transplantation," Lebanese American University, Beirut, Lebanon
- "Prometheus Myth under A20 fire... A Tale of Discovery and Translation in Liver Regeneration and repair," Transplantation Grand Rounds, the Transplant Institute, Medical University of Virginia, UVA, Charlottesville, VA
- "A20 and vascular homeodynamics: a tale of discovery and translation," Renal Grand Rounds, Brigham and Women's Hospital, HMS, Boston MA
- "An A20 suite: Insulin no longer in diabetes," Mass Biologics Seminar Series, University of Massachusetts Medical School, Mattapan, MA

- "A20 and vascular homeodynamics: a tale of discovery and translation," Molecular Medicine Series, Molecular Cardiology Research Institute (MCRI), Tufts Medical School, Boston, MA

Awards

- Christiane Ferran, MD, PhD: Avicenna Award in Health and Medical Sciences, Harvard Arab Alumni
- Jesus Revuelta-Cervantes, PhD: Abstract selected for oral presentation at the Clowes Visiting Professorship competition for his work on A20 and fatty liver diseases
- Brandon Wojcik, MD: Selected for oral presentation at the Harvard Surgery Research Day competition for his work on A20 and incidence/severity of thrombotic venous diseases

Patents

PCT/US2017/046938, international # WO 2018/035121 A1. "Novel therapies to achieve glycemic control." Inventors: Christiane Ferran MD, PhD, Cleide da Silva, PhD, and Alessandra Mele, MD

TEACHING, TRAINING, AND EDUCATION

For the past 20 years I have been training post-doctoral research fellows, surgical residents, undergraduate, graduate, and medical students, and research associates who rotate in my laboratory. I also mentor junior faculty in the Department of Surgery and the Center for Vascular Biology Research. Speaking to my commitment to teaching/mentoring, I serve on four NIH-funded T32 and one T35 training grants as:

- Co-director of the Longwood-Harvard T32 in vascular surgery (Director: Frank LoGerfo, MD, BIDMC)
- Faculty mentor in the Harvard trauma inflammation T32 (Director: Wolfgang Junger, PhD, BIDMC)
- Faculty mentor in the renal T32 (Director: Martin Pollak, MD, BIDMC)
- Faculty mentor in the transplantation biology T32 (Director: Joren Madsen, MD, MGH)
- Faculty mentor in the in vascular surgery T35 (Director: Frank LoGerfo, MD, BIDMC)

Moll HP, Lee A, Peterson CR, Cervantes JR, Wojcik BM, Parulkar A, Mele A, LoGerfo PJ, Siracuse JJ, Csizmadia E, da Silva CG, Ferran C. A20 haploinsufficiency aggravates transplant arteriosclerosis in mouse vascular allografts: Implications for clinical transplantation. *Transplantation* 2016;100(11):e106-e116.

LoGerfo PJ, Revuelta Cervantes JM, Mele A, Neidich A, Amr S, Chien V, Wojcik BM, da Silva CG, Ferran C, and Cooper JT. Donor and recipient polymorphisms in theTNFAIP3 (A20) gene correlate with risk of acute rejection and predict long term function in renal allografts. 2017;Submitted *Nephrology, Dialysis, Transplantation*.

da Silva CG, Kaczmarek E, Essayagh S, Daniel S, Choi L, Arvelo M, Wojcik BM, Patil M, Vora D, Moll HP, Ferran C. A20 increases eNOS transcription in an ERK5/KLF2 dependent manner to sustain endothelial cell function in the face of inflammatory insults. 2017; Submitted.

SELECTED RESEARCH SUPPORT

Novel therapies to achieve glycemic control; Juvenile Diabetes Research Foundation, 2016-2019; PI: Christiane Ferran, MD, PhD. (Co-investigator: Cleide G. da Silva, PhD)

Bioengineering of vein graft to resist intimal hyperplasia; NIH, 2018-2020. PI: Christiane Ferran MD, PhD. (Co-investigator: Mauricio Contreras, MD)

Mechanisms of prosthetic arterial graft failure; NIH, 1987-2021; PIs: Christiane Ferran MD, PhD; Frank W. LoGerfo, MD, David Mooney, PhD

Genetic engineering of vein bypass grafts in vascular and cardiovascular surgery, NIH, 2007-2018; Co-PI: Christiane Ferran, MD, PhD (Contact PI: Frank W. LoGerfo, MD)

A complete list of publications begins on page 13.



Raul J. Guzman, MD

Associate Professor of Surgery
Vice Chair, Resident Research

RESEARCH FOCUS

My research focuses on the role of arterial calcification in lower-extremity vascular disease. We are interested in the mechanisms by which smooth muscle cells in the arterial wall become transformed into more bone-like cells. This primarily occurs in patients with diabetes and renal failure.

In previous studies using cell culture systems and rodents, we showed that the matrix-degrading enzymes known as MMPs are critical factors in the development of medial artery calcification and that reducing MMP activity could prevent medial calcification *in vitro* and *in vivo*. We have been working to better understand how MMPs promote calcification and whether these inhibitors can be used in the clinical setting to prevent vascular calcification in patients. During our work on MMPs, we found that a class of bone-related factors known as bone morphogenetic proteins, or BMPs, is up-regulated during arterial calcification. Through collaborations with several investigators, we have begun to study the potential role of new synthetic small-molecule BMP inhibitors in our calcification models. The ultimate goal of our basic studies is to gain insight into mechanisms that control calcification so we can develop clinically relevant therapies for use in our patients with critical limb ischemia.

Through clinical studies we have undertaken over the last eight years, we have learned that the amount of calcification in lower extremity arteries is a better predictor of long-term amputation risk than demographic and vascular risk factors. More recently, our research has focused on the finding that extensive arterial calcium is associated with poor limb outcomes in a manner that is independent of occlusive disease. This finding is contrary to previous notions of how vascular disease affects lower extremity blood flow. Currently, we are evaluating the hypothesis that arterial calcification, perhaps by affecting vessel wall compliance, contributes to limb ischemia and increases amputation risk in vascular patients. Our ultimate goal is to develop pharmacologic therapies to decrease calcium accumulation, improve arterial wall compliance, and thus reduce amputations in patients with diabetic vascular disease.

RESEARCH GROUP

Yujun Cai, PhD
Tonghui Lin, PhD
Susan Wang

ACCOMPLISHMENTS 2016-2017

My laboratory moved to Boston from our previous home in Nashville, Tenn. in 2013. Over the past four years, we have begun new and exciting research collaborations with several investigators on campus. We are particularly fortunate to have entered into a new collaboration with Aristidis Veves, MD, from our Division of Podiatry, Research Director of the Microcirculation Lab and Director of the Rongxiang Xu, MD, Center for Regenerative Therapeutics. We are working together to initiate studies aimed at understanding the relationship between arterial calcification and ischemia in patients with diabetes. We have recently demonstrated that the association between calcification and foot ulcers is independent of arterial occlusion. Because this association remains undefined, however, we hope to develop a large clinical data set on diabetic patients with and without foot ulcers to study this problem. We are also currently initiating new protocols that quantify arterial calcification in patients undergoing endovascular interventions. Our hope is that we can use this unique data set to gain a more precise understanding of why calcification predicts increased amputation risk.

Our basic investigations have also been stimulated by the addition of Yujun Cai, PhD, Instructor in Surgery to our team. Dr. Cai has extensive experience in studies related to the role of phosphodiesterases in vascular remodeling. His work has been published in leading vascular journals including *Circulation Research* and *ATVB*. We plan to continue his work on phosphodiesterases as they related to osteogenic SMC transformation and calcification. Our hope is that these exciting findings will translate into novel therapies to reduce arterial calcification and in improve outcomes in patients with diabetes and renal disease.

TEACHING, EDUCATION, AND TRAINING

My educational contributions have primarily been in the teaching of general and vascular surgery residents in the operating room and on the inpatient wards. I also have been fortunate to mentor and supervise young surgery residents during their basic research experience. While much of my teaching is clinically oriented, I also enjoy teaching in the laboratory and, in particular, enjoy training our residents in methods of careful experimental design, execution, and interpretation of research results.

SELECTED RESEARCH SUPPORT

Role of MMPs in arterial calcification; NIH, NHLBI, 2017-2018; PI: Raul Guzman, MD (0Co-investigator Dr. Yujun Cai, PhD)

This purpose of this study is to investigate the role of MMPs in arterial calcification and the potential for a dedicated clinical trial to assess the role of MMP inhibition strategies to reduce calcification and improve outcomes in our patients with vascular disease. Our hypothesis is that MMP-3, induced by inflammation and elevated phosphate levels, promotes osteogenic transformation of vascular SMCs and medial calcification through both local and systemic effects.

SELECTED PUBLICATIONS

Zettervall SL, Soden PA, Ultee KH, Seldon C, Oh J, McGann K, Schermerhorn ML, Guzman RJ. Elevated serum phosphate levels are associated with decreased amputation-free survival after interventions for critical limb ischemia. *J Vasc Surg* 2017;65(2):431-437.

Zettervall SL, Marshall AP, Fleser P, Guzman RJ. Association of arterial calcification with chronic limb ischemia in patients with peripheral artery disease. *J Vasc Surg* 2018;67(2):507-513.

Wise ES, Wergin JE, Mace EH, Kallos JA, Muhlestein WE, Shelburne NJ, Hocking KM, Brophy CM, Guzman RJ. Upper extremity pulse pressure predicts amputation-free survival after lower extremity bypass. *Am Surg* 2017;83(7):804-811.

Lin T, Wang XL, Zettervall SL, Cai Y, Guzman RJ. Dorsomorphin homologue 1, a highly selective small-molecule bone morphogenetic protein inhibitor, suppresses medial artery calcification. *J Vasc Surg* 2017;66(2):586-593.

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Frank W. LoGerfo, MD

William McDermott Distinguished Professor of Surgery

Leena Pradhan-Nabzdyk, PhD, MBA

Assistant Professor of Surgery

RESEARCH FOCUS

Our group has been extensively involved in different areas of vascular biology, diabetes, and neuropeptide research: 1) evaluating mechanisms responsible for development of intimal hyperplasia (IH) in vein grafts and prosthetic grafts; 2) developing novel techniques to prevent IH in both vein grafts and prosthetic grafts using bioengineering methodologies' and 3) wound healing in diabetes.

IH is the most common cause of delayed prosthetic arterial graft failure and delayed failure of vein grafts. As graft healing occurs, genes are either up- or down-regulated as compared to a quiescent arterial wall. Our lab studies altered gene expression that results in endothelial cell activation as well as cellular proliferation, migration, and extracellular matrix production by smooth muscle cells, leading to vein graft IH and anastomotic IH (AIH).

Dr. Pradhan-Nabzdyk's main research focus is diabetic neuropathic complications. Peripheral neuropathy and peripheral vascular disease are the major contributors to diabetic foot ulcers and their failure to heal. Therefore, it is important to assess the individual and combined role of neuropathy and vascular disease and their intricate interplay that leads to diabetic foot ulcers (DFU).

To achieve this goal, Dr. Pradhan-Nabzdyk has successfully developed an *in vivo* diabetic rabbit model of ischemic and neuroischemic wound healing. She is conducting studies in rabbit models of wound healing aimed at understanding the role of neuropeptides in diabetic wound healing. Dr. Pradhan-Nabzdyk also collaborates with Aristidis Veves, MD, Division of Podiatry, using knock-out mice models to further understand the mechanisms underlying diabetic wound-healing complication.

In addition to understanding the mechanisms underlying diabetic wound healing, Dr. Pradhan-Nabzdyk is also developing novel therapeutics to treat non-healing ulcers in collaboration with Dr. Veves, Dr. Paula Hammond of the Massachusetts Institute of Technology (MIT), and Dr. David Mooney of the Wyss Institute for Biologically Inspired Engineering at Harvard University.

RESEARCH GROUP

Daniel Creighton
Mauricio Contreras, MD
Patric Liang, MD
Navneet Momi, PhD
Akshi Thakkar, MS

ACCOMPLISHMENTS 2016-2017

Based on their previous work, the LoGerfo-Pradhan group has identified gene targets that are upregulated in both vein graft IH and AIH. Current work is focused on understanding the biology of these molecules, including Thrombospondin-2 (TSP-2) and interleukin (IL)-18, and developing techniques to deliver silencing RNA (siRNA) to the vessel wall to silence those targets and thereby mitigate the development of IH. Results from these projects have been presented at several national and international meetings and have resulted in manuscripts. Dr. Pradhan-Nabzdyk through NIH funding is also developing small molecule inhibitors for prevention of IH.

In collaboration with Dr. Mooney, our group is developing novel heparin-based cryogels and hydrogels to which siRNA could be adsorbed. Their preliminary experiments suggest successful siRNA delivery to vascular endothelial and smooth muscle cells. Moreover, these cryogels and hydrogels could be coated upon existing clinical vascular graft materials for prevention of prosthetic graft intimal hyperplasia.

The diabetic rabbit model developed by Dr. Pradhan-Nabzdyk is being used not only to understand the mechanisms of this devastating problem, but is also being used to test therapies directed to improve wound healing. In collaboration with Harvard's Wyss Institute, Dr. Pradhan-Nabzdyk tested the efficacy of the neuropeptide Substance P that was encapsulated in modified alginate gel in neuroischemic wound healing. The goal was to deliver Substance P in a continuous manner for a period of 10 days using the alginate gel. In collaboration with Dr. Hammond of MIT, Dr. Pradhan-Nabzdyk is testing the efficacy of drug delivery to diabetic wounds through a layer-by-layer (LbL) system developed by Dr. Hammond.

TEACHING, TRAINING, AND EDUCATION

We have mentored several students and post-docs in the lab. Additionally Dr. LoGerfo is the Program Director of the Harvard-Longwood Research Training Program in Vascular Surgery NIH-T32 program and Dr. Pradhan-Nabzdyk is the member of the Training Program Executive Committee. Currently there are eight post-doctoral fellows in this program mentored in different labs in the Longwood Medical Area. Based on the success of the T-32 program and the past William J. von Liebig Summer Research in Vascular Surgery Fellowship program for medical students, we (Drs. LoGerfo and Pradhan-Nabzdyk as Co-Directors) received NIH T-35 funding in 2013 which was recently renewed for additional five years, 2018-2022. The goal of this T-35 program is to train medical students in vascular surgery research for a short (10-12 weeks) period.

SELECTED RESEARCH SUPPORT

Mechanisms of prosthetic arterial graft failure; NIH, 1987-2021; PIs: Frank W. LoGerfo, MD, Christiane Ferran, MD, PhD, David Mooney, PhD; Co-Investigator: Leena Pradhan-Nabzdyk, PhD, MBA

Genetic engineering of vein bypass grafts in vascular and cardiovascular surgery; NIH, 2013-2017; PI: Frank W. LoGerfo, MD; Co-Investigators: Christiane Ferran, MD, PhD; Leena Pradhan-Nabzdyk, PhD, MBA

Development of Small Molecule Inhibitors of IL-18 to Prevent Intimal Hyperplasia; NIH, 2016-2018; PIs: Leena Pradhan-Nabzdyk, PhD, MBA, Lijun Sun, PhD; Co-Investigator: Frank W. LoGerfo, MD

Harvard-Longwood Research Training in Vascular Surgery; NIH, 2014-2019; PI: Frank W. LoGerfo, MD; Training Program Executive Committee: Leena Pradhan-Nabzdyk, PhD, MBA

Harvard-Longwood Short-Term Research Training in Vascular Surgery; NIH, 2013-2018; Program Co-Directors: Frank W. LoGerfo, MD; Leena Pradhan-Nabzdyk, PhD, MBA

Mechanisms of neuropeptides action in diabetes; NIH, 2011-2016; Co-investigators: Frank W. LoGerfo, MD, Leena Pradhan-Nabzdyk, PhD, MBA

SELECTED PUBLICATIONS

You JO, Rafat M, Almeda D, Maldonado N, Guo P, Nabzdyk CS, Chun M, LoGerfo FW, Hutchinson JW, Pradhan-Nabzdyk LK, Auguste DT. pH-responsive scaffolds generate a pro-healing response. *Biomaterials* 2015;57:22-32.

Nabzdyk CS, Chun M, Pathan SG, Nelson DW, You JO, Phaneuf MD, LoGerfo FW, Pradhan-Nabzdyk L. Development of a composite electrospun polyethylene terephthalate-polyglycolic acid material: Potential use as a drug-eluting vascular graft. *Journal of Nanomaterials* Volume 2015 (2015), Article ID 340981, 7 pages.

Raof NA, Rajamani D, Chu HC, Gurav A, Johnson JM, LoGerfo FW, Bhasin M, Pradhan-Nabzdyk L. The effects of transfection reagent polyethyleneimine (PEI) and non-targeting control siRNAs on global gene expression in human aortic smooth muscle cells. *BMC Genomics* 2016;17(1):20.

Tellechea A, Leal EC, Kafanas A, Auster ME, Kuchibhotla S, Ostrovsky Y, Tecilazich F, Baltzis D, Zheng Y, Carvalho E, Zabolotny JM, Weng Z, Petra A, Patel A, Panagiotidou S, Pradhan-Nabzdyk L, Theoharides TC, Veves A. Mast cells regulate wound healing in diabetes. *Diabetes* 2016;65(7):2006-19.

Bodewes T, Johnson J, Hyunh C, Muralidharan S, Contreras M, LoGerfo FW and Pradhan-Nabzdyk L. Intraluminal delivery of thrombospondin-2 siRNA inhibits the vascular response to injury in a rat carotid balloon angioplasty model. *FASEB J* 2017;31(1):109-11.

Mammoo A, Bencheriff SA, Nabzdyk C, Shih TY, Huynh C, Mooney DJ, LoGerfo FW, Pradhan-Nabzdyk L. Heparin containing cryogels as surfaces for local cardiovascular drug delivery. *Acta Biomaterialia* (under revision).

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Marc L. Schermerhorn, MD

George H.A. Clowes, Jr. Professor of Surgery
Chief, Division of Vascular and Endovascular Surgery



RESEARCH GROUP

Thomas C. Bodewes, MD
Jeremy D. Darling, BA, MS
Sarah E. Deery, MD, MPH
Chun Li, MD
Patric Liang, MD
Thomas F.X. O'Donnell, MD
Alexander Pothof, MD
Katie E. Shean, MD
Peter A. Soden, MD
Nicholas J. Swerdlow, MD
Klaas Ultee, MD, PhD
Sara L. Zettervall, MD

RESEARCH FOCUS

My clinical research group has an active interest in vascular surgery outcomes research on a local and national level. As emerging technologies evolve the way we practice medicine, comparative effectiveness research has been instrumental in the identification of best practices from among an increasingly complex set of therapeutic options. Our main interest is to compare outcomes after open surgery and endovascular surgery for a variety of vascular diseases, including aortic aneurysms, carotid disease, and lower extremity arterial disease, in order to help guide patient selection for each type of procedure. We utilize a wide range of observational, registry, and administrative data from real-world settings to better understand the impact of vascular treatments on disease processes.

Our experience at BIDMC, boasting the world's largest series of distal bypass and tibial angioplasty procedures, provided rich data from which we have published on the effectiveness of primary endovascular therapy for critical limb-threatening ischemia and the benefits of statin dose intensities. We have used our institutional experience with novel imaging systems to show reduced radiation exposure and contrast dose for patients and providers. Joining other institutions in the region and nationally, we are an active participant in the Vascular Study Group of New England (VSGNE) and the Vascular Quality Initiative (VQI). These large databases provide detailed procedural and patient-related information from which we have investigated regional differences in patient selection, treatment, and outcomes of abdominal aortic aneurysms (AAA), carotid artery stenosis, and peripheral arterial disease (PAD), among other vascular diseases. We have developed and published work on risk prediction models that can be used in real-world settings to guide physicians in counseling a patient on his/her individual risk of surgery. Through the VQI as well as other databases such as the National Surgical Quality Improvement Project (NSQIP), we shed light on disparities in presentation, treatment selection, and outcomes across both genders and racial groups.

In addition, administrative data such as the Nationwide Inpatient Sample (NIS), a 20% sampling of all inpatient admissions, and the State Ambulatory Surgery Databases (SASD), a database of all ambulatory surgical encounters by state, have been invaluable in addressing population-based clinical questions, including the epidemiologic trends in the diagnosis and treatment of acute and chronic mesenteric ischemia. Importantly, we have partnered with the Centers for Medicaid and Medicare Services (CMS) to obtain Medicare data for the study of open versus endovascular AAA management, including a comparison of different endovascular stent grafts for AAA repair. We have also demonstrated that late rupture after endovascular repair is a subsisting concern that merits further research. Finally, we have also combined data from several of these sources to comment on data quality, as in our review of the accuracy of administrative data versus clinical data for assignment of neurologic symptom status in patients undergoing carotid revascularization. Expertise in the use of these datasets against the backdrop of our busy clinical practice has allowed our group to produce tangible improvements in the management of vascular disease by translating clinical issues into tangible research questions.



▲ Members of Dr. Schermerhorn's laboratory (left to right): Rens Varkevisser, Nicholas J. Swerdlow, MD, Patric Liang, MD, Marc L. Schermerhorn, MD, Thomas F.X. O'Donnell, MD, Chun Li, MD.

ACCOMPLISHMENTS 2016-2017

With over 55 peer-reviewed publications and over 35 presentations* at national and regional society meetings and international symposia in the last two years, my research group has continued to make significant contributions to vascular surgery in the area of comparative effectiveness research. This rich clinical activity has facilitated our participation in multi-center clinical trials in the areas of endovascular abdominal aortic aneurysm repair, best treatment for critical limb-threatening ischemia, and management of carotid artery atherosclerotic disease. Such activity has kept our Division of Vascular and Endovascular Surgery at the cutting edge of new advances in endovascular surgery and positioned us well to report on the effectiveness of these techniques in the literature.

Beyond our institution, I have taken on leadership positions in the Vascular Study Group of New England (VSGNE) and the Vascular Quality Initiative (VQI), innovative quality-improvement initiatives at the regional and national level, respectively. The VSGNE, a consortium of over 30 regional hospitals, collects granular clinical data across institutions from which participants have published novel insights on the management of vascular diseases. The success of the VSGNE has provided a model for quality-improvement efforts nationally through the formation of the VQI, a cooperative of 18 regional quality groups in the U.S. and Canada, and endorsed by the Society for Vascular Surgery. As a member of the Executive and Research Advisory Committees for both organizations, I have worked with our research group to develop projects utilizing these data, resulting in many peer-reviewed publications.

* *Vascular Annual Meeting for the Society for Vascular Surgery (9 presentations in 2016 and 5 presentations in 2017), and the Society for Clinical Vascular Surgery, Vascular Annual Symposium (11 presentations in 2016 and 10 presentations in 2017), Charing-Cross Symposium 2017 (2 plenary talks).*

TEACHING, TRAINING, AND EDUCATION

Under my mentorship, our research group has welcomed a number of tremendously productive clinical research fellows and PhD candidates in vascular surgery over the past years. Research fellows have come from our own general surgery residency as well as prestigious residency programs around the country. PhD candidates have come through an exciting international research exchange relationship with the University Medical Center Utrecht in the Netherlands, now in its seventh year of existence. In addition, we have developed research collaborations with Toronto, Rotterdam, Amsterdam, and Milan. All research fellows receive formal instruction in research methods and statistics through the Harvard T.H. Chan School of Public Health, and have gone on to present our work at national meetings in vascular surgery.

SELECTED RESEARCH SUPPORT

Carotid revascularization and medical management for asymptomatic carotid stenosis trial (CREST-2), NINDS, 2016-2017; PI: Marc L Schermerhorn, MD

Randomized, multicenter, controlled trial to compare best endovascular versus best surgical therapy in patients with critical limb ischemia (BEST-CLI); NHLBI, 2014-2017, Co-PI: Marc L. Schermerhorn, MD (PI: Allen D. Hamdan, MD)

Harvard/Longwood Training Grant in Vascular Surgery, NIH; Co-Investigator: Marc L. Schermerhorn, MD (PI: Frank LoGerfo, MD)

SELECTED PUBLICATIONS

O'Donnell TFX, Deery SE, Darling JD, Shean KE, Mittelman MA, Yee GN, Dernbach MR, Schermerhorn ML. Adherence to lipid management guidelines is associated with lower mortality and major adverse limb events in patients undergoing revascularization for chronic limb-threatening ischemia. *J Vasc Surg* 2017;66(2):572-578.

Deery SE, Soden PA, Zettervall SL, Shean KE, Bodewes TC, Pothof AB, Lo RC, Schermerhorn ML. Sex differences in mortality and morbidity following repair of intact abdominal aortic aneurysms. *J Vasc Surg* 2017;65(4):1006-1013.

Soden PA, Zettervall SL, Deery SE, Hughes K, Stoner MC, Goodney PP, Vouyouka AG, Schermerhorn ML; Society for Vascular Surgery Vascular Quality Initiative. Black patients present with more severe vascular disease and a greater burden of risk factors than white patients at time of major vascular intervention. *J Vasc Surg* 2018;67(2):549-556.

Pothof AB, Bodewes TCF, O'Donnell TFX, Deery SE, Shean K, Soden PA, de Borst GJ, Schermerhorn ML. Preoperative anemia is associated with mortality after carotid endarterectomy in symptomatic patients. *J Vasc Surg* 2018;67(1):183-190.

Deery SE, Schermerhorn ML. Open versus endovascular abdominal aortic aneurysm repair in Medicare beneficiaries. *Surgery* 2017;162(4):721-731.

Zettervall SL, Deery SE, Soden PA, Shean K, Siracuse JJ, Alef M, Patel VI, Schermerhorn ML; Vascular Study Group of New England. Editor's Choice - Renal complications after EVAR with suprarenal versus infrarenal fixation among all users and routine users. *Eur J Vasc Endovasc Surg* 2017;54(3):287-293.

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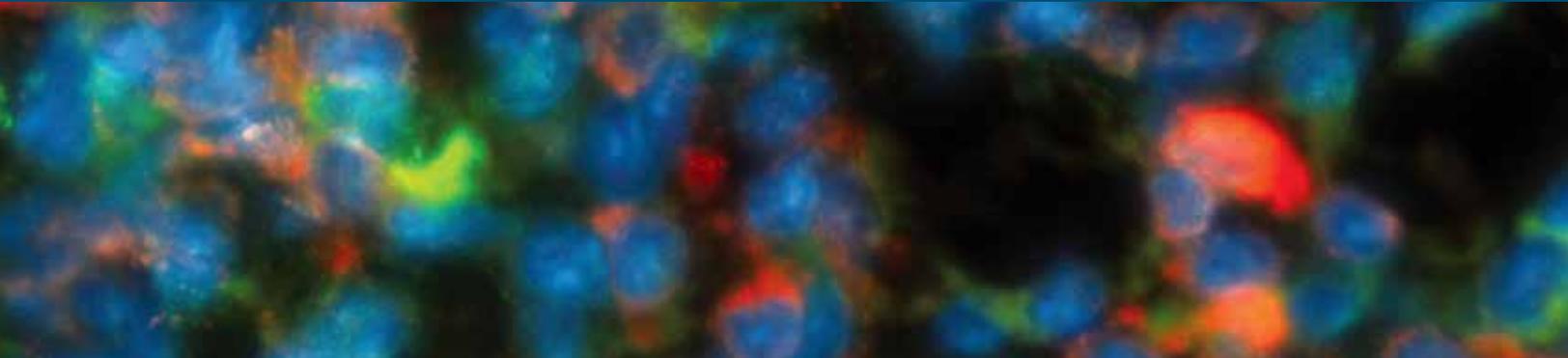
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