



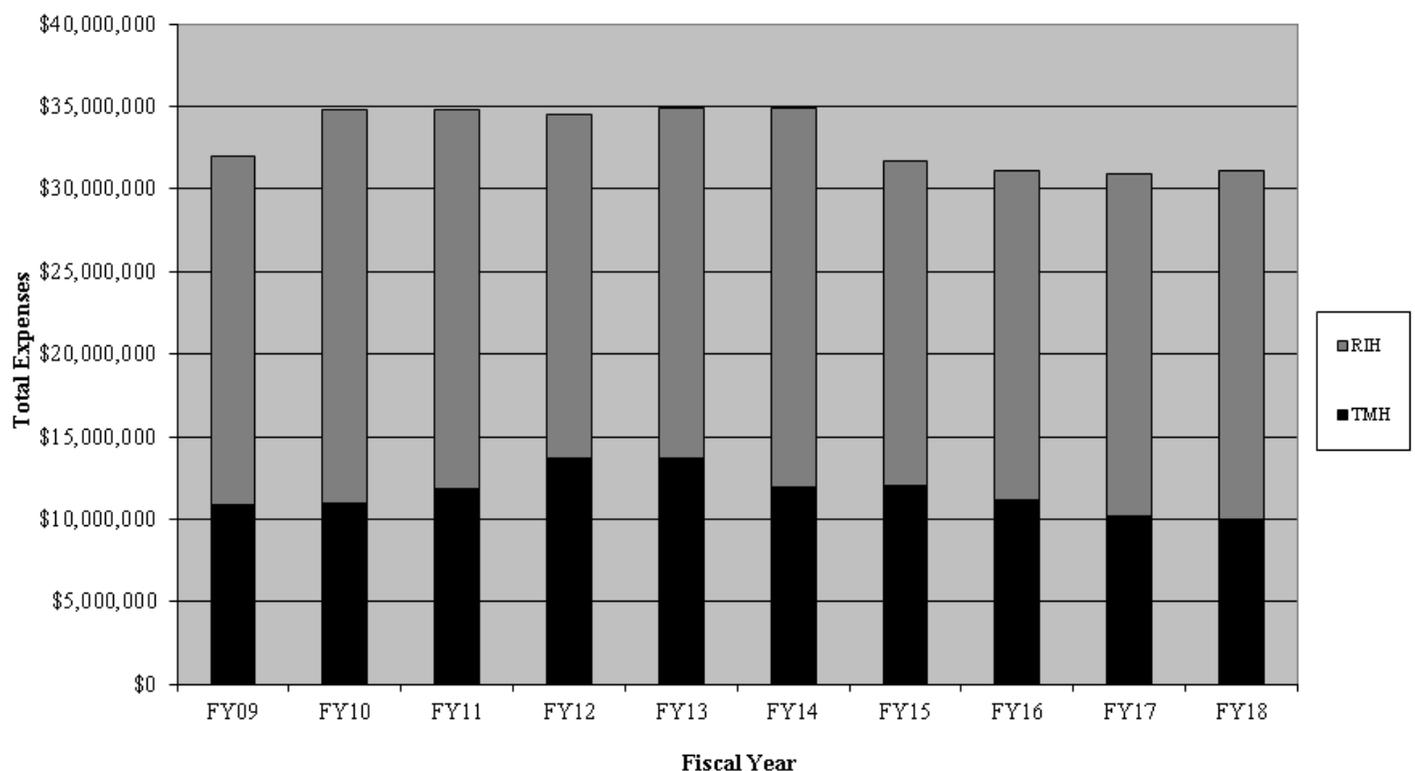
**Research Overview Fall 2019**

Brown University has long been regarded as a leader in all aspects of health care and teaching, including research. Leadership in the Department of Medicine including **Dr. Louis Rice**, Chairman for Medicine, and **Dr. Bharat Ramratnam**, Vice Chairman for Research in Medicine, strongly support research as part of the academic mission. Total research funding within the Department of Medicine at Brown affiliated hospitals (Rhode Island Hospital, Memorial Hospital of Rhode Island, Veterans Administration-Providence and The Miriam Hospital) has remained steady with 2018 funding of approximately \$31 million. Over 70% of funding comes from federal programs such as NIH, HRSA, CDC, and DHHS.

Laboratories are highlighted within the 'Knowledge District' in Providence. This enterprise involves key academic institutions including Brown University and Rhode Island Hospital. For Rhode Island Hospital, this includes a \$3 million laboratory construction of the Medical Oncology research program in the Coro facility, completed in 2012. Other programs in the Coro facility include the CardioVascular Research Center, the Genomics and Proteomics Center as well as the Lifespan Clinical Research Center (CRC). Lifespan has recently provided initial funding to develop significant additional new basic research space in the Coro facility, to be completed around 2020.

The other major research facility for Lifespan in the Knowledge district is the Galletti Research Building, which houses the Liver Research Center and Infectious Disease laboratories. Brown University has expansive research at the Ship street and Elm street facilities as well as the Warren Alpert (*next page*)

**Research Growth FY09 - FY18**



Medical School located in the area.

Both basic and clinical research are well represented in the Department. For basic research, major strengths include the **Liver Research Center** (directed by Dr. Jack Wands), the **Medical Oncology and Stem Cell Research Program** (directed by Dr. Peter Quesenberry) and the **Cardiovascular Research Laboratory** (directed by Dr. Gideon Koren). Academic aspects to research include NIH funded T-32 Training grants in Infectious Diseases and Gastroenterology. The training grant in Infectious Diseases was recently refunded until 2022. In November 2018, Wafik El-Deiry, MD, PhD, FACP joined the Department of Medicine and Brown University. In his role as the director of the unified cancer biology program, Dr. El-Deiry will design, recruit, and lead the cancer biology programs at Brown and Lifespan affiliates Rhode Island Hospital, Hasbro Children's Hospital and The Miriam Hospital. Within the past two years, three new COBRE grants have been funded within the Department of Medicine. These 5-year large collaborative grants receive several million dollars per year in funding from the National Institutes of Health. In 2017, Dr. Peter Quesenberry received a \$10 million COBRE grant for research in **Stem Cell Biology**. As of September 2018, Dr. Josiah Rich received a new \$11million COBRE grant to develop a **Center for Opioids and Overdose Research**. As of September 2018, Dr Elefterios Mylonakis received a new \$9.4 million COBRE grant to establish the **Center for Antimicrobial Resistance and Therapeutic Discovery (CARTD)**.

Clinical Research strengths include the Infectious Disease program under the direction of Drs. Elefterios Mylonakis and Karen Tashima, which has a major program in both domestic and international health including HIV/AIDS and the **Cardiology clinical research groups** under direction of Dr. Guarav Choudhary.

In 2016, Brown University and the affiliated hospitals were awarded a multi-million dollar NIH CTR grant which will provide significant resources to strengthening the clinical research enterprises at all institutions through core resources and support.

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**Basic Cardiovascular Research**

**Bum-Rak Choi, Ph.D.** His research is aimed at elucidating cardiac arrhythmia mechanisms with the long-term goal of identifying potential new therapeutic targets and strategies to suppress malignant arrhythmias. His lab currently investigates the roles of APD dispersion in initiating arrhythmias in long QT syndrome using multi-disciplinary approach including fluorescence mapping of action potential propagation and Ca<sup>2+</sup> handling from intact heart, cell voltage clamp and confocal imaging, and computer modeling. Dr. Choi's laboratory also investigates potential roles of cardiac fibroblasts and myocyte that potentiate triggered activity as well as conduction disturbances. In addition, his lab aims at developing highly predictive preclinical models of human drug-induced proarrhythmic risk using hiPSC-derived cardiac engineered microtissue system in collaboration with Dr. Coulomb's laboratory at Biomedical Engineering department of Brown University.

**Gaurav Choudhary, M.D.**'s focus of research is to evaluate the mechanisms underlying vascular, cardiac, and skeletal muscle dysfunction seen in pulmonary vascular diseases. His laboratory uses a variety of in vitro, ex vivo and in vivo approaches utilizing the preclinical models of pulmonary hypertension and emphysema. In clinical research, his team is attempting to characterize the role and impact of cardiac dysfunction in settings of lung diseases and study the epidemiology of pulmonary hypertension.

**Anatoli Kabakov, Ph.D.** is studying molecular, ionic and biophysical mechanisms of cardiac myocyte functions in normal and pathological conditions. He is interested in the effects of widespread mutations on functions of cardiac ion channels and subsequent effects on overall cellular ionic homeostasis.

**Gideon Koren, M.D.** He is interested in understanding the pathogenesis of cardiac arrhythmias through three main lines of investigation: 1) Mechanisms that underlie the increased prevalence of sudden cardiac death (SCD) in aged humans. The laboratory studies cardiomyofibroblasts senescence after myocardial infarction in aged rabbits. These studies may lead to the discovery of novel therapies for SCD; 2) Investigation of the transcription, trafficking, localization and degradation of voltage-gated ion channels in the cardiomyocytes and the effect of sex hormones on these processes. Specifically, the laboratory is studying the roles of three ubiquitine ligases (RNF207, LITAF and RFFL) in ion channels traffick-

## Cardiology (cont.)

ing and degradation; and 3) Creation and characterization of genetically modified large animal models for studying sudden cardiac death. The laboratory is characterizing the arrhythmogenic phenotype of novel transgenic rabbit models of long QT syndrome (LQT) including LQT type 1, type 2 and type 5. Specifically, the Dr.Koren's laboratory is interested in the role of dispersion of repolarization in generating triggered activity such as early after depolarizations (EADs) and polymorphic ventricular fibrillation in these models.

**Alan Morrison, M.D.**'s research is on atherosclerosis. He is PI on three ongoing studies, Calcific Atherosclerosis is Mediated by Macrophage Adhesion Signaling, Statins Influence Cardiovascular Outcomes by Modulation of Atherosclerotic Plaque Calcium Density and Development of Rac-Targeted Therapeutic Strategy for Treatment of Calcific Atherosclerosis.

**Glenn Radice, Ph.D.** He is interested in understanding the molecular, biochemical and cellular basis for how heart muscle cells sense and respond to mechanical force in normal physiological conditions and in heart disease. Specifically, we investigate how the N-cadherin/catenin cell adhesion complex together with the underlying cytoskeleton transmits force into the heart muscle cell to activate signaling pathways that control myocyte proliferation. Another major project in the Radice lab investigates how defects in intercellular adhesion and signaling cause heart disease, including arrhythmogenic cardiomyopathy. To understand the molecular mechanisms underlying the pathogenesis of this disease, genetically modified animal models are being created that better represent the genotype-phenotype relationship of the human disease.

**Karim Roder, Ph.D.** His research focuses on the role of (de)ubiquitination in cardiac excitation and disease. He is interested in delineating the molecular mechanisms of novel ubiquitin ligases, adapter molecules, or deubiquitinases affecting membrane proteins that underlie action potential duration and conduction velocity. He also shows interest in genome editing in iPS cells and mice to study cardiac excitation and disease.

### Clinical and Translational Research

#### Electrophysiology

**Antony Chu, M.D., F.A.C.C., F.H.R.S., F.A.H.A., F.A.C.P.** His clinical research focuses on mechanisms of cardiac arrhythmias and includes a diverse range of

innovative clinical therapies including cardiac device therapy, endocardial-epicardial cardiac ablation, spatial-temporal approaches to cardiac ablation for persistent atrial fibrillation and closure devices of the left atrial appendage.

**Nikhil Panda, M.D.** He is the co-PI of the multicenter Low Voltage Directed Catheter Ablation for Atrial Fibrillation (LD-CAF) trial, which is evaluating new ablation techniques for atrial fibrillation and a retrospective trial assessing patient factors associated with VT ablation. He studies emerging technologies, including a novel radiofrequency balloon catheter for pulmonary vein isolation. He is also involved in cell and tissue engineering for cardiac arrhythmias using animal models on a basic science level.

**Michael Wu, M.D.** His research interests include persistent atrial fibrillation (spatial temporal dispersion ablation), His bundle pacing/cardiac resynchronization therapy, and big data research.

**Cao Tach Tran, M.D., Ph.D.** His clinical and research interests include sudden cardiac death, potassium dynamics, and mechanisms of arrhythmias with special focus on modulators of cardiac repolarization.

#### Interventional Cardiology

**J. Dawn Abbott, M.D., F.A.C.C., F.S.C.A.I.** Her research interests include percutaneous coronary intervention (PCI), structural interventions and peripheral arterial disease. She is the site P.I. on several ongoing clinical research studies including: Myocardial Ischemia and Transfusion (MINT) trial evaluating a liberal versus restrictive transfusion strategy in patients with acute MI and anemia; AEGIS-II trial to investigate the Efficacy and Safety of CSL112 in Subjects with Acute Coronary Syndrome; OASIS 9 trial of CoLchicine and spironolactone in patients with ST elevation myocardial infarction/SYNERGY Stent Registry Organization to Assess Strategies for Ischemic Syndromes 9.

**Herbert D. Aronow, M.D., M.P.H., F.A.C.C., F.S.C.A.I., F.S.V.M.** Research interests include the safety and effectiveness of percutaneous vascular intervention (PVI), percutaneous coronary intervention (PCI), and structural heart intervention. He is involved in multiple registry-based research initiatives in these areas using resources such as NCDR Cath-PCI, PVI and TVT, SVS VQI, HCUP NIS, HCUP NRD, RI Current Care and the RI All Payer Claims Database. Dr Aronow also serves as site Principal

## Cardiology (cont.)

Investigator for a number of ongoing studies, including CALM-2, a randomized, sham-controlled, multicenter study to evaluate percutaneous implantation of a self-expanding carotid sinus device in patients with hypertension; SPYRAL PIVOTAL, a randomized, sham-controlled, multicenter study evaluating the effectiveness of renal denervation in patients with hypertension who are not on medical therapy; CREST-2, a randomized trial comparing carotid revascularization (stenting or endarterectomy) with medical therapy for asymptomatic carotid stenosis; ECLIPSE, a randomized trial comparing orbital atherectomy with conventional angioplasty before drug-eluting stenting in patients with calcified coronary arteries. Finally, Dr. Aronow is collaborating on pioneering work evaluating the role of artificial intelligence for the diagnosis and treatment of cardiovascular disease and is studying the role of the dysbiotic microbiome in atherosclerotic cardiovascular disease.

**Paul C. Gordon, M.D.**'s research interests include evaluating therapies and novel devices for coronary and structural heart disease. His current research focuses on transcatheter aortic valves with projects such as Transcatheter Aortic Valve Replacement to UNload the Left Ventricle in Patients With ADvanced Heart Failure (TAVR UNLOAD) and Edoxaban versus Standard of Care and Their Effects on Clinical Outcomes in Patients Having Undergone Transcatheter Aortic Valve Implantation-in Atrial Fibrillation. His other research project is on Physiologic Assessment of Coronary Stenosis Following PCI (DEFINE PCI).

**Peter A. Soukas, M.D., F.A.C.C., F.S.C.A.I., F.S.V.M., F.A.C.P., R.P.V.I.**'s clinical research focus is carotid stenting, endovascular treatment of PAD and venous disease. He is PI for the ongoing Sapphire-WW, Freedom flow-reversal, CANOPY, Choice and SCAFFOLD carotid studies and co-investigator for the CREST II trial. He is the site PI for the Lutonix below the knee paclitaxel coated balloon angioplasty RCT, the NHLBI-sponsored BEST-CLI RCT of open vs. endovascular therapy for CLI, and the LIFE study examining the use of Trivascular Ovation stent-graft for the percutaneous treatment of infra-renal abdominal aortic aneurysm.

### Non-invasive Cardiology & Cardiovascular Imaging

**Brian G. Abbott, M.D., F.A.C.C., M.A.S.N.C., F.A.H.A.** His clinical and research interests are cardiovascular imaging in the area of nuclear cardiology.

**Karen Aspry, M.D., M.S., F.A.C.C., F.N.L.A., F.A.H.A.** She has clinical and research interests in preventive cardiology and population management of CHD, diet and heart disease, and the treatment of lipoprotein (cholesterol) disorders. She conducts industry-sponsored lipid trials, and small clinical research projects with housestaff in the areas of familial hypercholesterolemia, and diet interventions to reduce cardiovascular risk.

**Michael Atalay, M.D., Ph.D.** has clinical and research interests in cardiac amyloid, atrial septal defects, pulmonary embolism, acute aortic syndromes, and the modalities of MRI and CT. Specific active research projects include: (1) Evaluating the potential utility of non-ECG gated contrast CT for detecting cardiac amyloidosis and other non-ischemic cardiomyopathies, (2) Correlating imaging biometrics with outcomes in patients with type A aortic dissection, (3) Correlation of anatomic metrics with ASD shunt severity, and (4) Using vessel density values on CTPA to estimate cardiac output.

**Sebhat Erqou, M.D. Ph.D.** [He](#) has interest in cardiac imaging and prevention. His research areas include preventive cardiology with a focus on cardiovascular disease risk factors, racial differences in outcomes, and HIV-associated cardiomyopathy.

**Katharine French M.D., M.P.H.** does research in echocardiography imaging.

**Philip G. Haines, M.D., M.P.H.**'s research interests include heart failure and non-invasive imaging. He has an Advance-Clinical Translational Research Pilot Project Program Grant: Post Hospitalization Community Pharmacy Medication Therapy Management for Heart Failure Multi-Site Collaboration between URI, Providence VA Medical Center, Brown, and Lifespan, Lifespan Echo Lab. Heart Failure with Preserved Ejection Fraction Pilot Mechanistic Cross-Sectional Study: The impact and interaction of female/male sex, hypertension, and diabetes on echocardiographic markers of HFpEF severity. Ancillary cardiac MRI study of the Jackson Heart Study focusing on basic and advanced evaluation of right ventricular structure and function Providence VA Medical Center and Brown Collaboration.

**Athena Poppas, M.D., F.A.C.C., F.A.S.E.** She is conducting studies focused on echocardiographic evaluation of valvular heart disease and heart disease in women. She is a co-investigator on multicenter and investigator initiated projects in conjunction

## Cardiology (cont.)

with the cardiac surgery, anesthesia, maternal fetal medicine and heart failure group. Her ongoing projects include echocardiographic predictors of recovery in peripartum cardiomyopathy patients, perioperative predictors of outcome of mitral and tricuspid valve repair, and a new application in 3D echocardiography. The echocardiography database is a resource for numerous residents and fellows.

**Raymond Russell, M.D.** does research in nuclear cardiology.

**Elena Salmoirago-Blotcher M.D., Ph.D., F.A.H.A.**, is interested in the study of behavioral strategies for the promotion of cardiovascular health (physical activity, medication adherence) in patients with, or at risk for, cardiovascular disease. She also conducts research on stress (takotsubo) cardiomyopathy as a model for the study of the complex interactions between psychological factors, reproductive factors and acute CV conditions in women. She collaborates with the Women's Health Initiative (WHI) study and can assist residents interested in exploring research questions related to cardiovascular health in women using the WHI dataset.

**Nishant R. Shah, M.D.** He is PI on Automated Assessment of Nuclear Stress Test Appropriateness and Downstream Patient Outcomes.

**Christopher Song, M.D., F.A.C.C.** His clinical and research interests include echocardiography, atrial cardiopathy, stroke, and quality improvement. He is the site PI for the ARTESiA trial (Apixaban for the Reduction of Thrombo-Embolism in Patients with Device-Detected Sub-Clinical Atrial Fibrillation) and a site co-investigator for the ARCADIA trial (Atrial Cardiopathy and Antithrombotic Drugs in Prevention After cryptogenic stroke).

**Wen-Chih Hank Wu, M.D., M.P.H.** He has conducted research work in the areas of cardiovascular epidemiology and outcomes with focus on system redesign to prevent adverse cardiovascular outcomes. He holds research grants from the VA Merit Review Process, non-for-profit organizations, and the industry.

### Heart Failure and Transplantation

**Daniel J. Levine, M.D.** He is interested in heart failure and transplantation. He is the site P.I. on several ongoing clinical research studies including: SOLOIST Trial, a randomized, double-blind, Placebo-controlled, Parallel-group, Multicenter Study to evalu-

ate the effects of SOTagLiflozin on clinical outcomes in Hemodynamically Stable Patients with Type 2 Diabetes POST Worsening Heart Failure; PARAGLIDE Trial, a multicenter, randomized, double-blind, double-dummy, parallel group, active controlled 8-week study to evaluate the effect of sacubitril/valsartan (LCZ696) versus valsartan on changes in NT-proBNP and safety and tolerability of in-hospital initiation of LCZ696 compared to valsartan in HFpEF patients with acute decompensated heart failure (ADHF) who have been stabilized during hospitalization; GUIDE-HF IDE, trial of Hemodynamic-GUIDEd Management of Heart Failure.

## Endocrinology, Diabetes and Metabolism

**Geetha Gopalakrishnan, MD, Division Director**, coordinates the clinical trials program for the Division of Endocrinology. There is a wide variety of research interests in clinical and basic investigation related to adult endocrine diseases, diabetes, thyroid diseases, obesity, hypertension, and women's health topics such as osteoporosis.

Studies include the effect of new pharmacological agents in the management of bone loss related to postmenopausal osteoporosis, hyperparathyroidism and cancer.

We have collaborated with other investigators to determine the bone and body composition of certain disease states like HIV infection, breast cancer and anorexia. More recently, research interests have broadened to include new treatments for diabetes.

## Gastroenterology

### Liver Research Center

**Jack R. Wands, MD** - Our research efforts involve the role of hepatitis B and C infection in the pathogenesis of hepatocellular carcinoma at the molecular level.

**Suzanne de la Monte, MD, MPH** is interested in the molecular mechanisms of programmed cell death as well as the role of aspartyl (asparaginy)-beta-hydroxylase (AAH) in cell motility and invasiveness of tumor cells as well as neuronal cells.

## Gastroenterology (cont)

**Jisu Li, MD, PhD** – Hepatitis B and C viruses are major causes of chronic hepatitis, liver cirrhosis and hepatocellular carcinoma. Our laboratory is interested in identifying hepatitis B virus receptors and cofactors.

**Steven Moss, MD** - Research interests are in the pathogenesis of gastrointestinal cancers in general and gastric cancer in particular. Since gastric cancer is the first malignancy related to a chronic bacterial infection, my laboratory examines the carcinogenic effects of *Helicobacter pylori* on gastric epithelial cells at cellular and molecular levels.

**Shuping Tong, MD, PhD** - Research interests involve investigations of hepadnaviral receptor proteins on hepatocytes. Using related duck hepatitis B virus (DHBV) as a model, we have identified p170, or duck carboxypeptidase D (DCPD), as a binding partner for viral pre-S envelope protein. Studies are in progress to define the contact site on the p170 for the pre-S1 region of DHBV.

**Chiung-kuei Huang, Ph.D.** – Interest is in the pathogenesis of cholangiocarcinoma and targeting such tumors with an antibody drug conjugate and studying the mechanism of action.

**Fusun Gundogan, M.D.** - My research interests involve insulin and IGF signaling in the placenta with particular reference to fetal alcohol spectrum disorders. Our group is also interested in aspartyl (asparaginyl)- $\beta$ -hydroxylase gene regulation during alcohol consumption in the placenta and neonate.

### Clinical Research

**Fadlo Habr, MD** - Clinical interests are mainly in interventional Gastroenterology, mainly pancreaticobiliary endoscopy and photodynamic therapy. We'll be looking at the effects of PDT on end-stage cholangiocarcinoma. The Division of Gastroenterology at Brown Medical School is part of a multicenter national prospective study looking at the role of EUS in the evaluation of cystic lesions of the pancreas. Fluid from the pancreatic cyst will be aspirated under EUS-guidance and tested for specific genetic markers as well as for monoclonal antibodies.

**Amanda Pressman, M.D.** – My focus is on women's health in gastroenterology, and gastrointestinal motility with clinical and translational research.

**Kittichai Promrat, MD** – Interests are in the natural history and therapy of chronic liver diseases, in particular hepatitis B, C and nonalcoholic steatohepatitis (NASH). Research efforts involve the roles of in-

ulin resistance and obesity in the pathogenesis of NASH. Another area of research interest is in identification of host immunogenetic factors that involve in clinical outcomes and treatment responses of viral hepatitis.

**Harlan Rich, MD** – Interests are in clinical Esophagology with an emphasis on gastroesophageal reflux disease and Barrett's esophagus, as well as general gastroenterology (including colorectal cancer screening, peptic ulcer disease, and irritable bowel syndrome). We are currently expanding the role of technology in clinical gastroenterology via the use of ambulatory telemetric pH and capsule endoscopy devices. Research includes creating a database on a large Barrett's surveillance population, studying the acute effect of esophageal acid perfusion on esophageal motility and LES function in humans, and studying genomic alterations in Barrett's epithelium.

**Colleen Kelly, M.D.** – My clinical research is focused on chronic *C. difficile* infection. I have developed a program of fecal transplantation wherein microbiota of the gut is analyzed before and after transplant; to date, results show that 95% of individuals undergoing this experimental procedure have total eradication of the infection.

**Sean Fine, M.D., M.S.** – Interest is in inflammatory bowel disease and new biologic therapy for this disease. He has a major interest in translational research and is engaged in several approaches to modify the disease progression and induce long term remission.

**Abbas Rupawala, M.D.** – Interest is in developing new approaches for predicting disease flairs in inflammatory bowel disease. He is involved in the construction and implementation of apps that could be used on a smartphone to identify early disease reoccurrence during therapy in collaboration with engineers at Boston Scientific.

**Suzanne Chan, MD, PhD** - My research interests include quality improvement in the inpatient management of patients with advanced liver disease.

**Zilla Hussain, MD** - My clinical and research interests include gastrointestinal reflux disease, esophageal motility disorders, Barrett's esophagus, Eosinophilic Esophagitis, and achalasia.

**Akwi Asombang, MD** – My clinical and research interests include ERCP and advances in Gastroenterology and Hepatology. My major interest is sharing my passion and experience with those in Zambia.

## General Internal Medicine

**Rebekah Gardner, MD** is interested in improving care transitions for patients across a variety of health care settings. Through her work at New England's Quality Improvement Organization, she helps to implement and then analyze interventions to reduce re-hospitalization rates. She also collaborates on statewide public reporting of physician use of health information technology and the impact of technology on workflow and stress.

**Meghan Geary, MD** is interested in women's health and addiction. Her primary care practice includes refugee patients and women who are in a residential treatment for substance use disorder.

**Ross Hilliard, MD** has interests focused on the Electronic Health Record, principally in the interactions of physicians and other healthcare providers with the EHR and the relationship of the EHR to burnout and stress. He is also interested in the ways in which the EHR can help drive clinical quality improvement, including opportunities for improving routine screenings such as for colon cancer as well as adherence to best practices and clinical guidelines in diagnostic testing. Lastly, he is involved in helping other physicians formulate questions and understand the data that is available in the EHR for their own research projects.

**Jennifer Jeremiah, MD** is interested in medical education, specifically in the areas of remediation, promotion of learner success and faculty development to improve evaluation of and feedback to learners. She has presented on these topics at AAIM/APDIM (Alliance for Academic Internal Medicine/Association of Program Directors in Internal Medicine). She is the Director of Faculty Development in Clinical Education. Dr. Jeremiah also is interested in promoting resident and practicing physician well-being and serves as the Wellness Champion for the State of Rhode Island ACP Chapter.

**Carol Landau, Ph.D.** interests include innovations in curricular development in residency training, depression in women and professional development. Her current projects include wellness and prevention of depression during residency training and she has developed curricula on professionalism and on refugee health. Her work in depression in young adults, has resulted in a forthcoming book from Oxford University Press.

**Suzanne McLaughlin, MD MSc** is interested in patient-centered medical home activities and resident learning in the continuity clinic environment. Her medicine-pediatrics colleagues and she have active research/QI projects in: SBIRT (Screening, Brief Inter-

vention and Treatment) for adolescent substance use in primary care, Integrated Behavioral Health (use of mental health screening tools and access to behavioral health services), and are part of a national collaborative of MedPeds residency programs to develop curriculum and evaluation tools for training residents in health care transition.

**Kelly McGarry, MD, FACP** has research interests in women's health, LGBT health and medical education. She also writes review articles on women's health topics including the prevention and treatment of osteoporosis and treatment of postmenopausal symptoms. She is a co-editor of the women's health textbook, *The 5-Minute Consult Clinical Companion to Women's Health*, by Lippincott Williams & Wilkins. She co-wrote "Women's Health Topics" in *Cecil's Essentials of Medicine*, 9th Edition. She is currently working on a project related to home visits and transitions of care and another project on faculty development.

**Susan Ramsey, PhD** conducts research aimed at developing and testing behavioral interventions to improve health. She currently serves as principal investigator on an ongoing NIH-funded study that aims to develop and test an intervention to promote use of HIV pre-exposure prophylaxis (PrEP) among at-risk women who are incarcerated and to link them to community-based PrEP care upon release from incarceration. She also served as principal investigator on a recently completed NIH-funded study that examined the impact of a smartphone-enhanced intervention to improve HIV medication adherence. In addition, she serves as a co-investigator or mentor on multiple NIH-funded studies focused on opioid use disorder and overdose risk reduction.

**Rahul Vanjani, MD** areas of interest focus on the impact of correctional control (incarceration, probation, parole) on health and the evaluation of multidisciplinary programs that center the role of the community health worker and provide wraparound services to patients.

**Sarita Warriar, MD** has an interest in medical education research, currently participating in two federally-funded grants focused on social determinants of health education and weight management counseling skills for medical students. She is one of the co-directors of the Clinician Educator Track for internal medicine residents and is the director of the medical education elective month, which helps residents implement educational innovations and improve teaching skills

## Geriatrics & Palliative Care

**Richard W. Besdine, MD**, the Division Director, oversees an \$18 M/year research program in health services research and aging at the Center for Gerontology and Health Care Research – one of 12 research centers of the Brown University School Public Health. Five faculty members from the Division of Geriatrics and Palliative Medicine conduct their research in the Center. Research foci include quality of care (especially nursing homes), end-of-life care, pharmaco-epidemiology and health care disparities. Many projects offer opportunities for resident participation. Most recently, he has led a grant from the Hartford Foundation and American Geriatrics Society (1/17-12/20, ~\$1.6 M) to disseminate nationally the geriatrics-orthopedics co-management program, which has reduced complications and mortality in elderly hip fracture patients at RIH.

**Sevdenur Cizginer, MD, MPH**, studies delirium in acute care settings, and outcomes of the Geriatrics-Colorectal Surgery Co-management program at the Miriam Hospital. Opportunities for residents to work with her are numerous.

**Julio Defillo-Draiby, MD** Evaluating impact of ACE unit at Kent Hospital for length of stay, readmission rates, overall patient/family satisfaction in a community hospital; Evaluating impact of an educational program to improve detection and management of Delirium in the ED, using a 15-minute educational intervention (Measuring attitudes, competencies; Collaborative program for preventing use of probable inappropriate medication in older adults in the Emergency Department

**David M. Dosa, MD, MPH**, is the Associate Director of the Providence VAMC Center of Innovation (COIN) for Long Term Services and Supports, one of 19 centers dedicated to research within the VA. He is the Principal Investigator of a 4-year VA MERIT Proposal to Evaluate Antibiotic Stewardship Efforts in VA nursing homes. A new NIH grant will examine outcomes for vulnerable elderly patients in disasters, using recent hurricanes as the model

**Stefan Gravenstein, MD, MPH**, Research interests are in aging, infection, inflammation, immunity and their intersection, mostly studied through the lens of vaccines, vaccine efficacy, non-targeted indications of vaccines in the nursing home setting; also interested in quality improvement, especially in the context of antimicrobial stewardship, care transitions and super-utilizers. Current research studies/grants include

comparing recombinant influenza vaccine to claims-based outcomes in long-term care residents; Designing and implementing strategies to reduce antibiotic overuse in the long-term care setting, developing and deploying communication and tracking support tools for better stewardship and scalability.

**Lynn McNicoll, MD**, oversees multiple quality improvement research projects. She is consultant to a national dissemination project for the geriatric-orthopedic comanagement program AGS CoCare: Ortho. She is also mentor for the geriatric-oncology outpatient evaluation clinic. She is Director for Quality Management and Outcomes for the Department of Medicine.

**Nadia Mujahid, MD**, leads the Geriatrics-Orthopedics Co-Management Program at RIH. She has developed pre- and post-operative management protocols to expedite the time to surgery; improve pain management; and reduce variability of care, thus reducing LOS, readmission rates and enhancing the overall patient experience. Data are being collected and analyzed with the assistance of Drs. Gravenstein and McNicoll. Several medical student research projects are underway to collect and analyze data on clinical outcomes. Resident project opportunities are considerable.

**Iva Neupane, MD**, leads the Geriatrics-Trauma Surgery Co-management program at RIH. She has published on outcomes of the program, which include a statistically significant reduction in mortality for patients >80 years of age. Resident project opportunities are considerable.

**Sakeena Raza, MD**, co-manages post-operative care for Elective Orthopedics Joint Replacement Center of Excellence at the Miriam Hospital. She co-managed the Urology service at the Miriam Hospital for 2 years (December 2016-December 2018) as a pilot project, and is currently in the process of analyzing data. Preliminary results show a decrease in hospital length of stay among older patients who had post-operative geriatrics co-management. Residents can work with her on these data, as well as a new project related to outcomes of the Joint Replacement Co-management program.

## Hematology & Oncology

The division of hematology/oncology is involved in clinical research, populations based research and basic laboratory research in cancer biology. We currently have approximately 50 clinical research studies of new anticancer drugs including first-in-man studies, and phase I and II studies. Research opportunities are available in these three areas.

**Howard Safran, MD – Division Director:** Dr. Safran is involved in investigator initiated studies in pancreatic and esophageal cancer. He is studying the regimen FOLFOX-A which he developed in pancreatic cancer and is collaborating an investigator initiated trial with neoadjuvant immunotherapy in esophageal cancer. He is developing a clinical trial with a novel agent for brain tumors. He also participates in biotech trials of immunotherapy and targeted in gastrointestinal cancers.

**Benedito Carneiro, MD,** is conducting a first-in-human study of a new TRAIL receptor agonist against solid tumors. He is also assessing an EGFR immunotoxin. He is also evaluating a CD40 antibody in combination with a PD-L1 inhibitor. Dr. Carneiro is involved in pharmacokinetics, pharmacodynamics and immunogenicity. He is collaborating with basic scientists at Brown University on DNA repair to develop new combinations of agents such as combining a PARP inhibitor with a PI3 kinase inhibitor.

**Don Dizon, MD** is evaluating immunotherapy in cervical and clear cell cancer. He is also studying intraperitoneal therapy for ovarian cancer. He also studies sexuality and cancer and is a world leader in on-line communication.

**Christopher Gerald Azzoli, MD,** is involved in clinical research in lung cancer and populations based research to reduce incidence of lung cancer in Rhode Island. Dr. Azzoli will be involved in strategies across the state to try to reduce the incidence of lung cancer. He is a leader in the American Society of Clinical Oncology establishing clinical care guidelines. In Rhode Island, he is developing an outreach to underserved populations and community health providers to try to reduce the incidence of lung cancer.

**John Reagan, MD** has been investigating cellular immune therapy for refractory leukemia and lymphoma. He is studying whether host tolerance to cancer is reversed by stem cell rejection.

**Adam Olszewski, MD** performs analysis of large

databases and populations based research. He is principal investigator of multiple studies including the use of a liposomal vincristine and bendamustine and rituximab for non-Hodgkins lymphoma. He is also performing a phase Ib/II of obinutuzumab + idasanutlin for relapsed or refractory follicular lymphoma and DLBC.

**Hina Khan, MD** is involved in lung cancer research that focus on immunotherapy. Clinically she is involved in a Phase 1B/2 Study of Viagenpumatumucel-L (Hs-110) in combination with multiple treatment regimens in patients with non-small cell lung cancer.

**Humera Khurshid, MD** has initiated a geriatric oncology program at RIH and TMH. This is a multidisciplinary program involving oncology, geriatrics, nutrition and pharmacology. This program evaluates whether early geriatric assessment can optimize the safe and effective administration of chemotherapy.

**Khaldoun Almhanna, MD,** will be developing novel investigator initiated studies in liver and esophageal cancer. He also studies immunotherapy for GI cancers

**Mary Anne Fenton, MD,** is involved in quality outcomes. Her assessments have been presented at major national meetings. Current focus are opioids, pain control and chemotherapy induced constipation. Dr. Fenton is also involved in weight loss in adjuvant treatment of overweight patients with breast cancer.

**Mary Lopresti, MD,** is involved in breast cancer and has set up a program for breast cancer in young women Her research involves adjuvant endocrine therapy and neoadjuvant chemotherapy.

**Rochelle Strenger, MD,** research focus is centered on treatment of adults with cancer with developmental disabilities such as autism. She studies strategies for care and team based approaches.

**Dr. Anthony Mega,** the head of the section of GU oncology. His research involved studying immune checkpoint inhibitors in the adjuvant setting in bladder cancer. He is also PI of an investigator initiated study of a PARP inhibitor in prostate cancer with defects in DNA repair genes.

**Andre Desouza, MD** research concentrates on GU oncology and phase I studies. He is also interested

## Hematology & Oncology (*cont*)

in genomic alterations in GU cancer.

**Tom Ollila, MD** is involved in research in CNS lymphomas. He is also studying opioid addiction in cancer patients.

**Alex Raufi, MD** is involved in investigator initiated research in gastric cancer. He is also involved in laboratory correlative studies.

### **BASIC RESEARCH**

The Hematology/Oncology Division has a broad basic research portfolio.

**Dr. Wafik El Deiry, MD, PhD** is the head of cancer biology at Lifespan and Brown University. His laboratory is involved in multiple aspects of translational research including apoptosis, novel cancer targets, immunotherapy and organoids.

**Peter J. Quesenberry, MD** focuses on the role of microvesicles in cellular communication in human cancers. He is interested in reversal of the oncogenic phenotype by microvesicles. He is also interested in using microvesicles to reduce damage by radiation and to treat pulmonary hypertension.

**Patrycja Dubielecka-Szczerba, PhD**, is working on approaches to reverse resistance to tyrosine kinase inhibitors in chronic myelocytic leukemia and more recently on a unique model of murine myelofibrosis. This latter model is unique and opens unique potential for understanding myelofibrosis and developing new therapeutic strategies to treat this disease.

**Sicheng Wen, PhD** He is studying the capacity of mesenchymal stem cell derived vesicles to reverse radiation damage to marrow and to treat murine models of aplastic anemia.

**Dr Olin Liang** is studying the role of microenvironment in supporting normal and malignant hematopoiesis and the impact of aging on the marrow microenvironment.

**Paul Bertone, PhD**, is studying brain tumors by investigating glioma. He is an expert in single cell technologies. He also performs computational biology

## Infectious Diseases

**Antimicrobial Drug Discovery** Groups in our Division are working to identify new classes of antimicrobials with antivirulence or immunomodulatory efficacy and evaluate toxicity/efficacy.

**Global Health** The Global Health Initiative (<http://brown.edu/initiatives/global-health>) is a multidisciplinary university-wide effort to reduce health inequalities among underserved populations locally and worldwide through education, research, service and development of partnerships with communities and institutions in Africa, India, Southeast Asia, the Caribbean, and the Pacific.

**HIV/AIDS** The Division has an in-depth focus in the area of HIV/AIDS. The NIH funded Lifespan/Tufts/Brown Center for AIDS Research (<http://192.138.176.29/cfar>), based at The Miriam Hospital supports laboratory and clinical HIV prevention and treatment research.

The AIDS Clinical Trials Unit (ACTU) at The Miriam Hospital/Brown conducts clinical trials in HIV-infected adults to test novel therapeutic interventions focused on HIV-associated inflammation and resulting end-organ disease, tuberculosis, viral hepatitis and HIV cure.

**Health Disparities, Advocacy and Policy** The Center identifies, initiates, and supports projects that respond to the epidemic of incarceration and recidivism in the criminal justice system and the associated complex public health crisis.

**Additional opportunities are available in the following areas: Infection Prevention and Control, Mycology, Sepsis Research, Sexually Transmitted Diseases, Travel Clinic**

**Curt G. Beckwith, MD** conducts NIH-funded research related to HIV and viral hepatitis among at-risk populations, including persons involved with the criminal justice system and substance users. Research interests include novel testing approaches for HIV and viral hepatitis and development and implementation of interventions to improve adherence to HIV treatment and care.

**Philip A. Chan, MD, MS** performs research in several areas including HIV and STD prevention, LGBTQ health, health disparities, and public health. Dr. Chan has specific expertise in HIV/STD prevention including diagnosis and testing, as well as pre- and post-exposure prophylaxis (PrEP and PEP, respectively). He is PI of seven NIH grants related to these topics.

## Infectious Diseases (cont)

**Cheston B. Cunha, MD**, Research interests include general infectious diseases, antimicrobial therapy, and antimicrobial stewardship including impact of rapid diagnostics and oral antimicrobial therapy.

**Susan Cu-Uvin, MD**. My main field of research is HIV in women. This includes understanding HIV dynamics and reservoirs in the female genital tract, sexually transmitted diseases in particular and Human Papilloma Virus infection (HPV). We have funding to assess HPV infection in HIV infected women, including cervical neoplasia and cervical cancer, and response to treatment. My research also involves assessment of microbicides to prevent HIV transmission to women. As Director of the Providence/Boston Center for AIDS Research, I coordinate efforts to support multidisciplinary HIV research at Brown and Boston University and their affiliated hospitals.

**Erika M. D'Agata, MD, MPH**, research focuses on the transmission dynamics of multidrug-resistant organisms in a variety of healthcare settings, including dialysis units and long-term care facilities. Her research focuses on characterizing and quantifying the most effective prevention strategies aimed at minimizing their spread, using both clinical epidemiological methods and mathematical modeling.

**Dimitrios Farmakiotis, MD**, research interests focus on infections in non-HIV immunocompromised patients (solid organ transplant recipients and patients with hematologic malignancies) and VAD recipients, specifically CMV, hepatitis-C and HIV in organ transplantation, invasive fungal infections, particularly mechanisms and clinical significance of resistance to antifungals in *Candida* species, and antifungal stewardship. Mentees have the opportunity to work with multi-institutional observational datasets on candidemia, invasive mold infections, CMV, as well as the Brown kidney transplant database, prospective clinical studies on antifungal agents and management of CMV, and interesting case studies.

**Timothy P. Flanigan, MD**. Major interests include HIV and other infectious diseases among marginalized communities. I participate in the Providence/Boston Center for AIDS research and a funded training program to prepare postdoctoral fellows (physicians and behavioral scientists) for research careers in the cross-disciplinary field of HIV and other infections associated with substance abuse. I also direct the Brown University Minority Health and Health Disparities International Research Training program with international ID work in Ghana, Ukraine, India and Liberia.

**Sara Geffert, MD** research interests include evaluation of innovative rapid diagnostics and quality improvement with respect to current microbiological testing.

**Joseph I. Harwell, MD** focuses his research on HIV and related complications in international settings. He has been funded by the Hong Kong government to study the local prevalence of drug resistant gonorrhea in community settings using molecular diagnostic methods. Through his work with the Clinton Health Access Initiative Dr. Harwell has helped to design an ANRS-funded study to explore the optimal approach to third line antiretroviral therapy in Cambodia. Working with the government of Lesotho and WITS Reproductive Health and HIV Institute of South Africa Dr. Harwell is studying the operational aspects of delivering oral pre-exposure prophylaxis (PrEP) for HIV to adolescent girls and young women in Maseru, Lesotho. Finally, Dr. Harwell has designed 2 operational research programs to describe the barriers and facilitators to the nationwide adoption of dolutegravir as initial HIV therapy in collaboration with the governments of Nigeria and Uganda.

**Rami Kantor, MD**, NIH-funded research in local and global settings including transmitted and acquired antiretroviral drug resistance in diverse HIV variants, populations and settings; HIV transmission networks; treatment-failure monitoring; and laboratory infrastructure, involving clinical research, bioinformatics, molecular epidemiology and basic science.

**Michelle A. Lally, MD, MSc**, Research interests include the integration of biomedical and behavioral interventions to prevent HIV, and quality improvement efforts that focus on disease prevention.

**Jerome M. Larkin, MD**, research interests include home-based intravenous antibiotic therapy, tick related infections and HIV infection in children and adults.

**John R. Lonks, MD**, research has explored the mechanism of pneumococcal resistance, particularly as it pertains to macrolide antibiotics. This program has characterized the clinical failure of therapy with macrolides among individuals with invasive pneumococcus treated with macrolide antibiotics.

**Leonard A. Mermel, DO, ScM**, Research is focused on understanding the epidemiology, pathogenesis, and prevention of healthcare-associated infections.

**Maria D. Mileno, MD**, is interested in returned travelers with illness. She is currently involved in a

## Immunology & Infectious Diseases (cont)

project that may help screen travelers for TB by using their smart phones.

**Jennifer Adelson Mitty, MD, MPH,** Clinical and research interests include general infectious diseases, HIV treatment and prevention, and Lyme disease.

**Eleftherios Mylonakis, MD, PhD,** is internationally recognized for his research on the study of host and microbial factors of infection and the discovery of anti-microbial agents, or substances that kill or inhibit the growth of microorganisms such as bacteria or fungi.

**Gerard Nau, MD, PhD,** is a physician-scientist with interests in innate immunity and genetic predisposition to infections. His laboratory studies host-pathogen interactions and bacterial pathogenesis, and is internationally known for its work on tularemia. The main objective is to translate information from pre-clinical studies into new therapies to treat infectious diseases, especially those caused by antibiotic-resistant bacteria.

**Steven M. Opal, MD,** Research interests are focused upon the immunopathogenesis of invasive bacterial and viral pathogens and septic shock research. He does primarily translational research from the basic cellular immunology and molecular pathogenesis of bacterial toxins and virulence factors, preclinical models of severe infection, up to late stage phase 2 and phase 3 clinical research investigations. He does research with biohazardous pathogens and their rapid molecular diagnosis and treatment. He also helps coordinate and direct international clinical trials in septic shock and severe infection.

**Bharat Ramratnam, MD,** currently has an NIH funded project which is focused on a better understanding the role of reproductive hormones on HIV-1 transmission (R01HD072693) and determining whether substance abuse alters a cell's capacity to support viral replication (P01AA019072). A separate interest is in better defining the cellular components of atypical responses to HIV such as those observed among individuals who become infected but are able to autonomously control viral replication.

**Louis B. Rice, MD,** is an international authority on antimicrobial resistance in bacteria. His research interests include understanding the mechanisms of antibiotic resistance in bacteria; preventing hospital infections; and developing antibiotic usage strategies that will minimize the emergence and spread of antibiotic resistance.

**Josiah D. Rich, MD., MPH.,** research focus is on the

overlap between infectious diseases and illicit substance use and disadvantaged populations, especially prisoners and others involved with the criminal justice system. He is also focused on addressing the Opioid overdose crisis. He is the Principal or Co-investigator on several research grants involving the treatment and prevention of HIV and other infectious diseases, as well as, the "COBRE" on overdose and Opioids.

**Ralph Rogers, MD** research interests include studying the intersection of infectious disease and immunology in immunocompromised hosts as well as the clinical application of novel assays of infectious disease diagnostics.

**Francine Touzard Romo, MD,** With an expertise in management of HIV and orthopedic devices associated infections, my research focus has been antiretroviral toxicity, orthopedic infections in HIV. I now actively participate on antimicrobial clinical research in conjunction with other Lifespan affiliates.

**Natasha Rybak, MD,** Research interests are in global health with a specific interest in tuberculosis (TB), HIV and TB, and multi-drug resistant (MDR) tuberculosis among adults and children in Eastern Europe. She helped to create the Brown University Ukraine Collaboration, a global health initiative program at Brown University to address these issues of TB, TB/HIV co-infection and MDR-TB in Ukraine. She will also serve as the Medical Director of the RISE TB Clinic.

**Martha Cristina Sanchez, MD,** Research interests include HIV - Care Continuum, Tropical Medicine, Global health. She oversees the Immunology Center Adherence and Retention Team (ICARE) that focuses efforts of re-engaging and maintaining HIV patients in care. She is the co-director of the Brown-Dominican Republic exchange program, a global health initiative involving medical residents and students as well as clinical research involving HIV infection and comorbidities in Santiago, DR.

**Karen T. Tashima, MD,** directs the NIH funded HIV Clinical Trial Unit at The Miriam Hospital to investigate new therapies for HIV, hepatitis C and novel approaches to HIV infection and its associated inflammatory state. She developed a national study to evaluate whether a class of antiretroviral medications should be included in regimens for patients with drug resistant virus.

**Edward J. Wing, MD,** Recent interests include Obesity and HIV and HIV and Aging. He has devel-

## Immunology & Infectious Diseases (*cont*)

oped international health programs within the Department to improve both education and clinical research in the Dominican Republic, Haiti, Brazil and Kenya. These programs have developed innovative approaches to HIV diagnosis and treatment, but also seek to improve general medical care in both the inpatient and ambulatory settings.

## Kidney Disease & Hypertension

**Douglas Shemin, MD** is the interim director of the Division of Kidney Diseases and Hypertension. His primary clinical and research interests are renal replacement therapy and end stage kidney disease. His current research projects include novel treatments for anemia of chronic kidney disease, measurement of solute clearance in end stage renal disease, and the effect of dialysis time on outcomes in end stage kidney disease.

**Shougang Zhuang, MD** serves as the director of the Renal Diseases and Hypertension Division's laboratory research program. He is interested in the mechanisms of acute kidney injury and renal regeneration after injury, and in developing therapeutic agents that promote renal recovery after acute kidney injury (AKI) and that attenuate progression of renal fibrosis. His current projects are focused on determining the intracellular signaling events critical for renal tubular cell death and development of renal fibrosis after injury, as well as defining the role of epigenetic regulation in renal epithelial cell regeneration and renal fibrosis. His research has been supported by the NIH grants.

**Reginald Gohh, MD** is actively involved in multiple studies pertaining to the clinical management of kidney transplant recipients. These include studies investigating the role of trepostinil in preventing the development of delayed graft function in deceased donor kidney transplant recipients. He is also studying the use of nicotinamide in preventing the recurrence of squamous cell skin cancer in this population. Other studies are investigating the natural evolution of ESRD-related elevated ferritin levels as well as the management of hypomagnesemia in the post-transplant setting.

**Susie L. Hu, MD** is interested in peritoneal dialysis outcome in relation to diuretic and ACEI and vitamin D use. She is also participating in a quality improvement project examining the utility of urgent start dialysis comparing outcomes between peritoneal dialysis and hemodialysis. She is also assessing adequacy, infection and catheter function. She has

## Kidney Disease & Hypertension (*cont*)

also doing research on renal transplant donor outcomes in relationship to kidney sizes.

**John O'Bell, MD** is interested in the use of novel educational tools to improve learning for fellows, residents and students. He is also involved in research about risk factors for recurrent kidney stones.

**George Bayliss, MD** research interests include learning whether there are ways to combine subjective and objective data to predict when someone will need to start dialysis or return to dialysis after the transplanted kidney fails and the use of immunosuppressant agents in the transplant patients with a failed kidney after return to dialysis.

**Mohammed Faizan, MD** is a pediatric nephrologist interested in hypertension in children, including the utility of ambulatory blood pressure monitoring in diagnosing and treating hypertension in children. He is also interested in novel treatments for nephrotic syndrome in children.

**Maroun Azar, MD** is interested in the role of palliative care in elderly patients with chronic kidney disease. Another interest is in outcomes in geriatric patients with end stage renal disease. He is also currently involved in a collaborative study on the incidence of acute kidney injury in women with pre-eclampsia in relation to NSAID use.

**Jie Tang, MD, M.Sc, MPH, FANS** is actively conducting epidemiological and prospective trials in kidney stone disease. The projects include studying the effects of dietary factors in various outcomes among prevalent as well as incident kidney stone formers, and the role of vitamin D, fibroblast growth factor 23 and klotho in the pathogenesis of kidney stone disease. Dr. Tang also leads a clinical study examining the cardiovascular biomarkers among CKD patients with obstructive sleep apnea.

**Matthew Lynch, MD's** research interests: treatment and prevention of acute kidney injury. He is currently the site PI on a large, international study examining timing of dialysis initiation in critically ill patients with acute kidney injury and its impact on patient survival and renal recovery.

**Ankur Shah, MD** is interested in peritoneal dialysis, home hemodialysis, and quality improvement. Dr. Shah is currently collaborating with Dr. Hu and together they are participating in a national registry to gather data about complications of peritoneal dialysis catheter placement.

**Basma Merhi, MD**, is a transplant nephrologist who

## Kidney Disease & Hypertension (*cont*)

has led a number of projects arising from the FAVORIT study, the largest clinical trial ever funded by the NIH in renal disease, which was run by our division's faculty. These projects have included calcium and phosphate metabolism in renal transplant recipients, and cardiovascular disease in renal transplant recipients.

**Yingjie Angie Guan, MD, PhD** is interested in understanding of the pathogenic mechanisms of chronic kidney disease—mineral bone disorder as well as renal fibrogenesis and inflammation. The laboratory is currently focused on the role of posttranslational modifications such as protein methylation in the expression of renal proteins related to CKD-MBD regulation.

## Pulmonary, Sleep Disorders & Critical Care

### Overview

We have many ongoing funded research projects in a wide variety of fields both within our own division and through collaboration with other divisions and departments in the Brown research community. Our Brown Respiratory Research Training Program (T32) is a demonstration of our commitment to mentoring young investigators in pulmonary, critical care, and sleep medicine.

### ***Active Areas of Research Include:***

- Sepsis (mechanisms and treatment)
- Knowledge translation
- Acute lung injury
- Pulmonary vascular disease (mechanisms and treatment)
- Pulmonary vascular permeability and endothelial dysfunction
- Extracorporeal life support
- Sleep medicine
- Systemic vascular co-morbidities of COPD
- Tuberculosis/NTM
- End-of-life care in the ICU
- Ethical & practical aspects of rationing medical care
- Health-related quality of life
- Role of Stem Cells, progenitor cells and extracellular vesicles in lung injury repair
- Pulmonary fibrosis and interstitial lung diseases

## Pulmonary, Sleep Disorders & Critical Care (*cont*)

### **The Brown Respiratory Research Training Program (T32 HL134625 01)**

The Brown Respiratory Research Training Program has as its overall objective the training of physicians and scientists to become independent investigators in the pathobiology of respiratory diseases and in the health services, outcomes, and epidemiology of these diseases. The Program aims to bridge gaps between biomedical, behavioral and public health disciplines to advance knowledge regarding how best to reduce disease burden among patients with diseases that affect the respiratory system.

### **Knowledge translation in sepsis**

**Mitchell Levy MD** (Division Chief) is conducting work on performance improvement techniques, and has been working with The Surviving Sepsis Campaign to improve the survival of sepsis. He has conducted several trials, testing the impact of these "sepsis bundles" and a multiple-faceted intervention in facilitating knowledge transfer. In partnership with the Institute for Healthcare Improvement (IHI), two sepsis bundles were developed in 2004, and revised in 2015 and 2018. His work with the New York State Sepsis Initiative was recently published (2017 and 2018) in the New England Journal of Medicine and the American Journal of Respiratory and Critical Care Medicine. He continues to access the 100,000 patients NYS DOH database to work with fellows and other collaborators for further manuscripts.

### **Biobank**

**Mitchell Levy MD and Corey Ventetuolo MD** are amassing a database for all patients admitted to the Medical Intensive Care Unit with sepsis and ARDS. Blood is being collected for Proteomic and Genomic evaluation.

### **Health services ICU research**

**Mitchell Levy MD** is examining large data sets of severely septic patients (Centers for Medicare and Medicaid services) to determine the viability of a disease-specific risk-adjusted mortality model in patients with severe sepsis and septic shock. Using recursive partitioning and regression analysis, statistical correlations with these features are being identified. The aim is to generate a predictive model incorporating these factors to identify mortality risk. These efforts are in collaboration with Stan Lemeshow and Gary Phillips, from Ohio State University School of Biostatistics.

**Nicholas Ward, MD** is currently working two

## Pulmonary, Sleep Disorders & Critical Care (cont)

studies of ICU utilization and practice. The first focuses on informed consent in ICUs and is part of multi-center study looking at this issue based out of Brown, the University of Chicago, and Beth Israel Deaconess Hospital. The second project is a quantitative and qualitative analysis of ICU admissions for non-critically ill patients using a data base created at Rhode Island hospital. This project is being done in conjunction with **Dr. Jason Aliotta**.

**Jason Aliotta, MD** is involved in several quality improvement projects that focus on ICU utilization and physician workflow and staffing at Rhode Island Hospital Medical ICU. In addition, he is the principal investigator in a funded randomized control trial that evaluates the utilization and effectiveness of breath-actuated nebulizers compared with standard nebulizers in patients admitted with acute COPD exacerbations.

### End-of-life care

**Mitchell Levy MD** is continuing his work in end-of-life care. Over the past several years, he has published numerous manuscripts in the field, including one on the visiting hours in the MICU, as well as several opinion pieces, describing the barriers to adequate end-of-life decision-making. Dr. Levy has completed a state-wide initiative on communication bundles in the ICU (with a research fellow as lead author) the results of which have been published in Critical Care Medicine.

### Extracorporeal life support

Rhode Island Hospital is an Extracorporeal Life Support Organization Center of Excellence. **Corey Ventetuolo, MD, MS** is the Medical Director of the Adult Extracorporeal Life Support Program. The research mission of the ECLS service is expanding, with participation in local and international registries and biorepositories, collaboration with the Center for Biomedical Informatics at Brown to apply machine learning algorithms to predict outcomes in extracorporeal life support (Adeel Abbasi, MD/T32 trainee), and work in best practice for anticoagulation monitoring modalities. A recent trial on Extra Corporeal Carbon Dioxide Removal (ECCO<sub>2</sub>R) was begun at Rhode Island Hospital. Drs. Levy and Ventetuolo are co-principal investigators for this study.

### Pulmonary vascular disease

The **Rhode Island Hospital Pulmonary Hypertension Center (RIHPHC)** was established in 1991, and has been under the leadership of **Dr.**

**James Klinger** since 2001 also includes **Drs. Corey Ventetuolo** (Associate Director), **Christopher Mullin, MD, MHS** and **Mary Whittenhall, MSN, APRN, AGACNP** (Center Coordinator). The RIHPHC was the first center in New England to be accredited as a Center of Comprehensive Care by the Pulmonary Hypertension Association. The Center participates in numerous clinical trials of new and approved therapies for the treatment of pulmonary arterial hypertension (PAH) and is currently enrolling patients in several local and national registries and bio-banking studies.

Dr. Klinger's research is concentrated on the natriuretic peptides, nitric oxide and downstream signaling mechanisms that are regulated by cGMP and cGMP-dependent protein kinase. His interest in these pathways is related to their role in modulating pulmonary hypertensive and right ventricular hypertrophic responses, as well as pulmonary endothelial barrier function. Presently, Drs. Klinger and Elizabeth Harrington, PhD are co-PIs on an RO1 that examines the role of natriuretic peptide C in ameliorating acute lung injury. In collaboration with Drs. Peter Quesenberry and Olin Liang (see Stem cell research below), Dr. Klinger also investigates the role of mesenchymal stem cells, endothelial progenitor cells, extracellular vesicles and microRNA in pathogenesis and treatment of pulmonary hypertension.

Dr. Ventetuolo's research includes both clinical and translational studies focused on the genetic and molecular mechanisms of sex hormone signaling and metabolism as a means for understanding sexual dimorphism in PAH and right ventricular function in health and disease. She serves as study co-chair for an NIH-funded clinical trial of anastrozole in PAH and is the Principal Investigator of the EDIPHY Study, the first NIH-funded clinical trial of a naturally occurring hormone, dehydroepiandrosterone, in PAH. Active collaborations include pulmonary artery endothelial cell culture and manipulation with Elizabeth Harrington, PhD and the Center for Stem Cell Biology, and quality of life research with Kate Guthrie, PhD in the Center for Behavioral and Preventative Medicine at Brown.

Dr. Mullin's research is focused on PAH related to systemic sclerosis (SSc) and other forms of connective tissue disease (CTD). He has ongoing clinical research projects examining and predicting outcomes and hospitalizations in SSc-PAH and CTD-PAH. He has interest and expertise in the use of

## Pulmonary, Sleep Disorders & Critical Care (cont)

pulmonary vascular responses to exercise (measurement of cardiopulmonary hemodynamics with exercise during right heart catheterization) to identify early pulmonary vascular disease in SSc and other patient populations at-risk for PAH.

### Venous thromboembolism

Led by **Dr. Christopher Mullin** and in conjunction with interventional radiology, emergency medicine, cardiothoracic surgery and cardiology, the Pulmonary Division has developed and plays an integral role in the **Pulmonary Embolism Response Team (PERT)** that evaluates all cases of pulmonary embolism (PE) admitted to Rhode Island Hospital. Dr. Mullin also oversees a **Post-PE Clinic** as part of the RIHPHC which includes an active population of patients with chronic thromboembolic pulmonary hypertension (CTEPH).

### Interstitial Lung Disease Program

**Barry Shea, MD** – Dr. Shea runs an active research program focused on interstitial lung diseases (ILDs), with an emphasis on idiopathic pulmonary fibrosis (IPF). Specific ongoing projects include: The use of positron emission tomography (PET) with a novel, fibrin-binding probe to assess lung fibrin deposition as a marker of ongoing lung injury and extravascular coagulation in IPF; The use of bronchoscopic optical coherence tomography (OCT) as a tool to noninvasively diagnose IPF and other interstitial lung diseases; Understanding the incidence and clinical features of interstitial lung disease with autoimmune features (IPAF), with a specific focus on ILD that occurs in the context of myositis-specific autoantibodies but without clinical evidence of dermatomyositis or polymyositis; Biobank of plasma, peripheral blood mononuclear cells, DNA and RNA from individuals with ILDs and from healthy controls; Industry-sponsored clinical trials in IPF

### Tuberculosis in Rural Africa

**E. Jane Carter, M.D.**, has a major interest in Tuberculosis- both domestically and internationally. Current projects in this area include (but are not limited to) intensified case finding and pediatric TB in high burden countries (focused in East Africa) as well as improved use of routinely collected TB data to “find the missing cases” by plugging the gaps in the TB care cascade. Although these major projects are centered outside the US, she is presently a mentor on trainee projects locally looking at determinants of TB mortality as well as adoption of IGRA testing for Latent TB infection screening. Related interests include Non-TB mycobacterial topics, pulmonary education in resource poor countries, and medical exchange/global health. Dr.

Carter has headed the Brown Kenya Program medical exchange program for 20 years which also contains a broad scope of research projects and opportunities.

### Vascular Research Laboratory, Providence VA Medical Center

The Vascular Research Laboratory (VRL) is a multidisciplinary group of investigators studying the pulmonary circulation and cardiopulmonary interactions using cells, animal models, clinical studies, and epidemiology studies using database approaches. Faculty include MD's, PhD's, pulmonary/critical care and cardiology specialists. Research is multidisciplinary with a focus on diseases resulting in pulmonary edema, pulmonary hypertension, and cardiac complications of pulmonary hypertension. The VRL faculty cumulatively have over \$2.3 million in direct costs per year of funding to support their research. In addition, the VRL is the site of the Cardio Pulmonary Vascular Biology Center for Biomedical Research Excellence (CPVB COBRE) with has \$1.5 million in direct costs per year. Website: [www.cpvb.org](http://www.cpvb.org)

**Gaurav Choudhary, MD**, is Chief of Staff for Research at the PVAMC. The focus of research in his laboratory is to evaluate the mechanisms underlying exercise intolerance, vascular dysfunction and cardiac dysfunction seen in pulmonary vascular diseases. The laboratory uses a variety of in vitro, ex vivo and in vivo approaches utilizing the preclinical models of pulmonary hypertension and emphysema. His NIH-funded research is focused on mechanisms of right ventricular fibrosis in pulmonary hypertension. He also performs epidemiological (using VA and non-VA data) and clinical studies in area of pulmonary hypertension and right heart function. He is site PI with Jankowich on a VA-funded Merit Review grant to study the effects of tadalafil on pulmonary hypertension associated with COPD, lung vascular remodeling, and RV dysfunction. Dr. Choudhary is funded by an RO1 and collaborates with Drs. Clements, Jankowich, Harrington, Lu, Rounds, and Wu.

**Richard Clements, PhD**, is expert in microvascular injury in diabetes and in mitochondrial function and collaborates with Choudhary.

**Elizabeth Harrington, PhD**, is PI on the Brown Respiratory Research T32 Training Program. Dr. Harrington is PI or co-PI on three training grants that support undergraduate, medical student, and graduate student research. The focus of her re-

search is characterization of intracellular signaling mechanisms regulating endothelial cell functions and/or responses to environmental cues. Current investigations include elucidation of the molecular mechanism by which NRP and Rab GTPases regulate endothelial monolayer permeability and apoptosis and elucidation of signaling pathways which are differentially activated in pulmonary and systemic microvascular endothelial cells in response to oxidative stress.

**Matthew Jankowich, MD**, studies conditions predisposing to pulmonary hypertension and RV failure with a focus on non-PAH PH, and also studies the interactions between systemic vascular disease and pulmonary vascular disease. He has been conducting epidemiologic research with cardiologists Gaurav Choudhary, M.D. and Wen-Chih Wu, M.D. using data from the Jackson Heart Study (JHS), the largest prospective observational study of cardiovascular disease in African-Americans. Brown University is a Vanguard data center for the JHS. Dr. Jankowich is a site investigator for the Tadalafil for Pulmonary Hypertension Associated with Chronic Lung Disease (TADA-PHiLD) multicenter randomized double-blind placebo-controlled clinical trial (co-PI Dr. Sharon Rounds). He is also a site investigator for the OPTIMAL-HF study (PI: Dan Gottlieb, M.D., Boston VAMC), a randomized parallel group study comparing CPAP, oxygen, or optimized medical therapy for patients with sleep apnea and chronic heart failure with a reduced ejection fraction.

**James Klinger, MD** is co-PI with **Elizabeth Harrington** on an RO1 to study the natriuretic peptides in regulation of endothelial permeability. He has active collaborations with Aliotta, Harrington, Lee, Ventetuolo, and Zhou. He is a mentor on the CPVB COBRE.

**Qing Lu, DVM, PhD**, the focus of her research is the molecular mechanism(s) underlying pulmonary endothelial dysfunction and injury. She is elucidating the molecular mechanism(s) by which adenosine and cigarette smoke regulate endothelial monolayer permeability, endothelial cell proliferation, and endothelial cell apoptosis. Dr. Lu has mentored several undergraduate students, several PhD and MD post-doctoral fellows, and is currently mentoring a PhD graduate student. Dr. Lu will co-mentor with Drs. Rounds and/or Harrington in the area of acute lung injury. Dr. Lu is a project PI on the CPVB COBRE. is PI on an NIH-funded RO1 to study mechanisms of cigarette smoke-induced endothelial cell injury. She is also co-Investigator with Dr. Rounds on a VA Merit Review award. Dr. Lu has established collabora-

tions with Drs. Kane, Choudhary, Klinger, Rounds, Harrington, Abid, Lee, and Ayala.

**Sharon Rounds, MD**, is interested in mechanisms of lung vascular injury in conditions causing pulmonary hypertension and acute lung injury. Her work focuses on mechanisms of lung endothelial cell injury. Current work in the laboratory focuses on the effects of cigarette smoke exposure on endothelial monolayer and pulmonary microvascular permeability. Dr. Rounds mentors in the area of endothelial cell injury and dysfunction, pulmonary edema, and pulmonary hypertension. Dr. Rounds is funded by the VA Merit Review to study cigarette smoke effects on lung function and by a second VA Merit Review to study the effects of Tadalafil on pulmonary hypertension associated with COPD. Sharon Rounds is PI of the Pilot Projects Program of the Advance Clinical Translational Research Program. She is PI of the CPVB COBRE, a \$10 million, 5 year grant to develop research on Cardio Pulmonary Vascular Biology. She collaborates with Drs. Choudhary, Harrington, and Lu.

**Wen-Chih (“Hank”) Wu, MD, MPH**, is an Investigator in the Center of Innovation in Long-Term Services and Supports for Vulnerable Veterans (COIN) at the PVAMC. Dr. Wu studies the relationship between anemia, blood transfusion and death in elderly patients undergoing non-cardiac surgery and delivery of care to patients with CHF. In collaboration with Drs. Choudhary and Jankowich, he also studies factors predisposing to pulmonary hypertension and RV failure. He is funded by VA Merit Review grants. He mentors in the areas of epidemiology and outcomes of pulmonary hypertension and CHF.

**Linda Nici MD** (Section Chief) is conducting work on interventions to improve patient-centered outcomes in COPD. Through the Pulmonary Rehabilitation Program as well as the Pulmonary Risk Reduction Initiative, COPD patients at risk for hospital admission or readmission are receiving additional health provider support through education initiatives, promotion of exercise, and identification of risk factors that can be modified to prevent hospitalizations. Studies have included: 1) Rates and predictors of hospital readmission among patients with COPD in the Department of Veterans Affairs using the national VINCI database; 2) The trajectory of physical activity following pulmonary rehabilitation; 3) Physician-led education interventions designed to prevent read-

## Pulmonary, Sleep Disorders & Critical Care (*cont*)

mission after COPD exacerbation. In addition, the VA has a robust lung cancer screening program which includes a patient registry of all positive screens. This has allowed for evaluation of interventions for positive screens as well as survival data for veterans with lung cancer.

**Eric Gartman MD** has research interests in airway disease, diaphragmatic dysfunction and exercise limitation. He is currently the principle investigator for a study evaluating the use of Cardiopulmonary Exercise Testing (CPET) in predicting outcomes after cancer diagnosis and treatment, as well as a collaborator in other clinical research studies using CPET as an outcome measure. He is a site co-investigator in the OPTIMAL-HF study above.

**Lung Cancer Screening Program:** The Providence VAMC implemented a clinical lung cancer screening program using LDCT starting in December 2013. We are currently evaluating the utility of lung cancer screening in the first years of implementation in terms of: rates of nodule detection and workup; prevalence of lung cancer at initial screening; sensitivity and specificity of lung cancer screening at the Providence VAMC; and outcomes of lung cancer diagnosis in the screened population compared to the pre-screening population.

### Sleep Medicine

**Richard P. Millman MD.** The relationship between obstructive sleep apnea and chronic renal disease is being pursued with a large grant to Brown from an anonymous donor. This study is trying to determine the relationship between stage 4 chronic renal disease, sleep disordered breathing, 24-hour blood pressure measurements and markers of potential cardiac disease. This is being done in conjunction with the Division of Renal and Hypertension in the Department of Medicine

**Katherine Sharkey MD, PhD** studies the interplay between mood regulation, circadian rhythms, and sleep. She recently completed a randomized controlled trial testing a chronotherapy intervention for treatment of perinatal depression, and currently is collaborating with colleagues in the School of Public Health on whether maternal sleep patterns influence perinatal weight gain and infant feeding. Her projects examine multiple factors associated with circadian rhythms and mood regulation, including hyperarousal, cognitive processing, hormone levels, biomarkers, and associated infant behaviors. Dr. Sharkey's other scholarly interests include sleep disorders and women's health and advancement and leadership among women in academic medicine.

## Rheumatology

### Ongoing Rheumatology Research Projects

**Joanne Cunha, M.D.** Focuses include quality improvement in identification of crystals in synovial fluid, clinical education regarding methotrexate, and ultrasound evaluation of the nail enthesis as a predictor of PsA.

**Deepan Dalal, M.D.** focuses on health-services and outcomes research. He collaborates with the Center for Gerontology Research and Health Services Policy and Practices division at the Brown School of Public Health, where he currently holds a joint appointment. The research focus is improvement of care of elderly patients suffering with inflammatory arthritis using large administrative database like Medicare and MDS Nursing Home data set. Simultaneously, he is also exploring clinical data from electronic medical records to address important health care outcomes as well as improve quality of care of patient with inflammatory arthritis. He has received funding from the School of Public Health - SURDNA award, Clinical and Transnational Unit at Brown University and Lifespan GME.

**Anthony M. Reginato, M.D. Ph.D.** is focused on areas including systemic sclerosis, rheumatoid arthritis, and Gout. Dr Reginato is also working on research pertaining to MSKUS.

**Stuart Schwartz, M.D.** focuses include reviewing discontinuation rate of allopurinol during hospitalizations.

