Department of Critical Care Medicine

ANNUAL REPORT

FY2017
Table of Contents

Critical Care Medicine General Description .................................................. 3
  Mission Statement ....................................................................................... 4
  Major Academic Achievements ................................................................. 4
  High-Impact Publications ...................................................................... 6
  Summary of Clinical Activities ............................................................... 8
  Summary of Research Activities ............................................................ 9
  Summary of Teaching Activities ............................................................ 13
  Summary of Faculty Data ...................................................................... 16

Clinical Activities .................................................................................. 18
  Adult Critical Care Division ................................................................. 18
  Pediatric Critical Care Division ............................................................ 22

Research Activities .............................................................................. 25
  Research Centers ................................................................................ 27
  Professional Conferences .................................................................. 31
  Training Grants ............................................................................... 33
  Individual Faculty Research Summaries ............................................. 37

Teaching Activities ................................................................................ 84
  Medical Students, Residents, APPs, & Observerships ..................... 84
  Adult Division Fellowship Program .................................................... 86
  Pediatric Division Fellowship Program .............................................. 100

Faculty Data .......................................................................................... 108
  Promotions & New Hires .................................................................. 108

Three-Year Bibliography ...................................................................... 109
  Adult Division .................................................................................. 109
  Pediatric Division ........................................................................... 131
Critical Care Medicine General Description

Introduction

The Department of Critical Care Medicine at the University of Pittsburgh was founded on December 5, 2001, and has remained an independent department for 16 years. Our department holds the distinction of being the first stand-alone department of critical care medicine in the United States. Since 2008 the Department has been led by Dr. Derek Angus, who holds the Mitchell P. Fink Chair of Critical Care Medicine, an endowed chair that was established to honor the founding chairman of the Department. Under Dr. Angus' leadership fiscal year 2016/2017 was a year of dynamic growth and positive change.

The Department contains 84 full-time faculty members within two divisions: Adult and Pediatric. The Department also has 22 secondary faculty members. On average, there have been 10 new faculty members recruited per year to support the Department’s three missions: clinical care, education, and research.

Cutting edge clinical care: The Department provides effective and efficient care to critically ill patients in the UPMC Oakland hospitals, the Veterans Affairs Pittsburgh Medical Center, UPMC Mercy Hospital, Children’s Hospital of Pittsburgh, and the various other facilities where our Hospitalist division provides services. In total, our faculty and fellows provided high quality critical care in 14 ICUs across six hospitals. We also provided an essential safety net to hospitalized patients outside the ICU by leading the hospital-wide rapid response teams. Our faculty lead nationally renowned programs in solid organ transplant, extracorporeal membrane support, and obstetric critical care, helping to position UPMC as a national leader in the care of the critically ill patient. Our faculty also actively contribute to various management committees for the UPMC Health System, ensuring seamless integration between UMPC ICUs and other important service lines.

Interdisciplinary education: We are proudly the oldest and largest critical care medicine training program in the country, emphasizing, from our inception 50 years ago, the necessity to be multidisciplinary and completely integrated into the workflow of acute care medicine. Our graduates leave with a level of expertise and competence based on real-world challenges and close mentorship that allows them to confidently take on leadership roles in critical care medicine around the world. Many of the present and past chairs of academic critical care medicine and anesthesiology departments (in many countries anesthesiology departments traditionally run critical care medicine programs) were or are our graduates. These highly visible and influential critical care medicine leaders amplify the impact our training program has outside our borders. Furthermore, we have two T32 research development training programs: one in pediatrics and the other in adult medicine. No other critical care medicine program can make this claim.

World leading research: Our faculty perform innovative, ground-breaking research in basic, translational, and clinical science, helping to advance the science of critical care medicine and leading to improved patient outcomes worldwide. Our research arm far exceeds national benchmarks, claiming an annual federal funding amount of more than $16 million, supported by multiple investigator-initiated awards. Specifically, we have currently active 25 R01 investigator-initiated awards; three R21 pilot awards; one R34 clinical trial planning grant; one R18 research demonstration and dissemination project; one DP2 NIH Director’s New Innovator Award; five K08, K23, and K24 career development awards; and 11 non-federal awards. This year alone, during a downturn in federal funding, we have received 30 new grants totaling $11.4 million. With this funding, our faculty and trainees combined to publish more than 400 peer-reviewed original research papers over the past 12 months. Furthermore, our faculty are widely sought as speakers at leading symposia and professional conferences. Thirty-six of our faculty members have given 233 major invited lectures at all the major meetings and conferences in the field, as well as many other national and international forums. Finally, our faculty hold eight editorships; eight associate editorships; six section, subject, and series editorships; and 29 memberships on editorial boards on all the major acute care journals, including JAMA, the
Mission Statement

The Mission of the Department of Critical Care Medicine is to provide exemplary care for critically ill patients, conduct cutting edge research related to life-threatening acute medical problems, and to educate tomorrow’s leaders in the field of critical care medicine. We believe that with the strong support of the University, the School of Medicine, and the UPMC Health System, the Department will continue to achieve our mission and contribute to the dramatic growth and prestige of the University.

Major Academic Achievements During the Past Year

Seventeen Faculty Named in Pittsburgh Magazine’s 2016 Best Doctors List
Critical Care Medicine faculty listed among the city’s best doctors by Pittsburgh Magazine include: Ali Al-Khafaji, MD, MPH; Rajesh K. Aneja, MD; Derek C. Angus, MD, MPH; Marie Baldisseri, MD, MPH; Hülya Bayır, MD; Michael J. Bell, MD; Arthur J. Boujoukos, MD; Joseph Carcillo, MD; Robert S. B. Clark, MD; Scott R. Gunn, MD; Melinda Hamilton, MD, MSc; John A. Kellum, MD; Ricardo Muñoz, MD; Holt N. Murray, MD; Richard A. Orr, MD; Penny L. Sappington, MD; and Lori A. Shutter, MD.

Leading National Guidelines on Mechanical Ventilation
Timothy Girard, MD, MSCI, co-chaired the collaborative effort between the American Thoracic Society and the American College of Chest Physicians to develop evidence-based clinical practice guidelines for liberation from mechanical ventilation in critically ill adults. These guidelines were published in the American Journal of Respiratory and Critical Care Medicine, the highest-impact journal in our field.

Faculty Elected to National Organizations
Derek Angus, MD, MPH, was elected to the Association of American Physicians.
Douglas White, MD, MAS, was elected to the American Society of Clinical Investigation.
Sherry Chou, MD, MMSc., and Raghavan Murugan, MD, MS, MRCP were inducted as Fellows of the American College of Critical Care Medicine by the Society of Critical Care Medicine.
Christopher Schott, MD, MS, was awarded Fellowship status in the American College of Emergency Physicians.

Editorial Board Membership
Christopher Seymour, MD, MSc., invited to join the Editorial Board of the journal Critical Care Medicine.

International, National and Local Recognition
Hülya Bayır, MD, received the Europe Clinical Award from the Society for Free Radical Research.
Sherry Chou, MD, MMSc., received the McGill Medical School Global Alumni Young Alumni Award.
John Kellum, MD, received the Carnegie Science Center Life Sciences Award.
Patrick Kochanek, MD, received the Certified Surgical Services Manager Lifetime Achievement Award.

CCM Young Investigator Receives National Awards
Jonathan Elmer, MD, MS, received the 2016 Young Investigator Award from the American Heart Association at the Scientific Sessions of the Resuscitation Science Symposium, and he was recognized for Outstanding Service and Leadership in 2017 by the Center for Organ Recovery and Education.
Industry Advisor
Hernando Gómez, MD was appointed an advisor to Edwards Lifesciences, and artificial heart valves and hemodynamic monitoring company.

Institutional Leadership
Douglas White, MD, MAS, chaired the University of Pittsburgh’s Tenured Faculty Promotions and Appointments committee.

Participation in the Marshall Webster Leadership Program
Brad Butcher, MD, was awarded a certificate for completing the Marshall Webster Physician Leadership Program, a 12-week program, a “Mini-MBA” program in the Katz Executive Education MBA Program.

Front and Center at the 46th Society of Critical Care Medicine Annual Congress
The Society of Critical Care Medicine (SCCM) is the world’s leading critical care-focused professional society. Faculty, fellows, and trainees from the Department of Critical Care Medicine delivered plenary lectures, received awards, acted as moderators, delivered research presentations, and took part in high-level panel discussions during the 46th SCCM Annual Congress in Honolulu, Hawaii from January 21 – 25, 2017. More than 6,000 members of the critical care community attended the Congress.

• Patrick Kochanek, MD, MCCM, received the Society's Lifetime Achievement Award and delivered the plenary session presentation “The Brain and Hypothermia: From Aristotle to Targeted Temperature Management, the Good Stuff Keeps Coming.”
• Michael R. Pinsky received the Star Research Achievement Award, and presented the 25th Asmund S. Laerdal Memorial Lecture “Personalized Precision Resuscitation.” He also presented “Functional Hemodynamic Monitoring,” “Heart-Lung Interactions During Mechanical Ventilation,” and co-presented “Case-Based Demonstrations: Septic Shock,” and was one of five panelists for the Experts Discussion during the Mechanical Ventilation: The Art Shrouded in Physiology session.
• Marie R. Baldisseri received the Safar Global Health Award, co-moderated The Changing Epidemiology of Sepsis Across the Globe: Are We Prepared for the Epidemic? session, and presented “Global Health Initiative and SCCM.”
• Sherry H-Y Chou received the Research Travel Award from the Society’s Neuroscience Section.
• Derek C. Angus presented “How Many Randomized Controlled Trials Do We Need to Create an Evidence-Based Treatment Guideline to Change Practice?” Robert S.B. Clark presented “Endothelial Activation in Brain Injury.”
• Lillian Emlet was one of five critical care educator-physicians leading the Adult Multidisciplinary ICU Simulation Bootcamp.
• Timothy Girard presented “Delirium: Is It the Next Never Event?”
• Hernando Gomez presented “Measures of Tissue Perfusion and Oxygenation” and co-presented “Case-Based Demonstration: Cardiogenic Shock.”
• Ruchira Jha, MD, presented “Infectious Diseases: Meningitis, Encephalitis, and Toxins” and presented “The Role of Corticosteroids in the Management of Meningitis.” She was also one of three expert panelists leading the discussion on Steroids Beyond Sepsis: What Is the Role?
• John Kellum delivered three presentations: “Are Biomarkers Ready for Prime Time?”, “When URine Trouble from Antibiotic Use: Antibiotic Nephrotoxicity” and “Hyperchloremic Metabolic Acidosis: Is It Really Bad for You?”
• Raghavan Murugan moderated the Modern Approach to the Diagnosis and Treatment of Shock and presented “Volumetric Assessment in Shock.”
• Joan Sanchez-de-Toledo presented “Clinical Cases” during the Critical Care Ultrasound Pediatric session.
• Christopher Schott presented “Basic Physics and Knobology” in a session on point-of-care ultrasound.
• Christopher W. Seymour presented “Respiratory Rate Variability to Predict Extubation Readiness.”
Lori A. Shutter co-moderated the What You Need to Know to Manage the Neurologically Critically Ill Patient session and presented “Traumatic Brain Injury and Acute Spinal Cord Injury.”

The 2017 SCCM Gold Snapshot Award went to second-year pediatric fellow, Jessica Wallisch, MD.

Multiple fellows who presented research abstracts, including Catherine Gretchen, MD MS; Jessica Wallisch, MD; Kendra Woods, MD; Alicia Alcamo, MD; Kathryn Kernan, MD; Andrew Prout, MD, Michael Wolf, MD.

Media Mentions
Mainstream news media often cover Departmental research results. That is especially so for the topic of sepsis, which is the research focus of many of our faculty and one of the most highly morbid acute care conditions in the United States. Chris Seymour’s paper, “Time to Treatment and Mortality during Mandated Emergency Care for Sepsis,” published this May in the *New England Journal of Medicine* to coincide with American Thoracic Society’s May 2017 conference in Washington, DC was a leading example. Seymour’s interviews with several reporters, including from *USA Today* and the *Associated Press*, resulted in stories in over 1,000 news outlets with an estimated total audience of more than 32 million. His sepsis research was covered in trade publications (e.g., *Nursing Times*, *Health Medicine Net*, and *Pharmacy Choice*), national outlets (e.g., *Pittsburgh Post-Gazette*, *Washington Post*, *NPR*, *Boston Herald*, *CBS News*, and *Fox News*) and their affiliated local outlets across the nation, as well as in international media (e.g.* China Post*, *Daily Mail UK*, *Shanghai Daily*, *Japan Today* and *Canadian Press*).

Our faculty are also called upon by journalists to provide expert opinion on issues in the news. For example, neurocritical care specialist Lori Shutter was interviewed and quoted by NBC News about the cause of death of Otto Warmbier: “What Killed Otto Warmbier? Maybe an Infection or Blood Clot,” June 20, 2017.

Additional news stories featuring Critical Care Medicine faculty during FY17 include:

- Douglas White was quoted by the *Washington Post*, “An elderly parent may struggle to recover from a stay in the ICU, but you can help,” September 16, 2017; and *California Health Online*, “Key Steps Can Help Patients Recover from a Stay in the ICU,” September 15, 2016.
- 2016 “Condition E” Early Warning System featured in *The Wall Street Journal* article “At the Hospital, Better Responses to those Beeping Alarms” by Laura Landro
- Sachin Yende and Florian Mayr were quoted by eight news outlets about their research into the long-term consequences of sepsis and readmissions. For example, the *Becker’s Infection Control & Clinical Quality* article “Sepsis causes more readmissions than COPD, heart failure, heart attack, and pneumonia,” January 23, 2017
- Derek Angus was quoted by the *Los Angeles Times* for a story on a superbug at an ICU at UC Irvine Medical Center, “UCI doctor's plan to stop superbugs is widely used. At her own hospital, it didn't work,” May 16, 2017

High-Impact Publications

Department of Critical Care Medicine researchers are highly influential in the field of sepsis, as demonstrated by the following three highly-cited pieces in the *New England Journal of Medicine*, the first two of which were published during the American Thoracic Society’s annual conference in Washington, DC.


Departmental investigators also performed a high-impact study published in JAMA demonstrating that readmissions for sepsis are at least as common as other major diseases and therefore worthy of a policy response.

Mayr FB, Talisa VB, Balakumar V, Chang CC, Fine M, Yende S. Proportion and cost of unplanned 30-day readmissions after sepsis compared with other medical conditions. JAMA. 2017 Feb 7;317(5):530-1.

Investigators at the Safar Center for Resuscitation Research continued to push the boundaries of our understanding of traumatic brain injury, pediatric neurological insults, and cardiac arrest in children, as well as chemical pathways leading to cell death. For example, Hülya Bayır, MD, was part of a team of investigators who authored two papers in the January 2017 issue of Nature Chemical Biology on the emerging topic of ferroptosis and its contribution as a previously unrecognized cell death pathway.


Ericka Fink, MD, also published two high-impact papers in the field of pediatric critical care this year. The first is a report on findings of a unique first-point prevalence study in the field of pediatric neurocritical care that described the global multicenter consortium called PANGEA. She was the lead investigator of the study, which generated data from 107 pediatric ICUs from 23 countries. The study was funded by the Laerdal Foundation.


Ericka Fink was also one of the co-investigators on the therapeutic hypothermia trial after in hospital cardiac arrest in children that was published in the New England Journal of Medicine. The study compared the efficacy of therapeutic hypothermia (target temperature, 33.0°C) with that of therapeutic normothermia (target temperature, 36.8°C) in comatose children and adolescents who were resuscitated after in-hospital cardiac arrest.


Junior faculty member and Safar Center investigator Dennis Simon, MD, published a comprehensive and high-impact review on the inflammatory response to the ‘silent epidemic’ of traumatic brain injury (TBI) in the journal Nature.
Reviews in Neurology. That review featured four Safar Center investigators as co-authors, along with other leading authorities on the inflammatory response. They propose a new framework of targeted immunomodulation after TBI for future exploration; it incorporates factors such as the time from injury, mechanism of injury, and secondary insults in considering potential treatment options.


Summary of Clinical Activities

Clinical activities for critical care medicine are separated into the Adult Division and the Pediatric Division.

Adult Division

Under the direction of Arthur J. Boujoukos, MD, Vice Chair for Adult Clinical Affairs and Chief of the Adult CCM Division, this Division’s 54 physicians provide care in 11 specialized ICUs totaling over 185 beds at UPMC Presbyterian, UPMC Montefiore, UPMC Magee-Womens Hospital, UPMC Mercy Hospital, and the Veterans Affairs Pittsburgh Medical Center. Mercy has three ICUs that can care for 53 patients. Holt Murray, MD, oversees the critical care activities at UPMC Mercy ICU. Scott Gunn, MD, is the Oakland Campus ICU Chief and is tasked with managing ICUs in UPMC Presbyterian, UPMC Montefiore and Magee-Women’s Hospital. Under the supervision of Dr. Raghavan Murugan, the highly efficient Rapid Response Team (RRT) provides extended point-of-care consultations and acute medical crisis management on a “24x7” basis. RRT provides expert care to a growing population of complex critically ill patients and also satisfies the administrative and triaging demands of a tertiary hospital that is routinely filled to capacity.

Achievements in FY17

In FY17, the Adult Critical Care Division made several notable achievements in its settings at UPMC Presbyterian, Montefiore, Magee, Mercy, and at the Oakland VA.

- Under the leadership of Derek Angus and Holly Lorenz, the ICU Service Center and the Adult clinical programs were successfully fused to create a lean oversight organization for critical care services across the UPMC health system. The goals of the ICU Serve Center are to reduce unnecessary ICU care; improving the quality of ICU and optimize the distribution of critical care services across the system.
- The development of the UPMC REMAP (Randomized Embedded Multifactorial Adaptive Platform) program enabled UPMC to conduct the next generation of clinical trials by embedding digital knowledge generation and translation into the electronic health record, facilitating the world’s smartest and leanest clinical trials for drug/device development and quality improvement initiatives.
- We also streamlined management of ICUs at partner hospitals in remote areas by providing on-site and telehealth physician intensivist coverage. UPMC Northwest ICU telemedicine support was successfully launched, serving to greatly increase the quality of critical care at this small hospital that would not otherwise have access to trained intensivists.

Pediatric Division

The Pediatric Division of Critical Care Medicine is recognized as one of the leading pediatric ICU services in the world. Under the direction of Robert Clark, MD, Chief of the Pediatric CCM Division, with assistance from Rajesh Aneja, MD, Director of the Pediatric ICU, and Ricardo Muñoz, M.D., Director of the Cardiac ICU, the Division is comprised of 18 faculty members, 2 research scholars, 17 pediatric critical care fellows, and two cardiac critical care fellows. Each year, they provide outstanding care to more than 3,200 critically ill infants and children ranging in age from newborn to young adult. The patient population is divided approximately evenly between medical and surgical subspecialties. Within these major groups, patient distribution reflects the activity of Children’s Hospital as a whole. Services using
the PICU most extensively include General/Trauma Surgery, ENT, Cardiovascular Surgery, Neurosurgery, Transplantation Surgery, and the full spectrum of pediatric medical subspecialties. The Pediatric Neurocritical Care Program reached its 10-year anniversary, having been established in 2007 as one of the first of its kind focused on a multidisciplinary program for neurologically critically ill infants and children.

**Achievements in FY17**

Clinical productivity continues to increase steadily and in keeping with our goal to expand pediatric ICU telemedicine services, we implemented a mixed model of telehealth support from Pittsburgh and on-the-ground staffing at St. Joseph’s Children’s Hospital in Tampa, Florida. This initiative was supported under the newly funded UVA PICU telemedicine service in Charlottesville, Virginia. We rolled out a pilot program for virtual house calls for “urgent care” with support from Verizon. As overall volume continues to rise, sedation and telemedicine services expand, and new NIH grants are implemented, we foresaw the need to recruit additional faculty. Per FY16 goals we recruited clinical assistant professor Yolandee Bell-Cheddar, MD, a pediatric cardiologist.

We also maintain remote pediatric cardiac ICU services in Colombia, and Brazil supported by CICU faculty; and PICU liver transplant telemedicine services in Colombia supported by PICU faculty. The division has also increased its commitment to CHP’s sedation service, in order to provide high level service and minimize practice variability.

**Summary of Research Activities**

The Department of Critical Care Medicine’s research ranges from fundamental cell and molecular biological studies of the basis for organ dysfunction due to inflammation, to translational research linking basic science advances to bedside care, to state-of-the-art clinical epidemiological studies of human critical illness, to population-based health services research. The Department continues to maintain its leadership role in cutting edge research, to be prolific in submitting proposals for funding and, even in these economic times with funding at a premium, to fare well in achieving awards.

Total grant support in FY17 was almost $16 million. Productivity toward achieving greater funding has continued in FY17 with 87 grants submitted (a 14% increase over FY16)) and 30 new grants awarded. Faculty have published more than 200 peer-reviewed manuscripts in the last year, many of which are both highly cited and in high impact journals. Given our track record over the last decade, we anticipate that success will continue in terms of rigorous scientific investigation and resultant contributions to the field of critical care medicine.

**Major awards**

In FY17, major award recipients included:

**Gilles Clermont, MD, MSc.**

“Physiologically Based Optimization of ICU Management”

*Funded by National Science Foundation, Role: Co-PI, beginning 9/1/2016.* This collaborative research project targets the heavy resource burden that ICUs place on a hospital system, carrying operating costs that may at times make up 20 percent of a hospital’s budget. The research team aims to model patient flow through a hospital system by employing methods that are often used in other cases to improve the efficiency of supply chains, flight schedules, or vehicular traffic while at the same time maintaining an optimized level of resource use. The research team will leverage the large repository of EHR data at UPMC, along with transfer request data and actual transfer times, in order to quantify the existing discrepancies between patient need and level of care. This information can then be used to design improved triage policies based on patient state, expected readmission rates, and outcomes.
Timothy Girard, MD, MSCI
“Mitochondrial Determinants of Cognitive Outcomes in ARDS and Sepsis”
Funded by: NIH, NHLBI R01 HL135144-01; Role: PI, beginning July 1, 2016. Mitochondrial dysfunction has been implicated in sepsis-induced lung injury as well as heart, muscle, and kidneys, but the most metabolically vulnerable organ—the brain—remains poorly studied in this context. The goals of this project are to determine whether specific mitochondrial DNA haplogroups and related alterations in mitochondrial oxidative metabolism, systemic oxidant injury, and mitochondrial injury as well as alterations in specific metabolic pathways affected by mitochondrial dysfunction are risk factors for delirium and long-term cognitive impairment due to ARDS and sepsis.

Jeremy Kahn, MD, MS
“Patient Oriented Research and Mentoring in Critical Care Implementation Science”
Funded by: NIH, NHLBI K24 HL133444, Role: PI, beginning 8/1/2016. This mid-career development award provides protected time and resources for Dr. Kahn to mentor the next generation of organizational scientists in critical care. Dr. Kahn is currently the PI of three NIH R01 awards. This award allows him to better leverage those resources to mentor junior faculty and fellows. Supported by this grant, Dr. Kahn is also developing new lines of research related to team science, focusing on how interprofessional care teams collaborate to provide critical care most effectively and efficiently.

Murat Kaynar, MD, MPH
“Aerobic Glycolysis and Long-Term Outcomes from Sepsis”
Funded by: UPP Foundation Grant 2017, Role: PI beginning July 1, 2016 Cost of Surviving Sepsis. This recently-funded project uses a Drosophila model of sepsis to explore inflammation, functional impairment, metabolic derangements, and lifespan in the recovery phase of sepsis. This innovative model replicates what humans experience after they survive an episode of sepsis and septic shock, providing a roadmap for improving long-term outcomes in patients with this deadly disease.

Ivy Lin, MD, PhD
“LRP1, an endocytic vesicle trafficking protein, is associated with congenital heart defects, an unexplored pathway”
Funded by: AHA 17SDG3367098, Role: PI, beginning July 1, 2017 Congenital heart diseases (CHDs) are the most common congenital defect and are the leading causes of neonatal death affecting more than 2 million children and adults in the US. The investigators are using a large-scale forward genetic screen of inbred mice chemically mutagenized with ethyl-nitrosourea to uncover the genetic etiology of CHDs. Specifically, they are testing the hypothesis that abnormal endocardial to mesenchymal transition results in endocardial cushion defects in mice with LRP1 mutations. LRP1 is ubiquitously expressed in all developing organs and is expressed in multiple cell lineages required for cardiac development. To delineate the crucial role of LRP1 in endocardial cushion defects, conditional gene ablation with several tissue-specific LRP1 mutants will be performed to identify the necessity of LRP1 for normal SHF, cardiac neural crest, and endocardial cushion development.

Christopher Seymour, MD, MSc.
Sepsis Endotyping Using Clinical and Biological Data
Funded by NIH/NIGMS (R35GM119519), Role: PI, beginning 8/2/2016. The project leverages our clinical translational laboratory to derive and validate novel sepsis endotypes using bioinformatics methods in electronic health record (EHR) data linked to a biorepository of residual blood. This innovative program of research translates findings from “big data” in the EHR and efficiently enrolled biologic specimens into generalizable bio-types for enrichment strategies in future clinical trials and EHR alerts. The program will be supervised by an external advisory board of experts in endotyping, inflammation, and computational and systems biology, while promoting the independence of my clinical-translational laboratory and mentoring of junior scientists.
Clinical Research, Investigation, and Systems Modeling of Acute Illness (CRISMA) Center

CRISMA is the Department’s clinical, translational, and health services research group that is home to 20 core faculty, seven postdoctoral research fellows, three visiting scholars, 45 staff, seven graduate students, and 10 undergraduate students. CRISMA is organized into five programs representing: Clinical Epidemiology, Ethics and Decision-Making, Health Policy and Management, Systems Medicine, and the Center for Critical Care Nephrology. These programs receive support services through four core teams: Administrative Core, Biostatistics and Data Management Core, Molecular Biology Core, and Long-Term Follow-Up Core. CRISMA faculty currently run 52 NIH grants and 17 grants from other foundational and industry sources, with annual direct costs exceeding $8.7 million.

Notable CRISMA Accomplishments

• CRISMA investigators submitted 53 grant proposals in FY17, totaling $37 million, of which 17 new grants at $8.2 million in total costs were awarded last year. The NIH funded an R21, K08, K24, R35, three R01s, and an R01 supplement, in addition to funding from the NSF (1 award), foundations (2 awards), and industry (6 awards).
• CRISMA researchers launched a major initiative to identify critical illness phenotypes using genomic, metabolic and clinical data. The PROFiling PHEnotypes in Critical Illness (ProPheCI) initiative will integrate principles for “big data” and clinical informatics to create a novel platform for precision medicine studies in the ICU.
• The CRISMA Program on Ethics & Decision making began enrollment in randomized, controlled trial in the UPMC Shadyside ICU entitled, “Developing a Web and Tablet based Tool to Improve Communication and Shared Decision Making between Clinicians and Surrogates in ICUs.” The project will test the use of an electronic patient portal as a strategy to improve family engagement.
• In collaboration with the University of North Carolina at Chapel Hill, enrollment began on the largest prospective cohort study of patients with chronic critical illness. “Prediction of Functional Outcomes from Chronic Critical Illness,” will develop and validate a tool to predict the combined outcome of long-term survival and physical and cognitive function in patients with chronic critical illness.
• The Center for Critical Care Nephrology strengthened collaborations with multiple industry partners, including RenalSense, Astellas Pharma Inc., Astute, and Bioporto Diagnostics, and LaJolla Pharmaceuticals with a goal of developing novel therapeutics to combat acute kidney injury.
• In total CRISMA investigators published of 150 manuscripts, plus an additional eight published online ahead of print that will be published in the next fiscal year. Twelve of those were first-authored abstracts by research fellows, including several in high impact journals.
• The Center for Critical Care Nephrology hosted the 6th Annual AKI Symposium with keynote addresses by University of Alberta's Sean M. Bagshaw, MD, MSc, FRCP, and Charig R. Parikh, MD, PhD, FACP, FASN, Yale University School of Medicine.

The Safar Center for Resuscitation Research

The Safar Center is the Department’s basic, translational, and clinical research group focusing on traumatic brain injury and cardiopulmonary arrest. Safar programs are internationally recognized and are leading their respective fields on a number of facets of both preclinical and clinical investigations. The focus is on bench to bedside investigations related to mechanisms involved in the evolution of secondary brain injury, translational neuroscience in the broadest sense, and the development of novel therapies and interventions that can be implemented from the field through to rehabilitation. Safar investigators lead several additional special programs addressing research training, along with research in both pediatric and adult neurocritical care, and resuscitation in combat casualty care.

Notable Safar Center Accomplishments

• After 38 years in the Hill Building on the main campus of the University of Pittsburgh, the Safar Center moved to 10,000 square feet of custom space on the 6th floor of the Rangos Research Center on the Children’s Hospital of Pittsburgh of UPMC campus.
• Hülya Bayır was awarded the Society for Free Radical Research Europe Clinical Award, for her novel work in the field of oxidative stress, presented by the Society for Free Radical Research-Europe and the Oxygen Club of California at their annual joint meeting in Berlin, Germany.
• In total Safar researchers published 51 peer-reviewed papers.
• Michael Bell, and Co-PI Stephen Wisniewski in the School of Public Health, entered 1,000 infants and children with severe traumatic brain injury at 50 sites nationwide into a large comparative effectiveness study designed to identify the optimal approaches to care for these high-risk patients.
• Safar hosted the 15th Annual Safar Symposium at which the 37th Peter and Eva Safar Annual Lectureship in Medical Sciences and Humanities” was presented by Donna M. Ferriero, MD, MSc, who is the W.H. & Marie Wattis Distinguished Professor and Chair, Department of Pediatrics; Physician-in-Chief, UCSF Benioff Children's Hospital, San Francisco.

Multidisciplinary Acute Care Clinical Research Organization

The Multidisciplinary Acute Care Clinical Research Organization (MACRO) is an internal clinical research organization specializing in 24/7 screening and enrollment for predominantly acute care clinical studies across the UPMC Pittsburgh hospitals, including clinical trials and prospective cohort studies. During the last year MACRO served 29 principal investigators in 10 departments/divisions conducting approximately 40 studies.

Notable MACRO Accomplishments
• MACRO acted Clinical Coordinating Center for five multicenter trials for a new, $90 million, Department of Defense contract to oversee all national trauma research (LITES).
• MACRO continued of Coordinating Center management of four federally-funded, multicenter, randomized trials led by investigators in Surgery, Emergency Medicine, CCM, and Infectious Diseases,
• MACRO expanded its collaboration with Pulmonary/Medicine for a novel enteral dextrose sepsis trial, and continued collaboration with ARDS studies, including the ROSE trial (the first trial of the NHLBI PETAL Network).
• As a strategy to engage young people in clinical research, MARCO employed 45 Pitt undergraduates in their innovative research associate program designed to provide early experiences in the health care field.

T32 Training Grants

The Department provides comprehensive, mentored research training for post-doctoral fellows supported by two NIH National Research Service Awards (T32). In FY17 these programs completed their 19th (adult program, PIs: Drs. Michael Pinsky and Jeremy Kahn) and 15th (pediatric program, PI: Kochanek) years.

CRISMA T32 Training Program
• Funded by the NHLBI, this T32 focuses on the epidemiology and outcomes of critical illness with a particular emphasis on clinical and translational science.
• Four trainees were supported in the entirety of the 2016-2017 academic year.
• The trainees published seven research manuscripts in peer-reviewed academic journals, including Heart Lung, American Journal of Hospice and Palliative Medicine, Journal of Gerontological Nursing, Current Treatment Options in Cardiovascular Medicine, and Critical Care Medicine.
• The trainees garnered several prestigious awards, including a CCM Innovation Grant, a Best Abstract in Clinical Research award at CCM’s Fink Scholar Day, and an American Thoracic Society Abstract Scholarship.
• Recent trainees have obtained highly prestigious academic positions at the University of Pittsburgh and the University of Michigan, among others.

Pediatric T32 Training Program
• Funded by NICHD, this T32 focus on pediatric brain injury and resuscitation. The grant is the longest standing T32 in the field of pediatric critical care medicine.
Three trainees were supported by the Pediatric T32 in the 2016-2017 academic year, and published a number of highly successful manuscripts:

- Christopher Horvat, MD, published a paper in the journal *Pediatric Research*; he will join the Department as an Assistant Professor.
- Diana Pang, MD, presented a paper at the Shock Society meeting was co-authored a report in *Critical Care Medicine*.
- Amery Treble-Barna, PhD, published 10 manuscripts on work prior to joining the T32 program; her research focuses on epigenetic consequences of childhood adversity and its impact on TBI outcomes.
- Jessica Wallisch received a Gold Snapshot Award for her presentation at the 2017 SCCM Congress; she published a manuscript in the journal *Neurocritical Care*.

Summary of Teaching Activities

The Department of Critical Care Medicine provides the highest-quality clinical education to learners at all levels of training, including medical students, residents, advanced practice providers, and post-doctoral fellows. Over 60 faculty contribute to providing core lectures, teaching at the bedside, and coordinating simulation training at the Peter M. Winter Institute for Education Research (WISER).

For medical students, CCM faculty provide instruction in the second-year clinical skills course, the third-year Critical Care component of the adult inpatient medicine clerkship, as well as the fourth-year four-week Critical Care Medicine elective course. The four-week -year elective continues to have one of the highest enrollments amongst senior medical students and is rated as one of the most valuable in their curriculum.

During FY17, 131 UPMC residents rotated through the Oakland-area ICUs. We also accepted visiting fellows and residents from Children’s Hospital of Pittsburgh of UPMC, Harvard Brigham and Women’s Hospital, University of Texas, University of Virginia, UPMC Hamot, and UPMC Horizon to participate in CCM elective rotations. We also have a robust international visiting observership program that attracts medical students, residents, fellows and faculty from institutions across the globes. This year welcomed visitors from Brazil, Colombia and France, who participated in the daily CCM educational program including lectures, workshops, Journal Club sessions, Grand Rounds, and simulation training at WISER as well as the observation visits to UPMC’s Oakland-based ICUs.

Active Fellows

The adult program welcomed 19 new fellows during the 2016–17 academic year across. The six specialty fellowships:

1. Critical Care Medicine - Internal Medicine / Emergency Medicine Fellowship, a two-year program open to trainees from either Internal Medicine (IM) or Emergency Medicine (EM) residencies. There is also a one-year training track for select physicians who have already completed one year of fellowship training in an
associated field. The IM fellowship program had seven IM and three EM second-year fellows and eight IM and two EM first-year fellows.

2. Surgical Critical Care and Acute Care Surgery Fellowships, a one-year program open to trainees who have completed surgical residencies. Four fellows completed the standard one-year surgical critical care fellowship in June 2017 and another four fellows were hired for FY18.

3. Anesthesiology Critical Care Medicine Fellowship, a one-year training program open to trainees who have completed anesthesia residencies. Four fellows completed the anesthesiology critical care fellowship in June 2017, and four more fellows were hired for FY18.

4. Neurocritical Care Fellowship, a one- to two-year program open to trainees from any accredited residency program without prior critical care training (two years) or trainees who have completed traditional critical care or neurosurgery training (one year). One fellow completed the neurocritical care training program in June 2017. In April 2015, the NCC Fellowship received a five-year re-accreditation approval from the United Council for Neurologic Subspecialties (UCNS).

5. Adult Critical Care ECMO Fellowship, a Special Institutional Education Program (SIEP) recognized by UPMC Graduate Medical Education as a component of the MCCTP. The Adult Critical Care ECMO Fellowship accepted its first fellow in 2013 and accepted a second fellow for FY18.

Graduated and Incoming Fellows
Since graduating its first fellows in 1964, the MCCTP at UPMC has trained over 700 critical care physician subspecialists. Twenty fellows graduated in June 2017 and were placed in positions at the following institutions:

- IM/EM Fellowship Program – Department of Critical Care Medicine, UPMC; Halifax Hospital, Daytona; University of Florida, Gainesville; Forrest General Hospital, Hattiesburg, Missouri; St. Vincent Hospital of the Allegheny Health Network, Erie; Advocate Christ Hospital, Chicago; Wellspan York Hospital, York; Drexel University College of Medicine, Philadelphia; Metropolitan Methodist Hospital, San Antonio, Texas; Barnes-Jewish Hospital, St. Louis; Stamford Hospital, Connecticut; and a Remote ICU in Israel.
- Surgical Fellowship Program – Department of Critical Care Medicine, UPMC; UPMC Hamot; and NYU School of Medicine.
- Neurocritical Care Fellowship Program – Stamford Hospital, Connecticut
- Anesthesiology Fellowship Program – St. Luke's Hospital University Health Network, Bethlehem; New York Presbyterian Hospital-Weill Cornell Medical Center; UPMC & Veterans Affairs Pittsburgh Healthcare System; AND University of Virginia, UVA Health System.

Curriculum
The educational curriculum for Adult Division fellows has been developed to ensure they gain the knowledge and skills required to manage all aspects of critically ill patients. To achieve this objective, fellows attend a structured array of lectures, interactive problem-solving workshops, and simulation sessions throughout the year.

Clinical Workshops
Fourteen different workshops cover topics such as routine and difficult airway management, central venous catheterization, chest tube placement, and bedside ultrasound. The “Intensivists as Teachers” workshop teaches fellows the skills to conduct teaching rounds and deliver proper feedback. The three-day “Critical Care Communications” course focuses on end of life discussions with families of patients in the ICU. All of these workshops use interactive learning, human simulation, human or cadaver models, and/or online educational experiences.

Professionalism and Leadership Course
A standard part of our second-year curriculum, and also offered to first-year fellows, is the Professionalism and Leadership course that provides fellows with the administrative, educational and research skills necessary to function as an intensivist, who is able to provide expert critical care services, develop clinical protocols, initiate Quality Improvement programs, coordinate educational activities for the unit, lead multidisciplinary committees and improve overall quality of patient care. The interactive small group sessions include topics from negotiating
contracts and finding the right job to grant writing and review, clinical decision making, the business of healthcare and malpractice legal process.

New Teaching Programs and Courses
Five new training programs were introduced this year: A point of care ultrasound training (training track for a senior fellow seeking to focus on clinical skills and translational research. The Emergency Neurological Life Support (ENLS) training program is open to any trainee or care provider interested in emergency neurological care. We broadened our Fundamental Disaster Management course by offering it to providers outside of the department, including emergency medical services, nurses, APPs and non-CCM physicians. An additional Global Health training track to a facility in Israel, which led to the development of a mass casualty plan for the department of CCM. A fellow-led procedural skills lab for medical students, held in collaboration with the WISER center, and formal bedside “Teaching” rounds.

Quality Measures of Teaching Efforts
In FY17, 469 evaluations were completed by fellows on 49 faculty. The average overall evaluation score was 4.55 on a 5-point scale, with nine faculty received an average overall score of 5.0. In terms of educational outcomes, the Department uses the Society of Critical Care Medicine’s Critical Care Knowledge Assessment Program, which enables program directors to better prepare fellows for subspecialty board examinations. Our fellowship program’s median score for all fellows was above the national median (154.5 vs. 144.0), and all of our specialty-specific mean scores exceeded their national equivalents.

Teaching Honors
• Chris Schott, MD – recipient of the Ake N. Grenvik Critical Care Medicine Faculty of the Year Award.
• Dana Fuhrman, MD – Pediatric Faculty of the Year.
• Alexandra Briggs, MD, first year surgery critical care fellow – Fellow of the Year award from CCM Faculty.
• Danish Malik, MD, first-year Adult IM Fellow – Outstanding Clinical Teaching Award by the 4th year medical students.
• Rajagopala Padmanabhan, MD, and Krystle Shafer, MD – Chief Fellows.
• Danish Malik, MD, and Ruth Musselman, MD – Chief Fellows for 2017-18.

Research
Fellows participated in various research opportunities through FY17, in additional to the research programs that are part of the educational curriculum. We celebrated the 6th Annual Mitchell P. Fink Scholar Day, on May 2, 2017, showcasing the scholarly work of our trainees, including research, educational development, and quality improvement projects.

Pediatric Fellowship Program
The Multidisciplinary Critical Care Training Program offers two tracks for pediatric fellowship training:
• A three-year program in Pediatric Critical Care Medicine, with a complement of 14 fellows,
• A one- to two-year program in Pediatric Cardiac Critical Care, with up to two fellows per year.

Both tracks are based at Children’s Hospital of Pittsburgh of UPMC. In July 2017, PCCM graduates will start faculty positions at Children’s Hospital of Michigan (Detroit), Betty Cameron Women’s and Children’s Hospital (Wilmington, NC), St. Joseph’s Children’s Hospital (Tampa, FL), Johns Hopkins All Children’s Hospital (St. Petersburgh, FL) and Children’s Hospital of Pittsburgh of UPMC. Pediatric fellows participate in multiple educational conferences throughout the year. In addition to the core conferences, we conducted high fidelity simulation sessions for pediatric residents and a Professionalism course in FY17.
Pediatric Critical Care Medicine Training Program

The prestige of our Pediatric Critical Care Medicine (PCCM) fellowship program is reflected in the record number of 109 applications for five openings for FY2017 training positions. The fellowship is one of the most highly-respected programs in the US, has been continuously accredited by the ACGME since 1990, and is one of the five largest of the 66 ACGME-accredited PCCM fellowship training programs. Trainees gain clinical experience in the management of pediatric patients with life-threatening illnesses in a 79-bed complex of intensive care and intermediate care units. The PCCM Training Program currently accepts four to five fellows per year. In the FY2017, we trained 18 clinical fellows (three pediatric cardiac critical care and 15 pediatric critical care) and graduated nine fellows (three pediatric cardiac critical care and six pediatric critical care) in the division in Pediatric Critical Care Medicine.

Presentations and Awards

- Pediatric Neurointensive Care and Resuscitation Research Scholars (5T32HD040686-11): Awarded to 2nd-year fellows Alicia Alcamo, MD, MPH and Michael Wolf, MD.
- Adult T32 (Experimental Therapeutics in Critical Illness, 5T32HL007820-19): Awarded to 2nd-year fellow Andy Prout, MD, MPH.

Honors and Recognition

- Kendra Woods, MD – Chief Fellow 2016–17, and 2017 Fellow of the Year by pediatric residency program.
- Jessica Wallisch, MD – 2017 SCCM Gold Snapshot Award, and 2017 Safar Symposium Best Abstract Award.
- Kate Kernan, MD – 2017 Fink Day Translational Research Award.
- Stefanie Ames, MD – 2017 McGrevin Scholarship.

Pediatric Cardiac Critical Care Training Program

The Pediatric Cardiac Critical Care fellowship program began in 2005. Pediatric Cardiac Critical Care is a complex task that requires expertise in several disciplines including pediatric cardiology, pediatric critical care, and neonatal critical care medicine. A sub specialty of medicine, this highly-selective program accepts a maximum of two fellows per year for one- or two-years of training. Thirteen applicants were invited to interview for one opening in our program.

Summary of Faculty Data

We hired seven new faculty in FY17, including five in the pediatric division, two in the adult division, and one at St. Joseph’s Children’s Hospital (Tampa). Four of these new faculty were already in the UPMC or University of Pittsburgh systems. We also promoted five faculty during FY17: two to professor, one to associate professor, and two received endowed chairs.

Notable New Faculty Recruit

Timothy Girard, MD, MSCI

Dr. Girard was recruited from Vanderbilt University School of Medicine, where he was an Assistant Professor of Medicine in the Division of Allergy, Pulmonary, and Critical Care Medicine and the Center for Health Services Research. He was also a staff physician and investigator in the Geriatric Research, Education and Clinical Center (GRECC) at the Department of Veterans Affairs Medical Center, Tennessee Valley Healthcare System, Nashville, Tennessee. While at Vanderbilt, Girard was an NIH-funded investigator in the ICU Delirium and Cognitive Impairment Study Group. He also chaired one of Vanderbilt’s Institutional Review Board committees, was co-director of Clinical
and Translational Research in the Office of Medical Student Research, served as Director of the Pulmonary Function Test Lab at the VA, and mentored several research trainees. His research interests include geriatric critical care, cognitive impairment after critical illness, delirium in the ICU, and sedation, and liberation from mechanical ventilation in the ICU. He is an international leader in the field of neurocognitive outcomes after critical care, with multiple high-impact publications including a first-authored clinical trial in the Lancet. Dr. Girard was recruited to develop a novel research program on neurocognitive outcomes after critical illness within CRISMA. Funded by an R01 from the NHLBI, he is leading the CRISMA Center’s LEGACI project on recovery and long-term outcomes.
Clinical Activities

Introduction

The Department of Critical Care Medicine’s primary clinical focus is to provide sophisticated, timely, compassionate and expert care to hospitalized and critically ill patients in our medical centers. Critical care medicine is unique in its clinical demands that include geographic ICU coverage and immediate direct patient consults. In FY17, the Critical Care Adult Division continued to fulfill its mission of high quality around the clock patient care in its settings at UPMC Presbyterian, UPMC Montefiore, UPMC Magee, UPMC Mercy, as well as providing care to veterans at the Veterans Affairs Pittsburgh Healthcare System. The Critical Care Pediatric Division accommodates the needs of the critically ill pediatric population at their state-of-the-art Pediatric ICU and Pediatric Cardiac ICU at Children’s Hospital of Pittsburgh of UPMC in Lawrenceville. Additionally, the Pediatric Division has operated a busy tele-ICU program with UPMC/ISMETT’s Transplant Center in Palermo, Italy as well as to subspecialized pediatric cardiac ICUs domestically and internationally.

The pie chart below depicts the distribution of clinical efforts, based on wRVUs, among the various hospitals where our Department physicians provide service. The majority of clinical services are provided at the UPMC Presbyterian and Montefiore Intensive Care Units. Over the course of FY17, the volumes at Children’s Hospital of Pittsburgh accounted for approximately 30% of the Department’s volume. The Department activity and volumes remained relatively flat at Magee for FY17.

Distribution of Clinical Efforts

- Children's CICU 9%
- Children's PICU 21%
- Hamot 1%
- Magee 10%
- Mercy 21%
- Presbyterian/Montefiore 39%

Adult Critical Care Division

The Adult Division continued to fulfill its mission of providing high-quality, around-the-clock care to some of our sickest patients in 11 specialized ICU settings with more than 185 beds at UPMC Presbyterian, Montefiore, Magee-Womens, and Mercy Hospitals, and at the Veterans Affairs Pittsburgh Healthcare System. ICU beds account for approximately 25% of the total beds available at UPMC Presbyterian and UPMC Montefiore. Our clinicians also provide emergent care to all patients in the medical center who experience a cardiac, respiratory or other life-threatening medical emergency through the Department’s Rapid Response Team (RRT).

Quality of patient care is optimized through a multidisciplinary approach, which includes intensivists working with surgical and medical colleagues, advanced practice providers (APPs), critical care fellows, nurses, respiratory and physical therapists, pharmacists, nutrition specialists, and social workers. This team approach, under the direction of the critical care faculty, provides our patients with the highest level of care based on the latest scientific evidence. The Adult Division of CCM supports specialized clinical programs including solid-organ transplantation, cardiac and
non-cardiac thoracic surgery, trauma and acute care surgery, artificial liver perfusion, ventricular assist devices, and neurocritical care. The CCM rounding teams are assigned to specific ICUs and consist of one CCM faculty member, one or more CCM fellows, APPs, medical students, and, in some cases, additional residents from a variety of other departments (surgery, anesthesiology, medicine, orthopedics, or obstetrics).

Achievements in FY17

ICU Service Center
Under the leadership of Derek Angus and Holly Lorenz, the ICU Service Center and the Adult clinical programs were successfully fused according to plan to create an ICU model that enables CCM to optimize acute care across our ICUs. Significant progress was made on all FY17 goals for the ICU Service Center:

- **Goal #1: Reduce Unnecessary ICU Care**
  - Family meeting initiatives: Achieved a 38 percent reduction in opportunity from baseline for discharge from the ICU and were able to boost system-wide compliance;
  - Admission/Discharge Criteria: Developed standardized criteria across the ICU Service Center to optimize resources while improving outcomes. Admission and discharge criteria have been collected per hospital and reviewed. “ Appropriateness” domains have been identified and digital flags are in development;
  - ICU Discharge: Developed a tracking process to identify patients no longer requiring ICU care, and are implementing processes to de-intensify care and staffing. Daily and monthly reports have been generated along with triggers for monitoring the intervention.

- **Goal #2: Improve Quality of ICU Care**
  - Sepsis, Delirium and Mobility QI Projects: For sepsis, use of the Emergency Department and inpatient PowerPlan usage doubled, and the sepsis mortality benchmark was achieved. For delirium, the PowerPlan went live in March, 2017;
  - Organized and supported the >70 ICU QI projects currently logged across the system;
  - ABDCEF Bundle: Developed eRecord strategies to support care of the ICU patient following the ABCDEF Bundle. Implementation of the eRecord build will occur in fall, 2017;
  - Chronic Critical Illness: Developed a proposal for the optimal management of chronically critical ill patients. Preliminary analyses have been conducted and a workgroup is developing a proposal with return on investment for the health system.

- **Goal #3: Examine ICU Distribution Across the System**
  - Reduced total ICU capacity, including planned conversion of four ICUs to step-down care at lower cost in the Oakland, Shadyside and East campuses;
  - Introduced APP-run ICU care models at Presbyterian and Magee. ICU clinical services in Oakland were restructured with increasing reliance on our APP model for patient groups whose care can be more easily protocolized.

- **Goal #4: Build ICU Service Center Structure and Brand**
  - With a strong working structure and broad engagement of stakeholders in place, we developed a system approach to management of the ICU Service Center to derive the highest value for the UPMC Health System. We have built the team and brand through shared governance structures, integrated staffing, cost savings initiatives, and communications.
The Adult Division provides services in the following ICUs:

UPMC Presbyterian and Montefiore Hospitals Campus

**Cardiothoracic/Surgical ICU (CTICU/SICU)**
Dr. Penny Lynn Sappington, Medical Director; Dr. Holt Murray, CTICU Co-Director
Other Team Members: Drs. Arthur Boujoukos and Hernando Gomez; APPs: Jane Guttendorf, Amanda Lombardi, Charmaine Pykosh, Kimberly Anderson, Heather Halle, Mitch Kampmeyer; PharmD: Ryan Rivoscechi

The 28-bed CTICU/SICU delivers care to adult cardiac, heart/lung transplantation, thoracic and vascular patients. These patients have undergone cardiac surgery, thoracic surgery, heart transplants, lung transplants and ventricular assist device placement. This ICU specializes in the support of patients with invasive cardiac monitoring, cardiac support devices and advanced support of ARDS. The CTICU team also provides all day-to-day ECMO support management. Under the leadership of Dr. Sappington, who is Medical Director of the ECMO program, with colleagues in CT Surgery and Perfusion Services, the CTICU team oversees our ECMO Center of Excellence, a recognized Extracorporeal Life Support Organization.

**Transplant Intensive Care Unit (TICU)**
Dr. Ali Al-Khafaji, Medical Director; Dr. David Huang, Associate Medical Director
Team Members: Drs. Derek Angus, Hyung Kim, Matthew Neal, Alan Rosenbloom and David Wallace; CRNPs: Kim Schatz, Lindsey Cornman, Edward Cornman; PharmDs: Catherine Kim and Heather Johnson

The 19-bed TICU provides a multidisciplinary approach to caring for critically ill patients with end-stage liver diseases, fulminant hepatic failure, acute alcoholic hepatitis, gastrointestinal bleeding and other complications related to liver disease. Our multidisciplinary team members provide management for liver, kidney, pancreas, small bowel and multi-visceral transplant patients. In addition, we care for complex head and neck, colorectal, orthopedic spine, surgical oncology and medical patients. Our staff provides Rapid Response for UPMC Montefiore. A variety of sophisticated artificial support devices including the Extracorporeal Liver Assist Device and Plasma Pheresis are used for patient care and are part of clinical trials. The TICU also participates in other clinical trials, including sepsis, acute kidney injury, Ischemic perfusion injury. Finally, the TICU team has been instrumental in conducting several quality improvement projects.

**Neurovascular ICU**
Dr. Lori Shutter, Medical Director; Dr. Marie Baldisseri, Co-Director
Team Members: Drs. Sherry Chou, Ruchi Jha and Brad Molyneaux; APPs: Danielle Bajus, Erika Bassett, Kyra Christensen, Trevor Nissley, Cecelia Ratay and Emma Schaus; PharmD: Joe Durkin

Critical Care Medicine faculty and fellows work collaboratively with faculty in the Departments of Neurosurgery and Neurology in the largest neurocritical care program in Western Pennsylvania. UPMC has been designated as a Comprehensive Stroke Center, and the core of the critical care services is located in this ICU. The CCM physicians in this 20-bed Neurological ICU manage patients with neurovascular diseases including subarachnoid and intracranial hemorrhage, acute ischemic stroke, status epilepticus/seizures, brain tumors, CNS infections, neuromuscular disorders, post-operative neurosurgical care, as well as provide determination and certification of death by neurological criteria. The unit based multidisciplinary QI projects for the last year focused on protocols to assist in the transition to comfort care during a terminal extubation, management of shivering during fever control, and hand-offs between the CCM team and neuro-anesthesia.

**Neurotrauma ICU**
Dr. Lori Shutter, Medical Director; Dr. Joe Darby, Medical Co-Director
Team Members: Drs. Jonathan Elmer, Ruchi Jha and Murat Kaynar; APPs: Emma Schaus, Timothy Rausch

The CCM physicians in this 10-bed ICU provide advanced care for critically ill patients with a neurological injury in conjunction with the Department of Neurosurgery and Division of General and Trauma Surgery. These patients have injuries to the brain or spinal cord secondary to trauma, as well as other traumatic injuries involving the chest,
abdomen, major vessels and long bones. This unique neuro-trauma patient population requires specialized management of hemorrhagic shock, sepsis, renal failure, adrenal suppression, and respiratory failure in order to optimize their potential for neurological recovery.

**Surgical Trauma ICU (ST ICU)**

Dr. Scott Gunn, Medical Director; Dr. Matthew R. Rosengart, Co-Director

Team Members: Drs. Louis Alarcon, Raquel Forsythe, Jason Sperry and Gregory Watson; APPs: Christa Cox and Tina Day

UPMC is a level I Trauma Center, as designated by the American College of Surgeons, and is the busiest trauma center in the state of Pennsylvania. The Surgical Trauma ICU provides state-of-the-art ICU care for 22 critically ill surgical and injured trauma patients. The unit is staffed by a dedicated team of intensivists, who provide and coordinate multidisciplinary, comprehensive critical care including hemodynamic monitoring and support, mechanical ventilation, prevention and management of shock, sepsis and acute respiratory distress syndrome.

**Rapid Response System**

Dr. Raghavan Murugan, Medical Director; Dr. Ali Al-Khafaji, Co-Director

The Rapid Response Team (RRT) is mainly responsible for responding to all Rapid Response System calls at Presbyterian and Montefiore Hospitals, Eye and Ear Institute, WPIC, and all surrounding UPMC buildings on the Presbyterian campus. The Rapid Response Team is led by adult CCM intensivists and first-year ICU fellows, ICU nurses, and respiratory therapists. A dedicated clinical rotation for first-year fellows provides fellows with an opportunity to gain experience in the evaluation, management, and triage of deteriorating patients outside the ICU environment. Each year, there are over 2,000 RRT calls including approximately 150 activations for cardiopulmonary arrest. Various specialized teams such as the difficult airway team, massive transfusion alert team, stroke team, and cardiac catheterization team are also secondarily activated as required.

**Mercy Hospital ICUs**

Dr. Holt Murray, Chief of Services, Critical Care Medicine; Dr. Chenell Donadee, Medical Director, Medical/Neuro ICU; Dr. Brad Butcher, Co-Director, Cardiovascular ICU

Other Team Members: Drs. Firas Abdulmajeed, Marie Baldisseri, Graciela Bauza, Joe Darby, Sean Dechancie, Cameron Dezfulian, Timothy Girard, Hernando Gomez, Gina Howell, Murat Kaynar, Linas Mockus, Dennis Phillips, Alex Preus, Mary Pryzbyz, Christopher Seymour, Matthew Siedsma, John Wallisch; PharmDs: Stephen Ganchuk and Robert Simonelli

Mercy is a full-service referral hospital with five ICUs—Stroke, Neurosurgical, Cardiovascular, Medical-Surgical, and Trauma—that can care for 53 patients. As a level 1 trauma center, UPMC Mercy uniquely provides the region with trauma services for pregnancy. Critical Care is an integral part of the multidisciplinary burn team providing comprehensive adult and pediatric burn services as a busy American Burn Association-verified center. The Adult Division has provided management of UPMC Mercy's ICUs since 2010.

**Magee-Womens Hospital of UPMC**

Dr. Raghavan Murugan, Magee Adult Medical-Surgical ICU Medical Director

Other team members: Drs. Luke Chelluri, Jeremy Kahn and Douglas White; APPs, Heather Becker, Jake Corbin, Robert Bauer, Jennifer Devore

The Magee Adult Medical-Surgical ICU is a 14-bed, state-of-the-art, multidisciplinary unit that admits critically ill patients from Internal Medicine and related sub-specialties such as Obstetrics, Gynecology and Oncology as well as General, Bariatric, Gynecologic/Oncology, Urology, Orthopedic, Breast and ENT surgical services. Critical Care Medicine attendings cover the separate six-bed specialized Obstetric ICU, admitting and managing critically ill obstetric patients with viable pregnancies. The Magee ICU prides itself in providing multidisciplinary patient-centered care aided in large part by the deliberate architectural design of the unit that was inspired by input from former patients, their family members and ICU care providers.
The Magee ICU patient care team manages the hospital Rapid Response System and, by ensuring that critically ill patients receive the right care in the right place and at the right time, plays a critical role in ensuring the Magee-Womens Hospital of UPMC remains a national leader in tertiary women’s health care. As reflected in the unit vision statement, all staff are committed to providing compassionate, patient centered, and evidence-based care driven by a commitment to lifelong learning.

Veterans Affairs Pittsburgh Healthcare System (VAPHS) Intensive Care Units

Drs. Sachin Yende, Vice President of Critical Care Service Line; Deanna Blisard, Director of Surgical Stepdown Unit; Christopher Brackney, Director of Surgical Intensive Care Unit 3A-ICU; Chester Hollinger, Director of Medical/Surgical Intensive Care Unit 3E-ICU

Other Team Members: Drs. Gilles Clermont, Lillian Emlet, John Hotchkiss, Florian Mayr, Jason Moore, Arjun Pennarthur and Christopher Schott

The Adult Division of the CCM department provides coverage of the 9-bed Surgical ICU and the 14-bed Medical/Surgical ICU, both of which provide state-of-the-art care for surgical and medical veterans patients. In 2015 and 2016, VAPHS received 5-star ratings for quality care allowing it to join the ranks of leading VA hospitals across the country. It has performed the highest number of liver and kidney transplants among the VA hospitals in the country in 2015 and 2016. A wide variety of patients receive care in the units including general surgery, cardiothoracic, vascular, neurosurgery, ENT, and transplant services patients. VAPHS serves as a tertiary referral center for the VA system in the tri-state area and serving VA hospitals in Erie, Altoona, Butler and Clarksburg. The Surgical ICU is one of the most sought-out rotations for fourth-year Pitt medical students. VAPHS is also an important site for educational activities for fellows and medical students, including teaching in bedside ultrasound.

Pediatric Critical Care Division – Children’s Hospital of Pittsburgh of UPMC

Children’s Hospital of Pittsburgh of UPMC (CHP) boasts the only multidisciplinary Medical-Surgical and Cardiac Pediatric Intensive Care Units (ICUs) in western Pennsylvania, in addition to the world’s first primary Pediatric Neurocritical Care service established in 2007. Our pediatric critical care complex comprises a 36-bed Pediatric Intensive Care Unit (PICU) and a 12-bed Cardiac Intensive Care Unit (CICU).

The Critical Care Pediatric Division is responsible for staffing, managing, and directing the PICU, CICU, and pediatric Neurocritical Care service. The Pediatric Division receives patients from all of western Pennsylvania, as well as much of West Virginia, Ohio, and Maryland. In addition, it serves as a referral center for patients from distant regions of the United States and many international sites. It is well recognized as one of the leading centers in the world for patient care, education, and research in pediatric critical care. Outcomes for our patients continue to far surpass that predicted by national norms.

Under the direction of Robert S. B. Clark, MD, Chief of the Pediatric CCM Division, 20 faculty members, two NIH T32 research scholars, 14 critical care fellows and two cardiac critical care fellows provide outstanding care each year for over 4,000 critically ill infants and children (ranging in age from newborn to young adulthood). The patient population is divided approximately evenly between medical and surgical subspecialties. Within these major groups, the distribution of patients reflected the activity of Children’s Hospital as a whole.

The 36-bed PICU, under the leadership of Dr. Rajesh Aneja, is a family-centered medical/surgical unit. Our physicians serve as the physicians of record for medical patients while they are in the ICUs and share management responsibilities with all surgical services. Services using the PICU complex included General/Trauma Surgery, ENT, Cardiovascular Surgery, Neurosurgery, Transplantation Surgery, and the full spectrum of pediatric medical subspecialties. PCCM is the primary service for all medical patients, with approximately one-third of the medical patients admitted directly from the emergency department or transport system. The Division achieves the lowest
adjusted mortality and morbidity figures for all Collaborative Pediatric Critical Care Research Network Pediatric ICUs, with network data published in August 2015 showing an impressive standardized morbidity and mortality ~40% lower than predicted in our patients (individual center data unblinded).

The 12-bed CICU, under the leadership of Dr. Ricardo Munoz, is for pediatric patients recovering from cardiac surgery or with a primary cardiac disorder as the indication for intensive care. As the need for cardiac intensive care beds increases, this unit affords physicians and staff the advantage of a space specially designed to care for critically ill heart patients or those recovering from cardiac surgery. Doctors have access to the latest technology, can operate at a moment’s notice, and are able to isolate patients who have recently received heart transplants and are in need of immunosuppressive drugs. The hospital accepts the toughest cases and performs the most demanding surgeries on some of the youngest patients. CHP’s highly trained heart specialists are centered in this one unit where they are able to focus their efforts to meet the unique needs of pediatric heart patients. Clinical efforts within our CICU also include an adult congenital heart disease program. The CICU utilizes six attending physicians to manage patient care, all with dual or additional focused-CICU training. The CICU also provides training to fellows in PCCM, Cardiology and Cardiothoracic Surgery. Fellows from institutions other than CHP rotate through the CICU to gain knowledge and experience from out complex cases.

Children’s Hospital of Pittsburgh boasts the world’s first primary Pediatric Neurocritical Care/Trauma service, established in 2007 by Dr. Michael Bell and now under the direction of Dr. Dennis Simon. The Pediatric Neurocritical Care/Trauma service manages patients with CNS trauma, cerebral hemorrhage, stroke, brain tumors, and complex neurological problems. Evidence-based clinical pathways have been implemented, and a world-renowned clinical research program has been established focusing on children with acute neurological disease.

The PCCM Division provides emergency transport for critically ill children as a major service to Children’s Hospital of Pittsburgh and the region. The CHP transport team transports over 1,500 children per year. The transport team, under the medical direction of the critical care physician, includes a PCCM fellow for those patients judged to be a particularly high risk for complicated illness or death. Research from the Pediatric Division has provided critically important, and perhaps startling, data that pediatric specialty transport teams not only minimize adverse events, but also significantly decrease in-hospital mortality.

The Pediatric Division established and continues to lead the medical emergency response team (Condition “A” and “C”) at CHP, responding to acute changes in patient status, particularly hemodynamic, respiratory, and neurologic. The team consists of a pediatric critical care fellow, an attending physician, ICU nurses, and a respiratory therapist. In 2016, we established and implemented one of the country’s first electronic medical record-triggered early warning alert known as “Condition E” to enhance the traditional human triggered system and provide “continuous electronic surveillance” for our hospitalized children.

The PCCM division also provides coverage and manages the PICU and CICU at St. Joseph’s Children’s Hospital (SJCH) in Tampa, Florida. Six recently hired BC/BE pediatric intensivists stationed in Tampa, along with both on-the-ground and telemedicine support from CHP will provide high-level critical care services at SJCH. In addition to SJCH, the Division also maintains contracted CICU services in Colombia and Brazil supported by CICU faculty; and PICU liver transplant telemedicine services in Colombia and in Charlottesville, Virginia, and soon in Orlando, Florida, supported by PICU faculty.

Finally, the division has launched three new unique services:

**Pediatric Critical Renal Research Team (pCRRT)**
Under the direction of Dr. Dana Fuhrman and Hülya Bayır, the pCRRT provides state-of-the-art renal replacement therapy and support for PICU and CICU patients. Dr. Fuhrman was recruited jointly with the Division of Nephrology, Department of Pediatrics and represents one of the few, if not the only pediatrician who is dual Board certified in critical care medicine and nephrology.
Healthcare Informatics and Clinical Effectiveness (HICE) team
Under the direction of Dr. Christopher Horvat, the HICE team capitalizes on the electronic health record and bioinformatics to improve patient care in real time.

Whole Child Center
Under the direction of Dr. Ericka Fink, the Whole Child Center is driven to provide the best quality of life beyond the child’s ICU stay, encompassing not only optimizing physical outcome, but psychosocial, emotional, and family-based outcomes as well.
Research Activities

Introduction

The Department of Critical Care Medicine continues to maintain its leadership role in cutting edge research, to be prolific in submitting proposals for funding, and, even in these difficult economic times with funding at a premium, to fare extremely well in achieving awards. CCM also continued to build partnerships toward diversifying future funding opportunities. Productivity toward achieving greater funding has continued in FY17 with 87 grants submitted, 30 of which were awarded totaling $11.4 million. Total grant support in FY17 was $15.3 million. Our publications most often stem from grant-funded projects, and CCM primary faculty have authored more than 200 peer-reviewed manuscripts during FY17, many of which are both highly cited and in high impact journals. Given our track record over the last decade, we anticipate the success of the past year will continue in terms of rigorous scientific investigation and resultant contributions to the field of critical care medicine.

Our research enterprise comprises some of the best known and most productive researchers in acute care medicine. CCM faculty continues to provide innovation and leadership across the spectrum of critical care, from basic science to clinical trials and outcomes research. Research activities are grouped into six primary domains: sepsis, resuscitation, computational biology, brain injury, organ dysfunction and support, and health services research. Two large centers form the foundation of the Department’s research endeavors: the Safar Center for Resuscitation Research, and the Clinical Research, Investigation, and Systems Modeling of Acute illness (CRISMA) Center, which are complemented by the four-year-old Center for Critical Care Nephrology (CCCN) as well as several smaller research programs and individual investigators. The Multidisciplinary Acute Care Research Organization (MACRO) performs industry-funded clinical trials and supports many National Institutes of Health trials. The continued growth of our MACRO is driven entirely by clinical investigator demand for clinical trials.

Sepsis and Septic Shock

Beginning with some of the earliest and still most widely quoted epidemiologic research in sepsis, and extending through to new definitions of sepsis released in February 2016, our T32 scientists are pursuing the basic mechanisms and conducting multicenter clinical trials to test new approaches for improving short and long-term outcomes for patients with sepsis. We have investigated the genetic and inflammatory profiles of thousands of patients and are studying different approaches to resuscitation, renal and respiratory support, and novel therapies to modify the immune response using either drugs or devices. We have explored therapeutic approaches in the pre-hospital setting, emergency department, and intensive care unit, to manipulate the immune response. We are also leading efforts to bring sepsis care into the age of personalized medicine, and to bring to bear computational biology along with the “omics package” to our translational research.

Resuscitation Research

An important theme in our multidisciplinary department is resuscitation. Several of our investigators are studying resuscitation in various shock states including sepsis, cardiac arrest, trauma and hemorrhage and organ donation. Furthermore, we have led the field in areas such as functional hemodynamic monitoring, medical emergency teams and even suspended animation. Our funding for this research has come from diverse sourcing including the National Institutes of Health, Health Resources and Services Administration, Defense Advanced Research Projects Agency, Department of Defense, US Army and Navy, American Heart Association, Laerdal Foundation, Robert Wood Johnson Foundation, and numerous industry partners.
Computational Biology, Mechanistic Modeling of Disease and Simulation

Our scientists are applying some of the most advanced techniques in systems modeling to problems in the field of critical care. We are using sophisticated computer simulations to unravel the mysteries of clinical problems from sepsis and hemorrhagic shock to mechanical ventilation and acute lung injury. Furthermore, we have exciting research programs using complexity analysis of patient vital sign monitoring aimed at developing early warning systems to detect clinical deteriorations in hospitalized patients. Finally, we are using our world-class WISER Simulation Center to study how best to train the next generation of intensivists and how to keep the current generation at the top of their game.

Brain Injury

Beginning with the seminal and ground-breaking work of the late Peter Safer, brain injury, both ischemic and traumatic, has been a centerpiece of research within our department. Hypoxic-ischemic encephalopathy remains an incurable disease and our researchers are studying both the causes of neuronal injury and life-saving treatments including gender specific approaches. Similar work is underway in traumatic brain injury and includes investigation into the mechanisms of cellular energy failure and the effect of novel therapies such as adenosine and other neuroprotective agents. Our investigators are leading multi-center pre-clinical studies funded by the US Army to define new therapies for traumatic brain injury and are carrying out the first multi-center comparative effective study in pediatric traumatic brain injury in the world. Finally, we are seeking to discover ways to improve recovery after brain injury and to reduce caregiver burden.

Organ Dysfunction, Support and Recovery

As critical illness and injury results in a diverse spectrum of organ dysfunction, so too are the research interests of our faculty similarly diversified. We have active research programs in brain, lung, heart, kidney, liver and gastrointestinal dysfunction and injury consequent to critical illness. Moreover, several of our investigators study the interplay between organ systems in health and disease such as heart-lung and kidney-lung interaction. Since critical care is supportive care, we have some of the world’s leading experts on the use of respiratory, cardiovascular and renal support. We are even studying emotional support in the wake of critical illness. Using applied physiology principles developed over the last 20 years by thought leaders from our department, we have spearheaded an international movement to approach assessment and management of acute cardiovascular insufficiency and acute renal injury. These applications have resulted in several published multi-center clinical trials and one US Air Force-funded air evacuation clinical trial. Finally, we are breaking new ground by looking past the acute care episode and studying how patient recover from critical illness. Recovery from acute illness is largely uncharted territory but critically important for patient long-term well-being. Whether recovering from neurological, respiratory or renal injury or from immune suppression in sepsis, survival is strongly associated with the extent of recovery.

Health Services Research, Health Policy, eResearch and Medical Ethics

Our researchers are leading the field in the study of health care delivery, health policy and decision making in acute illness both in adults and children. We are studying novel approaches to organize, manage and finance the care of acute illness in the United States and abroad using both traditional epidemiological methods and novel methods from sociology, behavioral economics, and the decision sciences. Funded by numerous federal and industry sources, we are leaders in the field of comparative effectiveness research in acute illness, using randomized clinical trials, observational studies using electronic medical record data and large administrative datasets to examine strategies to reduce mortality, lower costs and improve the patient and family experience in the ICU. We are leading the drive for state-wide sepsis regulations and to determine their effects on sepsis quality and costs. We are also doing innovative work in the area of quality improvement and patient safety, partnering with health care providers to measure and improve their performance using emerging methods including advanced analytics and “big data.” As part of this line of research, the Department runs the University’s Health Services Research Data Center (HSRDC)
that enables secure, high-throughput HIPAA-compliant computing for health services research projects making use of large public health datasets. Currently the HSRDC serves over 36 projects that represent over $52 million in federal and non-federal funding.

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**Research Centers in the Department of Critical Care Medicine**

**Clinical Research, Investigation, and Systems Modeling of Acute Illness Center**

The Clinical Research, Investigation and Systems Modeling of Acute Illness (CRISMA) Center is a clinical, translational, and health services research group conducting cutting-edge research into the optimal care of the critically ill. CRISMA was founded in 2001 concurrent with the founding of the Department.

The Center’s research is performed by world-class teams organized into five programs of research:

- Clinical Epidemiology
- Ethics and Decision-Making
- Health Policy and Management
- Systems Medicine
- The Center for Critical Care Nephrology

These programs receive support services through four core teams: Administration, Biostatistics and Data Management, Molecular Biology, and Long-Term Follow-Up.

The CRISMA Center continues to grow with research talent doubling over the last four years. At the end of FY17, CRISMA was home to 20 core faculty, seven postdoctoral research fellows, three visiting scholars, 45 staff, seven graduate students, and 10 undergraduate students collaborating across all programs and cores. During the past year, CRISMA researchers have upheld the tradition of leading critical care research advances, as well as garnering national attention and special recognition for their contributions to science.

**New Research Initiatives**

CRISMA launched two key research initiatives in FY17: Profiling Phenotypes in Critical Illness (ProPheCI) and Long-Term Evaluation of Goals After Critical Illness (LEGACI). Prior to these initiatives, researchers across the CRISMA Center were conducting numerous disparate efforts in these subject areas. Over the past year, we have improved research coordination and data analytic support to foster collaboration and potential gains, as well as future grant support, under these initiatives.

Through the ProPheCI Initiative, spearheaded by Christopher Seymour, CRISMA has successfully created the infrastructure for building and maintaining large datasets comprising EHR data (including GENEVA and HiDENiC). Not only investigators from CCM but also from across the schools of health sciences are collaborating with us to request data from these datasets for multiple novel QI and research projects.

Funded in late FY17, the team working with Douglas White (NIH/NIA R21) began recruitment at the Shadyside MICU for an innovative randomized, controlled trial, “Developing a Web and Tablet based Tool to Improve Communication and Shared Decision Making between Clinicians and Surrogates in ICUs.” The project is designed to determine the efficacy of a web-, tablet-, and mobile phone-enabled tool to enhance communication and shared decision making between clinicians and surrogates of incapacitated, critically ill patients.

**Research Funding Summary**

Investigators across CRISMA submitted 53 proposals in FY17, totaling $37 million, of which 17 new grants at $8.2 million in total costs were awarded last year. The NIH funded an R21, K08, K24, R35, three R01s, and an R01 supplement, in addition to funding from the NSF (1), foundations (2), and industry (6) to conduct research in basic
science, translational, clinical, and health services research, further demonstrating the breadth of research activities conducted by our multidisciplinary CRISMA investigators. These newly-funded CRISMA research projects include:

- Gilles Clermont, NSF, “Collaborative Research: Physiologically Based Optimization of ICU Management.”
- Tim Girard, NIH/NHLBI, R01,” Mitochondrial Determinants of Cognitive Outcomes in ARDA and Sepsis.”
- Jeremy Kahn, NIH/NHLBI, K24, “Patient Oriented Research and Mentoring in Critical Care Implementation Science.”
- Murat Kaynar, UPP Foundation, “Aerobic Glycolysis and Long-Term Outcomes from Sepsis.”

**Intramural and Extramural Collaborations**

By its very nature the CRISMA Center was designed to foster collaboration. Researchers cooperate extensively across program lines within CRISMA, intramurally at Pitt, and also with external constituents, including other research institutions and industry partners. In addition to ongoing collaborations, FY17 saw CRISMA PIs tapped for their expertise on new collaborations with other institutions including Jeremy Kahn and Douglas White (NIH/NINR R01) “Prediction of Functional Outcomes from Chronic Critical Illness,” a prospective cohort study designed to develop and validate a tool to predict the combined outcome of long-term survival and physical and cognitive function in patients with chronic critical illness. It is led by UNC at Chapel Hill.

While the Center for Critical Care Nephrology continues to foster the majority of research collaborations with industry partners. This year, John Kellum’s collaborations with RenalSense, Astellas Pharma Inc., Astute, and Bioporte Diagnostics, and Ragi Murugan’s collaboration with LaJolla Pharmaceuticals garnered new research funding for CCM.

**Publications and Productivity**

During the past year CRISMA Center researchers have upheld the tradition of leading critical care research advances, as well as garnering national attention and special recognition for their contributions to science. In the 2015-2017 three-year reporting period, CRISMA researchers have had 402 publications. Significant research accomplishments in FY17 included the publication of 150 manuscripts, plus an additional eight published online ahead of print that will be published in the next fiscal year. CRISMA investigators published in leading journals, including *New England Journal of Medicine* (4), *JAMA* (9), *Critical Care Medicine* (18), *CHEST* (6), *Intensive Care Medicine* (7), and *Critical Care* (6). Center investigators are not just publishing in high-impact journals, but their research is being recognized as influential. CRISMA research continues to influence health policy, practice guidelines and regulatory mandates about Sepsis care, as demonstrated by the following three highly-cited pieces in the New England Journal of Medicine:


The CRISMA Center has built an international reputation for providing robust training opportunities to critical care providers who want to develop a career in academic research. During FY17, the CRISMA Research Fellowship hosted a total of seven postdoctoral fellows working under the mentorship of CRISMA investigators, including four trainees sponsored on the T32 “Experimental Therapeutics and Critical Illness” which is now entering its 20th year.
The success of this interdisciplinary program is evidenced by the scholarly productivity of our research fellows, who this year first-authored 12 refereed articles and published abstracts, including several in high impact journals.

Being highly multidisciplinary in nature, CRISMA faculty actively contribute to the development of trainees hosted in another academic departments and institutions. In FY18, this included mentoring research fellows from the Department of Medicine’s Pulmonary Division, Pitt’s Health Policy Institute, and UPMC Hospice and Palliative Medicine.

The Safar Center for Resuscitation Research

The Safar Center was founded by the late Dr. Peter Safar in 1979, initially as the International Resuscitation Research Center. Our mission is to identify and promote ever-improving methods of preventing premature death and reducing associated disability from trauma and cardiac arrest in people with “hearts and brains too good to die.” Our programs in traumatic brain injury (TBI) and cardiopulmonary arrest (CA) are internationally recognized and are leading their respective fields on a number of facets of both preclinical and clinical investigations. We focus in these two areas on bench to bedside investigations related to mechanisms involved in the evolution of secondary brain injury, translational neuroscience in the broadest sense, and the development of novel therapies and interventions that can be implemented from the field through to rehabilitation. We feature several additional special programs addressing research training, along with research in both pediatric and adult neurocritical care, and resuscitation in combat casualty care.

FY17 was a special year for the Safar Center. In January of 2017, after being located in the Hill Building on the main campus of the University of Pittsburgh for 38 years, we moved our Center to impressive, newly renovated laboratory space on the 6th floor of the Rangos Research Center on the Children’s Hospital of Pittsburgh of UPMC campus. The new Safar Center includes ~10,000 square feet of custom space that features a large, multi-station pre-clinical surgical and ICU suite, a state-of-the-art behavioral outcome assessment facility, a unique blast-injury facility, along with conventional wet lab and office space. We are grateful to Children's Hospital of Pittsburgh of UPMC for welcoming us and supporting the renovation of this space, and to the Senior Vice Chancellor and Dean, and to the Departments of Critical Care Medicine, Neurosurgery, Physical Medicine & Rehabilitation, and Pediatrics for additional support. We are optimistic that this will lead to both continued productivity and successes, along with the development of many new collaborations with investigators in Children's Hospital.

There were many notable accomplishments by trainees and faculty in the Center and some of the highlights within our TBI, cardiac arrest, and other programs are discussed below.

On June 21, 2017, Hülya Bayır was awarded the Society for Free Radical Research Europe Clinical Award, for her novel work in the field of oxidative stress, presented by the Society for Free Radical Research-Europe and the Oxygen Club of California at their annual joint meeting in Berlin, Germany. Patrick Kochanek received the Lifetime Achievement Award for meritorious contributions to the field of critical care medicine, at the 46th Congress of the Society of Critical Care Medicine, on January 21, 2017 in Honolulu, Hawaii.

Among the 51 peer-reviewed papers published by Safar Center investigators this academic year, several high impact papers published by four associate directors were particularly noteworthy. Dr. Rachel Berger published an important multi-center study showing efficacy of the use of a serum biomarker panel to aid in identifying infants who are otherwise missed victims of abusive head trauma. That report represented the culmination of work supported by the NICHD and was published in JAMA Pediatrics. Hülya Bayır was part of a team of investigators who authored two papers in the January 2017 issue of Nature Chemical Biology on the emerging topic of ferroptosis and its contribution as a previously unrecognized cell death pathway. Ericka Fink, also published two high impact papers in the field of pediatric critical care this year including a report in Pediatric Critical Care Medicine on findings from the first point prevalence study in the field of pediatric neurocritical care. Her report described a global multicenter consortium called PANGEA. Dr. Fink was the lead investigator of that study, which generated data from 107 pediatric ICUs from 23 countries. She was also one of the co-investigators on the therapeutic hypothermia trial after
in hospital cardiac arrest in children that was published in the *New England Journal of Medicine*. Finally, junior faculty member and Safar Center investigator Dennis Simon published a comprehensive and high impact review on the inflammatory response to TBI in the journal *Nature Reviews in Neurology*. That review featured four Safar Center investigators as co-authors, along with other leading authorities on the inflammatory response.

We were also excited by the fact that Safar Center Associate Director Michael Bell, completed entry into the important ADAPT (Approaches and Decisions in Acute Pediatric TBI) trial. ADAPT, represents the first comparative effectiveness trial in the history of pediatric TBI. Dr. Bell and Co-PI Stephen Wisniewski in the School of Public Health entered 1000 infants and children with severe TBI at 50 sites into this landmark study. We look forward to seeing the findings as outcome data emerge. We are also pleased to report that Dr. Bell recently accepted the position of Director of CCM at Children’s National Medical Center in Washington, DC. We wish him the best of luck in this new endeavor and look forward to continuing to collaborate with him in pediatric TBI and neurocritical care.

As this annual report is going to press, we are pleased to report that Safar Center Associate Director Anthony Kline, Professor in the Department of Physical Medicine and Rehabilitation (PM&R), is currently president of the National Neurotrauma Society (NNTS). Remarkably, at the July meeting of the NNTS, Safar Center Associate Director Amy Wagner, also from the Department of PM&R, is now president-elect of the NNTS to follow Dr. Klein. It is unprecedented that back-to-back presidents of this prestigious society hail from the same Department and Center. This reflects the key role that University of Pittsburgh PM&R investigators at the Safar Center have had in shaping the TBI field.

This was also a good year for the acquisition of new grants by Safar Center investigators. Five new national grants for Safar Center investigators in the departments of CCM are particularly noteworthy for the FY17 academic year.

- Corina Bondi received an R21 award from NINDS for work titled “Multimodal assessment of behavioral flexibility after frontal brain trauma.”
- Corina Bondi also received an R03 award form NINDS for work titled “Sustained attention and executive function after brain trauma.”
- Travis Jackson received an R21 award from NINDS for work titled “FGF21 activates RBM3” and is a novel drug to revolutionize temperature management.
- Ruchira Jha, a young investigator in the Division of Neurocritical care, received a K23 award from NINDS titled “Translational assessment of sulfonylurea receptor-1 as a biomarker and therapeutic target for cerebral edema in TBI.”
- Anthony Kline received an R21 award from NINDS for work titled “Effects of chronic adolescent stress on cognitive and emotional behavior after adult TBI.”

The growth of funding support by our investigators over the past 22 years has been remarkable and is a testament to the hard work, dedication, and expertise of our faculty and trainees. The sources of grant support are broad and include the NIH, the Department of Defense, the Department of Veteran’s Affairs, the National Institute on Disability and Rehabilitation Research in the Department of Education, the Patient-Centered Outcomes Research Institute, the American Heart Association, the Ann Thompson Fund, among others. We continue to receive generous support from the Laerdal Foundation, which has been a supporter of our Center since its inception. We are grateful to all of the funding agencies for support, including the Grenvik Endowment. We would also like to extend our thanks to all the individuals who have donated to the Safar Legacy Fund.

Safar Center investigators were highly productive in FY17 publishing 51 peer-reviewed manuscripts, and seven editorials. A trainee was the first author on 28 of these publications. Our faculty are also authors and/or editors of many of the leading textbooks in the fields of acute brain injury, critical care, resuscitation, and rehabilitation. A brief summary of the TBI and cardiac arrest programs in our Center are described below.
**Traumatic Brain Injury**

The Safar Center is one of the leading centers in the world for the investigation of TBI. Research in TBI includes (1) both pre-clinical and clinical investigations addressing both mechanism and novel therapy development, (2) studies addressing questions across the continuum of care from the field through to rehabilitation, (3) investigations in both pediatric and adult arenas, and (4) also research germane to TBI resuscitation in combat casualty care. Although our work is predominantly focused on severe TBI, several projects addressing the emerging topic of mild TBI are also ongoing, given its world-wide importance.

**Cardiopulmonary Arrest**

The Safar Center is also a leading center in the world for the investigation of cardiac arrest, particularly in three areas of research: (1) pre-clinical modeling of cardiac arrest in pediatric and adult models (both asphyxia and ventricular fibrillation)—models highly relevant to the clinical condition, (2) pre-clinical investigation of ultra-advanced resuscitation strategies such as emergency preservation and the use of extracorporeal resuscitation in rat models, and (3) clinical studies of cardiac arrest in infants, children, and adults with a focus on investigation of hypothermia, biomarkers of brain injury—both serum and imaging, and novel therapy development.

**Multidisciplinary Acute Care Clinical Research Organization**

Directed by David Huang, MD, MPH, the Multidisciplinary Acute Care Clinical Research Organization (MACRO) is an internal clinical research organization that is driven entirely by clinical investigator demand for clinical trials. MACRO specializes in 24/7 screening and enrollment for predominantly acute care clinical studies, and has a consistently high enrollment of study participants, who are drawn from five local UPMC hospitals: Presbyterian, Montefiore, Mercy, Shadyside, and Magee. MACRO served 29 principal investigators in 10 departments/divisions conducting approximately 40 studies in FY17. Affiliated with the Clinical and Translational Science Institute and administratively housed within CCM, MACRO is an independent University of Pittsburgh cost center with a $1.74M annual budget. MACRO runs a Pitt undergraduate Research Associate Internship, and provides pro bono consultation for universities seeking to emulate our model (e.g. University of Michigan, University of Pennsylvania). Our future plans include continuous quality improvement to maximize enrollment and minimize costs, and continued organic client-demand driven expansion, including increased overall project management/coordinating center responsibility. Over the last 12 months, major accomplishments include:

- Serving as Clinical Coordinating Center for five multicenter trials for a new, $90 million, Department of Defense contract to oversee all national trauma research (LITES);
- Continuation of Coordinating Center management of four federally-funded, multicenter, randomized trials led by investigators in Surgery, Emergency Medicine, CCM, and Infectious Diseases;
- Expanded collaboration with Pulmonary/Medicine for a novel enteral dextrose sepsis trial, and continued collaboration with ARDS studies, including the ROSE trial (the first trial of the NHLBI PETAL Network); and
- Nurturing our new, highly cost-effective Research Specialists (“mid-levels” between a Coordinator and a Research Associate), including hiring of our first external Research Specialists.

**Professional Conferences on Issues in Critical Care Medicine**

In line with our mission of education, training and scientific advancement, each year the Department of Critical Care Medicine coordinates and hosts three professional conferences that feature national and international academic leaders as the keynote speakers. A key element of each conference is the opportunity for our junior faculty and fellows to gain experience presenting their research. These conferences are supported through funding from the National Institutes of Health, US Army, and Laerdal Foundation as well as and a number of industry and private sponsors. All conferences offer Continuing Medical Education credit.
**Fifteenth Annual Safar Symposium**

May 22-23, 2017  
Patrick Kochanek, MD, Program Director

The Safar Center for Resuscitation Research and the Peter M. Winter Institute for Simulation, Education and Research (WISER) jointly presented the 15th Annual Safar Symposium. To celebrate the Safar Center’s relocation from Oakland to Lawrenceville, the Symposium was held, for the first time, at the Rangos Center at Children’s Hospital of Pittsburgh of UPMC. The Symposium began with six talks focused on the theme of “Pediatric Neuroanesthesia, Neurocritical Care, Resuscitation and Rehabilitation: All Roads Lead to the CNS.” The 37th Peter and Eva Safar Annual Lectureship in Medical Sciences and Humanities” was presented by Donna M. Ferriero, MD, MSc, who is the W.H. & Marie Wattis Distinguished Professor and Chair, Department of Pediatrics; Physician-in-Chief, UCSF Benioff Children’s Hospital, San Francisco. Her lecture was titled “The Vulnerable Newborn Brain: Lesson from Neuroimaging.” Day 1 concluded with the Multi-Departmental Trainees’ Research Day, while day two featured five talks on the theme of “Improving Pediatric Patient Safety Through Simulation.”

**Fifth Annual Mitchell P. Fink Critical Care Scholar Day**

May 2, 2107  
Jeremy Kahn, MD, MS, Program Director

Fink Scholar Day is a celebration of the legacy of Mitchel P. Fink, the founding Chair of the Department of Critical Care Medicine who excelled as a teacher, clinician and scientist. In keeping with his vision for critical care medicine as a multidisciplinary field, Fink Scholar Day showcases the work of our junior faculty and fellows around the themes of Clinical Research, Health Services Research, Quality Improvement & Education, and Translational Science. Plenary speaker was Marc Moss, MD, the Roger S. Mitchell Professor of Medicine, Vice Chair for Clinical Research, Department of Medicine, Division of Pulmonary Sciences & Critical Care the University of Colorado, whose topic was “Burnout Syndrome in Critical Care Healthcare Professionals.” This year we had a record 36 abstract presentations in addition four oral presentations.
Sixth Annual AKI Symposium

October 13, 2016
John A. Kellum, MD
Now firmly established as an annual forum for cross-campus dialogue on acute kidney injury, the 2016 AKI Symposium drew more than 80 physicians, faculty, and researchers. Two guest lecturers were book-ended by nine University of Pittsburgh researchers and abstract presentations by post docs, residents, and fellows. The University of Alberta's Sean M. Bagshaw, MD, MSc, FRCP, spoke about “Strategies for Starting Renal Replacement Therapy in AKI,” and Charig R. Parikh, MD, PhD, FACP, FASN, Yale University School of Medicine spoke about “Three Lessons from the Long Term Follow-up of TRIBE-AKI Cohorts.” Dr. Bagshaw is Associate Professor, Critical Care Medicine, Faculty of Medicine and Dentistry, and School of Public Health, University of Alberta, and Canada Research Chair in Critical Care Nephrology. Dr. Parikh is Professor of Medicine and the Director of the Program of Applied Translational Research in the Department of Medicine at the Yale University School of Medicine, and Professor in the Clinical Epidemiology Research Center at the VA Connecticut Health Care System. The AKI Symposium was co-hosted by CCM’s John Kellum, MD with colleagues Thomas Kleyman, MD, Pittsburgh Center for Kidney Research - O’Brien Center; Fadi Lakkis, MD, Thomas E. Starzl Transplantation Institute; and Carlton Bates, MD, Children’s Hospital of Pittsburgh-Pediatric Nephrology Division.

Training Grants

Experimental Therapeutics In Critical Illness (5T32HL007820-19)

Directors: Michael Pinsky, MD CM, Dr hc, FCCP, MCCM, & Jeremy Kahn, MD, MS
The major goal of this program, which is entering its 21st year, is to train post-doctoral fellows for a period of two to three years in basic, clinical and translational research in the science of cardiopulmonary organ dysfunction and critical illness. Our program’s research focus is in three interrelated domains: (1) immunobiology and the cellular basis for organ injury; (2) organ systems modeling; and (3) clinical and health services research. These research areas intersect with the extramural research grants of our training faculty and reflect the essential translational basis of critical care medicine, which requires an integration of cell and molecular biology, organ system interaction, and novel therapies that impact patient-centered and socially relevant outcomes.

Scholars receive a high-quality, mentored critical care research experience in an inter-professional training environment. The program consists of four interrelated pillars: intensive mentoring, experiential research, didactic education, and participation in a community of learners.

- **Intensive mentoring:** Fellows meet weekly with their primary mentors, who are experts in the field and are expected to maintain active extramurally-funded research programs. Fellows meet quarterly with their trainer group (which includes primary mentor, any secondary mentors, and the program directors) to review recent accomplishments and set future milestones, ensuring effective career development.

- **Experiential research:** Fellow research projects are rooted in the scientific method, providing direct experience in how to design, execute, analyze and interpret experiments in order to answer specific questions related to real-world problems of critically ill patients. We emphasize cross-cutting “big science”
drawing off novel scientific disciplines including proteomics and metabolomics, information science, sociology and behavioral economics.

- **Didactic education:** Fellows typically enroll in formal coursework in the University of Pittsburgh Institute for Clinical Research Education, the University’s home for clinical and translational research training for clinician scientists. Coursework is selected by the fellow and their mentor to complement mentoring and research activities. In most cases fellows obtain an advanced degree (i.e. Master’s of Science) in their chosen discipline.

- **Participation in a community of learners:** We encourage and enable interaction among fellows and with program faculty by providing a shared research office in which fellows have a private desk and computer. Fellows present regularly at formal and informal departmental research conferences, enabling them to not only receive feedback on their work but also to learn how to provide constructive feedback to others.

Implementation of training objectives.

During FY17, we trained four post-doctoral fellows in critical care research:

**Matthew Siedsma, MD**  
Principal Trainer: Jeremy M. Kahn, MD, MSc; Appointment: 7/01/2015 – 6/30/2016; 2nd year appointment  
Dr. Siedsma completed a residency in internal medicine and emergency medicine at the University of Illinois, where he also served as chief resident. He joined the program from the Department of Critical Care Medicine’s clinical fellowship and is now in the second year of his research fellowship. His focus is on the intersection between critical care education and patient outcomes. Specifically, he is drawing on the fields of clinical epidemiology, implementation science, and behavioral economics to develop and test novel strategies for continuing medical education that optimize health care delivery and outcomes for patients with critical illness.

*Research projects:* “Adoption of neuromuscular blockade for treatment of the acute respiratory distress syndrome” is evaluating temporal trends in the adoption of neuromuscular blockade as a treatment for ARDS using clinical data from the UPMC health system, specifically examining the impact of publication of clinical trial results on usage patterns and clinical outcomes. This project is providing Dr. Siedsma with specific skills in clinical epidemiology and implementation science. His second research project, “Identification of critical care physician-specific cognitive task deficits and education to improve performance in a model of ARDS” uses high-fidelity simulation to assess physician performance in the management of hypoxic respiratory failure and ARDS. The long-term goal of this project is to test the effectiveness of different educational strategies designed to improve physician performance. This project is providing Dr. Siedsma with specific skills in high-fidelity simulation, adult education and behavior change.

**Jennifer Burgher Seaman, PhD, RN**  
Principal Trainer: Douglas White, MD, MAS; Appointment: 01/01/16 – 12/31/16; 2nd year appointment  
Dr. Seaman is a doctorally prepared nurse with PhD training from the University of Pittsburgh. Her research focuses on the clinical outcomes of older adults experiencing severe acute illness. Her career goals are to develop and test interventions to improve the experience of geriatric patients admitted to the ICU through interdisciplinary communication and palliative care education. Toward that end, she is receiving advanced training in intervention development, implementation science and clinical research design.

*Research projects:* “Exploring the perspectives of ICU clinicians on the conduct of interdisciplinary family meetings in the ICU: This qualitative study examines the barriers and facilitators to family meetings as a strategy to improve patient-centered outcomes in the ICU. Eleven interviews over five sites have been conducted thus far and data analysis is ongoing. Her second research project, “A national survey of barriers and facilitators to the conduct of interdisciplinary family meetings” will use a multi-modal survey to quantify the relative importance of key barriers and facilitators to family meetings in advance of an intervention. The survey domains are currently under development and a draft survey is in progress.
Daniel Kievlan, MD  
Principal Trainer: Derek C. Angus, MD  
Appointment: 07/01/15 – 6/30/16; 1st year appointment  
Dr. Kievlan received his medical degree from the University of Texas before completing a residency in emergency medicine at the University of California San Francisco. He then began a clinical fellowship in Critical Care Medicine at the University of Pittsburgh, from which he entered our research training program. Dr. Kievlan’s research interests are in the recognition and treatment of sepsis and acute lung injury in the pre-hospital setting. He is receiving advanced research training in clinical epidemiology, biostatistics, and physiological monitoring using the EHR.  
Research projects: “External validation of a prehospital risk score for critical illness” This project uses granular clinical data from the UPMC electronic health record to externally validate a widely-used but never validated risk-score to predict critical illness in the pre-hospital setting. A manuscript for this project has been submitted for publication and is currently under review. This project is providing Dr. Kievlan with specific training in predictive modeling and logistic regression. His second research project, “Relationship between repeated qSOFA evaluation and patient outcome” This work uses multicenter EHR data to define different organ failure trajectories in hospitalized patients with sepsis and acute lung injury. This project, which is currently in development, will provide Dr. Kievlan with specific training in trajectory analysis and bioinformatics.

Steven Keller, MD, PhD  
Principal Trainer: John Kellum, MD; 7/1/15 – 6/30/16; 1st year appointment  
Dr. Steven Keller received a PhD in medical engineering from MIT before obtaining a medical degree from Stanford University. He then completed a residency in Internal Medicine at Massachusetts General Hospital and a fellowship in Critical Care Medicine at the National Institutes of Health before coming to Pittsburgh to join our post-doctoral fellowship program. Dr. Keller’s research interests are in bio-engineering and organ support related to acute cardiopulmonary respiratory failure, specifically relating the development of novel medical devices for respiratory dialysis and right ventricular support. He is working with Drs. John Kellum and William Federspiel to develop and test novel respiratory dialysis devices in a small animal model of acute respiratory failure.  
Research projects: “Bench to beside development of a novel method for extra-corporal CO2 removal” involves a series of bench experiments to refine a respiratory dialysate, and a series of rodent experiments to demonstrate “proof of concept” for respiratory dialysis in acute respiratory failure.

Training in Pediatric Neurointensive Care and Resuscitation Research (T32HD040686-16)  
Our T32 program is in its 15th year. The program is directed by Dr. Kochanek, the Ake N. Grenvik Professor and Vice Chairman of CCM at the University of Pittsburgh School of Medicine and Director of the Safar Center for Resuscitation Research. It is co-directed by Robert S.B. Clark, MD, Chief of CM at Children's Hospital of Pittsburgh of UPMC and Dr. Anthony Kline, Professor of PM&R. Our T32 program trains clinicians, specifically, pediatric CCM, child neurology, pediatric neurosurgery, PM&R, pediatric emergency medicine, newborn medicine, pediatric radiology fellows, and selected other fellow-level clinician-scientists or scientists with related research interests, targeting investigations into TBI and cardiopulmonary arrest, which are central to the field of pediatric neurointensive care and resuscitation. Indeed, these are the two conditions that contribute the greatest morbidity and mortality to children across the field of pediatric neurocritical care.

The T32 program offers research opportunities in these two areas with 21 outstanding and highly experienced NIH-funded senior mentors, each of whom has successfully guided many trainees to academic careers and/or independent funding. Our program has the following five goals:

1. Education of the fellows is grounded in the sound principles of contemporary neuroscience.
2. Fellows become academic clinician-scientists in the field.
3. Fellows go on to successful independent funding.
4. Fellows ultimately become leaders in the field.
5. Fellows are fully equipped to bring the expertise to rigorously and ethically study novel neuroprotective, resuscitative, and regenerative therapies.

Each year, the program funds two new trainees for a two-year minimum duration of training. Thus, we typically fund four positions each year. In FY17 our T32 supported four outstanding fellows, all of whom have been highly productive.

Christopher Horvat, MD
Dr. Horvat completed two years on our T32 this year working under the mentorship of Drs. Robert Clark and Philip Empey, along with input from Dr. Derek Angus and the CRISMA group. His scholarly interests include evaluation of pharmacogenomics-based sedation strategies, electronic predictors of impending deterioration, and bedside ultrasound education in pediatric critical care. This year, Dr. Horvat published a manuscript in the journal Pediatric Research titled “ABCB1 genotype is associated with fentanyl requirements in critically ill children.” That work is part of an overall approach to phenotype use of sedation and analgesia in the pediatric ICU. We are pleased to report that Dr. Horvat will join our faculty as an Assistant Professor of Critical Care Medicine in July, 2017.

Diana Pang, MD
Dr. Pang completed three years of training on the T32 this year working under the dual mentorship of Drs. Raj Aneja and Robert Clark. She studied the emerging area of septic encephalopathy in the ICU. She presented a paper at the Shock Society meeting titled “Cytotoxic cerebral edema is correlated with microglial activation in a mouse model of sepsis” and also co-authored a report in Critical Care Medicine titled “Dietary supplementation with nonfermentable fiber alters the gut microbiota and confers protection in murine models of sepsis.” Dr. Pang will join the faculty of the Children’s Hospital of the King’s Daughters in Norfolk, VA.

Amery Treble-Barna, PhD
Dr. Treble-Barna is a clinical psychologist interested in pediatric TBI outcomes. She completed her PhD at the University of Houston, a clinical internship at Nationwide Children’s Hospital, and postdoctoral training at Cincinnati Children’s Hospital. Her work on our T32 is focused on epigenetic consequences of childhood adversity and its impact on TBI outcomes. She is examining the impact of epigenetic effects on expression of brain derived neurotrophic factor in these clinical investigations. She is being mentored by a multi-disciplinary and multi-institutional team including Drs. Amy Wagner, Yvette Conley, Amy Houtrow, Ericka Fink, Sue Beers and Rachel Berger from the University of Pittsburgh and Dr. Keith Yates from the University of Calgary. She published a remarkable 10 manuscripts in the 2016-2017 academic year addressing work prior to joining our T32 program.

Jessica Wallisch, MD
Dr. Jessica Wallisch began work on our T32 in July of 2016. Her research is mentored by Dr. Kochanek and has focused on the development of novel therapies targeting cerebral edema following TBI and cardiac arrest. She has been testing a novel aquaporin-4 antagonist (AER-271) being developed by Aeromics. Her findings suggest that this therapy has its greatest promise in the setting of cardiac arrest, where an impact on brain edema, the inflammatory response, and neurological outcome is suggested. She presented her findings at the 2017 SCCM Congress and received a Gold Snapshot Award. This year, she published a manuscript titled “Cerebrospinal fluid NLRP3 is increased after severe TBI in infants and children” in the journal Neurocritical Care.
Individual Faculty Research Summaries

Ali Al-Khafaji, MD, MPH

Dr. Al-Khafaji is a Professor of Critical Care Medicine and the Medical Director of the Transplant Intensive Care Unit at the University of Pittsburgh Medical Center. His research interests focus on clinical issues related to caring for critically ill patients with acute alcoholic hepatitis, end stage liver disease, acute kidney injury solid organ transplantation and multisystem organ failure.

Major Projects
- Extra corporeal liver assist device in patients with acute alcoholic hepatitis. (work in press in Liver transplantation)
- Significance of Oliguria in patients with chronic liver disease (work published in Hepatology)
- VTI 308: A Randomized, Open-label, Multicenter, Controlled, Pivotal Study to Assess Safety and Efficacy of ELAD\textsuperscript{®} in Subjects with Alcohol-Induced Liver Decompensation (AILD). Role: Principal Investigator. The primary objective of the study is to evaluate safety and efficacy of ELAD\textsuperscript{®} with respect to overall survival of subjects with a clinical diagnosis of alcohol-induced liver decompensation (AILD) through at least Study Day 91.

Raj Aneja, MD

Dr. Aneja’s research entails understanding the regulation of the heat shock response by a nuclear protein called Poly (ADP) Ribose Polymerase (PARP). Recent studies indicate that PARP-1 also acts as a co-transcription factor for many cellular proteins. He is also examining its impact on lipopolysaccharide mediated High Mobility Group Box 1 (HMGB-1) protein secretion. HMGB-1 is a DNA binding protein with cytokine like properties and is thought to be a key mediator of sepsis. Dr. Aneja’s clinical research interests include the use of plasma exchange in multi-organ failure associated with sepsis. Recent publications are in the Journal of Immunology and Journal of Leukocyte Biology.

Major Projects
- Regulation of LPS-Mediated HMGB1 Release by Poly (ADP-Ribose) Polymerase-1
  Funded by: NIH. The proposed research plan will define the role of PARP-1 in the modulation of Lipopolysaccharide (LPS)-mediated HMGB1 transcription, post-translational modification and secretion.
- Role of Danger Associated Molecular Patterns in Traumatic Brain Injury and Sepsis
  Working with Drs. Kochanek, Bayır, and Bell, this project will examine the role of danger associated molecular patterns in traumatic brain injury and sepsis.
- Dietary supplementation with non-fermentable fiber alters the gut microbiota and confers protection in a murine model of sepsis
  In collaboration with Dr. Michael Morowitz, we hypothesized that cellulose supplementation would improve animal survival in murine models of sepsis by modulating the microbiome and decreasing systemic inflammation.
Dr. Angus’ research interests include clinical, epidemiologic and translational studies of sepsis, pneumonia, and multisystem organ failure and health services research of the organization and delivery of critical care services. Dr. Angus has led several large NIH-funded multicenter studies in the critically ill, one of which is ProCESS (Protocolized Care for Early Septic Shock), a 40-center study focusing on how to best provide early resuscitation for septic shock.

Major Projects – Active (Federal)
- **Research training in anesthesiology and pain medicine**
  *Funded by: NIGMS T32GM075770, Role: Training Faculty, Principal Investigator: Xu.* Our primary goal is to continue training physician scientists to lead the future intellectual pursuits in anesthesiology beyond the confines of the traditional provision of anesthesia and to become independently funded investigators and leaders in the field.

- **Platform for European preparedness against (Re-)emerging epidemics (PREPARE)**
  *Funded by: European Union FP7 Program 602525, Role: Co-Investigator, Principal Investigator: Goossens.* By strengthening and integrating interepidemic research networks, PREPARE will enable the rapid coordinated deployment of Europe’s elite clinical investigators, resulting in a highly effective response to future outbreaks based on solid scientific advances.

- **Understanding regional critical care delivery in acute respiratory failure**
  *Funded by: NIH K08HL122478, Role: Primary Mentor, Principal Investigator: Wallace.* The overall goal of this project is to empirically evaluate the outcome benefit of regionalized critical care for patients with acute respiratory failure.

- **Procalcitonin antibiotic consensus trial (ProACT)**
  *Funded by: NIH/NIGMS, R01GM101197, Role: Co-I, Principal Investigator: Huang.* The major goal of this project is to determine which patients presenting with suspected acute infection require antibiotics. We are conducting a randomized trial to test implementation of a procalcitonin antibiotic algorithm, to safely reduce antibiotic exposure in lower respiratory tract infection. Study findings will have an immediate impact on the care of patients presenting with suspected acute infection and may significantly reduce antibiotic use and resistance.

- **Sedation strategy and cognitive outcome after critical illness in early childhood (RESTORE-Cognition)**
  *Funded by: NIH/NICHD, R01HD074757, Role: Co-I, Principal Investigator: Watson.* The major goal of this project is to determine the relationships between sedative exposure during pediatric critical illness and long-term neurocognitive outcomes. We will assess multiple domains of neurocognitive function 3 years post-discharge in 500 RESTORE subjects with normal baseline cognitive function aged 2 weeks to eight years at pediatric intensive care unit admission.

- **A trial to Improve surrogate decision-making for critically Ill older adults**
  *Funded by: NIH/NHLBI, R01AG045176, Role: Co-I, Principal Investigator: White.* This multi-center efficacy trial strives to improve key elements of decision making, decrease long-term psychological distress among surrogates, and achieve more patient-centered care near the end of life.

- **Model-based decisions in sepsis**
  *Funded by: NIH/NIGMS, R01GM105728, Role: Co-I, Principal Investigator: Clermont.* The overarching goal of the program is to validate computational models of human sepsis using data from the ProCESS study through advanced mathematical and computational methods. This study also provides an unprecedented opportunity to gain mechanistic understanding of the processes leading to organ failure and death, systemic recovery and unexpected failure.
• Identifying optimal care structures and processes in long-term acute care hospitals
  *Funded by: NIH, R01 HL096651, Role: Co-I, Principal Investigator: Kahn.* The major goal of this project is to investigate the impact of long-term acute care hospitals on survival and the costs of health care for critically ill patients with respiratory failure requiring prolonged mechanical ventilation.

• Preventive and early treatment of acute lung injury clinical trials network (PETAL)
  *Funded by: NIH, U01HL123020, Role: Co-I, Principal Investigator: Yealy.* As a Clinical Center in the PETAL Network, we will conduct two interventional studies for evaluation and implementation; a) A trial of nebulized DNAase as an ARDS-prevention strategy and b) a trial of protocolized neuromuscular blockade as an ARDS early treatment strategy. The goal is a shared mission to better understand treatment and outcomes for those with or at risk for acute lung injury (ALI) or acute respiratory distress syndrome (ARDS).

• Clinical and translational research training in late-mood disorders
  *Funded by: NIH, T32MH019986, Role: Mentor, Principal Investigator: Reynolds.* The primary goal of this fellowship program is to provide rigorous training in the basic foundations and methodologic tools necessary for successful clinical and translational investigation in geriatric mental health and psychiatry.

• Pre-hospital identification of high risk sepsis
  *Funded by: NIH/NIGMS K23 GM104022, Role: Primary Mentor, Principal Investigator: Seymour.* We will be developing an integrated model for sepsis and mortality risk, determining the incremental knowledge gained in a modest prospective study, and exploring novel mass-spectrometry-based, metabolomic biomarkers of prehospital sepsis and mortality to improve the emergency care of our highest acuity, most resource-intensive patients.

• Organizational Determinants of ICU Telemedicine Effectiveness
  *Funded by: NIH/NHLBI R01HL120980, Role: Co-I, Principal Investigator: Kahn.* The major goal of this project is to identify the key clinical and organizational factors associated with intensive care unit telemedicine effectiveness by conducting site visits and national survey of ICU telemedicine providers.

• A Stepped Wedge trial of an intervention to support family members in UCUs
  *Funded by: NIH R01NR014663, Role: Co-I, Principal Investigator: White.* The major goal of this proposal is to conduct a multi-center, randomized stepped wedge trial testing the PARTNER intervention in 5 ICUs among 1000 patients with advanced critical illness and their surrogates.

• Novel approaches to profiling hospitals on critical illness mortality
  *Funded by: NIH R01HL14945, Role: Co-I, Principal Investigator: Kahn.* The major goal of this project is to develop and validate novel measures of hospital-specific mortality for critical ill patients. We will use a unique state-wide hospital dataset from Pennsylvania containing detailed clinical and administrative data, as well as innovative statistical models that account for care transitions and have not yet been applied to the field of performance assessment.

• Immunotherapy of sepsis using anti-PD-L1 antibody
  *Funded by: NIH/NIGMS R34GM107650, Role: Principal Investigator.* The major goal in this planning grant is to execute detailed simulations to finalize the trial design. It will also finalize study logistics, including procedures to standardize biomarker assays at the six sites and the oversight procedures.

• A novel intervention to make heuristics a source of power for physicians
  *Funded by: NIH DP2LM102339, Role: Co-Investigator, Principal Investigator: Mohan.* A novel intervention to make heuristics a source of power for physicians. The overall objective will be to translate behavioral science principles into a new method of modifying physician judgment.
• **Re-evaluation of systemic early neuromuscular (ROSE) blockade trial PETAL Network**
  
  *Funded by: NIH/NHLBI, U01HL123009, Role: Co-Principal Investigator, Co-Principal Investigator: Moss.* The major goal of ROSE is to assess the efficacy and safety of early neuromuscular blockade with cisatracurium besylate in reducing mortality and morbidity in patients with moderate-severe ARDS in comparison to usual care.

• **Sepsis endotyping using clinical and biological data**
  
  *Funded by: NIH/NIGMS, R35GM119519 Role: Co-Investigator, Principal Investigator: Seymour.* The major purpose of this project is to translate findings from "big data" in the EHR and efficiently enrolled biologic specimens into generalizable bio-types for enrichment strategies in future clinical trials and EHR alerts.

### Major Project – Active (Non-federal non-competitive)

• **A phase 1b/2a, randomized, double-blinded, placebo-controlled, multicenter study to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of BMS-936559 in subjects with severe sepsis**
  
  *Funded by: Bristol Myers Squibb, Role: Co-Investigator, Principal Investigator: Mayr.* The major goal of this project is the completion of Data Collection Form/Case Report form and completion of training materials.

### Major Projects – Recently Completed (Federal)

• **University of Pittsburgh Clinical and Translational Science Institute**
  
  *Funded by: NIH CTSA Program UL1TR000005 and UL1RR024153, Role: Clinical Mentor, Principal Investigator: Reis.* The University of Pittsburgh's Clinical and Translational Science Institute will facilitate integrative collaboration to coalesce clinical and translational research and education programs that enable investigators to conduct visionary clinical and translational research.

• **Genetic variants in zinc proteins and racial differences in infectious diseases**
  
  *Funded by: NIH KL2TR000146, Role: Mentor, Principal Investigator: Palmer.* Multidisciplinary clinical research scholars program. The goal of the research is to determine the role that SNPs in zinc proteins play in racial disparities in susceptibility to community-acquired pneumonia and risk of severe sepsis.

• **Estimating the national burden of sepsis using electronic health record data**
  
  *Funded by Harvard Pilgrim Health Care/CDC U54CK000172, Role: Co-Investigator, Principal Investigator: Seymour.* The major purpose of this project is to estimate the current national burden of sepsis and septic shock using electronic clinical data, characterize trends in sepsis incidence and mortality using electronic clinical data from diverse hospitals and compare the incidence, agreement and mortality rates of EHR-based sepsis surveillance definitions versus the SCCM/EICM's forthcoming clinical sepsis definitions and traditional claims-based definitions.

• **Novel diagnostic and stratification tools for septic shock**
  
  *Funded by NIH/NIGMS R01GM108025, Role: Co-Investigator, Principal Investigator: Wong* The major goal of this proposal will be to use complementary aims that are aligned with the overarching theme of our longstanding translational sepsis research program. They build upon data generated during the previous funding period to move in new directions.

• **Protocolized goal-directed resuscitation of septic shock to prevent AKI**
  
  *Funded by NIH/NIDDK, R01 DK083961, Role: Co-I, Principal Investigator: Kellum.* We are conducting a study to examine the natural history of Acute Kidney Injury (AKI) arising in patients with sepsis. We will determine if protocolized resuscitation is more effective in improving long term outcomes (survival, renal recovery, reduced progression of Chronic Kidney Disease).
• Late cardiovascular consequences of septic shock (Consequences)
  
  *Funded by: NIH/NIGMS, R01GM097471, Role: Co-I, Principal Investigator: Yende. We will address: a) with what frequency and in which patients does the delayed immune resolution observed at discharge persist beyond discharge, b) what might be the cause for delayed immune resolution, c) which immune pathways are more strongly associated with cardiovascular outcomes and d), do early sepsis interventions have long-term beneficial effects? Survivors of severe sepsis hospitalization have high long-term morbidity and mortality.*

Alicia Au, MD, MS

Dr. Au’s research focuses on the study of neurological injuries in children, with an emphasis on the use of biomarkers for prediction of outcome in traumatic brain injury and for early detection of neurologic system failure in diagnostically diverse patients in the Pediatric Intensive Care Unit (PICU).

Major Projects

• Mixed Graphical Models for the Prediction of Neurological Morbidity in the PICU
  
  *Funded by: Submitted for NIH, NINDS K23, Role: PI; Co-Mentors: Robert S.B. Clark, Takis Benos. This study is based on my preliminary work regarding the use of serum biomarkers for detection of neurological morbidity, as determined by Pediatric Cerebral Performance Category (PCPC) score of 3-6 with a deterioration from baseline, among diagnostically diverse patients admitted to the PICU. Serum samples were collected daily (days 1-7) and concentrations of neuron-specific enolase (NSE), myelin basic protein (MBP), and S100B, specific for neurons, oligodendrocytes, and glia, respectively, were measured. As published in *Neurocritical Care,* “Brain-Specific Serum Biomarkers Predict Neurological Morbidity in Diagnostically Diverse Pediatric Intensive Care Unit Patients,” peak biomarker levels were greater in patients with unfavorable versus favorable neurological outcome and peak levels were each independently associated with unfavorable neurological outcome when controlling for presence of primary neurologic admission diagnosis and poor baseline PCPC using logistic regression analysis. Receiver operating characteristics with these models had an area under the curve ranging from 0.75-0.81. As such, we are proposing the use of mixed graphical modeling for the integrative analysis of biomarkers and clinical data variables (e.g. heart rate, pH) to better determine direct associations and probabilistic outcomes for the development of neurological complications and enhanced predication of neurologic morbidity in the PICU.*

• Autophagy Biomarkers in TBI
  
  *Role: PI; Mentors: Robert Clark. This study explored the role of autophagy after TBI in humans, through the evaluation of Beclin 1 and p62. Beclin 1 is a Bcl-2 interacting protein with early involvement in the nucleation phase of phagophore formation through complex formation with Vps34/class III PI3 K and p62 functions further downstream from beclin 1 and is consumed during the elongation phase through its interaction with LC3. Pediatric TBI CSF was collected in 30 patients on days 1, 3, and 7 after admission, and enzyme-linked immunosorbent assays were performed for beclin 1 and p62. Mean and peak CSF beclin 1 and p62 levels were increased compared to controls. Peak p62 levels were higher in patients with unfavorable versus favorable outcome and were independently associated with outcome when controlling for age and initial Glasgow Coma Scale score. This suggests increased autophagy with impairment of, and/or exceeding the capacity for, autophagic flux. The association of increased p62 with unfavorable outcome suggests that autophagy in excess of the capacity to clear degradation products may be deleterious after TBI.*

• Approaches and Decisions in Acute Pediatric TBI Trial (ADAPT) – Co-Site PI and Member of Steering Committee
  
  *Funded by: NIH, NINDS U01NS081041; Role: Co-Site PI for University of Pittsburgh Site and Member of Steering Committee; PI: Michael Bell, Stephen Wisniewski. ADAPT is a multicenter, comparative effectiveness pediatric trial of severe TBI. Through the enrollment of 1,000 children with severe traumatic brain injury with ICP monitor placed as standard of care, its aims are to determine the effectiveness of (1) first-line intracranial hypertension strategies, (2) strategies that mitigate iatrogenic ischemia and hypoxia, and (3) strategies that*
provide metabolic support on outcome. Enrollment is currently complete, with follow-up assessments ongoing. The University of Pittsburgh Site is additionally participating in ancillary ADAPT microbiome, genetic and MRI studies.

• **Epilepsy Bioinformatics Study for Antiepileptogenic Therapy (EpiBioS4Rx)**
  *Funded by: NIH, NINDS; Role: Co-site PI for University of Pittsburgh Site, PI: Paul Vespa.* This multicenter study investigates the development of post-traumatic epilepsy (PTE) following moderate-severe TBI through early underlying biomarkers (electrical [EEG], structural [MRI], and metabolic [blood]) in humans. It will enroll 600 patients age ≥ 6 yrs, with GCS between 3-12 and hemorrhagic contusional injuries to the frontal and/or temporal lobes. We expect to begin enrollment in the next few weeks.

Marie Rosanne Baldisseri, MD, MPH

Major Projects

- University of Pittsburgh Medical Center site co-investigator for the PRINCE study sponsored by the Neurocritical Care Society that is looking at the practices of neurointensivists worldwide and identifying areas for future research.

Ian Barbash, MD MS

Dr. Barbash is an intensivist interested in designing, implementing, and evaluating system-level interventions to optimize processes of care and clinical outcomes for patients with critical illness.

Major Projects

- **Evaluating Behavioral Incentives in the ICU**
  *Funded by: none; Mentor: Jeremy Kahn.* This study used electronic health record data to evaluate the impact of a physician-targeted financial incentive on the completion of spontaneous breathing trials in mechanically ventilated patients. The primary finding was that the incentive was associated with an improvement in performance driven largely by increases in the documentation of eligibility exclusions, a phenomenon known as exception reporting. This project led to a publication in the *American Journal of Respiratory and Critical Care Medicine.*

- **Evaluating the Effect of the ICU Supply on ICU Utilization**
  *Funded by: NIH, NHLBI F32 HL132461; Role: PI; Mentor: Jeremy Kahn.* This study uses administrative data to evaluate the association between changes in the supply of ICU beds and the probability of admission to the ICU for patients with “discretionary” indications for ICU admission. The analysis is ongoing and manuscript is in process.

- **Understanding Hospitals’ Perceptions of Sepsis Health Policy**
  *Funded by: none; Mentor: Jeremy Kahn.* This study used semi-structured interviews with hospital quality officials to understand how hospitals perceive and are responding to Medicare’s SEP-1 quality measure. The primary finding is that hospitals find some aspects of the measure challenging and are investing substantial resources to meet the measure’s requirements. The findings are accepted for publication and serve as preliminary data for a K08 that is currently under review.

Hülya Bayır, MD

Dr. Hülya Bayır’s research continues to focus on the primary themes of mitochondrial injury and oxidative stress. She has organized a multidisciplinary team of investigators to study novel approaches to the treatment of mitochondrial dysfunction by targeting oxidative stress. Her laboratory integrates the work of clinical and basic science
researchers. Her group has recent publications in *Cell Death and Differentiation*, *Journal of Neurochemistry* and *Nature Chemistry*, among others.

**Major Projects**

- **Oxidative Lipidomics in Pediatric Traumatic Brain Injury**  
  *Funded by: National Institute of Neurological Disorders and Stroke (NINDS). 2R01NS061817, Role: PI; Co-Is: P. Kochanek; D. Stoyanovsky (EOH/GSPH); V. Kagan (EOH/GSPH).* This project employs the newly developing technology of oxidative lipidomics to provide important mechanistic information on the role of oxidized phospholipids in neuronal apoptosis after pediatric traumatic brain injury.

- **University of Pittsburgh CMCR Project 3, Radiation mitigators targeting regulated necrosis pathways of necroptosis and ferroptosis**  
  *Funded by: National Institute of Allergy and Infectious Diseases (NIAID), 2U19AI068021, Role: PI; Co-Is: V. Ritov (EOH/GSPH), Z. Huang (EOH/GSPH).* The central hypothesis of this project is that necroptosis and ferroptosis are important pathogenic mechanisms of acute radiation injury syndrome triggered by pro-inflammatory responses (cytokines, lipid mediators) thus representing new targets for radiomitigation.

- **Mapping Lipid Oxidation in Traumatic Brain Injury by Mass Spectrometric Imaging**  
  *Funded by: National Institute of Neurological Disorders and Stroke (NINDS). 1R01NS076511, Role: PI; Co-PI: VE Kagan; Co-Is: P Kochanek, A. Amoscato (EOH/GSPH), A. Kline (PM&R), S. Watkins (Cell Biology).* The goal of this application is to develop and apply a new technology – imaging mass spectrometry (IMS) – for spatial and temporal mapping of diverse molecular species of phospholipids and their oxidation products and superimposing them onto neuropathology of the injured brain.

- **Mitochondria-Targeted Redox Therapy for Cerebral Ischemia in the Developing Brain**  
  *Funded by: National Institute of Neurological Disorders and Stroke (NINDS). 1R01NS084604, Role: PI; Co-PI: RSB Clark; Co-Is: P Kochanek, P. Wipf (Chemistry), M Manole (Pediatrics), D. Stoyanovsky (EOH/GSPH), A. Kline (PM&R).* The aim of this research is to synthesize and develop novel mitochondria-targeting therapeutics, toward meaningfully improving neurological outcome and quality of life in infants and children suffering from cerebral hypoxia-ischemia.

- **Oxygenated Species of Cardiolipins As Biomarkers Of Mitochondrial Dysfunction, Role: Co-Investigator**  
  *Funded by: National Institute of Environmental Health (NIEHS). R01ES020693. Role: Co-I; PI: YY Tyurina and VE Kagan.* The central hypothesis of this project is that exposure to rotenone, a pesticide, causes time- and dose-dependent selective oxidation of cardiolipin and accumulation of its oxidized molecular species associated with mitochondrial dysfunction through enzymatic reactions triggered early in apoptosis.

- **Overcoming Membrane Transporters to Improve CNS Drug Therapy**  
  *Funded by: National Institute of Neurologic Diseases and Stroke R01NS069247, Role: Co-I; PI: Robert Clark, MD; other Co-Is: Patrick Kochanek, MD; Michael Bell, MD.* There is a sense of urgency to move forward with pharmacological therapies that improve outcome after brain injury. This project tests combinational strategies that overcome membrane transport barriers to synergistically improve bioavailability and efficacy of both clinically used and novel therapies after traumatic brain injury. We aim to define the capacity of the combination of probenecid and N-acetylcysteine (NAC) to synergistically reduce oxidative stress and improve neurological outcome in experimental models, and to define the capacity of the combination of probenecid and NAC to safely and synergistically reduce oxidative stress in children (Phase I/II Pro-NAC trial), after traumatic brain injury.
Major Projects

**The role and effectiveness of point of care ultrasound (POCUS) in our pediatric cardiac intensive care unit.**

The overall goal is to educate and assist in implementation of point of care ultrasound in the cardiac intensive care unit. The initial goal for trainees would be to determine indications for focused ultrasound; and demonstration of knowledge of the limitations of focused ultrasound.

Trainees will demonstrate proper probe choice and positioning; with goals being:

- To obtain four basic images - subcostal four-chamber, parasternal long, parasternal short and apical for chamber views.
- Assess obvious morphologic abnormalities, assess for effusions – both pericardial and pleural, determine qualitative left ventricular and right ventricular systolic function. Also, to aid in determination of fluid status of the heart.
- The basic questions to be answered – is the left and right ventricular systolic function normal, is there pericardial or pleural effusion with potential for hemodynamic compromise. Is there potential evidence of intravascular volume depletion?
- Trainees will be given a pre-test evaluation of basic ultrasound technique and physics
- Post – training they will be given a similar post-test. and after 5 different sessions will be required to obtain similar images on their own.
- An echocardiographic attending{blinded} will determine whether images pre- and post-training are of similar quality and are valuable enough to sufficiently answer the above questions.
- Trainees will include cardiac intensive care fellows, PICU fellows, cardiology fellows and attendings in the unit without formal ultrasound training.

**Assessing and Increasing the effectiveness of educating fellows and other learners rotating through the cardiac intensive care unit.** There is an ongoing challenge to educate medical trainees – residents and fellows – to ensure that all trainees get the same or similar core pediatric cardiac intensive care exposure. A pediatric cardiac critical care curricula is being undertaken via use of the six-step approach.

Christopher Brackney, DO

Dr. Brackney is involved as a clinician-educator with teaching medical students, residents, nurse practitioners, and fellows in the Multidisciplinary Critical Care Training Program. Currently, serves as CCM Fellowship site director at VA Pittsburgh. He has experience in teaching utilizing high-fidelity simulation. He co-directs the Critical Care Medicine Elective rotation for medical students and has participates in medical simulation research. Dr. Brackney currently serves as the director of the VA Surgical Intensive Care Unit, VA Respiratory Therapy, and VA ECLS Program.

**Major Projects**

- **Simulation Approaches to mechanical Ventilation: Metrics and Evolution (SAVE-ME)**
  
  *Funded by: 2014-2017 R18 (Hotchkiss). Role Co-I, 3 years.* This project will deploy an Internet-based simulation environment to train physicians and care partners in the management of those with critically compromised cardiopulmonary function. A multiyear, multicenter AHRQ demonstration project that will
  
  - Refine and extend the current simulator;
  - Develop a large database of expert and novice practice patterns spanning a range of provider types;
  - Apply novel pattern recognition and cognitive assessment tools to characterize expertise and the trajectory of learning;
  - Assess the feasibility and effects of dynamically adaptive simulation based training;
  - Elucidate the effects of common environmental stressors on provider cognitive performance.

- Educational research and development: The educational simulator developed in CANVENT was the foundation for the new SAVE-ME grant, and has seen steadily increasing web traffic despite only word of
mouth promotion. Currently, the most frequently downloaded simulator on Bing and #1 on Google; approximately 20 downloads per day that have spanned 98 countries. This is up from approximately 30 downloads per week as of July. In early stages of negotiation with large healthcare organization to promote denser dissemination within US.

Joseph A. Carcillo, MD

Dr. Carcillo is a founding member and the present UPMC-CHP site PI for the Eunice Kennedy Shriver National Institute of Child Health and Human Development Collaborative Pediatric Critical Care Research Network. The site has contributed over 24,000 patients over 10 years to NICHD clinical studies in critically ill children. Dr. Carcillo has successfully competed for another 5 years of funding in the third cycle beginning December 1, 2014, bringing the total to 15 years of continuous funding. He is also presently funded by NIGMS to study ‘Inflammation Phenotypes in Pediatric Sepsis induced Multiple Organ Failure. Sepsis remains a leading killer of children worldwide. Dr. Carcillo’s research interest is in using improved understanding of host-pathogen interactions to develop individualized or phenotype specific therapies for pediatric sepsis. His clinical goal is to apply this research to bedside development of practice methods that reduce global child mortality and morbidity. He. Carcillo is the taskforce chair for the ACCM-PALS Hemodynamic Support in Newborns and Children Clinical Practice Guidelines, the Pediatric group leader for the Surviving Sepsis Campaign, and co-chair of the World Federation of Pediatric Intensive Care and Critical Care Societies Global Sepsis Initiative. These guidelines have been effective vehicles for bringing his prior research on individualizing therapy for pediatric septic shock to bedside practice. Presently, Dr. Carcillo’s research is directed to understanding the role of systemic inflammation related to host-pathogen interactions in the development of sepsis-induced multiple organ failure. Using the NICHD collaborative research network of pediatric centers to test the generalizability of clinical research findings already attained at the UPMC-CHP site, Dr. Carcillo hopes to inform bedside practice in the prevention and reversal of pediatric sepsis induced multiple organ failure. The basic tenet of his ongoing research is that just as hemodynamic therapies directed to specific cardiovascular dysfunction phenotypes have reduced mortality from septic shock, so too can therapies directed to specific inflammation pathobiology phenotypes reduce mortality from sepsis induced multiple organ failure.

Major Projects
- Collaborative Pediatric Critical Care Research Network at Children’s Hospital of Pittsburgh
  - THAPCA Clinical Trial (Therapeutic Hypothermia After Pediatric Cardiac Arrest)
    Funded by: NICHD as a sub-award to Dr. Carcillo and the University of Pittsburgh. This trial started in Sept. of 2009 and enrolled 80 children nationwide. Four children have been enrolled at Children’s Hospital of Pittsburgh. The THAPCA Trials are two prospective randomized controlled trials of therapeutic hypothermia after cardiac arrest in children. Each THAPCA Trial will be analyzed as an intention to treat study. The THAPCA Trials include one for out-of-hospital cardiac arrests (THAPCA-OH Trial), and one for in-hospital cardiac arrests (THAPCA-IH Trial). These trials will be analyzed separately, because etiologies and patient outcomes of these groups are substantially different.
  
  - Critical Illness Stress induced Immune Suppression Trial
    Funded by: NICHD as part of the CPCCRN Network. The project’s primary goal is to determine if enteral zinc, selenium, and glutamine and parenteral metoclopramide will delay the onset of nosocomial infection/sepsis compared to enteral whey proteins. The study has been closed to enrollment. The project has recruited 293 patients at seven centers (67 at the University of Pittsburgh) and has generated one manuscript in the Journal of Parenteral and Enteral Nutrition.
  
  - Bereavement in Parents of Critically Ill Children
    Funded by: NICHD as part of the CPCCRN Network. The goal is to identify patterns of grieving in parents who have lost their child in the Pediatric Intensive Care Unit. This is the fourth year of this study which has generated three publications in peer reviewed journals Pediatrics, Pediatric Critical Care Medicine, and Journal of Pediatrics.
The Critical Pertussis Trial
*Funded by: NICHD as part of the CPCCRN Network.* Investigators seek to describe the course of critical Pertussis illness and outcomes in survivors. CPCCRN investigators plan to enroll 200 children with critical Pertussis at the 7 CPCCRN sites across the US. Data on morbidity, mortality, and developmental sequelae will be collected and characteristics of childhood critical illness from Pertussis will be described in detail. The study aims to characterize the acute course of critical Pertussis during PICU admission and assess reported health status and family impact following PICU discharge in survivors.

Date Registry Study
*Funded by: NICHD as part of the CPCCRN Network.* This project is in its sixth year and is funded by the National Institutes of Child Health and Development. The University of Pittsburgh has contributed over 6,000 patients. The goal of this project is to provide a registry of critical illness at the seven sites for both epidemiology and study design purposes. This work generated 1 publication in *Pediatric Critical Care Medicine*.

Asthma Study
*Funded by: NICHD as part of the CPCCRN Network.* Following admission to a Pediatric ICU (PICU), some critically ill children with asthma progress to death. The purpose of this study is to review all admissions related to an asthma diagnosis requiring ventilation support from 2003-2008 occurring in the 7 Collaborative Pediatric Critical Research Network PICUs. It is believed the information gleaned from careful analysis of details surrounding the circumstances of these admissions can be extracted retrospectively, will better inform prospective studies on critical asthma assessment, and pharmacologic therapy in the future. The Pittsburgh team and other CPCCRN sites will retrospectively review the medical records of children identified to have an asthma diagnosis which required ventilator support. Each PICU will examine its admissions for asthma over the past 5 years (2003-2008). Post-mortem data will be reviewed where available. There have been 31 patients enrolled at Children’s Hospital of Pittsburgh during the past fiscal year.

Life After Pediatric Sepsis Evaluation
It is well known that sepsis represents the leading cause of childhood mortality worldwide. However, as distinct from adult medicine, there exists a large knowledge gap regarding long-term health-related quality of life (HRQL) and functional status (FS) following pediatric sepsis. This lack of sepsis outcomes data is critical because failure to identify children at risk for sepsis-associated HRQL/FS deterioration may delay delivery of crucial rehabilitation medicine efforts to facilitate recovery. Moreover, failure to identify mechanisms of sepsis-associated HRQL/FS deterioration may impede development of novel, effective interventions for these children. For the first time the LAPSE investigation will longitudinally measure health-related quality of life (HRQL) and functional status (FS) alterations in this population and examine potential clinical risk factors that may be associated with adverse sepsis outcomes. LAPSE will derive a contemporary natural history for pediatric septic shock that will facilitate early identification of children at high risk for sepsis-associated HRQL/FS deterioration, and inform design of future interventional trials to maximize HRQL/FS among children surviving sepsis.

Inflammation Phenotypes in Pediatric Sepsis induced Multiple Organ Failure
The major goals of the project are to 1) Determine the incidence and outcomes of three unique sepsis MOF phenotypes: Thrombocytopenia Associated MOF defined by three organ failure with new onset thrombocytopenia, renal dysfunction, and an ADAMTS 13 activity < 57%; Immunoparalysis / Lymphoid Depletion associated MOF defined by an ex vivo whole blood endotoxin stimulated TNF response < 200 pg/mL after 3 days; and Sequential MOF defined by respiratory distress followed by liver dysfunction with sFasL level > 200 ng/mL, in children with severe sepsis; 2) Determine the relative contribution of genetic and environmental risk factors to the development of each of these three sepsis induced MOF phenotypes; and
3) Demonstrate that systemic inflammation reflected by CRP and/or Ferritin levels is increased in children with these sepsis induced MOF phenotypes with changes in CRP and Ferritin levels over time being associated with outcomes.

Sherry H-Y Chou, MD, MMSc FNCS

Dr. Chou’s research focuses on the use of human molecular biomarkers to probe mechanisms and predict outcome in acute brain injury conditions such as subarachnoid hemorrhage (SAH). The need for better bedside-to-bench translational investigations in SAH is dire, evidenced by several recent large SAH clinical trials that showed no neuroprotective effects in multiple therapeutic agents such as statins, magnesium, and selective endothelin-1a inhibitor clozopentan that had shown significant effects in pre-clinical studies. Dr. Chou contributed to this effort by designing and building a prospective SAH cohort with clinical phenotyping, bio-specimen banking, and extended long-term outcome evaluation up to 36-months post SAH. She is funded with a K23 career-development award. Dr. Chou has also contributed to patient-oriented research in intracerebral hemorrhage and ischemic stroke and published on the efficacy of acute reversal of anti-oxidation in the setting of ICH and examined susceptibility candidate genes that correlated with neuropathologically confirmed ischemic stroke subtypes. Dr. Chou also actively participates in research collaboration and serves as site primary investigator, co-investigator, clinical endpoint committee member, or data-safety monitoring board member in multicenter clinical trials and in research networks in neurocritical care including the US Neurocritical Care Research Network.

Major Projects

- **Biomarkers of Vasospasm and Outcome Following Subarachnoid Hemorrhage**
  
  *Funded by*: NIH/NINDS K23NS073806 (4/15/2011 – 12/31/2016) Subarachnoid hemorrhage (SAH) affects over 30,000 Americans per year and is one of the major causes of stroke-related potential life-years lost in people age 65 and younger. Despite advances in critical care for SAH patients, more than half of SAH survivors still live with significant disability. Vasospasm, which can occur in up to 70% of SAH survivors, is one of the most important causes for additional brain injury and disability after SAH. Her work will lay the foundation for potential discovery of new non-invasive bedside tests that can better diagnose and predict vasospasm and patients at risk for greater disability following SAH. Ultimately, we hope advances in understanding of molecular mechanisms of vasospasm and secondary brain injury following SAH will help us identify new therapies that may improve survival and reduce disability in SAH patients.

Robert S. Clark, MD

Dr. Clark’s current research interests include mechanisms of cell death and neurological dysfunction after traumatic and ischemic brain injury, particularly in the developing brain. Laboratory efforts have been supported by the NIH consecutively since 1996, and encompass in vitro and in vivo models of brain trauma and ischemia, and translational studies in patients suffering from these injuries. He has established an infrastructure for studying mechanisms of traumatic and ischemic cell death in the developing brain, training young clinical investigators, and translating innovative therapies from clinically relevant models to patients. Recent endeavors include exploring the mechanistic basis for innate sex-dependent differences in response to acute brain injury (currently an area of emphasis at the NIH), translating novel mitochondria-targeting therapeutics for the treatment of hypoxic-ischemic brain injury, and translating repurposed therapeutic adjuncts using ATP binding cassette membrane transporter inhibitors (e.g. probenecid) to improve brain bioavailability of potentially neuroprotective drug substrates (e.g. N-acetylcysteine, NAC).

Major Projects

- **Mitochondria-targeted Redox Therapy for Cerebral Ischemia in the Developing Brain**
  
  *Funded by*: NIH/NINDS R-01 NS084604. Multi-PI: R. Clark and H. Bayır (CCM). This project is in its first year. The goals of this project are to design, develop and test novel mitochondria-targeting nitrooxide therapeutics
toward improving neurological outcome after pediatric cardiac arrest. Novel therapeutics are developed under GLP by Dr. Peter Wipf in the Department of Chemistry at Pitt.

- **Overcoming Membrane Transporters to Improve CNS Drug Therapy**
  *Funded by: NIH/NINDS R01 NS069247. PI: R. Clark.* In this “bench-to-bedside” study, the overall goal is to determine if combinational therapeutics for traumatic brain injury can increase drug delivery into the CNS. We have established that detectable NAC levels can only be achieved in brain with an intact blood-brain barrier when used in combination with probenecid, and a phase I clinical trial—the “Pro-NAC Trial” (ClinicalTrials.gov identifier: NCT01322009)—is ongoing in children age 2-18 with severe traumatic brain injury.

- **Regulation of LPS-Mediated HMGB1 Release by Poly (ADP-Ribose) Polymerase-1**
  *Funded by the NIH/NIGMS R01 GM098474. Co-I: R. Clark, PI: R. Aneja (CCM).* The proposed research plan will define mechanisms that regulate the secretion of a crucial late-mediator of sepsis, high mobility group box-1 (HMGB1).

- **CYP450-mediated CBF Dysregulation and Neurotoxicity in Pediatric Cardiac Arrest**
  *Funded by: NIH/NICHD R01 HD075760. Co-I: R. Clark, PI: M. Manole (Pediatrics).* This grant will explore molecular mechanisms of cerebral blood flow dysregulation after cardiac arrest in the developing brain.

- **Training in Pediatric Neurointensive Care and Resuscitation Research**
  *Funded by: NIH/NICHD T32 HD40686. Co-PI: R. Clark, PI: P. Kochanek (CCM).* The purpose of this training grant is to develop Clinician Scientists in Pediatric Neurointensive Care research.

**Gilles Clermont, MD, CM, MSc**

Dr. Gilles Clermont’s systems medicine program seeks to explore the intersection of advanced quantitative methods and bedside care with the ultimate vision of leveraging mathematical, computational and engineering expertise to deliver improved personalized care to the critically ill. Fundamental to this goal is the belief that such work is best accomplished by scientists that can bridge cultural differences between clinical medicine and quantitative sciences. The systems medicine program is necessarily transdisciplinary and maintains a diversified portfolio of projects. Within CRISMA, the program has overlapping interests and shares resources with the Bioengineering and Organ Support program and the Healthcare Policy and Management. These projects are supported through federal agencies (NIGMS, NIAID, NLM, NSF, NIDDK, NHLBI) and through industry collaborations. The genesis of the systems medicine program was itself transdisciplinary through a privileged collaboration with investigators from the Departments of Mathematics (Carson Chow, PhD) and Surgery (Yoram Vodovotz, PhD) supported by an exploratory grant “Modeling the acute inflammatory response” 2002. This project was an early contribution to the NIH Roadmap Initiative seeking the integration of quantitative methods and systems approaches to improving patient care. Since then, our portfolio and resources have expanded considerably with a variety of collaborations, locally, nationally and internationally.

**Major Projects**

- **Machine Learning of Physiological Variables to Predict Diagnose and Treat Cardiorespiratory Instability**
  *Funded by: R01GM117622 NIH/NIGMS. Role: Co-I (PI: Pinsky)* This project proposes to apply machine learning modeling to ICU patients. We have previously applied machine learning (ML) modeling to our clinically-relevant porcine model of hemorrhagic shock to characterize responses to hypovolemia, hemorrhage, and resuscitation, predict which animals would or would not collapse during hypovolemia, and identify occult bleeding 5 minutes earlier than with traditional monitoring. We now propose to apply our work to vulnerable and invasively monitored ICU patients. We will develop multivariable models through ML data-driven classification techniques such as regression, Fourier and principal component analysis, artificial neural networks, random forest classification, etc. as well as more novel approaches (temporal rule learning
developed by our team; Bayesian Aggregation) to predict CRI in ICU patients. We envision a basic monitoring surveillance that identifies patients most likely to develop CRI to apply focused clinician attention and targeted treatments to deliver highly personalized medical care.

- **Physiologically Based Optimization of ICU Management**
  
  *Funded by: National Science Foundation. PIs: Gilles Clermont, MD; Andrew Schaefer, PhD, MCAM; Guodong Pang, PhD.*

  This collaborative research project targets the heavy resource burden that ICUs place on a hospital system, carrying operating costs that may at times make up 20 percent of a hospital’s budget. The research team aims to model patient flow through a hospital system by employing methods that are often used in other cases to improve the efficiency of supply chains, flight schedules, or vehicular traffic while at the same time maintaining an optimized level of resource use. In the case of hospital systems, ensuring that patients are assigned to the proper level of care, such as an ICU, is vital for achieving an optimal trade-off between outcomes and resource use. The research team will leverage the large repository of EHR data at UPMC, along with transfer request data and actual transfer times, in order to systematically quantitate the existing discrepancies between patient state and level of care. That information can then be used to design improved transfer request policies based on patient state, expected readmission rates, and outcomes.

- **Endotypes of Thrombocytopenia in the Critically Ill**
  
  *Funded by: R21HL133891 NIH/NHLB. PIs: Clermont & Robert Parker, PhD.*

  The role of platelets is crucial in coagulation and the inflammatory response, and thrombocytopenia, or a deficiency of platelets, is a condition often seen in the critically ill. This study will investigate the dynamics of thrombocytopenia in an attempt to determine how it affects the development and outcomes of disease. The project employs a computational approach, in which the investigators will employ large electronic health record databases in order to construct clinical endotypes of thrombocytopenia and uncover how the evolution of platelet counts corresponds to mechanisms of disease. Ultimately, the research conducted by Clermont and Parker could lead to more focused therapeutic approaches for treating the critically ill.

- **Model-based Decision Support for Tight Glucose Control without Hypoglycemia**

  This proposal will use systems engineering tools to provide a robust answer to the following questions: given the characteristics of a minimally invasive glucose measuring device, what is the tightest glucose control achievable while avoiding hypoglycemia, and what is the strategy to achieve this control? We propose to use a very large multi-center dataset of critically ill patients receiving insulin, aiming to (1) calibrate and validate a mathematical model of glucose and insulin dynamics and (2) characterize between-patient variations as embodied in model parameters. Such a model will then be used to (3) design and deliver a patient-tailored decision support system, in the form of a portable interface that would forewarn clinical practitioners of potential hypoglycemic episodes and recommend insulin or dextrose dose administration. The ultimate goal of this proposal is to put all necessary tools in place for a randomized clinical trial of tight glucose control in critically ill patients, while completely avoiding episodes of hypoglycemia. It is expected that a successful completion of this proposal will have high translational impact and contribute to systems engineering science, specifically in the tailoring of sophisticated algorithms to patient-specific needs.

- **Evaluate and develop computational and conceptual processes to identify and treat critically ill patients**

  The goal of this project is to formalize an integrated monitoring and management system (IMMS). This system is designed for the use of existing and novel biosensors (clinical input data), and associated expanded emergent parameters created by interfacing these biosensor read outs with defined stressor perturbations, referred to a functional hemodynamic monitoring, identifying hemodynamic parsimony (minimal data set, sampling frequency and lead time) and progress in an interactive fashion though large animal models and human data to create a library of patterns of response defined health and, disease, specific disease processes relative to effective treatments and end-points of therapy. The IMMS product will incorporate mathematical modeling in a decision support structure to identify likelihood of instability,
potential utility of additional physiological measures, most likely effective treatment and parameters to
monitor to define treatment success and disease process resolution.

- **Predicting Patient Instability Noninvasively for Nursing Care**
  The purpose of this study is to develop multivariate models through state-of-the-art data-driven
  mathematical classification techniques and determine which models most effectively and parsimoniously
  predict cardiorespiratory instability earlier in SDU patients using noninvasively monitored vital sign,
  demographic, and clinical data domains.

- **Discovering Complex Anomalous Mappings**
  The purpose of this project is to develop and extensively test algorithms for identifying informative
  correlations between multiple streams of large multivariate data. These machine learning algorithms will
  extend the currently available set of statistical tools which fall short in producing useful predictive models in
  large disparate datasets.

- **Model-Based Decisions in Sepsis**
  The overarching goal of the program outlined in this proposal is to validate computational models of human
  sepsis using data from the ProCESS study through advanced mathematical and computational methods.
  Leveraging data and preliminary analyses from the ProCESS trial on the one hand and an extensive existing
  transdisciplinary effort at expanding existing computational models of the acute inflammatory response on
  the other will also provide an unprecedented opportunity to gain mechanistic understanding of the
  processes leading to organ failure and death, systematic recovery and unexpected failure.

- **Real-time detection of deviations in clinical care in ICU data streams**
  The research work in this proposal offers computational, rather than expert-based, solutions that build alert
  systems from data stored in patient data repositories, such as electronic medical records. Briefly, our
  approach uses advanced machine learning algorithms to identify unusual clinical management patterns in
  individual patients, relative to patterns associated with comparable patients, and raises an alert signaling this
  discrepancy.

_Cameron Dezfulian, MD_

Dr. Dezfulian is interested in ways of reducing cerebral and cardiac injury resulting from cardiac arrest. In the lab, he
has developed mouse and rat models of cardiac arrest to study the effects of nitrite, an ischemic reservoir for nitric
oxide and potent S-nitrosating agent, in achieving this organ protection. Active areas of investigation surround
signaling related to nitrite and inhaled nitric oxide through the pathways of S-nitrosation (particularly of
mitochondria), cGMP production and nitrated conjugated linoleic acid formation. Dr. Dezfulian studies these
signaling pathways within the context of two phase 2 randomized controlled trials which were funded based on his
prior pre-clinical work. These trials examine intravenous sodium nitrite and inhaled nitric oxide in out-of-hospital
cardiac arrest (OHCA) patients. Other projects under development include characterizing mechanistic differences
that account for increased brain injury in asphyxia vs cardiac etiology cardiac arrest. In collaboration with Hulya
Bayir, MD, we are characterizing the CL signature of brain (vs cardiac) injury after cardiac arrest as a novel early
biomarker and possible signaling pathway. In collaboration with Sruti Shiva, PhD, we have characterized the
generation of nitrite after remote ischemic conditioning and the mitochondrial/ROS effects of this technique. In
collaboration with Robyn Domsic, MD, we are examining the endothelial function of patient with early systemic
sclerosis and the effects of statin therapy. In collaboration with Cecilia Lo, we are examining the relationship
between nasal NO and plasma nitrite in children with congenital heart disease. Clinically, Dr. Dezfulian is interested in
aspects of post-resuscitation care which may affect these organ injuries. Current projects examine the role for
coronary intervention after cardiac arrest.
Major Projects

- **Evaluating the Effect of Oral Atorvastatin on Microvascular Endothelial Function and Raynaud in Early Diffuse Systemic Sclerosis (TAMER)**
  
  *Funded by: R21AR066305. Role, Co-I; (PI: Domsic).*

  Systemic sclerosis is a disease characterized by blood vessel injury, immune system activation and fibrosis of the skin, and internal organs; blood vessel injury is thought to be important early in the disease process. Vascular complications of systemic sclerosis include Raynaud phenomena, finger and toe ulcers, and pulmonary hypertension. This project is designed to assess the effect of oral statin drugs given over 4 months to patients with very early diffuse scleroderma on: 1) noninvasive measurements of small blood vessel function and 2) Raynaud symptoms. We hope that by targeting therapy early in the disease we may delay blood vessel changes and improve Raynaud symptoms.

- **University of Pittsburgh Undergraduate Student Research Program (USRP)**
  
  *Funded by: AHA USRP 15UFEL23750003.*

  The United States has for generations been a world leader in science and biomedical research. This position has been maintained through the farsighted support of private agencies including the American Heart Association and federal programs. Crucial to the process is the inspiration and recruitment of the next generation of ambitious and high-quality trainees. The purpose of this proposal is to expose talented undergraduate students, including women and minority students, to the art and practice of cardiovascular sciences at the University of Pittsburgh, one of the nation’s premier research institutions. The experience will partner the students with leaders in the field of vascular and cardiac sciences spanning the gamut from basic scientists to transitional and clinical investigators. The students will participate in cutting edge studies and be part of the day to day routine of top flight science. In the process, the experience will inspire and motivate these young minds to pursue biomedical and cardiovascular research.

- **Randomized clinical trial of inhaled nitric oxide after out of hospital cardiac arrest**
  
  *Funded by: NCT03079102 Mallinckrodt Pharmaceuticals, Inc. Investigator Initiated Research Award Role, PI.*

  This is a phase 2 double blind (participants and investigator) placebo controlled randomized (1:1) clinical trial of inhaled nitric oxide (iNO) 20 ppm administered over 12h beginning as soon as possible but within 4 h of return of spontaneous circulation (ROSC) from out-of-hospital cardiac arrest (OHCA). Planned enrollment is 130 subjects over 24 months at University of Pittsburgh Medical Center (UPMC) Presbyterian and UPMC Mercy with randomization stratified in blocks of 8. Recruitment will be performed under exception from informed consent (EFIC) to facilitate early enrollment and treatment. Subjects will be screened by members of the University of Pittsburgh post-cardiac arrest service (PCAS), all of whom will serve as the study co-investigators, and the Research Coordinators. Primary outcome measure is a composite of in-hospital death OR unfavorable discharge location defined as a skilled nursing facility (SNF), long term acute care (LTAC) or hospice OR New York Heart Association (NYHA) class III/IV heart failure at the time of discharge.

- **Randomized clinical trial of sodium nitrite for out of hospital cardiac arrest**
  
  *Funded by: NCT02987088 1R01HL129722-01A1 Role, Site PI [Co-I] (PI: Francis Kim).*

  This is a phase 1/2 study to determine whether administration of IV sodium nitrite is safe and efficacious during resuscitation. Phase 1 recently completed with results being organized into manuscript form. We dosed sodium nitrite IV (25 and then 60 mg) to a total of 120 subjects who suffered OHCA during CPR. Based on our results we plan a randomized trial of a two doses of sodium nitrite (45 and 60 mg) during resuscitation versus identically-appearing placebo. We plan to enroll 1500 subjects (500/treatment group). All OHCA subjects will be recruited by Seattle city and King county paramedics who will attempt cardiac resuscitation (both VF and non-VF) and with established IV access will perform standard ACLS with dosing of study drug after epinephrine. The primary efficacy endpoint will be survival to discharge and the primary safety endpoint will be assessed by measuring survival to hospital admission. Data will be collected from review of paramedic run reports and hospital records.
• **ThreadRite IV**
  
  *Funded by: Coulter @ Pitt Foundation, Role: PI.* ThreadRite IV is an invention conceived of by Dr. Dezfulian and designed in cooperation with Dr. William “Buddy” Clark (engineering), Ehsan Qaium and Dennis Wist. This device is an IV catheter which uses a novel technology to assist users in peripheral IV cannulation. The device is presently under development for human testing and a provisional patent was filed.

Jonathan Elmer, MD, MS

Dr. Elmer works to improve recovery after cardiac arrest by reducing the burden of neurological injury on these patients. His research focuses on translating existing best practice neurocritical care to this patient population, while in parallel developing and testing novel treatment strategies for anoxic brain injury.

**Major projects**

• **Quantitative electroencephalography after cardiac arrest (K23)**
  
  *Funded by: K23NS097629. Role, PI.* Brain injury is the most dreaded result of critical illness. For more than half a million Americans who suffer sudden cardiac arrest each year, current therapies are inadequate and outcomes are abysmal. Among more than 100,000 patients who regain pulses, severe global brain injury is common and the major driver of both morbidity and mortality. This is a major public health problem. This work addresses two important, potentially preventable causes of death and disability due to post-arrest brain injury. The first of these problems is secondary brain injury from ongoing tissue hypoxia and hypoperfusion in the days after resuscitation. Outcomes are further worsened by inaccurate neurological prognostication, which directly increases mortality through premature withdrawal of care in patients who might otherwise have had favorable recoveries. Quantitative electroencephalography (qEEG) is a tool that measures individual components or overall characteristics of electrical brain activity, and may help overcome both of these problems. Currently, accurate prognostication is optimal only days after arrest. This is burdensome for families, resource intensive and often leads to premature withdrawal of life-sustaining therapy in patients who would otherwise have awakened and been able to live independently had they been given more time to recover.

• **NEurologic MOnitoring and Resuscitation after Cardiac Arrest**
  
  This work is a single center prospective study evaluating the effect of comprehensive neurologic monitoring (intracranial pressure, brain tissue temperature and oxygen, jugular venous oxygen saturation, depth electrocorticography, cerebral blood flow and surface electroencephalography) and protocolized treatment on outcomes of deeply comatose survivors of cardiac arrest.

• **Intracortical electroencephalographic monitoring in high-risk survivors of cardiac arrest**
  
  This work seeks to evaluate the utility of intracortical electroencephalographic monitoring for the detection of occult seizures, spreading depolarization and early brain hypoxia in high-risk survivors of cardiac arrest.

• **Swine model of multimodal neurological monitoring and goal-directed treatment after cardiac arrest**
  
  This work translates our human research to a large animal model, allowing controlled testing of specific interventions and measurement of a range of surrogate outcome measures (serum and CSF antioxidant reserves, platelet mitochondrial function, brain microdialysis) and treatment responsiveness (e.g. reduction of spreading depolarization frequency with ketamine treatment).

• **Trajectory modeling of quantitative electroencephalography after cardiac arrest**
  
  This work applies advanced statistical modeling methods to high-resolution EEG trends derived from a cohort of over 600 post-arrest survivors. Our aim is to identify novel combinations of EEG biomarkers predictive of disease progression and clinical outcome. Specifically, this work focuses on developing multi-trajectory models that incorporated time-varying risk factors to generate iterative estimates of the posterior probability of trajectory group membership over time.
Yuliya Domnina, MD

Major Projects

- **Epidemiology of pressure ulcers in pediatric patients with heart disease: A Report from the Pediatric Cardiac Critical Care Consortium**
  
  **Role:** PI; Co-PI: Parthak Prodhan, David Cooper, Melita Viegas. **Purpose of Project** is to describe the prevalence, incidence, and risk factors of acquiring pressure ulcer injuries in congenital and acquired heart disease patients admitted to the Pediatric Cardiac Intensive Care Units participating in PC4 registry. Studies systematically examining risk factors beyond low skin assessment scores associated with acquiring a pressure in pediatric cardiac patients are lacking. Information from 23 institutions and more than 25,000 CICU encounters will be included.

- **Clinical epidemiology and center variation in chylothorax rates after cardiac surgery in children**
  
  **Role:** Co-PI. The purpose of this study is to provide a multicenter analysis of chylothorax after cardiac surgery in children. The analysis includes incidence, associated risk factors, management, and the effect of chylothorax on clinical and resource utilization-related outcomes from 4,864 surgical hospitalizations. Information from 15 institutions was included.

David Emlet, PhD

Dr. Emlet’s expertise is in cellular and molecular biology, with an emphasis on signal transduction. He has over 15 years of PhD experience, and have contributed significantly to a number of successful projects and grant applications. In 2014, Dr. Emlet was recruited as a Research Associate by Dr. John Kellum into the Center for Critical Care Nephrology to develop an in vitro model systems program to research acute kidney injury, and was promoted to Research Assistant Professor in February 2017. Dr. Emlet established an in vitro studies research program from the ground up, and have established and maintained a University-approved collaboration with the Center for Organ Recovery and Education (CORE) for the receipt and processing of human kidneys for research. Since July 2014, he has received and processed 39 human kidney samples (68 whole human kidneys) for current research and collaboration, as well as for archiving for future in vitro, proteomic, and genomic studies. He has conceived and lead or performed all of the molecular and cellular based studies that have resulted in the first publication in 2016. Additionally, by establishing and maintaining this human kidney tissue/cell resource, he has established 6 separate collaborations for research that cross a gamut of kidney-related diseases.

Major Project


  Dr. Emlet is one of the few researchers leading the molecular and cellular biology-based investigation of the potential biological role of the biomarkers IGFBP7 and TIMP2 in acute kidney injury. The group was the first to clearly identify the expression and secretion patterns of these proteins in the proximal and distal tubule cells of the kidney, and to demonstrate that they indeed are modulated by clinically relevant kidney insults, having demonstrated their modulation by oxygen/nutrient depravation and reperfusion. This is the major focus of his current research.

Lillian Liang Emlet, MD

Dr. Emlet’s areas of interest include simulation education, difficult airway management, communication skills training, and teaching palliative care medicine. Other areas of interest include mentorship of Emergency Medicine-Critical Care Medicine dually trained physicians, and fostering the collaboration of multiple disciplines to promote multi-disciplinary critical care medicine.
Major Projects

- **Observational Study of Inpatient Airway Management**
  Unfunded. Internal QI, Role: PI; Co-PI: Hernando Gómez. This study aims to review the intubations performed at UPMC and specifically of our critical care trainees to determine the rate of success, exposure, and quality of airway management in our multidisciplinary fellowship training program.

- **Simulation Use in Critical Care Medicine Education: A Scoping Review**
  Unfunded. Role: PI; Co-PI: Ilana Harwayne-Gidansky, Adrian Zurca, Deepa Malaiyandi, Arti Sarwal, Jeff Carter, Sage Whitmore. This study aims to performing a scoping review of the current state of science for simulation use in interdisciplinary delivery of critical care medicine across the spectrum of care (neonatal to adult).

**Ericka L. Fink, MD, MS**

Dr. Fink’s research focus is pediatric resuscitation, neurocritical care, and outcomes. She performed translational science in an animal model of asphyxial cardiac arrest during fellowship, and was subsequently awarded a K12 from the Pediatric Critical Care Scholar Development Program in 2006, followed with grants from the NINDS (K23) and Laerdal Foundation in June 2008 to study different durations of therapeutic hypothermia after cardiac arrest in children. For this K23, she assembled a multidisciplinary team to investigate tissue biomarkers of brain injury and novel applications of magnetic resonance imaging and spectroscopy to classify outcomes. In 2016, Dr. Fink was awarded an NIH R01 for a program titled Development of Serum, Imaging, and Clinical Biomarker Driven Models to Direct Clinical Management After Pediatric Cardiac Arrest. This multicenter study, now enrolling subjects, will validate promising brain-based biomarkers leading to a panel that will personalize the prognostication of outcome after pediatric cardiac arrest. Dr. Fink recently completed an innovative study funded by the Patient-Centered Outcomes Research Institute (PCORI). This was a multicenter randomized, controlled trial of early rehabilitation interventions vs. usual care for children with acute brain injury in the pediatric ICU. Complimenting this effort was a multinational survey of clinician approach to rehabilitation resources and outcomes assessment for critically ill children. Finally, Dr. Fink’s research focus includes pediatric brain injury in the context of global health. The Laerdal Foundation and CCM funded PANGEA, a prospective, multinational (n=107 centers) cross-sectional study of the epidemiological burden and outcomes of pediatric brain injury in critical care. The objectives of PANGEA-Developing Countries, also funded by the Laerdal Foundation, were in assessing epidemiology and outcomes of pediatric traumatic brain injury in four hospitals in Africa.

Major Projects

- **Early Rehabilitation Protocol (ERP) in the Pediatric ICU for Children with Acute Brain Injury (ABI)**
  Funded by: Patient-Centered Outcomes Research Institute (PCORI), Role: Primary Investigator. This study will (1) Perform a multicenter survey to characterize the current practices, barriers to care, and resources for physical, occupational, speech, and behavioral assessment and therapies needed for ERP implementation in pediatric ICUs; and (2) Evaluate ERP versus usual care to improve outcomes for children admitted to the ICU with ABI in a multicenter center randomized, clinical trial.

- **Development of Serum, Imaging, and Clinical Biomarker Driven Models to Direct Clinical Management After Pediatric Cardiac Arrest (Personalizing Outcomes after Child Cardiac Arrest (POCCA) study)**
  Funded by: R01 from NIH (NINDS) Role: PI. This multicenter study will validate a panel of serum, imaging, and clinical biomarkers to classify patient outcome early after out-of-hospital pediatric cardiac arrest. This work will provide clinicians, families, and researchers with superior tools to assess the severity of brain injury early after resuscitation in order to know who is at risk of disability or death and may benefit from neuroprotective interventions, to monitor response to these interventions, to plan rehabilitation strategy, and to optimize the design of research studies that test novel interventions to improve neurological outcome after cardiac arrest.
Dana Fuhrman, DO, MS

Dr. Fuhrman is a pediatric intensivist and nephrologist with an overall research interest in predicting and preventing kidney disease in children and young adults. Specifically, she is interested in establishing a method to predict a kidney’s response to stress and decline in glomerular filtration rate (GFR) over time. Dr. Fuhrman previously studied and published a method to quantify renal functional reserve in healthy young adults. She plans to determine if renal functional reserve values and differences in baseline tubular biomarkers may serve to identify a kidney with favorable ‘renal fitness’, defined by the ability to respond well to renal stress and, therefore, show a decreased risk of acute kidney injury (AKI) and chronic kidney disease (CKD). The patient population that she is currently studying is the young adult congenital heart disease population, a group of patients that are at risk for numerous kidney insults across a lifetime and the development of CKD.

Major Projects

- **Quantifying Renal Reserve in Healthy Young Adults**
  Dr. Fuhrman and colleagues published data showing a significant mean increase in GFR in healthy individuals ages 18-25 years after eating 60 grams of protein quantified with a cystatin C protocol. She subsequently studied an additional 10 healthy young adults using an iohexol infusion method in order to validate the cystatin C protocol. The results have been published in *The Journal of Renal Nutrition*.

- **Epidemiology of Young Adults with Congenital Heart Disease**
  Dr. Fuhrman is working to determine the incidence of AKI in patients 18-35 years of age with congenital heart disease admitted to the Cardiac Intensive Care Unit at the Children’s Hospital of Pittsburgh after cardiopulmonary bypass and/or cardiac catheterizations. Additionally, she plans to identify susceptibilities and exposures associated with AKI in this patient group. She is currently in the process of preparing a manuscript for publication reporting these findings.

- **Urinary Biomarkers in Healthy Young Adults as Compared to Young Adults with Congenital Heart Disease**
  Prior studies suggest that the urinary biomarkers TIMP-2, IGFBP7, IL-18, KIM-1, NGAL, beta 2-microglobin, alpha 1-microglobin, and N-acetyl-B-D-glucosaminidase may be different during times of no renal stress when comparing healthy young adults to young adults with congenital heart disease. Dr. Fuhrman is working with the CRISMA Molecular Core Laboratory to compare baseline values of these urinary biomarkers in healthy young adults as compared to young adults with congenital heart disease. She has enrolled 30 healthy young adults and 20 young adults with congenital heart disease in this study. She plans to complete a manuscript reporting these findings in the coming months.

- **International Network for Simulation-based Pediatric Innovation, Research, & Education (INSPIRE) member.** This is group of pediatric investigators across the globe working to improve the care delivered to all neonates, infants, and children, using simulation. Dr. Hamilton’s current projects have involved a survey study and scoping review related to pediatric trainee knowledge of pediatric anaphylaxis.

- **Graduate Medical Education Research Collaborative (GMERC) at UPMC.** This is a local UPMC collaborative of program directors, associate program directors, and medical educators in the UPMC GME community. Dr. Hamilton is co-founder and organizer with Dr. Julie McCausland. Currently, the collaborative meets monthly, and uses UPMC GME and faculty resources to help promote medical education research in the UPMC medical education community.
Dr. Girard's research interests include cognitive impairment after critical illness, delirium in the ICU, sedation, and liberation from mechanical ventilation. His research efforts have included a randomized clinical trial evaluating the effect of a paired sedation and ventilator weaning protocol on short- and long-term outcomes among medical ICU patients as well as a multicenter prospective cohort study of long-term cognitive impairment in survivors of critical illness. He is currently funded by the National Heart, Lung, and Blood Institute.

**Major Projects**

- **Mitochondrial determinants of cognitive outcomes in ARDS and sepsis**  
  *Funded by: NIH, NHLBI R01 HL135144-01; Role: PI.*  
  Mitochondrial dysfunction has been implicated in sepsis-induced injury of lung (i.e., ARDS) as well as heart, muscle, and kidneys, but the most metabolically vulnerable organ—the brain—remains poorly studied in this context. The goals of this project are to determine whether specific mitochondrial DNA haplogroups and related alterations in mitochondrial oxidative metabolism, systemic oxidant injury, and mitochondrial injury as well as alterations in specific metabolic pathways affected by mitochondrial dysfunction are risk factors for delirium and long-term cognitive impairment due to ARDS and sepsis.

Dr. Gómez’s research interests are centered in the pathophysiology of septic and hemorrhagic shock and the repercussions of these biologic processes on organ function. His primary project is focused on establishing the role of metabolic re-programming mitochondrial dysfunction and microvascular dysfunction in the origin of sepsis-induced organ dysfunction. He is investigating the natural metabolic response of renal tubular epithelial cells to sepsis, and re-programming of such response may alter the course of organ dysfunction. In addition, he is investigating the role of the denudation of the glycocalyx in the origin of microvascular dysfunction during sepsis, and how this microvascular dysfunction relates to the metabolic and energy profile of adjacent renal tubular epithelial cells using intravital microscopy techniques. He is exploring the effects of novel resuscitation adjuncts, like inhaled carbon monoxide, nebulized sodium nitrite and intravenous anti-histone antibodies, on organ dysfunction in the context traumatic hemorrhagic shock using a porcine model. In addition, Dr. Gómez is interested in studying the microcirculatory, mitochondrial and tissue-specific metabolic consequences of traumatic hemorrhagic shock using side-stream, dark-field microscopy and microdialysis techniques. Dr. Gómez is investigating if the use of unsupervised approaches can lead to the understanding of the natural structure of large datasets of critically ill patients, and most importantly, to identify clinically relevant phenotypes.

**Major Projects**

- **The role of energy regulation in the epithelial cell response to sepsis and the origin of multiple organ dysfunction**  
  *Funded by: NIH/NHLBI, 1K08GM117310-01A1; Role: PI.*  
  The goal of this proposal is to determine the mechanisms by which the epithelial cell re-programms metabolism to adapt to inflammatory injury, and to understand the impact of these modifications on cell and organ function, and cell survival. We hypothesize that: 1. The Sirt-1 mediated shift from the acute, glycolytic inflammatory phase to the adaptive phase is dependent on AMPK activation. 2. Activation of autophagy is necessary to limit cell death in the early inflammatory phase.

- **The role of glycocalyx shedding and platelet adhesion in sepsis-induced microvascular dysfunction**  
  *Funded by: Vascular Medicine Institute P3HVB, Supplemental Innovation Award – Department of Critical Care Medicine, Role: PI.*  
  This study aims to investigate the effect of glycocalyx shedding and platelet adhesion on microvascular flow distribution, as well as to determine if the loss of the glycocalyx is necessary for increased P-selectin-mediated platelet adhesion during sepsis. Tubular epithelial cell (TEC) injury has been found to be temporally and spatially associated with heterogeneously localized areas of sluggish microvascular peritubular blood flow, suggesting that altered microcirculatory blood flow distribution may
be a key driver of tissue injury. In support of this, sepsis has been consistently associated with endothelial activation and with profound alterations in microcirculatory blood flow distribution across multiple microvascular beds including the renal capillary network, which could constitute a key mechanism of tissue injury in the absence of macro-circulatory abnormalities. Importantly, changes in microvascular flow secondary to pathology or therapy, cannot be predicted from the assessment of macrohemodynamic parameters like arterial pressure, cardiac output or mixed venous oxygen saturation, which could explain the failure of protocolized care to affect outcome in recent trials. These observations have profound clinical implications because microcirculatory dysfunction has been consistently associated with increasing organ dysfunction and worse outcome in human sepsis, and because reversal of such microcirculatory abnormalities has been associated with organ function recovery and improved survival. Together these data not only support the involvement of microvascular dysfunction as a plausible driving mechanism of tissue injury and organ dysfunction, but also, as a mechanism susceptible of therapeutic intervention. With the support of the Vascular Medicine Institute P3HVB award, and utilizing intravital microscopy as a core tool, Dr. Gómez will determine the role of shedding of the glycocalyx and platelet adhesion on the development of microvascular dysfunction in the renal peritubular capillary system, and its association to the development of acute kidney injury during sepsis. The aims of the study will be 1) to determine if the loss of the glycocalyx is necessary for increased P-selectin-mediated platelet adhesion during sepsis; 2) to investigate if inhibition of platelet adhesion in the setting of a shed glycocalyx layer can reverse microvascular dysfunction during sepsis.

**Trans-Agency Research Consortium for Trauma-Induced Coagulopathy (TACTIC)**

*Funded by: NIH/NIGMS, UMtHL120877-01, Role: Co-I, Brian Zuckerbraun: PI.*

The TACTIC Research Program includes 10 Basic Science Projects conducted by 14 investigators across 10 different institutions, in a trans-agency partnership between the NIH and Department of Defense (DoD). This enterprise was intended to coincide with a large DoD clinical trials program to answer therapeutic questions about early administration of plasma and the use of tranexamic acid to fibrinolysis. The clinical trials will have practical implications on patient care; moreover, they provide opportunities for standardized acquisition of well-phenotyped clinical samples from civilian trauma patients in the minutes immediately following injury. The TACTIC basic science projects will utilize these biological specimens and clinical information obtained from civilian trauma patients, along with parallel studies in model systems, to advance mechanistic research in TIC. The University of Pittsburgh is one site where some of the basic science and clinical studies are being conducted. We have developed a swine model of traumatic hemorrhagic shock with the aim to determine the role of histone release from platelets or damaged tissues to the development of coagulation abnormalities and inflammation following trauma, and to investigate if the administration of anti-histone antibodies as an adjunct to therapy will result in better organ protection.

Melinda Hamilton, MD, MSc, FAHA

Dr. Hamilton is interested in research pertaining to graduate medical education and pediatric simulation. This includes multidisciplinary, and often multicenter simulation studies involving care of critically ill children in the PICU or PED. In addition, Dr. Hamilton is a co-founder of the Graduate Medical Education Research Collaborative (GMERC) here at UPMC. The goal of this collaborative is to pool our resources and interests into medical education research projects. The major goal of the group is to collaborate between education programs within the entire UPMC institution on topics for GME research and development.

**Major Projects**

- **Improving Pediatric Acute Care Through Simulation (IMPACTS) site investigator**

  This is a multicenter pediatric collaborative created to improve health outcomes and survival for acutely ill and injured infants and children through simulation-based interventions and quality improvement processes. The first phase of this work has described, measured, and compared the factors associated with high quality care of a set of simulated infant patients across a spectrum of emergency department teams. This
information will be used to develop multifaceted simulation-based education and quality improvement interventions. Dr. Hamilton coordinated the study here in Pittsburgh, wrote manuscripts, and continues to be a committee member.

- **Educators in Pediatric Intensive Care (EPIC) site investigator**
  This is a multicenter research collaborative focused on educational projects related to Pediatric Critical Care Medicine Training Programs. Past projects for which Dr. Hamilton was involved include investigation into PCCM fellow communication and leadership skills. Dr. Hamilton is study coordinator in Pittsburgh, part of the manuscript writing committee, and a committee member, active in meetings and project development.

Christopher Horvat, MD, MHA

Dr. Horvat is interested in electronic health record (EHR) data storage and retrieval for applications in clinical research and performance improvement. This work is characterized by three major elements: 1) Effectively leveraging the accumulating, granular data harbored by the EHR will bring a new era of pediatric research by increasing cohort sizes and significantly improving capabilities of covariate adjustment; 2) Pairing this data with novel biologic information, such as patient genotypes, will lead to new, personalized approaches to care; and 3) Generating reliable summaries of EHR data offers better characterization of practice patterns that can guide institutional decision making.

**Major Projects**

- **Personalized Sedation Strategies for Critically Ill Children**
  *Funding: Applications in progress.* An individualized approach to sedative-analgesic administration relies on predicting dose-response relationships of commonly used medications such as fentanyl through characterization of pharmacokinetic and pharmacodynamic profiles. Pairing EHR data with patient genotype, we previously identified ABCB1 single nucleotide polymorphism (SNP), rs1045642 genotype AA, that is associated with reduced fentanyl requirements in a diagnostically diverse sample of PICU patients. ABCB1 codes for p-glycoprotein, a xenobiotic efflux pump present in multiple tissues, including the liver, intestines, kidney, and the blood-brain barrier. As such, it is known to be a key determinant of systemic drug exposure and central nervous system disposition for several medications, including fentanyl. We also demonstrated that ADRA2A SNP rs1800544 GG is associated with greater fentanyl requirements. ADRA2A codes for alpha adrenergic receptor 2A, which is known to play a role in pain perception. We hypothesize that prospective, pragmatic characterization of fentanyl pharmacokinetic profiles and relevant clinical covariates in critically ill children using remnant laboratory samples and existing EHR data can be paired with novel pharmacogenomic factors to craft a precision approach to sedative-analgesic administration. The aims of this study are (1) Characterize fentanyl pharmacokinetic profiles of critically ill children receiving fentanyl infusions using remnant blood samples; (2) Identify clinical characteristics deterministic of fentanyl requirements in critically ill children; and (3) Identify pharmacogenomic traits deterministic of fentanyl requirements in critically ill children.

- **Electronic predictors of critical care outcomes.**
  Dr. Horvat has worked to understand electronic clinical data storage and retrieval and have conducted analyses shedding insight into clinical features of DKA that can help predict neurologic decompensation from cerebral edema. He has also worked to identify electronically retrievable biochemical characteristics of patients at high risk for mortality from inflammatory disease.

John Hotchkiss, MD

The underlying theme of Dr. Hotchkiss’ work is the application of contemporary computational and bioengineering techniques to complex biological and clinical systems. His goal is to produce computational tools that can be used to improve patient care, either directly or by guiding the application of extant or novel technologies in the clinical
setting. Foci of interest have expanded from individual patients to include healthcare facilities and networks, focusing on access and economic issues.

Major Projects

- **Simulation Approaches to Ventilator Education: Metrics and Evolution (SAVE-ME)**
  
  *Funded by: R18HS023453 AHRQ, Role: PI.*
  
  Mechanical ventilation is a complex and lifesaving medical intervention with great capacity to cause harm. Acquisition of expertise in this invasive therapy is largely experiential, slowing the acquisition of expertise, restricting the number of skilled providers, and complicating the assessment of competence. We will refine and deploy an educational simulator focusing on mechanical ventilation that is coupled to state of the art assessment tools. We will develop a database to detail patterns of care adopted by experts and novices, assess degradation of provider performance by environmental factors, and explore different approaches to accelerate the acquisition of expertise in this critical intervention.

*David T. Huang, MD, MPH, FACEP, FCCM*

Dr. Huang’s research focuses on the resuscitative and biomarker aspects of sepsis, ARDS, and clinical trials. He is the Director of the Multidisciplinary Acute Care Research Organization (MACRO), an Executive Committee member of the CRISMA Center, a funded member of the Pitt CTSI. Dr. Huang works extensively with Dr. Derek C. Angus, his mentor since his NIH T32 Fellowship, and Dr. Donald M. Yealy of the Department of Emergency Medicine.

Major Projects

- **Procalcitonin Antibiotic Consensus Trial (ProACT)**
  
  *Funded by: NIH/NIGMS 1R01GM101197, Role: PI.*
  
  This multicenter randomized-controlled trial will determine the effect of implementation of a procalcitonin algorithm on antibiotic exposure in clinically diagnosed lower respiratory tract infection in the emergency department.

- **Microbiome and Procalcitonin Long term outcomes Epidemiology (MAPLE)**
  
  *Funded by: Thermo Fisher I#0052116, Role: PI.*
  
  This research study will help answer how a new blood test (procalcitonin) can provide insight into the presence and variety of bacteria of the mouth and GI tract, and how outcomes related to those bacteria interact and change over time.

- **Prevention and Early Treatment of Acute Lung Injury (PETAL) – U. Pittsburgh Clinical Center**
  
  *Funded by: NIH/NHLBI 1U01HL123009-01, Role: Co-I, Pls: D.A. Angus, D. M. Yealy.*
  
  The PETAL network consists of approximately 11 Clinical Centers and 1 Clinical Coordinating Center (CCC), with an emphasis on early enrollment and ED-ICU collaboration. PETAL is the immediate successor to the ARDS Network (ARDSNet). PETAL will develop and conduct at least 3-5 randomized controlled clinical trials to prevent, treat, and/or improve the outcome of adult patients with, or at risk for, acute respiratory distress syndrome (ARDS).

  - **Reevaluation of Systemic Early neuromuscular blockade (ROSE)**
    
    *Funded by: NIH/NHLBI 1U01HL123009-01, Role: PI.*
    
    This study aims to assess the efficacy and safety of early neuromuscular blockade in reducing mortality and morbidity in patient with moderate-severe ARDS in comparison to a control group with no routine early neuromuscular blockade. Dr. Huang is lead author of the ROSE protocol paper.

  - **Vitamin D to Improve Outcomes by Leveraging Early Treatment (VIOLET)**
    
    *Funded by: NIH/NHLBI 1U01HL123020, Role: Co-I*
    
    To assess the efficacy and safety of early administration of vitamin D3 (cholecalciferol) in reducing mortality and morbidity for vitamin D deficient patients at high risk for ARDS and mortality.
• **Linking Investigations in Trauma and Emergency Services (LITES) Network**  
   *Funded by: Department of Defense (DoD) W81XWH-16-D-0024, Role: Co-I*  
   A research network of US trauma systems and centers with the capability to conduct prospective, multicenter, injury care and outcomes research of relevance to the Department of Defense (DoD).

**Travis C. Jackson, PhD**

Dr. Jackson's laboratory utilizes cutting edge molecular tools to discover novel apoptotic and survival signaling mechanisms in primary CNS cells with the goal to patent and advance new therapies for treatment of brain injury. Promising targets are characterized in vivo using transgenic KO mice. A current area of interest is to understand the deleterious effects of altered RNA splicing due to a dysfunctional spliceosome in brain injury, and develop strategies to repair splicing mechanisms. He is currently funded by a National Scientist Development Grant from the American Heart Association to study the role of pleckstrin homology domain and leucine rich repeat protein phosphatase 1 (PHLPP1) splice variants as targets for treatment of cardiac arrest induced global brain ischemia. He is also funded by an R21 from the National Institutes of Health to study the role of RNA binding proteins (key nuclear splicing factors) in traumatic brain injury (TBI).

**Major Projects**

- **FGF21 Activates RBM3 and is a Novel Drug to Revolutionize Temperature Management**  
   *Funded by: NIH, NINDS, R21 NS098057-01A1; Role: PI.* Cold-shock protein RNA binding motif 3 (RBM3) as a key mediator of cognitive and histological benefits associated with deep cooling in models of neurodegenerative disease. Dr. Jackson reported that fibroblast growth factor 21 (FGF21), a hormone involved in torpor in hibernating mammals, augments cooling induced upregulation of RBM3 in primary rat neurons (Jackson et al., 2015). This proposal is investigating the ability of FGF21 to augment TH induced neuroprotection in the setting of neuronal/brain injury.

- **Pharmacological inhibitors of PHLPP1: Novel Therapies to Treat Brain Injury after Cardiac Arrest**  
   *Funded by: American Heart Association Scientist Development Grant (14SDG20210000), Role: PI.* This study is examining the role of pro-death protein Pleckstrin homology domain and leucine rich repeat protein phosphatase 1 (PHLPP1) in the setting of global cerebral ischemia. Dr. Jackson is currently testing if a novel small-molecule PHLPP inhibitor (NSC74429) decreases CA1 hippocampal neuronal death following asphyxia CA (ACA) or ventricular fibrillation (VF) CA in rats.

- **2',3'-cAMP in Traumatic Brain Injury**  
   *Funding: NIH, NINDS, 1R01NS87978; Role: Co-I (Co-PIs, Edwin K. Jackson and Patrick M. Kochanek).* This study is examining the role of 2',3'-cAMP metabolism in the setting of TBI. Dr. Jackson's contribution to this project involves training (e.g. teaching technicians on culture techniques and lentivirus production), data collection, data interpretation, manuscript preparation, and attending team meetings.

**New Grant Under Review**

- **The Role of RNA binding Motif 5 in Traumatic Brain Injury**  
   *NIH, NINDS, R01; Role: PI.* This new application seeks to continue Dr. Travis Jackson’s research on the role of RBM5 in TBI. This new grant will study the role of RBM5 in vivo using novel conditional KO mice which were created during the course of a highly productive preceding R21 on the same topic (i.e. a 2yr exploratory NIH R21 which recently expired; NIH/NINDS grant R21NS088145).

**Ruchira Jha, MD**

Dr. Jha’s research focus is on cerebral edema using traumatic brain injury as a model. Her specific interest is on a pathway involving sulfonylurea receptor-1 and evaluating the role of this pathway from multiple translational angles in human subjects as well as animal models. She is also exploring this and related pathways in other neurological
diseases that involve cerebral edema such as cardiac arrest, ischemic stroke, and subarachnoid hemorrhage. Her current work is supported by the NIH KL2 TR001856 grant.

Major Projects

- **Characterization of the role of Sulfonylurea Receptor (SUR1) in cerebral edema in a combined injury mouse model of controlled cortical impact and hemorrhagic shock**
  This project involves evaluation of attenuation of cerebral edema by SUR1 blockade using the existing FDA approved medication, Glyburide/Glibenclamide. A temporal-spatial map of Surr1 expression is also being generated.

- **Investigating whether SUR1 is measurable/quantifiable in human cerebrospinal fluid from patients with severe traumatic brain injury**
  We have demonstrated that it is feasible to quantify SUR1 protein in human CSF in traumatic brain injury. Levels are undetectable in controls, and elevated in traumatic brain injury. The trajectory of Surr1 appears to correlate with measures of cerebral edema. Current studies are ongoing in a larger cohort of patient to validate our findings.

- **Investigating the impact of genetic polymorphisms in the SUR1 gene (ABCC8) on the development of cerebral edema in patients with severe traumatic brain injury**
  Our work has revealed multiple single nucleotide polymorphisms (SNP) that are associated with measures of cerebral edema and outcomes. The goal of this project is to explore the potential functional significance of these SNPs. This work has expanded to include TRPM4 SNPs (associated with ABCC8).

Jeremy M. Kahn, MD, MS

Dr. Kahn’s research program focuses on the organization, management, and financing of critical care services in the United States. Specific areas of interest include ICU workforce and staffing, quality measurement, telemedicine, and regionalization of critical care. His work integrates approaches from the fields of epidemiology, health services research, health economics and organizational psychology to investigate novel strategies for increasing the quality and efficiency of critical care.

Major Projects

- **Contributors to Effective Critical Care Telemedicine (ConnECCT)**
  *Funded by: NIH, NHLBI R01 HL120980, Role: PI, Co-Is: Derek Angus, Marilyn Hravnak, Tina Batra Hershey.*
  Intensive care unit telemedicine uses audio-visual technology to provide critical care from a remote location. Although telemedicine has great promise, particularly in small rural hospital, many ICU telemedicine programs fail to improve outcomes, leaving clinicians with little guidance about how and where to best apply this technology. In this project, Dr. Kahn and his team are using both qualitative and quantitative research methods to understand the organizational factors that contribute to successful telemedicine programs and develop a “toolkit” to help hospitals effectively use telemedicine to improve the quality of critical care.

- **Determinants of Effective Long Term Acute Care (DELTA)**
  *Funded by: NIH, NHLBI R01 HL120980, Role: PI, Co-Is: Derek Angus, Nicholas Castle, Tina Batra Hershey.*
  Long-term acute care hospitals (LTACHs) provide specialty inpatient care to patients Recovering from severe acute illness. However, little is known about to organize and manage in order to optimize care for these high-risk, high-cost patients. In this project, Dr. Kahn and his team are using a mixed-methods approach to look with within LTACs to identify the factors associated with improved survival for patients with chronic critical illness.
• **Novel approaches to benchmarking hospitals on their critical care mortality**  
  *Funded by: NIH, NHLBI R01 HL126694, Role: PI, Co-Is: Derek Angus, Chung-Chou Chang.*  
  The lack of robust performance measures for the care of critically ill patients is a major hindrance to ICU comparative effectiveness research, particularly research in how to optimally design regional systems of care. In this project Dr. Kahn’s team is using state-of-the-art statistical modeling approaches to develop novel critical care performance measures that account for the complex trajectories of acutely ill patients through the health system, addressing a key barrier to progress in the fields of comparative effectiveness research.

• **Understanding Intensive Care Team Effectiveness and Dynamics (UNITED)**  
  *Funded by: NIH, NHLBI K24 HL133444, Role: PI.*  
  This mid-career development award provides protected time and resources for Dr. Kahn to mentor the next generation of organizational scientists in critical care. Supported by this grant, Dr. Kahn is developing new lines of research related team science, focusing on how interprofessional care teams collaborate to provide critical care most effectively and efficiency. His mentees, which includes medical students, residents, post-doctoral fellows, and junior faculty, are building off these resources to receive research training and mentorship in critical care implementation science.

• **Experimental therapeutics in critical illness**  
  *Funded by: NIH NHLBI, T32HL007820, Role: Principal Trainer, Principal Investigator: Pinsky.*  
  The major goal of this project is to further train physician scientists to more thoroughly understand the science of organ dysfunction and its consequences in critical illness. Trainees focus on the biology of acute severe illness and its response to therapy in inter-related levels of investigation: (1) immunobiology and the cellular basis for organ injury; (2) organ systems modeling; and 3) clinical and health services research.

A. Murat Kaynar, MD, MPH

Dr. Kaynar’s overarching research program continues to focus on the long-term effects of sepsis and acute respiratory distress syndrome (ARDS). He is studying the role of zinc and matrix metalloproteinases (MMP) to elucidate their role in sepsis and ARDS, with the subsequent aim of applying the findings to the management of these diseases. Recently, he added a Drosophila model of sepsis to his armamentarium to dissect the long-term outcome after sepsis (*Cost of surviving sepsis: a novel model of recovery from sepsis in Drosophila melanogaster, Intensive Care Med Exp. 2016*). This model provides the added advantage of an innate immunity-only model system. His work involves small animal models of the aforementioned diseases and he has recently published in the *American Journal of Respiratory and Critical Care Medicine, Journal of Critical Care, PlosOne, and American Journal of Respiratory Cell and Molecular Biology*. He was awarded an R01 at the end of FY15 to study zinc in mouse models of pneumonia, and progress is encouraging, with Dr. Kaynar’s team having developed a novel model of resolution of sepsis in Drosophila with promising preliminary work in mice towards a follow-up competitive grant. Along the same line of long-term effects of acute inflammatory events, Dr. Kaynar is exploring the role of intra-operative anesthetic variables (mechanical ventilation, types of anesthesia) in the operating room to outcomes in patients using data from anesthesia electronic medical records. This work aligns with his role as the program director of the anesthesiology critical care medicine fellowship and quality initiatives in which he took part in the Departments of Anesthesiology and Critical Care Medicine.

Major Projects

• **Combined Viral and Bacterial Infection and Zinc Homeostasis in Distal Lung**  
  *Funded by: R01HL126711 NIH/NHLBI, Role: PI.*  
  This project is focusing on the role of zinc in resolution of pneumonia (H1N1 and S. aureus) in mouse models. The current project is also aligning with an ongoing clinical trial.

• **Aerobic Glycolysis and Long-Term Outcomes from Sepsis**  
  *Funded by: UPP Foundation Grant 2017, Role: PI.*  
  Cost of Surviving Sepsis. This recently-funded project uses a Drosophila model of sepsis to explore inflammation, functional impairment, metabolic derangements, and lifespan in the recovery phase of sepsis. The preliminary data have been translated to a mouse model.
• Neutrophil Collagenase in Sepsis and Ventilator Induced Lung Injury  
  *Funded by: K08 NIH, Role: PI.* The primary goal of this career development award (K08) is to develop a better understanding of the mechanisms of sepsis leading to more effective therapies for patients. Although the grant is completed, Dr. Kaynar is planning to expand it to a follow-up grant.

• Cardiovascular Consequences of Infection and Sepsis  
  *Funding: BaCoCoR (CTSI Basic to Clinical Collaborative Research Pilot Program), Role: PI.* This recently completed project is exploring cardiovascular disease in sepsis survivors, from the standpoint of the immune response.

• MMP Polymorphisms in sepsis  
  *Role: PI.* The project’s primary goal is to bridge the bench findings of animal models of sepsis to the available large data set of human sepsis established in the Department of Critical Care Medicine.

• Long-term effects of mechanical ventilation in minimally invasive esophagectomy  
  *Role: PI.* The project’s primary goal is to test the hypothesis that high intra-operative tidal volumes lead to increased 28- and 90-day mortality.

John A. Kellum, MD, MCCM

Dr. Kellum’s research focuses on translational research and personalized medicine for critical illness. He has organized a multidisciplinary team of investigators to study novel approaches to the treatment of sepsis, to understand the pathogenesis of acute kidney injury and to explore novel interventions for acute kidney injury. He directs the Center for Critical Care Nephrology, which integrates the work of epidemiology and health service research with studies of basic mechanism of disease and new methods of treatment. The Center’s research has a focus on fluid, electrolyte, acid-base and renal disorders in the critically ill and injured. His group has publications in the *New England Journal of Medicine*, *JAMA*, *Lancet*, and *Archives of Internal Medicine*, among others. Dr. Kellum’s program has enjoyed federal funding since 2003 and has active research grants from multiple NIH institutes and HRSA.

Major Projects

• **Phenotyping REnal Cases in Sepsis and surgery for Early Acute Kidney Injury (PReCISE AKI)**  
  *Funded by: National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) UG3DK114861*  
  *PIs: J Kellum, P Palevsky, M Rosengart.* This project, as part of the KPMP consortium, seeks to study patients with AKI including obtaining biopsies for interrogation, careful clinical and molecular phenotyping, and long-term follow-up.

• **Biomarkers Effectiveness Analysis in Contrast Nephrology (BEACON)**  
  *Funded by: National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) R01DK106256*  
  *PI: R Murugan; Co-Is: J Kellum, P Palevsky, F Pike, S Weisbord.* The main objective of this proposal is to advance NIDDK’s mission of early detection, risk-stratification, and prognostication of CIAKI. It will provide new scientific knowledge on using biomarkers to monitor patients undergoing angiography and will have a high impact on clinical practice, physicians, and policy makers.

• **Sepsis Endotyping Using Clinical and Biological Data**  
  *Funded by: National Institute of General Medical Sciences (NIGMS) R35GM119519.*  
  *Pl: C Seymour; Co-Is: J Kellum*  
  The major purpose of this project is to translate findings form "big data" in the EHR and efficiently enrolled biologic specimens into generalizable bio-types for enrichment strategies in future clinical trials and EHR alerts.
• **Inflammation Phenotypes in Pediatric Sepsis Induced Multiple Organ Failure**  
  *Funded by: National Institutes of Health (NIH), 1R01GM108618. PI: Carcillo; Co-Is: J Kellum.* Presently, we direct therapy to killing the germ and supporting organ function while ignoring inflammation. Our study will document whether inflammation is related to failing organs. This insight will provide evidence for a paradigm shift to investigate use of inflammation directed therapies to reduce child morbidity and mortality from sepsis.

• **Transforming the Medication Regimen Review Process of High-Risk Drugs using a Patient-Centered Telemedicine-Based Approach to Prevent Adverse Drug Events in the Nursing Home**  
  *Funded by: National Institutes of Health Agency for Healthcare Research and Quality, R18HS024208. PI: Gill; Co-Is: J Kellum.* The major goal of this project is to conduct a cluster-RCT, to determine the impact of patient-centered telemedicine-based medication reviews on ADE reduction in four nursing homes.

• **Late cardiovascular consequences of septic shock**  
  *Funded by: National Institute of General Medical Sciences (NIH/NIGMS), R01GM097471-01A1. Role: Co-I, Principal Investigator: Yende.* The work proposed will extend our preliminary work and address four questions. First, with what frequency, and in which patients, does the delayed immune resolution observed at discharge persist beyond discharge? Second, what might be the cause for delayed immune resolution? Third, are particular immune pathways more strongly associated with cardiovascular outcomes? Fourth, do early sepsis interventions have long-term beneficial effects?

• **Discover and Validation of Biomarker of Acute Kidney Injury and Dialysis Recovery**  
  *Funded by: Astute Medical Inc. PI: Kellum.* The specific aims of the program are to conduct a series of clinical trials that will be used to support development and commercialization of diagnostic assays for the early detection and risk stratification of acute kidney injury and recovery.

• **Epidemiology and Outcomes of Catecholemine-Resistant Hypotension in Critically Ill Patients**  
  *Funded by: La Jolla Pharmaceutical Co. PI: R Mururgan; Co-Is: J Kellum.* Using a large dataset of critically ill patients admitted to the intensive care units at the University of Pittsburgh Medical Center, we will examine the epidemiology and various phenotypes of CRH and its association with outcomes.

• **Adjudication of Acute Kidney Injury and Etiology**  
  *Funded by: BioPorto Diagnostics, PI: J Kellum.* Major goal of this project is to develop a method of adjudication for Acute Kidney Injury (AKI) (presence or absence) and most likely etiology in critically ill patients; determine the rates AKI using the methods developed in aim 1 on data derived from a new clinical trial; provide input on the design and analysis of the clinical trial especially with regard to outcome adjudication.

• **Investigation of the relation between individual patient characteristics and the occurrence of different stages of acute kidney injury and clinical outcome after cardiovascular surgery**  
  *Funded by: Astellas Pharma PI: J Kellum.* The project will identify and characterize clinical parameters associated with the occurrence of Acute Kidney Injury (AKI) within 72 hours and first 7 days after cardiovascular (CV) surgery and the subsequent clinical outcomes such as Major Adverse Kidney Events (MAKE), death and dialysis at 30, 90, and 180 days.

**Major Projects – Recently Completed (Federal)**

• **Protocolized Goal directed Resuscitation of Septic Shock to Prevent AKI (ProGReSS AKI)**  
  *Funded by: National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) R01DK083961. PI: J Kellum; Co-Is: P Palevsky, F Pike, S Yende.* The major goal of this project is to examine the natural history of Acute Kidney Injury arising in patients with sepsis. Sepsis is found in more than 50% of critically-ill patients with AKI.
Hyung Kook Kim, MD

Major Projects

- **Selepressin Evaluation Programme for Sepsis-Induced Shock – Adaptive Clinical Trial (SEPSIS-ACT)**
  
  *Funding: FerringPharmaceutical; Role: Site PI*

  This study is a double-blind, randomized, placebo-controlled, phase 2b/3 adaptive clinical trial investigating the efficacy and safety of selepressin as treatment for patients with septic shock. The primary objective is to demonstrate superiority of selepressin plus standard care versus placebo plus standard care in the number of vasopressor and ventilator-free days in patients with vasopressor-dependent septic shock.

Nahmah Kim-Campbell, MD

Major Projects

- **The role of cell-free hemoglobin in acute kidney injury after pediatric cardiopulmonary bypass**

  This is an ongoing prospective observational study designed to determine the independent association of cell-free hemoglobin with acute kidney injury which is a common and problematic morbidity associated with extracorporeal therapies. The role of cell-free hemoglobin needs to be evaluated amongst other risk factors for AKI including but not limited to age, gender, bypass duration, cross-clamp duration, surgical complexity, blood prime, ischemia/reperfusion.

- **Use of an animal model of extracorporeal therapy to help determine the mechanism behind acute kidney injury**

  An animal model of extracorporeal therapy (essentially a rodent version of veno-arterial ECMO) has been established over the past couple of years at the Safar center. This model is valuable because very little data is available in terms of the exact mechanism behind the kidney injury that occurs during and after extracorporeal therapies. This is, in part, because of the lack of indications for and actual data related to the information that can be gained from humans after a kidney biopsy (histopathology, cell death, etc.). Once the degree and type of cellular injury is established in this model, targeted therapies (against cell-free hemoglobin production and cell-free hemoglobin associated oxidative injury) will be tested.

Patrick M. Kochanek, MD, MCCM

Dr. Kochanek’s research addresses studies in experimental and clinical traumatic brain injury (TBI) and cardiopulmonary arrest (CA) across pediatric and adult arenas. He has mentored trainees at all levels for 30 years, many of whom are NIH funded and/or have gone on to careers of national prominence. His work focuses on the secondary injury response in TBI and CA and the development of novel therapies and biomarkers. His work involves pre-clinical and clinical investigations. He has pioneered the concept of multi-center, multi-model, pre-clinical therapeutic and biomarker screening in TBI through his involvement as principal investigator of Operation Brain Trauma Therapy (OBTT). OBTT represents a partnership between civilian and DoD investigators to produce the first pre-clinical multicenter consortium evaluating novel therapies and biomarkers for TBI across multiple models. OBTT is a groundbreaking approach to multicenter preclinical investigations in TBI as evidenced by its publications, its recognition by others in major publication and editorials, and through numerous invited lectures across disciplines such as stroke and spinal cord injury. Dr. Kochanek has also been PI of a T32 titled Training in Pediatric Neurointensive Care and Resuscitation Research since 2000. It has supported training a number of highly successful faculty in pediatric neurocritical care and resuscitation. He is the primary mentor for three junior faculty members (Travis Jackson, PhD, Ruchira Jha, MD, and Cameron Dezfulian, MD), along with T32 fellow Jessica Wallisch. Dr. Kochanek was also one of the five editors of the 7th edition of the Textbook of Critical Care, published by Elsevier in 2017. He received the Lifetime Achievement Award from the SCCM in 2017.
• **Operation Brain Trauma Therapy**  
  *Funded by US Army W81XWH-10-1-0623, Role: PI; Co-I: C. Edward Dixon, PhD; Statistical Consultant: Stephen R. Wisniewski, PhD.* Dr. Kochanek is the head of a $7 million multicenter pre-clinical drug screening consortium for the United States DoD titled OBTT. The consortium includes investigators at the University of Pittsburgh, The University of Miami (Miami project to cure paralysis), Walter Reed Army Institute of Research, the Virginia Commonwealth University, the University of Florida, Messina University in Sicily, and Banyan Biomarkers, LLC. OBTT is testing therapies across multiple TBI models and species to define a potent therapy for TBI for ultimate use in combat casualty care. The focus is on drugs that are FDA approved for other uses and thus could be rapidly translated to clinical trials. In each therapeutic study, the consortium is also testing serum and/or plasma biomarkers of brain injury for theranostic utility.

• **Operation Brain Trauma Therapy Extended Studies**  
  *Funded by US Army W81XWH-14-2-0018.* Role: PI; Co-Is: C Edward Dixon, TC Jackson, Samuel Poloyac, PharmD, PhD. Based on the success of OBTT, the United States DoD funded an additional $2.99 million for supplemental investigations by the OBTT consortium, to expand its drug testing and include higher risk drugs that may have the potential for high reward. The same investigative team as OBTT is involved supplemented by additional support in pharmacology/pharmacy.

• **Training in Pediatric Neurointensive Care and Resuscitation Research**  
  *Funded by the NIH (National Institute of Child Health and Human Development, T32 HD 040686).* Role: PI; Co-directors: Robert Clark, MD, and Anthony Kline, PhD. Acute life-threatening insults in children such as TBI and CA are leading causes of morbidity and mortality. Injury to the central nervous system from these insults is the key determinant of outcome. These insults require a multidisciplinary and multi-departmental response that must be coordinated from the field through to rehabilitation. Research training in pediatric neurointensive care and resuscitation is best served by a parallel multidisciplinary and multi-departmental program. Our unique postdoctoral program at the Safar Center for Resuscitation Research, supported by a T32 since 2000, establishes important links across the continuum of care of brain injured children and facilitates rigorous scientific investigation across the key disciplines including PCCM, neurology, neurological surgery, emergency medicine, neonatology, radiology, and physical medicine and rehabilitation. We train fellows in these pediatric disciplines in basic and clinical research in neurointensive care and resuscitation. The research focus is on injury mechanisms, novel therapies, and outcomes after TBI and CA. We capitalize on the unique interaction between the Safar Center and the training programs at Children's Hospital of Pittsburgh and the University of Pittsburgh School of Medicine. The research areas of each mentor ask important questions, suitable for career development and hypothesis testing. We integrate a curriculum in neurointensive care and involvement on a unique pediatric neurocritical care clinical service.

• **2',3'-cAMP in TBI**  
  *Funded by NIH R01NS087978, Role: Dual PI with Edwin Jackson, PhD, Co-I: C. Edward Dixon, PhD, Travis Jackson, PhD.* Drs. Kochanek and Jackson, using studies in cell culture and a mouse model of TBI, are elucidating which CNS cell types produce 2',3'-cAMP, what kinds of injury trigger 2',3'-cAMP production, how 2',3'-cAMP is transported out of cells, how downstream AMPs are converted to adenosine, and if manipulating the 2',3'-cAMP-adenosine pathway alters secondary damage after TBI. The overall hypothesis is that the “2',3'-cAMP-adenosine pathway” is an endogenous cytoprotective mechanism after TBI.

• **Research by Dr. Kochanek as a Co-investigator on NIH- or US DoD funded projects, for PIs within the department of CCM and in other departments.** This includes the following grants:  
  - Oxidative Lipidomics in Pediatric TBI (Hülya Bayır, MD, PI)  
  - ADAPT Trial – Approaches and Decisions in Acute Pediatric TBI (Michael Bell, MD PI)  
  - CYP 450-mediated CBF Dysregulation and Neurotoxicity in Pediatric CA (Mioara Manole, MD, PI)  
  - Emergency preservation and resuscitation (EPR) (Samuel Tisherman, MD, PI, University of Maryland)  
  - Novel Approaches to Screening for Inflicted Childhood Neurotrauma (Rachel Berger, MD, MPH, PI)
- Mapping Lipid Oxidation in Traumatic Brain Injury by Mass Spectrometric Imaging (Hülya Bayır, MD, and Valerian Kagan, PhD, Dual PIs)
- Mitochondria-Targeted Redox Therapy for Cerebral Ischemia in the Developing Brain (Hülya Bayır, MD, and Robert Clark, MD, Dual PIs)
- Targeted Evaluation Action & Monitoring of TBI (TEAM-TBI) (David Okonkwo, MD, PhD, PI)
- The mRNA splicing factor RBM5: A new therapeutic target for TBI (Travis Jackson, PhD, PI)
- FGF21 Activates RBM3 and is a Novel Drug to Revolutionize Temperature Management (Travis Jackson, PhD, PI)
- Early Rehabilitation Protocol in the Pediatric ICU for Children with Acute Brain Injury (Ericka L. Fink, MD, PI)
- Development of Serum, Imaging, and Clinical Biomarker Driven Models to Direct Clinical Management after Pediatric Cardiac Arrest (Ericka Fink, MD, PI)
- Multifunctional Rehabilitative Therapy to Reduce Alzheimer Pathology after TBI (Milos Ikonomovic, PhD, PI)
- CYP 450-mediated CBF Dysregulation and Neurotoxicity in Pediatric Cardiac Arrest (Miora Manole, MD, PI)

• Research mentoring of Extramurally Faculty by Dr. Kochanek

Dr. Kochanek is the primary faculty mentor of Dr. Ruchira Jha, who is supported by a new K23 award; Dr. Travis Jackson, who is funded by a new R21; Dr Cameron Dezfulian, who is funded by a grant from Mallinckrodt Pharmaceuticals and a subcontract on an R01 at the University of Washington; and T32 fellow Jessica Wallisch, who is funded by NICHD and the Laerdal Foundation for Acute Medicine.

Jiuann-Huey Ivy Lin, MD, PhD

Dr. Lin’s research interests include understanding the mechanism and processes of congenital heart diseases (CHD). Mice, derived from ENU mutagenesis and CRISPR/cas9 gene editing, are utilized to understand various forms of CHD. Recent endeavors include exploring the mechanisms of endocytic vesicle trafficking proteins, LRP1/LRP2, that have been associated with various CHD phenotypes including malalignment, outflow tract anomalies and septation defects (Project 1,2). In addition to the ENU mouse models, Dr. Lin is working on solidifying the hypoplastic left heart syndrome mouse model using CRISPR mouse lines (Project 3).

Major Projects

- LRP1, an endocytic vesicle trafficking protein, is associated with congenital heart defects, an unexplored pathway

Congenital heart diseases (CHDs) are the most common congenital defect and are the leading causes of neonatal death which affect over 2 million children and adults in the United States. Despite a strong indication of genetic contribution to CHDs, the developmental processes and genetic etiology are poorly understood. This largely reflects the difficulty in conducting genetic studies in the human population. Given the difficulties with human genetic analysis, we used a large-scale forward genetic screen of inbred mice chemically mutagenized with ethyl-nitrosourea (ENU) to uncover the genetic etiology of CHDs. From this large-scale screen, we uncovered mutations in endocytic trafficking genes, including LRP1 (lipoprotein receptor protein 1), associated with CHD. Endocytosis plays an important role in modulating cell signaling by regulating the internalization, recycling, and degradation of receptor-ligand complexes. LRP1 regulates the trafficking of the internalized endocytic vesicles to different endosomal compartments, with some destined for fusion with lysosomes and degradation, while others are recycled to the surface by recycling endosomes. Mutations in LRP1 cause a spectrum of CHDs comprising of outflow tract abnormalities and alignment defects. Supporting the findings from the LRP1<sup>−/−</sup> mutant mice, we also identified rare LRP1 coding variants in patients with CHD. With the support of her recent funded AHA award, Dr. Lin will test the hypothesis of abnormal endocardial to mesenchymal transition (EMT) will result in endocardial cushion defects in the LRP1<sup>−/−</sup> mice. LRP1 is ubiquitously expressed in all developing organs and is expressed in multiple cell
lineages required for cardiac development. Mutations in LRP1 result in embryonic lethality and multiple developmental abnormalities, including cardiovascular defect, omphalocele, craniofacial abnormalities and abnormal vessels formation. To delineate the crucial role of LRP1 in different cell lineages, conditional gene ablation with several tissue-specific LRP1 mutants to identify the necessity of LRP1 for normal SHF, cardiac neural crest, and endocardial cushion development.

- **LRP2, an endocytic vesicle trafficking protein, is associated with Truncus arteriosus**
  From a large-scale forward genetic screen of inbred mice chemically mutagenized with ethyl-nitrosourea (ENU), we identified mutation in lipoprotein receptor protein 2 (LRP2) associated with truncus arteriosus which correlated with LRP2 knockout phenotype. To delineate the pathway responsible from the phenotype, changes in gene expression in the isolated outflow tract within LRP2<sup>m/m</sup> and controls will be investigated. Tissue-specific LRP2 mutants in different cell lineages for cardiac development demonstrated ablation of LRP2 in anterior heart field (AHF) recapitulate the phenotype of LRP2<sup>m/m</sup> indicate the critical role of LRP2 during cardiac development.

- **HLHS – Generate a mouse model for hypoplastic left syndrome**
  This project aims to develop a mouse model using 3 different genes, HNRNPAB, NRD1 and CYGB, with mutations induced by CRSPR/cas9. These proteins appear to be integral in engineering a transgenic mouse and recuperating the human hypoplastic left heart syndrome phenotype. This project still in its breeding infancy.

Alejandro Lopez-Magallon, MD

Major Projects

- **Telemedicine in pediatric critical care patients supported by ECMO**
  *Role: PI. Mentor: Ricardo Munoz.* Mechanical cardiopulmonary support with extracorporeal membrane oxygenation (ECMO) is an invaluable tool during medical care of critically ill children with imminent or present cardiopulmonary collapse due to systemic or cardiac disease, but significant expertise is needed to maximize results and decrease complications. Furthermore, associated financial costs remain substantial. Telemedicine has demonstrated to be an excellent tool to deliver a wide array of health-related services, and may enable a faster improvement in the performance of remote ECMO teams with the resultant reduction of costs for patients, their families and health-system. The current research of Dr. Lopez-Magallon, and the tele-CICU team at Children's Hospital of Pittsburgh, is to explore the relationship of telemedicine-assisted interventions in outcomes from a pediatric ECMO program in the international setting.

- **Adverse events prevention for single ventricle infants in the CICU with artificial intelligence algorithms**
  *Role: co-PI. Mentor: Ricardo Munoz.* Children and adults with congenital heart disease (CHD) are a very diverse and complex patient population presenting a challenge to medical teams. Their survival and quality of life will vary depending on the medical approach by specialized physicians, but even in the most expert hands, potentially catastrophic events (e.g., cardiac arrest, emergent intubation, ECMO cannulation) are common and frequently present without anticipation. Infants with single-ventricle physiology are a particularly vulnerable population, and at the same time these patients are not prone for adverse event prevention with algorithms developed for the general pediatric population. With the currently CHP funded Cardiac Intensive-Care Unit Warning Index (C-WIN), Dr. Lopez Magallon is participating with the teams from CHP and the University of Pittsburgh to develop an artificial intelligence algorithm with self-learning capabilities with the aim to anticipate and avert adverse events in these very sick patients.

- **Therapeutic plasma exchange as adjuvant therapy in children with heart disease and multi organ dysfunction syndrome**
  *Role: Co-I. Mentor: Ricardo Munoz.* The overall reported survival rate to hospital discharge for pediatric cardiac patients supported by ECMO ranges from 38% to 73%, with good functional results. However, a
distinct subset of very sick patients presents with clinical manifestations of multiple organ dysfunction syndrome (MODS), not unlike those observed in non-cardiac patients with MODS or thrombocytopenia-associated multi organ failure (TAMOF). Dr. Lopez Magallon's, and the CICU team at CHP, current research aims are review their institutional experience with the use of therapeutic plasma exchange in children with heart disease and MODS while on ECMO in anticipation of targeted interventions during a prospective multicenter RCT.

Florian B. Mayr, MD

Major Projects

- **Towards precision medicine for improving long-term outcomes after sepsis**
  *Funded by: In preparation, Role: PI.* Sepsis, defined as a severe infection that results in life-threatening organ failure, is a significant public health burden that affects over 1 million Americans annually. Despite recent improvements in short-term mortality, long-term outcomes remain poor: a third die within 90 days, and of those who survive, many experience exacerbation of pre-existing chronic diseases, leading to frequent rehospitalizations and premature death. Early identification of patients at high risk for poor long-term outcomes may help clinicians initiate early interventions to improve their quality of life and reduce unplanned readmissions. The goal of this project is to use machine-learning to identify subgroups of sepsis survivors with similar characteristics (phenotypes) and predict common outcomes including premature death and cause-specific unplanned readmissions. I will subsequently design and simulate an adaptive platform trial that will test multiple phenotype-specific interventions.

- **Home-based palliative care intervention to reduce unplanned hospital readmissions in Veterans after critical illness**
  *Funded by: VAPHS, Role: PI.* This project is a quality improvement project to assess whether a high intensity home-based palliative care intervention in Veterans with recent admission to the ICU for pneumonia, COPD, heart failure or sepsis have lower 30-day unplanned readmission rates compared to Veterans treated with usual post hospitalization care. 15 Veterans will be enrolled into the pilot study and outcomes will be compared to 30 propensity matched controls.

- **A Phase 1b/2a, Randomized, Double-Blinded, Placebo-Controlled, Multicenter Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of BMS-936559 in Subjects with Severe Sepsis**
  *Funded by: Bristol-Myers Squibb, Role: Site PI.* The purpose of this study is to evaluate the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) and potential efficacy signal of a single dose (range 10 to 900 mg) of the programmed cell death-1 (PD-1) ligand monoclonal antibody BMS-936559 in subjects with severe sepsis.

- **Randomized, Double-Blind, Parallel Group Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of BMS-936558 (Nivolumab) in Participants with Severe Sepsis or Septic Shock.**
  *Funded by: Bristol-Myers Squibb, Role: Site PI.* The purpose of this study is to evaluate the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of two different doses (480mg vs. 960mg) the programmed cell death-1 (PD-1) monoclonal antibody BMS-936559 in subjects with severe sepsis or septic shock.

Deepika Mohan, MD MPH

Dr. Mohan is interested in how doctors make decisions for their patients. Most quality improvement efforts assume that doctors weigh information about the patient, knowledge of best practices, external incentives, and system constraints. Her clinical experience as a surgical resident and critical care fellow suggest that other variables influence decision making, particularly under conditions of time-pressure. She is using behavioral science methods,
such as signal detection theory, to identify these variables and to design novel interventions that might reduce variability in care.

Major Projects

- **Developing a novel intervention to recalibrate physician heuristics in trauma triage.**
  Funding: DP2LM012339, NIH New Innovators Award (Role: PI). The goal of this program is to improve the quality of care provided to trauma patients. Trauma disproportionately affects the young and healthy, consuming over $400 billion annually in direct medical costs and lost productivity. Treatment of severely injured patients at high-level academic centers reduces mortality, improves functional outcomes, and increases the cost-effectiveness of care. For the last 40 years, stakeholders have intervened at the system- and provider-level to right-size care: severely injured patients receive treatment at trauma centers, while minimally injured patients receive treatment at non-trauma centers. Despite these efforts, almost 50% of all severely injured patients receive their care at non-trauma centers (under-triage), in part because of physician decision making.

  Our research suggests that emergency medicine physicians rely on intuitive judgments (heuristics) when triaging patients. Heuristics allow rapid decision making, under conditions of time-pressure and uncertainty. However, when poorly calibrated, they result in predictable errors. Heuristics do not respond to traditional didactic programs, which may explain why existing quality improvement efforts have failed. One of the most promising techniques for recalibrating heuristics involves serious games, interactive computer applications that allow structured role-playing in virtual environments. Researchers in threat detection have successfully used serious games to recalibrate the heuristics of baggage screeners at the Transportation Security Administration.

  We plan to test the hypothesis that we can use a similar strategy to recalibrate the heuristics of emergency medicine physicians. Improving adherence to trauma triage guidelines will improve the care provided to the 2 million patients hospitalized after injuries each year. Additionally, trauma represents a specific type of decision – one where physicians act under conditions of time-pressure and uncertainty. Other examples include the early management of patients with acute myocardial infarction, stroke, and sepsis. Better understanding of how to modify physician decision-making in trauma may have broader applicability to other clinical conditions.

**Raghavan Murugan, MD, MS, FRCP, FCCM**

Dr. Murugan is a core faculty and member of the executive committee of the Center for Critical Care Nephrology and has authored more than 60 peer reviewed publications. His research interests include acute kidney injury, sepsis, fluid overload, biomarkers, and inflammation-induced organ dysfunction after critical illness. Dr. Murugan is also a recipient of the National Institute of Health’s KL2 career development award as well as an R01 to study biomarkers in contrast induced acute kidney injury. Dr. Murugan employs a highly innovative and paradigm shifting approaches from systems biology, biostatistics, bioengineering, epidemiology, and translational methods to understand complex dynamics of critical illness, develop hypotheses, and examine new therapies in critical illness

Major Projects

- **Biomarker Effectiveness Analysis in Contrast Nephropathy (BEACON)**
  Funded by: R01 DK106256-01A1, Role: PI; Co-Is: Steven Weisbord, John Kellum, Paul Palevsky, Joyce Chang.
  Contrast-induced acute kidney injury (CIAKI) is a serious complication occurring in patients with chronic kidney disease undergoing angiography and is associated with adverse renal and cardiovascular outcomes. We have been recently funded by the Department of Veterans Affairs to conduct a multicenter, randomized, clinical trial in 7,680 high-risk patients undergoing angiography to compare the effectiveness of intravenous sodium bicarbonate with isotonic sodium chloride, and oral N-acetylcysteine with placebo, for the prevention of serious adverse outcomes associated with CIAKI. The NIDDK has funded an associated
biorepository to examine known and yet-to-be identified biomarkers for CIAKI. We propose to leverage these resources to conduct an ancillary observational study entitled Biomarker Effectiveness Analysis in Contrast Nephropathy (BEACON). Aim 1 will examine the accuracy of urinary TIMP-2, IGFBP7, and select other plasma biomarkers in predicting the composite renal outcome of death, dialysis dependence, or persistent renal injury at day 90 after contrast exposure (1a); biomarker reclassification of risk for adverse renal outcomes and develop a risk score (1b); and predicting the progression of chronic kidney disease (1c). Aim 2 will examine the accuracy of urinary TIMP-2 and IGFBP7 in predicting the composite outcome of hospitalization with acute coronary syndrome; heart failure; cerebrovascular accident; or all-cause mortality within 90 days (2a); and biomarker reclassification of risk for cardiovascular events (2b).

- **Phenotyping REnal Cases In Sepsis and surgery for Early Acute Kidney Injury (PReCISE AKI)**
  
  *Funded by: RFA-DK-16-026: Kidney Precision Medicine Project—Recruitment Sites (UG3/UH3). Role (Co-I) Kellum JA, Palevsky PM, Rosengart M (Multi-PIs).* This application is in response to RFA-DK-16-026: Kidney Precision Medicine Project—Recruitment Sites (UG3/UH3). Specifically, this application entitled PReCISE AKI (Phenotyping REnal Cases In Sepsis and surgery for Early Acute Kidney Injury) seeks to enroll patients with Early Acute Kidney Injury (AKI) as well as to contribute to enrollment of patients with established AKI as part of the UG3/UH3 consortium. The specific aims include to obtain biopsies from patients with a range of AKI syndromes in a safe and ethical manner, to test the hypothesis that specific clinical phenotypes of AKI have differing biopsy findings, and to determine whether biopsy findings can predict early resolution and subsequent risk for CKD.

- **Epidemiology and Outcome of Catecholamine Resistant Hypotension in Critically Ill Patients**
  
  *Funded by: La Jolla Pharmaceuticals Company Inc., Role: PI; Co-Is: John Kellum, Gilles Clermont. This study comprises a retrospective cohort study using a large, heterogeneous population (n~45,000) of critically ill patients admitted to the ICU over an 8-year period at the University of Pittsburgh Medical Center. It will determine epidemiology and outcomes associated with catecholamine-resistant hypotension in critically ill patients.*

- **Adjudication of Acute Kidney Injury and Etiology**
  
  *Funded by: Bioporto Diagnostics Inc., Role (Co-I) Kellum (PI), Palevsky PM (Co-I). Major goal of this project is to develop a method of adjudication for Acute Kidney Injury (presence or absence) and most likely etiology in critically ill patients using an observational study.*

- **Fluid Balance and Outcomes**
  
  *Unfunded, Role: PI. The goal of this project is to examine the epidemiology of fluid overload in critically ill patients and examine association between intensity of ultrafiltration and outcomes in patients receiving renal replacement therapy.*

- **Evaluation of MDW for Early Detection of Patients Having or Developing Sepsis Pivotal Trial**
  
  *Funded by: Beckman Coulter, Role: Blinded Adjudicator. The objective of this study is to validate the utility of Monocyte Distribution Width (MDW) to detect sepsis in a multi-center large prospective study of ED adults who have CBC ordered upon presentation, and to validate the cut-off value established in the feasibility trial which was established with the goal of maximizing sensitivity at an optimal level of specificity. Septic patients are identified as those with values equal to or above the MDW threshold and non-septic patients are those with MDW values below the threshold.*

- **A randomized, double-blind, placebo-controlled, four-arm, parallel group, proof of concept, and dose-finding adaptive phase 2a/2b study to investigate the safety, tolerability and efficacy and effect on quality of life of human recombinant alkaline phosphatase in the treatment of patients with sepsis-associated acute kidney injury**
Funded by: AM Pharma, Role: Site Investigator. Sepsis is a leading cause of AKI and is associated with increased risk of death. Alkaline phosphatase is an endogenous enzyme present in many cells and organs that exerts detoxifying effects through dephosphorylation of endotoxins including extracellular adenosine triphosphate. There is increasing evidence that the protein plays a significant role in host defense and innate immunity, particularly against inflammatory reactions due to lipopolysaccharide (LPS) release. Dr. Murugan is a site investigator for this multicenter, randomized, double-blind, placebo-controlled, four-arm, parallel-group, proof of concept, and dose-finding adaptive phase 2a/2b study to investigate the safety, tolerability and efficacy and effect on quality of life of human recombinant alkaline phosphatase in the treatment of patients with sepsis-associated AKI.

- A phase 3, placebo-controlled, randomized, double-blind, multi-center study of angiotensin II infusion in patients with catecholamine-resistant hypotension
  
  Funded by: La Jolla Pharmaceuticals Company Inc., Role: Site Investigator. Catecholamine-resistant hypotension is an often a fatal condition resulting from an underlying cause such as septic shock, trauma, or severe drug reactions. Approximately, 6-7% of patients will require excessive doses of vasopressors and will be deemed to be resistant. Angiotensin II is a hormone produced by the renin angiotensin aldosterone system that modifies blood pressure via regulation of vascular smooth muscle tone and extracellular fluid homeostasis. As a site investigator of this phase 3, placebo-controlled, randomized, double-blind, multi-center study, Dr. Murugan is investigating the role of angiotensin II infusion in patients with catecholamine-resistant hypotension.

Michael R. Pinsky, MD, Dr hc

Dr. Pinsky’s work spans various aspects of critical care medicine but centers on hemodynamic monitoring based on cardiopulmonary physiology, sepsis and acute organ dysfunction and focuses on using machine learning principles to diagnose and treat critical illness. Since 198, he has organized multidisciplinary teams of investigators to study novel approaches to the diagnosis of left and right ventricular dysfunction, circulatory shock, long-term outcome form critical illness, complexity modeling of critical illness and the use of complex modeling feedback to diagnose and treat critical illness in humans.

Dr. Pinsky’s Cardiopulmonary Research laboratory integrates the work of computation biology, health service research and minimally invasive hemodynamic monitoring to understand the basic mechanism of cardiovascular collapse and response to therapies in all forms of circulatory shock. Recent research foci have been on endothelial dysfunction, mitochondrial dysfunction and microcirculation imaging in trauma, sepsis and hemorrhagic shock in porcine models; pattern recognition of physiologic responses to defined stressors, and microcirculatory and mitochondrial injury and repair. Other research interests include the use of integrated monitoring systems to improve recognition of cardiorespiratory instability and highly invasive human models assessing both left and right ventricular dysfunction prior to left ventricular assist device insertion.

Major Projects

- Experimental therapeutics in critical illness
  
  Funded by: NIH NHLBI, T32HL007820, Role: Principal Trainer, Principal Investigator: Pinsky. The major goal of this project is to further train physician scientists to more thoroughly understand the science of organ dysfunction and its consequences in critical illness. Trainees focus on the biology of acute severe illness and its response to therapy in inter-related levels of investigation: (1) immunobiology and the cellular basis for organ injury; (2) organ systems modeling; and 3) clinical and health services research.

- Machine Learning of Physiological Variables to Predict Diagnose and Treat Cardiorespiratory Instability (MLADI)
  
  Funded by: NIH NIGMS 1R01GM117622-02, Role: PI; Co-Is: Marilyn Hravnak, Gilles Clermont, Artur Dubrawski. If one could accurately predict who, when and why patients develop shock then effective preemptive treatments
could be given to improve outcome and more effectively use healthcare resources. But signs of shock often occur late once organ injury is already present. The purpose of this study is to first develop multivariable models through data-driven classification techniques to parsimoniously predict cardiovascular insufficiency, etiology and response to treatment.

- **Predicting patient instability noninvasively for nursing care (PPINNC)**  
  *Funded by: NIH, NRI R01 NR013912-01, Role: PI; Co-PI: Marilyn Hravnak; Co-Is: Gilles Clermont, Artur Dubrawski.*  
  This study aims to mine the existing clinical database of one year’s continuous non-invasive vital sign data base from one step-down unit to create identification algorisms based on machine learning to identify earlier cardiorespiratory insufficiency, stability and vital sign artifact with a high degree of specificity.

- **Microvascular alterations in severe hemorrhagic shock**  
  *Funded by: NIH, NHLBI 5-K12 HL109068-03; Role: Mentor; PI: Hernando Gómez; Mentors: John A. Kellum, Brian Zuckerbraun.*  
  This study uses porcine and murine models of sepsis and circulatory shock to study the link between mitochondrial dysfunction and its microcirculatory changes asking which comes first or do both occur at the same time.

- **The Role of Energy Regulation in the Epithelial Cell Response to Sepsis and the Origin of Multiple Organ Dysfunction**  
  *Funded by: NIH, NIGMS 1K08GM117310-01A1; Role: Mentor; PI: Hernando Gómez; Mentors: John A. Kellum, Brian Zuckerbraun.*  
  Sepsis, a syndrome estimated to affect 750,000 people in the United States and about 19 million people worldwide every year, presents high mortality rates that have been consistently associated with increasing organ dysfunction. Efforts are needed to better understand the mechanisms by which sepsis causes organ dysfunction, because this will lead to the identification of more effective and targeted diagnostic, preventive and therapeutic strategies. By establishing the role of known cellular defense mechanisms in sepsis-induced organ dysfunction, this project will provide key evidence, fundamental to developing such strategies that will improve the care for the critically ill patient and reduce mortality.

- **Trans-Agency Research Consortium for Trauma-Induced Coagulopathy (TACTIC)**  
  *Funded by: NIH DoD NHLBI 1 UM1 HL120877-01, Role: Co-I; Overall PI: Kenneth Mann. Project 9: “Trauma-induced endothelial injury and inflammation that results in coagulopathy and end-organ damage”; Co-Is: Brian Zuckerbraun, Hernando Gómez.*  
  This large program project grant focuses on the pathophysiologic mechanisms for trauma-induced coagulopathy. Our project is to examine the endothelial injury as measured by cell surface receptor expression, activation of coagulation cascades and microcirculatory changes.

- **Developing Goal-Directed Perfusion Therapy for Neurocardiac Injury in Sub-Arachnoid Hemorrhage**  
  *Funded by: NIH NHLBI 2-R01 HL074316-06-At, Role: Co-I; PIs: Marilyn Hravnak, Robert Friedlander; Co-Is: Yuefang Chang, John Gorcsan, Paula Sherwood, Samuel Poloyac, Brian Jankowitz.*  
  This clinical observational trial measures the multiple cardiovascular changes associated with the initial sub-arachnoid hemorrhage injury asking the question: Does neurogenic cardiac injury occur during sub-arachnoid hemorrhage and to what extent is it minimized by neuroprotective therapies.

**Armando James Rotondi, PhD**

Dr. Rotondi’s research program focuses on the continuity of care and how to improve the long-term outcomes of patients with severe chronic illness, including once they are discharged from the hospital. This research program has involved five related areas: understanding the influences of family caregivers’ on patient long-term outcomes; identifying the unmet needs of both patients and their family caregivers while in the hospital and once back in the community; designing long-term therapies and services for both patients and caregivers; designing innovative ways to use e-health technologies (e.g., websites, smart phones, interactive voice response systems, home telemedicine devices) to improve availability of treatments, support, and continuity of services; and developing designs and
design models to reduce the cognitive load and meet the cognitive needs of individuals with chronic illnesses, including those with severe mental illness, and cognitive impairment. He is also involved in research on the design and evaluation of Medical Emergency Teams, and the dissemination of a program to promote uncontrolled donation after cardiac death.

Major Projects

- **Rapid Adaptation of Treatments to Optimize Chronic Illness Management and Community Recovery in Schizophrenia**
  
  *Funded by: VA HSR&D, Project Number LIP 72-089. Role: Principal Investigator; Haas GL, Kasckow J.*

- **Questionnaire Development: Knowledge of Appropriate Illness Self-Management in Schizophrenia**
  
  *Funded by: VA HSR&D, Project Number: LIP 72-089. Role: Principal Investigator; Haas GL, Kasckow J.*

- **E-Health Delivery of Social Skills Training to Veterans with SMI**
  
  *Funded by: Veterans Administration, Center for Health Equity Research, Pilot Grant, Role: Principal Investigator; Haas G, Glynn S, Kasckow J, Mueser K, Spring M, Hanusa B. The goal of this study is to conduct a 2-arm randomized controlled trial of delivering social skills training (SST) via a web-based intervention (term e-SST) vs. treatment as usual (TAU).*

- **Secure Messaging Impact on Access: A Supported Adoption Intervention**
  
  *Funded by: Veterans Administration, Office of Telehealth Services/Connected Health, and Quality Enhancement Research Initiative (QUERI), eHealth Program Evaluation Initiative, Role: site Principal Investigator. The goal of this study is to evaluate the impact of communication through secure messaging on Veteran's access to VA healthcare and well-being. The goal of this project is to evaluate the impact, in a 2-arm randomized trial, of a Supported Adoption Intervention on veterans’ utilization of, and communications via, secure messaging. Outcomes will include utilization of VA healthcare, and well-being.*

- **Comparison of e-health vs in-person delivered family psychoeducational treatment**
  
  *Veterans Administration, Health Services Research and Development, Role: PI; Co-Is: Haas G, Glynn S, Kasckow J, Chinman M, Spring M, Hanusa B. The goals of this study are to conduct: (1) a 2-arm randomized comparative effectiveness trial of an e-mental health treatment (termed the Daily Support Website) vs. the standard for care, an in-person treatment (termed Multi-Family Group Psychoeducation); and (2) exploratory secondary analyses to identify Veteran and family individual characteristics that are associated with decreased levels of psychiatric symptoms and caregiver burden.*

- **Online Treatments for Mood and Anxiety Disorders in Primary Care**
  
  *Funded by NIMH. Depression and anxiety are common in primary care practice and are associated with substantial reductions in health-related quality of life. This project will test the comparative effectiveness of two on-line treatments for these conditions provided through the context of a Collaborative Care program: (1) moderated access to a proven-effective computerized cognitive behavioral therapy (CCBT) program; versus (2) moderated access to CCBT plus an Internet support group (CCBT+ISG). The Project will also compare the effectiveness of these treatments to PCPs’ "usual care" for these conditions, and evaluate the adoption and maintenance of CCBT+ISG by practices following the conclusion of the trial to provide a greater understanding of how to best scale the delivery of these interventions into a variety of primary care settings.*

Joan Sanchez-de-Toledo, MD, PhD

**Major Projects**

- **Inflammatory response associated to CPB and its relationship with end organ perfusion**
  
  *Kidney Injury*

Redefining AKI criteria that will apply to our pediatric population – Retrospective analysis of more than 2500 patients with renal function and diuresis data. Status: Data has been collected. Manuscript preparation.

Heart-Brain interactions


Incidence of Acute neurologic events in the CICU. This is a retrospective analysis over more than 1,500 CICU admissions looking at the incidence of acute neurologic events and their associated factors. Paper submitted to Pediatrics.

Analysis of the quality of life of patients who survived after a cardiac arrest and extracorporeal resuscitation. This is a retrospective analysis of all patients that underwent ECPR at our institution. A prospective evaluation of their quality of life was undertaken 3 years after hospital discharge.

• Respiratory Ciliary Dysfunction and Pulmonary Risks in Congenital Heart Disease Patients,” Funded by: W81XWH-15-1-0649 Department of Defense; PI: Cecilia Lo, 9/30/2015 to 9/29/2018

• Point of Care Ultrasonography

Implementation of the ultrasound program in the ICU, in particular the utility of lung ultrasonography in the Intensive Care Unit and of a new composite score using point of care ultrasonography to better identify readiness for extubation.

Jennifer B. Seaman, PhD RN

Dr. Seaman is a nurse scientist committed to advancing the field of primary palliative care, in particular improving care for critically-ill intensive care unit patients and their families by bringing evidence-based palliative care practices to the bedside. Her current work focuses on interventions to ensure timely interdisciplinary family meetings in the ICU.

Major Projects

• Ensuring Timely Interdisciplinary Family Meetings in the ICU; Development and Testing of a Nurse-led Intervention

Funded by: Cambia Health Foundation, Role: PI; Mentors: Robert Arnold, Douglas White. This study aims apply principles of implementation science and organizational behavior to findings from our preliminary studies in order to develop and pilot test a scalable nurse-led intervention to ensure timely interdisciplinary family meetings in the ICU.

• Survey of Barriers, Facilitators, Practices and Processes of Care Associated with the Conduct of Interdisciplinary Family Meetings in the ICU

Funded by: CCM Innovation Grant; Role: PI; Mentors: Douglas White, Robert Arnold. The goal of this study is to survey, via on-line or telephone, a representative national sample of ICU medical directors and nurse managers about barriers, facilitators, practices and care processes related to the conduct of interdisciplinary family meetings in the ICU.

Christopher W. Seymour, MD, MSc

Dr. Seymour’s research program focuses on early recognition and treatment of those with acute illness, particularly sepsis. Specifically, he seeks to develop a research and acute care paradigm for prehospital sepsis similar that for acute cardiovascular disease, and develop novel strategies in the emergency department. He has been awarded
grants from the National Institutes of Health, Society of Critical Care Medicine, American Heart Association, MedicOne Foundation, the Surgical Infection Society, and the University of Pittsburgh CTSI. His science has been published in the New England Journal of Medicine, JAMA, and the American Journal of Critical Care Medicine.

Major Projects

- **Sepsis Endotyping Using Clinical and Biological Data**
  *Funded by NIH/NIGMS (R35GM119519), Role: PI, beginning 8/2/2016.* This project proposes to leverage our clinical translational laboratory to derive and validate novel sepsis endotypes using bioinformatics methods in electronic health record (EHR) data linked to a biorepository of residual blood. This innovative program of research translates findings from “big data” in the EHR and efficiently enrolled biologic specimens into generalizable bio-types for enrichment strategies in future clinical trials and EHR alerts. The program will be supervised by an external advisory board of experts in endotyping, inflammation, and computational and systems biology, while promoting the independence of my clinical-translational laboratory and mentoring of junior scientists.

- **Estimating the National Burden of Sepsis Using Electronic Health Record Data**
  *Funded by: Harvard Pilgrim Health Care/CDC, sub-award, Role: PI, (Michael Klompas, overall PI) (Project period: 9/30/2015 – 6/30/2016)* The major purpose of this project is to estimate the current national burden of sepsis and septic shock using electronic clinical data, characterize trends in sepsis incidence and mortality using electronic clinical data from diverse hospitals and compare the incidence, agreement and mortality rates of EHR-based sepsis surveillance definitions versus the SCCM/EICM's forthcoming clinical sepsis definitions and traditional claims-based definitions.

- **Prediction of High Risk Sepsis During Prehospital Care**
  *Funded by the NIH/NIGMS as a K23 Career Development, Role: PI.* This project has two aims: (1) to link a regional database of prehospital records of more than 21 EMS agencies to the UPMC electronic health in CERNER. Using more than 3 years of data, this large clinical/administrative dataset allows detailed study of prehospital exposures, organizational characteristics and interventions on patient-centered outcomes. (2) to conduct a prehospital cohort study in collaboration with Pittsburgh City EMS to measure a panel of prehospital biomarkers to identify those at greatest risk of sepsis and death. The dataset for Aim 1 is complete and undergoing analysis, and the cohort study in Aim 2 recently completed enrollment of more than 450 EMS patients with prehospital blood sampling.

- **Immune Regulation by RNA Metabolites in Severe Sepsis**
  *Funded by the University of Pittsburgh CTSI, this Basic to Clinical Collaborative Research Pilot Program, Role: PI.* This project is a collaboration with Dr. Melanie Scott in the Department of Surgery studying how plasma RNA metabolites may act as damage associated molecular patterns in severe sepsis. The will use state of the art techniques to measure global metabolic profile of patients at risk for organ dysfunction in sepsis, and pair these human studies with in vitro work to explore how RNA metabolites may alter the immune system. Current analyses with Metabolon Inc. are analyzing 12 matched pairs of critically ill, septic patients with and without organ failure for their global metabolomics profile. Validation will occur in samples banked during the ProCESS randomized trial (NEJM, 2014)

- **Is Very Early-goal Directed Therapy Superior to Early-goal Directed Therapy in Septic Shock?**
  *Funded by the Surgical Infection Society, Role: Co-PI.* This project aims to use a cecal ligation and puncture murine model of prehospital sepsis to determine whether early administration of fluids and/or antibiotics is associated with improved survival. In a collaboration with Dr. Matt Rosengart from the Department of Surgery, the project uses continuous physiologic monitors embedded in the peritoneum of mice to wirelessly determine the point of illness severity at which the mouse would call “911.” We then randomize in our factorial experiment to test our treatment approaches. This is key preliminary data for an upcoming prehospital human clinical trial.
Major Projects

- **Evaluation of Implementation of a National Point-of-care Ultrasound Program Training**
  Despite its potential advantages, POCUS has not been universally adopted in healthcare due to limited numbers of providers trained in use of POCUS. This project will evaluate the effectiveness of an immersive POCUS training course developed by the VHA’s Simulation Learning, Education and Research Network (SimLEARN) on provider skill acquisition and retention, frequency of use, and identify barriers/facilitators to POCUS use at participating VHA facilities. Pre- and post-course testing will be used to assess acquisition of knowledge and technical skills to perform POCUS exams. Post-course testing for knowledge and skill retention, and frequency of use, will be performed 6 months after the training course with a secondary objective to identify the effect of the POCUS Training Course and implementation facilitation on facility-level frequency of POCUS use. Data collection is presently ongoing.

- **Focused Evaluation with echo for New Onset Anuria and Oliguria (FENA)**
  Oliguria is a common and multifactorial reflection of organ dysfunction in the acutely-ill patient. Ultrasonography allows for rapid bedside assessment of organ function. To date, no standardized protocol has been published to assess the etiology of oliguria. Using five previously validated US windows, the investigators have developed a protocol to evaluate the cause of oliguria. The standardized sequence has been designed to allow for rapid determination of post-renal, pre-renal and intra-renal causes of oliguria (Focused Evaluation for New onset Anuria or oliguria- FENA). The resultant protocol is intended to be quick to perform with minimal training and high reliability and accuracy. Data collection is presently ongoing.

- **Teaching vs. Learning: The impact of deliberate practice and formative feedback on developing POCUS skills**
  This study is being done to evaluate the impact of creating an ultrasound image portfolio on the acquisition of cognitive and psychomotor skills required for trainees to learn Point of Care Ultrasonography (POCUS). The development of an image portfolio requires deliberate practice by the trainee as well as providing direct and indirect formative feedback aimed at enhancing the skills of image acquisition and interpretation accuracy through longitudinal learning. We hypothesize that this more longitudinal approach to ultrasound education, with practice and feedback, is key to achieving competence in these skills. We designed a stepped wedge study to examine the effects of this educational intervention on our fellows’ acquisition of both cognitive and psychomotor POCUS skills. Data collection is presently ongoing.

- **Ultrasonographic Measurement of Optic Nerve Sheath Diameter as a Non-invasive Means to Assess Patients for Intracranial Hypertension**
  Diagnosis of raised intracranial pressure (ICP) is a challenge for clinicians, as the established diagnostic tests have significant shortcomings. Assessment of intracranial pressure via ultrasonographic measurement of optic nerve sheath diameter (ONSD) is a promising technique that has attracted much research in the past decade. It is inexpensive, non-invasive, rapid, and can be performed at a patient’s bedside with evidence suggesting that ultrasonography of ONSD has high discriminative value. Herein, we seek to use a prospective cohort convenience sample design of patients already scheduled to receive therapeutic or diagnostic lumbar puncture to assess the dynamics of ICP change through pre- and post- measurements of their ONSDs in comparison to their opening and closing pressure measurements as well as amount of cerebral spinal fluid removed. Data collection is presently ongoing.

Lori Shutter, MD

Dr. Shutter’s research focus is the area of traumatic brain injury and neurocritical care, with a special interest in spreading depolarizations and advanced neuro-monitoring. Since 2016, she has published articles in *Neurocritical Care, Critical Care Medicine, Brain Imaging and Behavior, Neurosurgery, NeuroImage*, and *Cerebral Blood Flow &*
Metabolism. She actively participates in guideline development for the management of neurocritical care patients, and has served as a co-author of the Brain Trauma Foundation’s Guidelines for Management of Severe Traumatic Brain Injury (2007 & 2016), the Neurocritical Care Society’s Guidelines on Medical Management of Subarachnoid Hemorrhage (2011) and Management of Status Epilepticus (2012), and the Society of Vascular and Interventional Neurology’s Developing practice recommendations for endovascular revascularization for acute ischemic stroke (2012).

Major Projects

- **Stroke Hyperglycemia Insulin Network Effort (SHINE) Trial Protocol**
  *Funded by: NIH (through the NETT) 1U10NS069498, Role: PI.* The major goal of this project is to determine if using IV insulin to treat high blood sugar in patients after an acute ischemic stroke will result in better recoveries when compared to the current standard of care for blood sugar management.

- **Neurological Emergencies Treatment Trial (NETT) Network Pittsburgh Clinical Hub**
  *Funded by: NIH/NINDS 5U10 NS080371-03, Role: Co-I; Site PI: Cliff Callaway.* The University of Pittsburgh has extensive resources and expertise in studying emergency conditions, and specifically neurological emergencies and aims to provide infrastructure and reduce start-up time for the testing treatments of neurological disorders and will facilitate the performance of clinical trials and preselect clinical sites with specific expertise relevant for specific types of trials.

- **Developing Goal-Directed Perfusion Therapy for Neurocardiac Injury in Sub-Arachnoid Hemorrhage**
  *Funded by: NIH 1R01NR014221-01A1, Role: Co-I; PI: Marilyn Hravnak.* The study goal is to develop perfusion goal-directed therapeutic recommendations for SAHMI patients based upon the optimal hemodynamic parameters associated with better patient functional outcomes.

- **HOPES: Hypothermia for Patients Requiring Evacuation of Subdural Hematoma: a Multi-center, Randomized Clinical Trial**
  *Funded by: UT Health, Role: Co-I; Site PI: David Okonkwo.* The primary objective of HOPES is to determine if rapid induction of hypothermia prior to emergent craniotomy for traumatic subdural hematomas (SDH) will improve outcomes as measured by Glasgow Outcome Scale-Extended (GOSE) at 6 months.

- **Targeted Evaluation, Action & Monitoring of Traumatic Brain Injury**
  *Funded by: USAMRAA W81XWH-14-2-00020, Role: Co-I; Site PI: David Okonkwo.* The goal is to confirm efficacious targeted therapies for TBI and provide deployable protocols and technology for large-scale cost-effective diagnosis and management.

- **Improving Clinical Decisions for Critically Ill Traumatic Brain Injury Patients**
  *Funded by: NICHD 1K23HD080971-01A1, Role, Co-I and mentor; PI: Susanne Muehlschlegel.* The goal is to apply shared decision-making principles to the critically ill traumatic brain injury patient, and develop decision aide tools to use in this setting.

- **SDII: Development and Validation of Spreading Depolarization Monitoring for TBI Management**
  *Funded by: DoD DMRDP W81XWH-13-PH-TBIRA; Role: Co-I; Site PI: David Okonkwo.* The objective is to develop quantitative data processing algorithms for automated bedside detection of spreading depolarizations (SD) in non-invasive EEG recordings that can be applied to all TBI patients, and to characterize SD across the spectrum of mild-moderate-severe TBI patients to determine its relevance to neurologic outcomes.
Matthew Siedsma, MD

Dr. Siedsma’s research interests focus on creating and investigating novel education strategies within critical care medicine for use by medical students and house staff trainees. This includes applying contemporary pedagogical models such as asynchronous learning and flipped learning to critical care specific education. He utilizes computer and model based simulation to then test the efficacy of knowledge translation from these pedagogical models.

Major Projects
- **Creation of a novel critical care curriculum for use across multiple residency programs differing in base specialty and training year as well across multiple hospital sites**
  This is a unique challenge requiring the investigation of critical care education needs of residents in multiple specialties (internal medicine, emergency medicine, anesthesia, neurology, general surgery, obstetrics and gynecology) across multiple training levels (PGY-1 through PGY-5) and across multiple hospital sites (Presbyterian University Hospital, Montefiore University Hospital, Mercy, and Magee). To accomplish this, he explores the needs of the residents in each specialty and during each year of their training as well as the expectations of their educational program leadership and the expectations of their specialty boards. He is further challenged as these residents are spread across 4 separate hospitals. To overcome the first set of obstacles he has performed a needs assessment of each of the residency programs by discussing the needs perceived by the residents in various training levels and the program leadership. He is now analyzing these needs assessments to determine areas of commonality that will allow him to build a common core curriculum in critical care medicine, then will involve a panel of experts from our department that will involve members of these various specialties to ensure that there is agreement and buy in. We will then begin to develop the curriculum via a combination of asynchronous learning and flipped learning methods to be delivered in a 4-week block. Finally, Dr. Siedsma plans to test the efficacy of such a curriculum via simulation performance in three to five key areas. Ultimately, he will develop a fully modular curriculum that includes intermediate and advanced topics in critical care medicine as appropriate for more senior trainees that is also targeted to their specific base specialties.

David J. Wallace, MD MPH

Dr. Wallace's research focuses on structure, process and outcome relationships in critical care delivery, with the goal of improving regional care for time-sensitive medical emergencies. He is in the third year or a four-year K08 award from NIH/NHLBI. Dr. Wallace recently received a notice of grant award for an R03 through NIH/NHLBI. Dr. Wallace has an RWJF application under review (PI: Wallace), with notification expected in September 2017.

Major Projects
- **Referral Regions for Time-Sensitive Acute Care Conditions in the United States.**
  *Funded by: NHLBI K08 HL122478, PI: Wallace.* The overall goal of this project is to empirically evaluate the mortality benefit of regionalized critical care for patients requiring mechanical ventilation. To do so he will take advantage of existing variation in regional care patterns - regions currently vary in the degree to which care for mechanically ventilated patients is centralized in high volume hospitals. Using innovative geographical tools and state-of-the-art hierarchical statistical modeling, he will (a) define novel referral regions for mechanical ventilation; (b) identify the regional determinants of care centralization within these regions; and (c) determine the relationship between regional care centralization and patient outcomes. Together, the results will provide clinicians and policy makers with essential tools to develop, implement and refine regionalized care systems for mechanically ventilated patients.

- **Causes and Effects of Hospital-Level Changes in Intensive Care Bed Supply**
  *Funded by: NHLBI R03-HL-16-020, PI: Wallace.* The overall goal of this project is to determine the causes and effects of hospital-level changes in the number of ICU beds from the perspectives of key decision makers. To accomplish this goal, he will conduct and analyze semi-structured interviews with administrators from
hospitals with increasing, unchanged and decreasing intensive care bed supply. To understand the interplay between local and regional factors we will employ a novel, context-driven sampling frame that samples hospitals across regions with overall increasing, unchanged and decreasing ICU bed supplies. The study has two specific aims: (1) Determine the causes of hospital-level changes in the number of ICU beds, and (2) Evaluate the effects of hospital-level changes in the number of ICU beds. Successful completion of these aims will produce new insight into how changes in ICU infrastructure may affect operations, financial metrics and clinical outcomes, providing new hypotheses and guiding future research projects examining organizational strategies to improve the care of patients with critical illness.

- **Accessing Critical Care and Emergency Service Systems (ACCESS) Maps**
  
  *Funded by Department of Critical Care Medicine, PI: Wallace.* The overall objective of the project is to create the preferred online service for evaluating, comparing, and planning the delivery of critical care and emergency services worldwide. Such a resource is urgently needed, as an integrated catalogue of hospital locations, emergency medical service locations and their respective capacities is not available in the majority of countries. Where information is available, it is often years out of date, greatly reducing its value. ACCESS MAPS will include information from three data sources: internet-sourced, crowd-sourced, and publicly available databases. ACCESS MAPS will inform decisions by policy analysts, public health planners, and disaster relief workers.

**Douglas B. White, MD, MAS**

Dr. White directs the University of Pittsburgh Program on Ethics and Decision Making in Critical Illness. His research program encompasses both empirical research on and normative ethical analysis of decision-making for patients with life threatening illness. He has several ongoing NIH funded studies and a strong research infrastructure for the implementation and assessment of behavioral health interventions. He has published widely using both quantitative and qualitative methods to examine the process of medical decision making in intensive care units. In conducting this work, he collaborates with a multi-disciplinary group of investigators, which includes faculty with expertise in bioethics, law, philosophy, sociology, biostatistics, and health services research.

**Major Projects**

- **Family Support Intervention in Intensive Care Units: A randomized trial to improve surrogate decision-making for critically ill elders**
  
  *Funded by: National Institute on Aging - 1RO1AG045176-01, Role: PI.* The goal of this study is to conduct a multicenter efficacy trial of the Four Supports Intervention among 400 critically ill older adults to reduce their long-term symptoms of depression and anxiety. The Four Supports Intervention is a multifaceted intervention in which a specially trained nurse intensively provides four types of support to surrogates in coordination with the clinical team: emotional support, communication support, decision support, and anticipatory grief support. The central hypothesis is that by intensively supporting surrogates in this highly stressful circumstance, the Four Supports Intervention will improve key elements of decision making, decrease long-term psychological distress among surrogates, and achieve more patient-centered care near the end of life.

- **Developing a Communication and Shared Decision Making Tool to Prepare Family Members in ICUs for the Role of Surrogate Decision Makers**
  
  *Funded by: National Institute on Aging- R21-AG050252-01, Role: PI.* The purpose of this project is to find ways to improve the quality of Surrogate Decision Makers in the ICU by developing and deploying a web based Communication and Decision Support (CDS) tool and a reliable care process to integrate the tool into routine practice.
• **PARTNER II: Improving Patient and Family Centered Care in Advanced Critical Illness**  
*Funded by: NIH/NINR - 1R01NR014663 - 01A1, Role: PI.*  
The overall purpose of this research study is to assess health care quality and health outcomes following a protocolized, ICU team-based quality improvement initiative to improve patient and family centered care in patients with advanced critical illness (PARTNER). We will test the effect of the PARTNER Quality Improvement Intervention on surrogates’ 6-month psychological outcomes. We will test the effect of the PARTNER Quality Improvement Intervention on communication about end-of-life decisions and patients’ end-of-life experiences. We will assess the effect of the PARTNER Quality Improvement Intervention on healthcare resource use, both during the index hospitalization and over 6 months of follow-up.

• **Communicating with Surrogate Decision Makers About Incapacitated ICU Patients’ Values**  
*Funded by: National Heart, Lung, and Blood Institute (NHLBI) - 2T32HL007820-16A1 and National Institutes on Aging (NIA) – 1F32AG047806-01A1 - Role: Mentor; PI: Leslie P. Scheunemann, MD.*  
The goal of this project is to develop three research tools for future interventions to improve this problem: 1) a high-fidelity simulation, which is a laboratory for studying and intervening on how clinicians elicit and incorporate incapacitated patients’ values into life support decisions; 2) consensus from a diverse group of stakeholders about which communication skills for physicians to use to elicit patients’ values and preferences are most important for interventions to target; and 3) a checklist outcome measure to quantify intervention effectiveness.

• **Improving Psychological Distress Among Critical Illness Survivors and Their Informal Caregivers**  
*Funded by: Patient Centered Outcomes Research Institute (PCORI) - Funding Award 195, PI: Christopher E. Cox, MD.*  
The purpose of this randomized trial is to reduce distress and improve quality of life for the ICU survivor-informal caregiver (family) dyad. Dyads will be randomized to receive one of two 6-week, telephone-based interventions: an ICU survivor-specific coping skills training (CST) program or a critical illness educational program. Both programs were developed with patient input and are promising interventions for this high-risk group.

• **Improving Decision Making for Patients with Prolonged Mechanical Ventilation**  
*Funded by: National Institutes of Health - 1 ROI HL109823, PI: Christopher E. Cox.*  
Testing the efficacy of a tablet computer-based decision aid to usual care control in improving the quality of the decision-making process for surrogates of incapacitated prolonged mechanical ventilation (PMV) patients, and their ICU physicians and nurses.

• **Exploring the perspectives of ICU clinicians on the conduct of multidisciplinary family meetings in the ICU**  
*Funded by: National Heart, Lung, and Blood Institute (NHLBI) – T32-HL007820 - Role: Mentor; PI: Jennifer Seaman, PhD, RN.*  
The overall purpose of this research study is to explore the perspectives of ICU clinicians (nurses, physicians, and social workers) on perceived barriers and facilitators related to scheduling and conducting timely multidisciplinary family meetings in the ICU and elicit their thoughts and opinions about interventions that might improve the rate of interdisciplinary family meetings in ICU.

Xiaoyan Wen, MD MSc

Dr. Wen is a faculty member in the Center for Critical Care Nephrology. She has a research background in experimental nephrology, with additional training and expertise in cell and molecular biology obtained through work in the Division of Cell and Molecular Biology, Department of Pathology, and the CRISMA Center. Her research interests lie primary in mechanism of acute kidney injury and its recovery through both in vivo and in vitro models. Specific studies include but not limited to signaling pathways of cell-transdifferentiation-phenomena in the process of fibrosis and explored in their roles in the secondary inflammatory responses in cell culture system, data analysis of the associations between biological markers with AKI-outcome in critically ill patients treated with dialysis, inflammatory cell phenotype transition and their roles in kidney injuries, rodent models of nephrotoxic AKI and
sepsis-associated acute kidney injury induced by cecal ligation and puncture surgery, and zebrafish model of AKI. Dr. Wen has authored more than 30 publications.

Major Projects

- **Zebrafish model of septic AKI**
  
  *Funded by: Internal funding, Role: PI; Mentors: Neil Hukriede, John Kellum.* This study aims to establish a multi-cellular model of sepsis AKI by micro-injection of zebrafish pathogens into zebrafish larvae blood circulation at age of 5-day post fertilization. The success of this model will enable applications of novel genetic tools in septic AKI study.

- **Tubular epithelial cell cycle arrest and its secretion of TIMP2&IGFBP7 in septic AKI progression**
  
  *Funded by: Astute Medical, Inc. Role: co-investigator; PI: John Kellum.* This study uses murine models of sepsis to study renal tubular epithelial cell and infiltrated inflammatory cell’s cell cycle arrest over time and the linkage between the cell cycle arrest with TIMP2&IGFBP7 secretion in sepsis associated AKI.

- **Mouse model of AKI non-recovery in sepsis and UPHD186 intervention**
  
  *Funded by: Internal funding; Role: Co-Investigator; PI: John A. Kellum, Neil Hukriede.* This study uses murine models of sepsis and follow-up to 2-4 weeks to better understand the underlying mechanisms of AKI non-recovery in sepsis. Histone deacetylase inhibitors (HDACi) are small molecule chemical compounds that inhibit histone deacetylation. Recent researches have shown inhibition of deacetylation could attenuate kidney injury and reduced interstitial fibrosis in both nephrotoxic and ischemia-reperfusion AKI models. We have identified HDACi methyl-4-(phenylthio) butanoate (m4PTB), UPHD186, that is efficiently metabolized to the active analog PTBA, act as PTBA prodrugs in vivo. Septic AKI is believed to have unique mechanisms for AKI. This project sought to better understand whether UPHD186 could affect both renal tubular epithelial cell differentiation and infiltrated macrophage phenotype transformations during recovery.

- **AB103 modulated Th/Treg cell phenotype and its effects in sepsis**
  
  *Funded by: AtoxBio; Role: Co-Investigator; PI: John Kellum.* Immune checkpoint inhibitors synergistic innate and adaptive immune and therefore believed play important roles in determining sepsis outcome and its associated organ dysfunctions. This project applied one of the AtoxBio products, AB103, to murine model of sepsis to study the role of checkpoint inhibitor during sepsis.

- **Ferroptosis in septic AKI.**
  
  *Funded by: NIAID, 5U19AI068021-12; Role: collaborator; PI: Kagan, Valerian E. 15-Lipoxygenases (15LO)* oxygenate free polyunsaturated fatty acids (PUFA) but can change their substrate specificity to generate hydroperoxy-PUFA-phosphatidylethanolamines (PUFA-PEs) which - under conditions of GPX4 deficiency - trigger ferroptosis, a form of non-apoptotic cell death. We sought to identify the important role of ferroptosis in septic AKI using our established model of mouse CLP and hopefully prove a novel PEBP1-dependent regulatory mechanisms in kidney epithelial cell death during septic AKI.

- **Biomarker for AKI and its recovery in critically ill patients**
  
  *Funded by: NIDDK, 5R01DK070910; Role: Researcher; PI: John Kellum.* This study randomized 1164 patients at 27 centers in ARF Trial Network (ATN) study CSP530, aimed to better understand the role of two key pathways, inflammation and oxidative stress, in survival and recovery of renal function after ARF and build a clinical risk prediction model that will consider plasma mediator levels, urine markers, genetic, and clinical variables.
Sachin Yende, MD, MS

Dr. Yende’s research focuses on improving short and long-term outcomes of sepsis. He is conducting several epidemiologic and translational studies to understand how an episode of sepsis worsens chronic diseases. He is also leading a large consortium to test personalized strategies for sepsis using adaptive trial design.

Major Projects

- **Immunotherapy of sepsis**
  
  *Funded by: National Institutes of Health - R34GM107650-A1, Role: PI. Began 7/1/15.* Programmed death-(PD)-1 receptor and its ligand, PD-L1 play an important role in suppressing the innate and adaptive immune in cancer and sepsis. This project is a planning grant to finalize study design, logistics, and oversight activities to design a trial to test multiple immunotherapies for sepsis. This proposal will use an innovative study design (adaptive enrichment design) and novel therapy that will reverse immunosuppression in severe sepsis.

- **Late cardiovascular consequences of septic shock with additional supplemental funding**
  
  *Funded by: National Institutes of Health - R01GM097471, Role: PI.* This project will focus on long-term cardiovascular outcomes after severe sepsis. We will determine the duration of resolution of immune response after severe sepsis and its relationship with acute cardiovascular events during recovery, and whether early interventions for severe sepsis alter long-term cardiovascular outcomes by affecting immune response resolution.
Teaching Activities

The Department of Critical Care Medicine is committed to providing the highest quality education to all trainees including medical students, residents and critical care fellows. Over 60 faculty contribute to teaching at the bedside, providing core lectures, and coordinating sessions at the Peter M. Winter Institute for Education Research (WISER) and Veteran's Administration Simulation Center.

Our faculty also provide instruction to medical students in the second-year clinical skills course, the third-year critical care component of the medicine clerkship and the fourth-year critical care elective.

We continue to increase the integration of educational opportunities between the adult and pediatric fellowships, which allows us to share valuable knowledge and resources. The integration efforts focus on particular lectures, workshops, our learning management system, and special events with the collaboration of faculty, chief fellows, and program directors. This integration has proven to be successful and led to the development of an innovative combined internal medicine/pediatric critical care training curriculum.

Medical Students

Critical Care Medicine Component of Adult Inpatient Medicine Clerkship (MS-3)

Medical students must learn to assess unstable patients and initiate appropriate therapies. Since crisis situations are relatively infrequent and students are rarely allowed to participate in the management of patients with respiratory or hemodynamic compromise, most students never acquire these important skills. To overcome these obstacles, the Critical Care component of the third-year medicine clerkship is taught at WISER. Educational objectives include assessing and managing simulated patients with respiratory distress, hypotension and arrhythmias. Evaluations of this component of the medicine clerkship are consistently superior.

Critical Care Medicine Elective Clerkship (MS-4)

The Critical Care Medicine clerkship is a four-week elective for fourth-year medical students designed to teach the cognitive and technical skills needed to initially evaluate and manage unstable patients in the ICU. Students participate in an orientation, daily interactive, problem-solving conferences, bedside teaching rounds, direct patient care with CCM faculty/fellow supervision, and intermittent sessions at WISER with a computerized whole-body mannequin. This year, revisions to the MSIV CCM 5430 course saw the introduction of a procedural skills lab in collaboration with the WISER Center, and the initiation of formal bedside “Teaching” rounds that were led by the CCM fellows with faculty input to review interesting cases and reinforce crucial aspects of clinical decision making.

Medical students are assigned to a specific ICU for their clinical activities where they actively participate in patient care. Supplemental didactic sessions are provided during each block, which augment education in cardiac resuscitation, airway management and other topics including hypotension, anaphylaxis, arrhythmias and sepsis. The course remains one of the school’s most popular electives and continues to be rated as one of the most valuable in the medical student curriculum. Sixty-five students completed the CCM elective during the past year.

Residents

CCM offers elective rotations in the ICU for residents from surgery, neurosurgery, neurology, anesthesiology, internal medicine, emergency medicine, pediatrics, dental anesthesia, radiology and others. In the last year, 131
residents rotated through the ICUs covered by CCM faculty. In addition to internal and local residents, we also accepted visiting fellows and residents from Children’s Hospital of Pittsburgh of UPMC, Harvard Brigham and Women’s Hospital, University of Texas, University of Virginia, UPMC Hamot, and UPMC Horizon to participate in CCM elective rotations.

Advanced Practice Providers

We continue to administer our advanced critical care training program for acute care advanced practice providers (APPs; nurse practitioners or physician assistants). This competitive program only accepts one or two trainees per year. The APP critical care residents train at the bedside with their physician counterparts allowing the APPs to learn intensive care medicine across a broad patient population including medical, general/cardiac/specialty surgical, trauma, solid organ transplant, and neurocritical care. APPs also participate in our fellowship lecture series, simulation sessions at WISER, and all training workshops.

International Observership Program

CCM offers an opportunity for international observers to travel to Pittsburgh and become immersed in our departmental activities. From two weeks to three months, these visitors vary from medical students to full professors, and represent various primary specialties such as internal medicine, anesthesiology, general practice, surgery, pulmonary medicine, and obstetrics and gynecology. For the past several years, our observers have come from Asia (China, Japan, South Korea, India, Bangladesh), Africa (Egypt, Libya, Swaziland), Europe (Spain, the Netherlands, Denmark, France), the Middle East (Turkey, Jordan) and Latin America (Brazil, Columbia, Panama, Peru). In addition to participating in the daily CCM educational program including lectures, workshops, Journal Club sessions, Grand Rounds, and simulation training at WISER, they are able to observe rounds in ICUs of their choice. During FY17, we had two clinical observers in our department, coming from Colombia and Brazil.

The CCM research-focused observership is a new addition to the program. Recent medical graduate from the University of Paris, Amelie Cambriel, MD, visited Murat Kaynar’s research lab for two months. She returned to France with knowledge of the project to study the impact of exercise on the metabolomics and lifespan of fruit flies surviving sepsis. Cambriel was afforded the opportunity to observe lab experiments in John Kellum’s lab and also participated in many of the department’s educational activities.

On April 24, 2012, the Department of Critical Care Medicine and the China Society of Critical Care Medicine entered into an agreement to build collaboration between China and the US in critical care medicine training, and to build a foundation for the future research cooperation between China and the US. The China Society of Critical Care Medicine will typically select one to two outstanding ICU physicians from the People’s Republic of China who are fluent in English to attend a two-month observership (no direct patient care or management). The visit will include sessions similar to those given to our full-time clinical critical care medicine post-doctoral trainees, with exposure to bedside critical care medicine, systematic didactic courses in critical care, and patient simulation. To date, CCM has hosted 14 Chinese physicians and a group of 10 are being processed to visit next year.

Critical Care Fellowships

Since graduating its first fellows in 1964, the Multidisciplinary Critical Care Training Program (MCCTP) at UPMC has trained over 700 critical care physician subspecialists. MCCTP has maintained continuous accreditation by the ACGME in Critical Care Medicine-Internal Medicine, Critical Care Medicine-Emergency Medicine, Anesthesiology Critical Care Medicine, and Surgical Critical Care. The Training Program is also accredited by the United Council of
Neurological Subspecialties in Neurocritical Care. In addition, the MCCTP offers training in extracorporeal membrane oxygenation (ECMO). The MCCTP is one of the world’s leading training programs, attracting candidates from around the globe and enabling graduates to attain leadership positions at well-respected institutions throughout the world.

The MCCTP is under the direction of Lori Shutter, MD, who is Vice Chair of Education. Jason Moore, MD, serves as Associate Director of the Adult Division, and Melinda Hamilton, MD, is the Associate Director of the Pediatric Division.

**Adult Division Fellowship Program**

**Critical Care Medicine-Internal Medicine Fellowship and Emergency Medicine Fellowship**

The Critical Care Medicine fellowship is a two-year program that is now open to trainees from either Internal Medicine (IM) or Emergency Medicine (EM) residencies. Clinical experience includes required rotations through medical, trauma/general surgery, neurovascular, abdominal organ transplantation, cardiothoracic surgery and obstetrical ICUs. Elective rotations in medical toxicology, radiology, and several of the medical subspecialties are also available. We also offer a one-year training track option for select physicians who have already completed a year of fellowship training in an associated field, such as cardiology or nephrology. A collaborative arrangement has been created with the UPMC Heart and Vascular Institute to provide a dedicated single year of critical care training for interested Cardiology fellows effective July 1, 2017. The field of Cardiology Critical Care is an innovative concept that is being advance by this integrated program.

Fellows enrolled in the two-year program select one of three possible pathways for their senior year: research, education or leadership. Fellows entering the research track pursue a mentored research project and didactic research training with a goal of becoming an NIH-funded clinician scientist. Fellows entering the education track pursue mentored curriculum development and didactic training in adult education with a goal of a career in academic medicine as a clinician-educator. Fellows entering the leadership track complete a quality improvement project and obtain training and health administration with a goal of a career as an ICU director or quality improvement specialist. These pathways deliberately approximate directions for advancement in academic medicine with fellows working with faculty mentors to acquire leadership skills in their area of interest.

Eleven IM/EM fellows graduated from our program on June 30, 2017 (10 fellows in the two-year track, and one fellow in the one-year track). Nine fellows completed their first year of training and advanced to their second year this past June. A full class of eleven fellows was hired for FY2018; the two-year program has six fellows from IM residencies, one from Cardiology, one from combined IM/EM training, and three from EM.

The demand from EM-trained physicians to be board-eligible in Critical Care has led to very highly qualified EM residents applying to our program. EM residents now make up about 25% of the Critical Care IM program. The American Board of Internal Medicine (ABIM) and American Board of Emergency Medicine co-sponsor critical care training and the ABIM subspecialty exam for Critical Care Medicine.

**Surgical Critical Care and Acute Care Surgery Fellowships**

The Surgical Critical Care fellowship is a one-year program that includes rotations through trauma/general surgery, neurotrauma, neurovascular, surgical, abdominal organ transplantation, cardiothoracic surgery and burn ICUs. Electives in pre-hospital care, infectious disease, pediatric and obstetrics/gynecology ICUs are also available.

In place since 2008, the Acute Care Surgery Fellowship is recognized as a combined GME and OZ program by the UPMC Graduate Medical Education Program because these fellows become clinical instructors in Surgery during their second year. The fellowship includes the one-year surgical critical care fellowship and a second year devoted to
trauma, emergency and elective general surgery, and surgical subspecialties (pediatric, thoracic, vascular, and hepatobiliary).

Four fellows completed the standard one-year surgical critical care fellowship in June 2017. Two fellows are continuing their training for the second year of the acute care surgery fellowship. We hired four surgery fellows for 2017-2018.

Anesthesiology Critical Care Medicine Fellowship

The Anesthesiology Critical Care fellowship is a one-year training program that includes rotations through trauma/general surgery, surgical, neurosurgical/neuro-trauma, abdominal organ transplantation, cardiothoracic surgery, and burn care ICUs. Elective options include infectious disease, nephrology, radiology, cardiology, post-cardiac arrest service, echocardiography, operating room, and additional ICU time including the pediatric and obstetrics/gynecology ICUs. Four fellows completed the anesthesiology critical care fellowship in June 2017, and four fellows were hired for 2017–2018.

Neurocritical Care Fellowship

Accredited by the United Council for Neurologic Subspecialties, the Neurocritical Care Fellowship recruits one fellow per year. The fellow is selected through the SF Match system. The program offers three training options in neurocritical care: (1) A traditional two-year training track for physicians from any background residency without prior critical care training, (2) A one-year track providing specialized neurocritical care training for those who have already completed critical care training through another board (IM/EM, Surg, Anes, Peds), and (3) A one-year concentrated critical care training track for neurosurgery residents, who can complete the training during their residency.

All neurocritical care fellows rotate through a variety of clinical rotations including neurovascular, neurotrauma, cardiothoracic, trauma/general surgery, and general medical-surgical ICUs. In addition, they rotate on the Stroke Service, neurointerventional, neuro-anesthesia/neurosurgery, and neuro-electrophysiology. Additional electives include post-cardiac arrest service, toxicology, and additional ICU time including the pediatric and obstetrics/gynecology ICUs. The program graduated one fellow in June 2017, and had a very successful match with 42 applicants for the single position with our highest-ranking applicant matching for June 2018. Plans for FY18 include developing a dedicated pediatric neurocritical care track that will be integrated with the pediatric CCM training program.

Adult Critical Care ECMO Fellowship

The Adult Critical Care Extracorporeal Membrane Oxygenation (ECMO) fellowship is a component of CCM’s Multidisciplinary Critical Care Training Program. One fellow each year is admitted to the program and is appointed as a UPMC Clinical Instructor. The Adult Critical Care ECMO fellowship began in 2013.

ECMO trainees spend the vast majority of their 12 months of clinical time in the Cardiothoracic ICU (CTICU). This ICU is the primary local site for all ECMO patients and also has a large regional catchment area. Fellows may be asked to see patients on any of the adult ICUs within Presbyterian and Montefiore University Hospitals (PUH/MUH), UPMC Mercy, or Magee Women’s Hospital of UPMC.

International Multidisciplinary Program in Advanced Critical Care Training

The International Multidisciplinary Program in Advanced Critical Care Training (IMPACCT) program is now an OZ and is open to physicians who have completed residency programs (anesthesiology, general/internal medicine, general surgery, or intensive care medicine) in their respective countries, are eligible or certified with their national medical
registration (i.e. “boards”) authorities, in good standing within their professional societies, and eligible for an independent medical license in the state of Pennsylvania. The candidate should have also completed at least six months of critical care training within their specialty.

Trainees are provided with a local CCM mentor as well as an advisor from their home country to ensure their return to their home-country institution upon completion of the fellowship. This in-depth clinical and research experience prepares the trainee to master the essentials of critical care medicine.

Curriculum

The educational curriculum for fellows in the Multidisciplinary Critical Care Training Program (MCCTP) was developed to teach the knowledge and skills required to manage all aspects of critically ill patients. Fellows attend lectures, interactive problem-solving workshops and simulation sessions throughout the year.

### Core Lectures Subject Areas

<table>
<thead>
<tr>
<th>Airway</th>
<th>Cardiothoracic</th>
<th>Cardiovascular</th>
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</thead>
<tbody>
<tr>
<td>Disaster Management</td>
<td>GI / Hepatology</td>
<td>ICU Administration / Quality Improvement</td>
</tr>
<tr>
<td>ID &amp; Transplant</td>
<td>Neuro</td>
<td>Obstetrics</td>
</tr>
<tr>
<td>Palliative Care and Ethics</td>
<td>Renal</td>
<td>Respiratory</td>
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<tr>
<td>Toxicology</td>
<td>Trauma</td>
<td>Ultrasound</td>
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</table>

Additional conferences include: EMS/CC Transportation Interactions, Bioterrorism, Long Term Acute Care, Creating a Teaching Portfolio, Clinical Trials 101, and Fatigue 101

### Clinical Workshops

The development of a culture of patient safety is a key focus of the MCCTP curriculum. Fellows participate in 14 different workshops throughout the year to achieve this objective, including routine and difficult airway management, central venous catheterization, chest tube placement, and bedside ultrasound. We have continued to provide the relatively new “Intensivists as Teachers” (In’AT) workshop designed to teach our fellows the skills to conduct teaching rounds and deliver proper feedback. All of these workshops involve the use of interactive learning, human simulation, human or cadaver models, and/or online educational experiences.

In addition to patient safety, developing outstanding communication skills is also an important component of the program. For the last several years, fellows have attended the “Critical Care Communications” (C3) course that focuses on end of life discussions with families of patients in the ICU. The three-day course is conducted off campus in a relaxed atmosphere and features live actors along with learner-directed teaching by the instructors. The learners demonstrate and practice the skills needed to deliver bad news, establish goals of care, talk about forgoing life sustaining therapy, and manage conflict. This course continues to be a collaborative effort between Palliative Care Medicine and Critical Care Medicine. It is the only experience of its kind directed toward CCM fellows and it is one of the highlights of the CCM curriculum. The course consistently receives outstanding evaluations from the fellows.

### Professionalism and Leadership Course

The Critical Care Medicine Professionalism and Leadership course is now in its seventh year and is a standard part of our second-year curriculum and is also offered to first-year fellows. The objective of the curriculum is to teach fellows the administrative, educational and research skills necessary to function as an Intensivist, who is expected to provide expert critical care services, develop clinical protocols, initiate Quality Improvement programs, coordinate educational activities for the unit, lead multidisciplinary committees and improve overall quality of patient care.
Interactive small group sessions provide fellows with these important skills. The course has received excellent evaluations from our graduates, who have found the skills they learn highly valuable in their first years after graduation.

### 2016–17 CCM Professionalism and Leadership Course Curriculum

<table>
<thead>
<tr>
<th>Topic</th>
<th>Instructor</th>
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<tbody>
<tr>
<td>Finding the Right Job in a Variable Market</td>
<td>John Hoyt, MD</td>
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<tr>
<td>Advancement in the Professional Environment</td>
<td>Ann Thompson, MD</td>
</tr>
<tr>
<td>Graceful Self Promotion: PARs and Executive Summaries</td>
<td>Lori Shutter, MD</td>
</tr>
<tr>
<td>Contracts</td>
<td>Kelly Gottschalk, JD</td>
</tr>
<tr>
<td>Negotiating Compensation</td>
<td>Derek Angus, MD, MPH</td>
</tr>
<tr>
<td>Manuscript Review</td>
<td>David Huang, MD, MPH</td>
</tr>
<tr>
<td>Principles of Experimental Design and Controlled Observations</td>
<td>Michael Pinsky, MD</td>
</tr>
<tr>
<td>The Art of Presentation</td>
<td>Michael Pinsky, MD</td>
</tr>
<tr>
<td>Grant Writing and Review</td>
<td>John Kellum, MD</td>
</tr>
<tr>
<td>Teaching Efficiently on Rounds</td>
<td>Jason Moore, MD, MS</td>
</tr>
<tr>
<td>Providing Feedback</td>
<td>Lillian Emlet, MD, MS</td>
</tr>
<tr>
<td>Curriculum Design</td>
<td>Jason Moore, MD, MS</td>
</tr>
<tr>
<td>Supervision vs. Autonomy in the ICU</td>
<td>Jason Moore, MD, MS</td>
</tr>
<tr>
<td>eRecords, CPOE, &amp; Decision Support</td>
<td>Steve Hasley, MD</td>
</tr>
<tr>
<td>Clinical Decision Making</td>
<td>Jeremy Kahn, MD, MS</td>
</tr>
<tr>
<td>Principles of Triage</td>
<td>Jason Moore, MD, MS</td>
</tr>
<tr>
<td>Hospital Administration and Leadership</td>
<td>John Hoyt, MD</td>
</tr>
<tr>
<td>How to Work with Senior Hospital Administration</td>
<td>John Hoyt, MD</td>
</tr>
<tr>
<td>Collaborative Practice Principals in Acute Care Medicine</td>
<td>John Hoyt, MD</td>
</tr>
<tr>
<td>Balancing Personal and Professional Life</td>
<td>Panel of CCM attendings, facilitator Jason Moore, MD, MS</td>
</tr>
<tr>
<td>Understanding the Business of Healthcare</td>
<td>Arthur Boujoukos, MD</td>
</tr>
<tr>
<td>Billing and Coding</td>
<td>Arthur Boujoukos, MD</td>
</tr>
<tr>
<td>The Malpractice Legal Process and Effects on the Physician</td>
<td>Richard Kidwell, Catherine Hampel, DrPH, MPH</td>
</tr>
<tr>
<td>Healthcare Financial Statements: A Primer</td>
<td>Catherine Hampel, DrPH, MPH and Bill Thompson</td>
</tr>
<tr>
<td>Graceful Self-Promotion</td>
<td>Lori Shutter, MD</td>
</tr>
</tbody>
</table>

### New Teaching Programs and Courses

The multidisciplinary critical care fellowship training program introduced or expanded five training programs this year.

1. The point of care ultrasound training (POCUS) curriculum continues to expand. A dedicated POCUS training track has been added for a senior fellow who wants to focus on clinical skills and translational research in this area.
2. The Emergency Neurological Life Support (ENLS) training program is extremely popular with three courses held throughout the UPMC facilities. This course is open to any trainee or care provider interested in emergency neurological care.
3. We broadened our Fundamental Disaster Management (FDM) course by offering it to providers outside of the department. Registration for this course was at capacity, and we welcomed the participation of providers from emergency medical services (EMS), nurses, APPs and physicians from other departments.
4. The Global Health training track for critical care fellows remains a popular focus of the senior fellows. The foundation of this effort is a collaboration with Partners Health and Vanderbilt University that provides critical care services to a hospital in Mirebalais, Haiti. An additional global rotation added to the program was to a facility in Israel, which led to the development of a mass casualty plan for the department of CCM based on the experiences of our colleagues in Israel.

5. As mentioned above under the Medical Students section, we introduced a fellow-led procedural skills lab in collaboration with the WISER center, and formal bedside “Teaching” rounds. Fellows, with faculty input, review interesting cases and re-inforce crucial aspects of clinical decision making.

Other Educational Innovations

**Flipped Classroom** – One of the biggest recent innovations is our flipped classroom approach, which was initiated three years ago as a pilot program. This novel approach improves the educational experience of our fellows in several aspects: (1) as a contemporary educational strategy, it was better suited to fellows’ expectations and learning styles, (2) it enabled us to leverage our existing online material, and (3) it allowed for better assessment of the fellows’ learning experiences.

Having just completed our second official year of using a flipped classroom, we have found it to be extremely successful. Notably, our median scores on the Multidisciplinary Critical Care Knowledge Assessment Program well exceeded the national median (see “Excellent Scores in Critical Care Knowledge Assessment Program” below). It has been so successful that we expanded the approach through the recent purchase of a learning management system called Canvas.

**Learning Management System** – Canvas was acquired to further link all of our educational activities, and has created an efficient and cutting-edge learning environment for fellows, residents, medical students, faculty, APPs and alumni. This learning management tool greatly enhances our ability to employ our extensive array of instructional resources as we provide high-quality, learner-centered, and sustainable instruction in critical care. The use of Canvas fully supports and expands our “flipped classroom” model and allows all levels of learners to interact with hundreds of video-, text- and image-based content assets.

Our department has a long history of providing a rich array of online resources to support our Multidisciplinary Critical Care Training Program. We began to integrate technologies for teaching and learning into our educational program about 10 years ago, when we created podcasts from our daily lecture series. The approximately 150 lectures recorded annually since then constitute one of the most extensive array of online resources supporting a fellowship program.

We continue to expand Canvas, which currently supports the Adult Division of our Education program and the Medical Student training options. Future expansions will provide support to the Pediatric Division, our resident and APP education programs, future faculty development and continuing educational initiatives, and eventually connect our alumni.

**Development of Research Education Infrastructure** – We have also begun to initiate the development of an education research infrastructure. Working in partnership with the research wing of our department, in particular Jeremy Kahn and Michael Pinsky, who oversee our Adult T32 training program, we are developing our education research capabilities so as to be able to critically assess the effectiveness of our educational activities. This includes advanced course work in the theory of medical education, statistics, and development of education specific knowledge assessment tools.

One distinct example of this initiative is our participation in the Medical Education Research Certificate (MERC) program, through the Association of American Medical Colleges. For the second year, a faculty member from the Critical Care Medicine Fellowship Program was accepted into the MERC program. Murat Kaynar, MD, MPH, Associate
Professor and Director of the Anesthesiology Critical Care Fellowship Training Program participated in a series of six workshops over three separate days in fall 2016. The workshops, which are sponsored by UPMC Medical Education, are designed to strengthen participants’ knowledge of medical education research and to encourage stronger participation in medical education research. The participation of our faculty has been so successful that we will continue to encourage faculty to participate, with the goal of having one or two attend every year.

As another example of the emphasis on education research, we had two education-related presentations at our departmental Grand Rounds: our own Lillian Emlet, MD, MS, FACEP, presented “iTeach CCM: Teaching & Learning in the Age of FOAMed” and a distinguished external presenter, Nicole Roberts, PhD, Assistant Dean of Medical Education and Faculty Development, City College of New York, spoke on “Medical Education in the 21st Century.” The inclusion of a Grand Rounds presentation specifically focused on education research is a new initiative that represents our increased emphasis on developing a world-class education research program.

**Participation in Marshall Webster Leadership Course** – We frequently have a fellow and faculty member participate in the Marshall W. Webster Physician Leadership Program, a 12-week program, which is based on the “Mini-MBA” program in the Katz Executive Education MBA Program. The Marshall Webster Physician Leadership Program is a collaborative venture between the Physician Services Division and the Katz Graduate School of Business at the University of Pittsburgh. This Program provides physicians with business training. We have had trainees participate in five of the last five years; in FY17 CCM faculty member Brad Butcher, MD, and 2nd year IM fellow Rajagopala Padmanabhan, MD participated.

**Real-time Delivery of our Educational Lectures** – Many of our faculty and staff provide daily patient care throughout the UPMC system, so in order to provide our departmental educational activities we live stream many events from the Oakland campus to all of our members. Our Grand Rounds and Journal Club lectures are webcast across campus (and soon to our alumni).

**Quality Measures of Teaching Efforts**

**Fellow Evaluations of Faculty** – We have consistently asked our fellows to provide evaluations of faculty. In FY17, 469 evaluations were completed by fellows on 49 faculty. The number of evaluations per faculty ranged from 1 – 24. The average overall evaluation score was 4.55 on a five-point scale. Nine faculty received an average overall score of 5.0, and 34 faculty had scores above 4.55. Feedback is provided to faculty about their scores with the goal to improve the educational experience of the fellows.

**Excellent Scores in Critical Care Knowledge Assessment Program** – The MCCTP also participates in The Society of Critical Care Medicine’s Multidisciplinary Critical Care Knowledge Assessment Program (MCCKAP), an online examination used to assess critical care fellowships across the country. The results of the MCCKAP also enable program directors to better prepare fellows for subspecialty board examinations. Our fellowship program’s median score for all fellows was above the national median (154.5 vs. 144). In addition, all of our specialty-specific MCCKAP mean scores exceeded their national equivalents. We had four fellows with scores over 170, which represents over 80% of questions answered correctly by these fellows. We feel that these scores are an objective measure of the effectiveness of our Flipped Classroom approach to graduate medical education.

**Teaching Honors**

Chris Schott, MD, was the recipient of the Ake N. Grenvik Critical Care Medicine Faculty of the Year award. Dana Fuhrman, MD was voted Pediatric Faculty of the Year. Alexandra Briggs, MD, first year surgery critical care fellow, received the Fellow of the Year award by the CCM faculty. The Outstanding Clinical Teaching The award from 4th year medical students went to Danish Malik, MD, first-year Adult IM Fellow. Kendra Woods, MD, named the 2017 Fellow of the Year by the pediatric residency program. Rajagopala Padmanabhan, MD, and Krystle Shafer, MD, were honored for their roles as Chief Fellows, Adult Division, and Kendra Wood, MD, was honored for her role as Chief
Fellow, Pediatric Division. Chief fellows for the upcoming year are: Danish Malik, MD, and Ruth Musselman, MD, for the Adult Division, and Alicia Alcamo, MD, for the Pediatric Division.

Participation in Leadership Conference

Our department continued a significant presence at the UPMC Leadership Conference, with Jason Moore, MD, Lillian Emlet, MD, and Melinda Hamilton, MD, participating in the presentations and training.

Adult Critical Care Medicine Fellows 2016–17

Graduating Adult Fellows (on June 30, 2017) for two-year fellowships

**Critical Care Medicine / Internal Medicine & Emergency Medicine**

### Mary Assad, MD
- **Medical School:** St. Christopher Iba Mar Diop College of Medicine, Dakar, Senegal
- **Residency:** University of Illinois at Chicago/ Louis A. Weiss Memorial Hospital, Chicago, IL
- **Future Position:** Attending Intensivist, ICU Clinical Clerkship, and Residency Rotation Director, Forrest General Hospital, Hattiesburg, MS

### Torben Becker, MD, PhD
- **Medical School:** Medizinische Fakultät Heidelberg, Ruprecht-Karls-Universität, Heidelberg, Germany
- **Residency:** University Hospital Mannheim, Germany & St. Joseph Mercy Hospital, University of Michigan, MI
- **Future Position:** EMS Fellow, Department of Emergency Medicine, University of Florida, Gainesville, FL

### Abhishek Freyer, MD
- **Medical School:** Ross University School of Medicine, Portsmouth, Dominica
- **Residency:** MedStar Franklin Square Medical Center, Baltimore, MD
- **Future Position:** Attending Intensivist, Halifax Hospital, Daytona, FL

### Hitesh Gidwani, MD
- **Medical School:** Pravara Institute of Medical Sciences, Loni Maharashtra, India
- **Residency:** UPMC, Pittsburgh, PA
- **Future Position:** Attending Intensivist, St. Vincent Hospital of the Allegheny Health Network, Erie, PA

### Daniel Glass, MD
- **Medical School:** Sackler School of Medicine, Tel Aviv, Israel
- **Residency:** Staten Island University Hospital, Staten Island, NY
- **Future Position:** Attending Physician, Remote ICU, Israel

### Rajagopala Padmanabhan, MD, Chief Fellow
- **Medical School:** Katsurba Medical College, Karnataka, India
- **Residency:** UPMC, Pittsburgh, PA
- **Future Position:** ECMO Fellowship, UPMC, Clinical Instructor, Department of Critical Care Medicine, UPMC, Pittsburgh, PA

### Debjit Saha, MD
- **Medical School:** Kolkata Medical College & Hospital, Kolkata West Bengal, India
- **Residency:** Mount Sinai Medical Center, NY
- **Future Position:** Attending Intensivist, Advocate Christ Hospital, Chicago, IL
Krystle Shafer, MD, Chief Fellow  
**Medical School:** University of Maryland School of Medicine  
**Residency:** Wellspan York Hospital, York, PA  
**Future Position:** Physician Director of ER Critical Care, Emergency Medicine Attending, and Open Heart ICU & Med Surg ICU Attending, Wellspan York Hospital, York, PA

Muhammad Tahseen, MBBS  
**Medical School:** Allama Iqbal Medical College, Lahore Punjab, Pakistan  
**Residency:** Crozer-Chester Medical Center, Upland, PA  
**Future Position:** Assistant Clinical Director, Intensive Care Unit, Crozer-Chester Medical Center, Upland, PA & Assistant Professor, Drexel University College of Medicine, Philadelphia, PA

Pavan Thangudu, MD  
**Medical School:** Temple University School of Medicine, Philadelphia, PA  
**Residency:** Tulane University School of Medicine, New Orleans, LA  
**Future Position:** Attending Physician, Metropolitan Methodist Hospital, San Antonio, TX

Fadi Tohme, MD  
**Medical School:** Université Saint-Joseph Faculté de Médecine, Beirut, Lebanon  
**Residency:** University of Iowa Hospitals and Clinics, Iowa City, IA  
**Future Position:** Assistant Professor, Washington University, Barnes-Jewish Hospital, St. Louis, MO

**Neurocritical Care**  
**Joshua Keegan**  
**Medical School:** Brown University, Providence, RI  
**Residency:** Emergency Medicine, Yale University, New London, CT  
**Future Position:** Staff Physician, Stamford Hospital; Stamford, CT

**Graduating Adult Fellows (on June 30, 2017) for one-year fellowships**

**Anesthesiology Critical Care Medicine**  
**Christopher Johnson, MD**  
**Medical School:** Georgetown University School of Medicine, Washington DC  
**Residency:** Medstar Union Memorial Hospital, Baltimore MD  
**Future Position:** Attending Intensivist and Anesthesiologist, St. Luke's Hospital University Health Network, Bethlehem, PA

**Rohan Panchamia, MD**  
**Medical School:** The George Washington University School of Medicine, Washington, DC  
**Residency:** New York Presbyterian Weill Cornell Medical Center, New York, NY  
**Future Position:** Clinical Instructor of Anesthesiology and Critical Care Medicine, New York Presbyterian Hospital-Weill Cornell Medical Center, New York, NY

**Alexander Preus, MD**  
**Medical School:** State University of New York Upstate Medical Center, Syracuse, NY  
**Residency:** UPMC, Pittsburgh, PA  
**Future Position:** Attending Intensivist and Anesthesiologist UPMC & Veterans Affairs Pittsburgh Healthcare System, Pittsburgh, PA
Yiyu Zhao, MD
Medical School: Northwestern University Feinberg School of Medicine, Chicago IL
Residency: University of Virginia, Charlottesville, VA
Future Position: Assistant Professor of Anesthesiology, University of Virginia, UVA Health System, Charlottesville, VA

**Surgical Critical Care Medicine**
Alexandra Briggs, MD
Medical School: The University of Chicago Pritzker School of Medicine, Chicago IL
Residency: Brigham and Women's Hospital, Boston, MA
Future Position: Trauma/Acute Care Surgery Fellowship, UPMC, Clinical Instructor, Department of Critical Care Medicine, UPMC, Pittsburgh, PA

Benjamin Kautza, MD
Medical School: Medical College of Wisconsin, Milwaukee WI
Residency: UPMC, Pittsburgh, PA
Future Position: Trauma/Acute Care Surgery Fellowship, UPMC, Clinical Instructor, Department of Critical Care Medicine, UPMC, Pittsburgh PA

Melissa Loveranes, DO
Medical School: Lake Erie College of Osteopathic Medicine, Erie, PA
Residency: UPMCHorizon, Greenville, PA
Future Position: Surgical Intensivist and Trauma and Acute Care Surgeon, UPMC Hamot, Erie, PA

Michael Klein, MD
Medical School: University of Medicine and Dentistry of New Jersey, New Jersey Medical School, Newark, NJ
Residency: SUNY Downstate Medical Center, Brooklyn, NY
Future Position: Assistant Professor of Surgery, NYU School of Medicine, New York, NY

1st Year Fellows (Beginning July 1, 2016)

**Neurocritical Care**
Namir Khandker, MD
Medical School: Wayne State University School of Medicine, Detroit, MI
Residency: University Hospitals Case Medical Center, Cleveland, OH

**Critical Care Medicine / Internal Medicine & Emergency Medicine**
Vikram Balakumar, MD
Medical School: Stanley Medical College, Chennai, Tamil Nadu, India
Residency: UPMC, Pittsburgh, PA

Nicholas Goodmanson, MD
Medical School: University of Pittsburgh School of Medicine, Pittsburgh, PA
Residency: UPMC, Pittsburgh, PA

Timothy Kaselitz, MD
Medical School: University of Michigan Medical School, Ann Arbor, MI
Residency: University of Michigan Health Center, Ann Arbor, MI
### CRITICAL CARE MEDICINE

**Annual Report FY17** | 95

<table>
<thead>
<tr>
<th>Name</th>
<th>Medical School</th>
<th>Residency</th>
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<tbody>
<tr>
<td>Karthik Kode, MD</td>
<td>American University of the Caribbean, Cupecoy, St. Maarten</td>
<td>Case Western Reserve University (MetroHealth), Cleveland, OH</td>
</tr>
<tr>
<td>Ryan Lapointe, MD</td>
<td>Ross University, School of Medicine, Dominica, West Indies</td>
<td>New York Methodist Hospital, Brooklyn, NY</td>
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<tr>
<td>Syed Shad Mahmood, MD</td>
<td>The Aga Khan University Medical College, Karachi, Sindh, Pakistan</td>
<td>Northshore University Health System, Evanston, IL</td>
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<tr>
<td>Danish Malik, MD</td>
<td>Rutgers-New Jersey Medical School, Newark NJ</td>
<td>Mt Sinai St Lukes-Roosevelt, New York, NY</td>
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<tr>
<td>Ruth Musselman, MD</td>
<td>St. George's University School of Medicine, Grenada</td>
<td>Norwalk Hospital, Norwalk, CT</td>
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<tr>
<td>Aaron Skolnik, MD</td>
<td>University of Pittsburgh School of Medicine, Pittsburgh PA</td>
<td>Brigham and Women's/Harvard, Boston, MA</td>
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<tr>
<td>Fadi Tohme, MD</td>
<td>Université Saint-Joseph Faculté de Médecine, Beirut, Lebanon</td>
<td>University of Iowa Hospitals and Clinics, Iowa City, IA</td>
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**Incoming Fellows (Beginning July 2017)**

### Anesthesiology Critical Care Medicine

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<thead>
<tr>
<th>Name</th>
<th>Medical School</th>
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<tbody>
<tr>
<td>Hassan Aijazi, MD</td>
<td>Shifa College of Medicine, Islamabad, Pakistan</td>
<td>University of Texas at Houston, TX</td>
</tr>
<tr>
<td>Jessica Cassavaugh, MD</td>
<td>University of Vermont, Burlington, VT</td>
<td>University of Pittsburgh Medical Center, Pittsburgh, PA</td>
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<tr>
<td>Devin Caswell, DO</td>
<td>New York College of Osteopathic Medicine, Old Westbury, NY</td>
<td>Cleveland Clinic Foundation, Cleveland, OH</td>
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<tr>
<td>Rachel Pool, MD</td>
<td>University of Washington School of Medicine, Seattle WA</td>
<td>UPMC, Pittsburgh, PA</td>
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### Neurocritical Care

<table>
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<tr>
<th>Name</th>
<th>Medical School</th>
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<tbody>
<tr>
<td>Mohammad Hirzallah, MD</td>
<td>University of Jordan, School of Medicine, Amman, Jordan</td>
<td>University of Texas at Houston, TX</td>
</tr>
</tbody>
</table>
Christian Ricks, MD  
Medical School: Baylor College of Medicine, Houston, TX  
Residency: University of Pittsburgh Medical Center, Pittsburgh, PA

**Surgical Critical Care**  
Kristen Arnold, MD  
Medical School: Medical University of South Carolina, Charleston, SC  
Residency: University of Texas Southwest, Dallas, TX

Letitia Bible, MD  
Medical School: University of Miami Miller School of Medicine, Miami, FL  
Residency: Rutgers University- New Jersey Medical School, Newark, NJ

Erin Fitzgerald, MD  
Medical School: Tufts Medical Center, Boston, MA  
Residency: Tufts Medical Center, Boston, MA

Cathline Layba, MD  
Medical School: The Ohio State University College of Medicine, OH  
Residency: University of Texas Medical Branch, Galveston, TX

**Critical Care Medicine / Internal Medicine & Emergency Medicine**  
Sabrina Arshed, MD  
Medical School: Universidad Iberoamericana School of Medicine, Santo Domingo, Dominican Republic  
Residency: Raritan Bay Medical Center, Perth Amboy, NJ

Emily Brant, MD  
Medical School: Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, PA  
Residency: University of Pittsburgh Medical Center, Pittsburgh, PA

Meshe Chonde, MD  
Medical School: George Washington University School of Medicine and Health Sciences, Washington DC  
Residency: Cedars Sinai, Los Angeles, CA

Garima Gupta, DO  
Medical School: Touro University College of Osteopathic Medicine, Mare Island, Vallejo, CA  
Residency: White Memorial Medical Center, Los Angeles, CA

Bachar Hamade, MD  
Medical School: American University of Beirut Faculty of Medicine, Beirut, Lebanon  
Residency: John Hopkins School of Medicine, Baltimore, MD

Alexander Kobzik, MD  
Medical School: Tufts University School of Medicine, Boston, MA  
Residency: University of Illinois at Chicago, IL

Matthew Niehaus, DO  
Medical School: Philadelphia College of Osteopathic Medicine, Philadelphia, PA  
Residency: Lehigh Valley Health Network, Bethlehem, PA
Critical Care Grand Rounds

Critical Care Medicine Grand Rounds represents a bi-weekly department-wide clinical and research conference series. 2016 - 2017 lectures included:

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<tr>
<th>Grand Rounds / Research Conferences</th>
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<td>Grand Rounds</td>
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<tr>
<td>AKI Symposium Keynote Speaker, Grand Rounds</td>
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<td>Distinguished Alumnus, Research Conference</td>
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<td>Distinguished Alumnus, Grand Rounds</td>
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<td>Grand Rounds</td>
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<tr>
<td>Annual Ethics, Research Conference</td>
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<td>Annual Ethics, Grand Rounds</td>
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<td>Grand Rounds</td>
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<tr>
<td>Grenvik Lecture, Research Conference</td>
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<td>Grenvik Lecture, Grand Rounds</td>
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<tr>
<td>Fink Scholar Day, Research Conference</td>
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<td>Fink Scholar Day, Grand Rounds</td>
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Research Training

National Research Service Award - Experimental Therapeutics in Critical Illness

Director: Michael R. Pinsky, MD
This NHLBI-funded postgraduate training program, now entering its 19th year of continuous funding, offers motivated physicians and scientists interested in an academic career in Critical Care Medicine (CCM) or related fields an excellent opportunity to work in one of the oldest and best established academic CCM training programs nationwide in the world. This training program is multi-disciplinary and accepts up to 4 trainees per year, over a period of up to 3 years. Trainees should have completed training in anesthesiology, emergency medicine, internal medicine, or surgery. Training for a period of 1-3 years is provided in research theory and practice in basic science research relevant to the pathophysiology or treatment of critical illness. The program runs in parallel with our clinical training program in adult CCM. Fellows can share a common clinical first year that leads to certification eligibility in CCM.

Our program’s research focus is in three interrelated domains: (1) immunobiology and the cellular basis for organ injury; (2) organ systems modeling; and (3) clinical and health services research. These research areas intersect with the extramural research grants of our training faculty and reflect the essential translational basis of critical medicine,
which requires an integration of cell and molecular biology, organ system interaction, and novel therapies that impact patient-centered and socially relevant outcomes. Examples of ongoing research include: molecular mechanisms of enterocyte intestinal epithelial barrier dysfunction; endothelial-vascular muscle cell interactions; inflammatory cell-mediated vascular endothelial interactions; myocardial function during ischemia and ventricular pacing; cardiopulmonary interactions in shock states; and long-term outcome of ventilator-dependent patients from critical illness; and use of novel resuscitation techniques to improve survival and organ function in critical illness. These research plans are based on broad questions on which precise, well-targeted individual research training efforts can be developed. Interdisciplinary approach to investigation is a unique feature of our training program. The impressive list of principal trainer faculty form a diverse and expert group of senior scientists, all of whom have strong track records as effective basic science investigators and educators with long-term extramural funding for their research. More information about the Adult T32 program is in the Research section of this Annual Report.

**Evidence-Based Medicine Journal Club Series**

Clinical fellows are paired with experienced faculty members for our evidence-based medicine Journal Club Series. Each fellow selects a recent article from the medical literature, reviews it in detail with their faculty mentor, and then presents a critical review for the Department. Through this process the fellows learn the basics of clinical research and how to interpret the medical literature, while at the same time staying up-to-date with current practice.

<table>
<thead>
<tr>
<th>Fellow</th>
<th>Preceptor</th>
<th>Journal Club</th>
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<tbody>
<tr>
<td>Hitesh Gidwani, MD</td>
<td>Cameron Dezfulian, MD</td>
<td>Targeted therapeutic mild hypercapnia after cardiac arrest: A phase II multi-center randomized controlled trial (the CCC trial)</td>
</tr>
<tr>
<td>Debjit Saha, MD</td>
<td>David Huang, MD</td>
<td>Initiation Strategies for Renal-Replacement Therapy in the Intensive Care Unit</td>
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<tr>
<td>Abhishek Freyer, MD</td>
<td>David Wallace, MD</td>
<td>Effect of Early Vasopressin vs Norepinephrine on Kidney Failure in Patients with Septic Shock: The VANISH Randomized Clinical Trial</td>
</tr>
<tr>
<td>Alexander Preus, MD</td>
<td>Murat Kaynar, MD and William Wallisch, MD</td>
<td>Effect of Noninvasive Ventilation Delivered by Helmet vs Face Mask on the Rate of Endotracheal Intubation in Patients with Acute Respiratory Distress Syndrome</td>
</tr>
<tr>
<td>Pavan Thangudu, MD</td>
<td>Scott Gunn, MD</td>
<td>ICU Attending Handoff Practices: Results from a National Survey of Academic Intensivists</td>
</tr>
<tr>
<td>Muhammad Tahseen, MD</td>
<td>Cameron Dezfulian, MD</td>
<td>Practice Patterns and Outcomes Associated with Use of Anticoagulation Among Patients with Atrial Fibrillation During Sepsis</td>
</tr>
<tr>
<td>Rohan Panchamia, MD</td>
<td>Hernando Gomez, MD</td>
<td>Association Between Overnight Extubations and Outcomes in the Intensive Care Unit</td>
</tr>
<tr>
<td>Melissa Loveranes, MD</td>
<td>Matthew Rosengart, MD</td>
<td>Effect of Posttextubation High-Flow Nasal Cannula vs Noninvasive Ventilation on Reintubation and Posttextubation Respiratory Failure in High-Risk Patients, A Randomized Clinical Trial</td>
</tr>
<tr>
<td>Alexandra Briggs, MD</td>
<td>Jason Sperry, MD</td>
<td>Tranexamic Acid in Patients Undergoing Coronary-Artery Surgery</td>
</tr>
<tr>
<td>Name</td>
<td>Co-Authors</td>
<td>Title</td>
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<tr>
<td>Yiyu Zhao MD</td>
<td>Dennis Phillips, MD</td>
<td>Vasopressin versus Norepinephrine in Patients with Vasoplegic Shock after Cardiac Surgery</td>
</tr>
<tr>
<td>Fadi Tohme, MD</td>
<td>David Huang, MD</td>
<td>Video Laryngoscopy vs Direct Laryngoscopy on Successful First-Pass Orotracheal Intubation Among ICU Patients: A Randomized Clinical Trial</td>
</tr>
<tr>
<td>Michael Klein, MD</td>
<td>Matthew Rosengart, MD</td>
<td>Ultrasound Assessment of Volume Responsiveness in Critically Ill Surgical Patients: Two Measurements are Better Than One</td>
</tr>
<tr>
<td>Mary Assaad, MD</td>
<td>David Huang, MD</td>
<td>Association Between Tracheal Intubation During Adult In-Hospital Cardiac Arrest and Survival</td>
</tr>
<tr>
<td>Krystle Shafer, MD</td>
<td>Jonathan Elmer, MD</td>
<td>Prevalence and Localization of Pulmonary Embolism in Unexplained Acute Exacerbations of COPD: A Systematic Review and Meta-analysis</td>
</tr>
<tr>
<td>Christopher Johnson, MD</td>
<td>Hernando Gomez, MD</td>
<td>Prevalence and Localization of Pulmonary Embolism in Unexplained Acute Exacerbations of COPD: A Systematic Review and Meta-analysis</td>
</tr>
<tr>
<td>Timothy Kaselitz, MD</td>
<td>David Wallace, MD</td>
<td>Impact of 24/7 In-Hospital Intensivist Coverage on Outcomes in Pediatric Intensive Care</td>
</tr>
<tr>
<td>Benjamin Kautza, MD</td>
<td>Matthew Neal, MD</td>
<td>Every Minute Counts: Time to Delivery of Initial Massive Transfusion Cooler and Its Impact on Mortality</td>
</tr>
<tr>
<td>Namir Khandker, MD</td>
<td>Sherry Chou, MD</td>
<td>Platelet Transfusion Versus Standard Care After Acute Stroke Due to Spontaneous Cerebral Haemorrhage Associated with Antiplatelet Therapy (PATCH): A Randomized, Open-label, Phase 3 Trial</td>
</tr>
</tbody>
</table>

Pediatric Division Fellowship Program

Pediatric Critical Care Medicine Training Program

The Multidisciplinary Critical Care Training Program (MCCTP) also includes two pediatric fellowship programs. The Division of Pediatric Critical Care Medicine (PCCM) is well recognized as one of the leading academic programs worldwide for patient care, education, and research in pediatric critical care. In the 2016-17 academic year, we trained 18 clinical fellows in the division.

PCCM has two fellowship training program tracks: a three-year program in pediatric critical care medicine, with a complement of 14 fellows, and a one- to two-year program in pediatric cardiac critical care, with up to two fellows. In both, the program is designed to provide fellows with the knowledge, clinical experience, and training to acquire the competency of a pediatric intensivist and the skills to pursue an academic career. In so doing, the fellows will fulfill the requirements needed for Pediatric Critical Care Board eligibility. We intend that all pediatric critical care fellows will obtain board certification. Our fellowship program is included in website listings of fellowship programs on the ACGME, American Board of Pediatrics, Society of Critical Care Medicine, and Pediatric Critical Care Medicine. In addition, our recruiting program benefits from a strong national reputation, a large number of alumni practicing throughout the US, and the prominence of program faculty in the field of pediatric critical care medicine.
The PCCM Fellowship is among the five largest of the 66 ACGME-accredited pediatric critical care fellowship programs in the US. Sixty-four of these programs are currently training 400 fellows. The PCCM fellowships participate in the National Residency Matching Program. Fellowship applications are accepted via the Electronic Residency Application System in the late summer and fall prior to starting fellowship the following July.

Program News
The 2017 Academic Year was a year of positive change for the PCCM Program. In response to the fellow's request for additional education on new technologies available in critical care medicine (diagnostic ultrasound and imaging modalities), we have now scheduled an additional one hour of protected educational workshop time focused on ICU technology. A total of 12 hours of this activity has been added to our educational curriculum. Fellow workshop evaluations have shown positive results.

The PCCM leadership partnered with the Children’s Hospital of Pittsburgh of UPMC (CHP) administration to streamline the fellow role in transport calls. Previously, PCCM fellows triaged all transport calls coming into CHP and now using an algorithmic approach, these calls have been reduced by at least 50%. The PCCM fellows now take only ICU related calls, therefore complementing the defined learning goals and objectives of the fellowship program. Fellow response has been overwhelmingly positive to this change.

In April 2017, PCCM held the Pediatric Communication Course (PC3) in Mt. Washington. The course is a three-day, intensive course with “actor” parents and the course focuses on preparing learners to have difficult conversations with families. The course has been held six times and generally consists of second and third year fellows.

The PCCM department was honored to have several visiting professors this year, including Mark Hall, MD (October, 2016), Melanie Bembea, MD (April 2017), and Jeff Burns, MD (March 2017). PCCM fellows had the opportunity to present their current research topics to these distinguished visitors, and receive feedback on their projects, helping them to refine their projects and develop next steps.

Recruitment
In the fall 2016 match for fellows starting July 2017, we received a record number of 109 applications for five openings in our program. Twenty-six applicants accepted invitations for a full day of interviews, primarily with faculty from the PCCM division as well as with faculty from the Department's Adult Division and other divisions within the UPMC system. Applicants attend part of morning ICU rounds and have lunch and dinner with current fellows. These opportunities to spend time with current fellows have been touted as important and effective aspects our recruiting efforts. Our program’s applicant rank list is based on input and consensus from all division faculty, augmented by the opinions of current fellows and conversations with attendings at applicants’ residency institutions. We strongly consider an applicant’s academic potential, record of clinical work, and demeanor, with an emphasis on ability to provide effective care in a stressful, busy environment while working collegially with a large team of providers from multiple disciplines.

Presentations and Awards
- Pediatric Neurointensive Care and Resuscitation Research Scholars (5T32HD040686-11): Awarded to 2nd-year fellows Alicia Alcamo, MD, MPH and Michael Wolf, MD.
- Adult T32 (Experimental Therapeutics in Critical Illness, 5T32HL007820-19): Awarded to 2nd-year fellow Andy Prout, MD, MPH.

Honors and Recognition
- Chief Fellow 2016–17: 2nd year fellow, Kendra Woods, MD
- 2017 SCCM Gold Snapshot Award: 2nd year fellow, Jessica Wallisch, MD
- 2017 Safar Symposium Best Abstract Award: 3rd year fellow, Jessica Wallisch, MD
• 2017 Fink Day Translational Research Award: 2nd year fellow, Kate Kernan, MD
• 2017 McGrevin Scholarship: 2nd year fellow, Stefanie Ames, MD
• Kendra Woods named 2017 Fellow of the Year by pediatric residency program
• Alicia Alcamo, MD, MPH named Chief Fellow for 2017–18

Pediatric Critical Care Medicine Fellows 2016–17

**Graduating PCCM Fellows, graduated June 30, 2017**

Jamie Bell, MD
Medical School: Michigan State University College of Human Medicine, East Lansing, MI
Residency: Pediatrics, Children’s Hospital of Pittsburgh of UPMC, Pittsburgh, PA
Future: Assistant Professor, Pediatric Critical Care Medicine, Children’s Hospital of Michigan
Presented Abstract: PAS Annual Conference

Idris Evans, MD, MS
Medical School: Drexel University College of Medicine, Philadelphia, PA
Residency: Pediatrics, Children’s Hospital of Pittsburgh of UPMC, Pittsburgh, PA
Future: NIH Scholar, University of Pittsburgh School of Medicine; Clinical Instructor, Children’s Hospital of UPMC
Presented Abstract: ATS Annual Conference

Catherine Gretchen, MD, MS
Medical School: LSU Health New Orleans School of Medicine, New Orleans, LA
Residency: Pediatrics, Johns Hopkins Children Center, Baltimore, MD
Future: Clinical Fellow, Pediatric Cardiac Critical Care Medicine, Children’s Hospital of Pittsburgh of UPMC
Presented Abstract: SCCM 46th Annual Critical Care Congress, Fink Scholar Day

Bradley Podd, MD, PhD
Medical School: University of Virginia School of Medicine, Charlottesville, VA
Residency: Boston Children’s Hospital, Boston, MA
Chief Residency: Boston Children’s Hospital, Boston, MA
Future: CCM physician, Coastal Children's Services, Betty Cameron Women's and Children's Hospital, Wilmington NC
Presented Abstract: PAS Annual Conference, Fink Scholar Day

Jessica Wallisch, MD
Medical School: University of Kansas School of Medicine, Kansas City, MO
Residency: Pediatrics, Children’s Hospital of Pittsburgh of UPMC, Pittsburgh, PA
Future: NIH Scholar, Safar Center, University of Pittsburgh School of Medicine; Clinical Instructor, Children’s Hospital of Pittsburgh of UPMC
Presented Abstract: SCCM 46th Annual Critical Care Congress, Fink Scholar Day, Safar Symposium

Kendra Woods, MD
Medical School: Southern Illinois University School of Medicine, Springfield, IL
Residency: Pediatrics, Children’s Hospital of Pittsburgh of UPMC, Pittsburgh, PA
Chief Residency: Pediatrics, Children’s Hospital of Pittsburgh of UPMC, Pittsburgh, PA
Future: Clinical Instructor, Children's Hospital of Pittsburgh of UPMC
Presented Abstract: SCCM 46th Annual Critical Care Congress, Fink Scholar Day
2nd Year PCCM Fellows
Alicia Alcamo, MD
Medical School: Ohio State University of College of Medicine, Columbus, OH
Residency: Pediatrics, Cincinnati Children’s Hospital, Cincinnati, OH
Presented Abstract: SCCM 46th Annual Critical Care Congress, Fink Scholar Day, Quality Symposium

Stefanie Ames, MD
Medical School: Southern Illinois University School of Medicine, Springfield, IL
Residency: Pediatrics, University of Utah Health Care, Salt Lake City, UT

Kathryn Kernan, MD
Medical School: Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA
Residency: St. Louis Children’s Hospital/Washington University, St. Louis, MO
Oral Presentation: Fink Scholar Day
Presented Abstract: SCCM 46th Annual Critical Care Congress

Andrew Prout, MD
Medical School: Wayne State University School of Medicine, Detroit, MI
Residency: Pediatrics, C.S. Mott Children's Hospital, University of Michigan, Ann Arbor, MI
Presented Abstract: SCCM 46th Annual Critical Care Congress, Fink Scholar Day, Safar Symposium

Michael Wolf, MD
Medical School: Vanderbilt University School of Medicine, Nashville, TN
Residency: Pediatrics, Monroe Carell Jr. Children's Hospital, Vanderbilt University, Nashville, TN
Presented Abstract: SCCM 46th Annual Critical Care Congress, Fink Scholar Day

1st Year PCCM Fellows
Zachary Aldewereld, MD
Medical School: University of Alabama, Birmingham, AL
Residency: Lurie Children’s Hospital, Chicago, IL

Justin Azar, MD
Medical School: George Washington University School of Medicine, Washington, DC
Residency: DC Children’s National, Washington, DC

Katelyn Even, MD
Medical School: University of Massachusetts, Worcester, MA
Residency: Children’s Hospital of Pittsburgh of UPMC, Pittsburgh, PA

Catherine Madurski, MD
Medical School: Robert Wood Johnson Medical School, Rutgers University, Newark, New Jersey
Residency: AI duPont Hospital for Children, Wilmington, DE

Incoming Fellows
Monique Gardner, MD
Medical School: New York Medical College, New York, NY
Residency: Children’s Hospital of Philadelphia, Philadelphia, PA
Fellowship: Cardiology, Children’s Hospital of Philadelphia, Philadelphia, PA

Tim Kaselitz, MD, MPH
Medical School: University of Michigan, Ann Arbor, MI  
Residency: University of Michigan, Ann Arbor, MI  
Fellowship: Critical Care Internal Medicine, University of Pittsburgh

Joe Lynch, MD  
Medical School: West Virginia University, Morgantown, WV  
Residency: West Virginia University, Morgantown, WV

Neil Munjal, MD  
Medical School: Washington University School of Medicine, St. Louis, MO  
Residency: Pediatrics & Child Neurology, Children’s Hospital of Pittsburgh of UPMC

Madiha Raees, MD  
Medical School: Medical College of Georgia, Augusta, GA  
Residency: Johns Hopkins, Baltimore, MD

Pediatric Cardiac Critical Care Medicine Training Program

The Division of Pediatric Cardiac Critical Care is recognized for providing excellent critical care for infants, children, adolescents, as well as adults with congenital heart problems. Cardiac Critical Care is a complex task that requires expertise in several disciplines including pediatric cardiology, pediatric critical care, and neonatal critical care medicine. Established in 2003, the 12-bed Cardiac Intensive Care Unit (CICU) is among the very few units in the US that provides training for experts in this crucial sub-specialized field of medicine.

The Pediatric Cardiac Critical Care SIEP/OZ fellowship began in 2005. Our graduated pediatric cardiac intensivists have assumed leadership positions nationally and internationally. In addition to clinical expertise, the fellowship provides an unmatched environment for clinical and translational research with trainees producing several publications and presenting in national meetings. In the fall of 2016, the fellowship program was converted to solely an OZ fellowship program. Oversight of the program now falls under UPP and the Department of Critical Care Medicine, not the GME office. There is no impact on training, requirements, or opportunities; the change merely alters the management and hiring process from an administrative perspective.

The Pediatric Cardiac Critical Care Fellowship program provides a comprehensive training program for fellows interested in leading the field of pediatric cardiac critical care. Educational opportunities are tailored to suit the needs and interests of each fellow. The CICU is staffed by five pediatric cardiac intensivists responsible for more than 700 admissions a year. We have world-renowned cardiac surgeons, an unparalleled artificial heart (ventricular assist device) and ECMO program, and a heart-lung transplant program. The fellowship program is integrated with other fellowships, including pediatric cardiology, critical care medicine, neonatology, and anesthesiology thus providing a broad range of interdisciplinary expertise and several research opportunities from the basic sciences to translational and clinical research.

Fellow Recruitment

In the fall/winter, eight applicants were invited to interview for one opening in our program. All applicants accepted invitations for a full day of interviews, primarily with faculty from the PCCM Division but also with faculty from Cardiology and Surgery. Applicants attended part of morning CICU rounds and, like the pediatric critical care applicants, they had lunch and dinner with current fellows.
Pediatric Cardiac Critical Care Medicine Fellows 2016–17

Graduating Fellows, graduated June 30, 2017
LaTasha Lewis, MD
Medical School: Meharry Medical College, Nashville, TN
Residency: Pediatrics, Riley Hospital for Children, Indianapolis, IN
Fellowship: Pediatric Critical Care, Pediatric Critical Care, Children’s Hospital of Michigan, Detroit, MI
Future: Pediatric Intensivist, St. Joseph’s Children’s Hospital, Tampa, FL

Julia Mercer Niebauer, MD
Medical School: University of South Florida College of Medicine, Tampa, FL
Residency: Pediatrics, Florida State University Sacred Heart Hospital, Tallahassee, FL
Fellowship: Pediatric Critical Care, University of Alabama at Birmingham, Birmingham, AL
Future: Pediatric Intensivist, Johns Hopkins All Children’s Hospital, St. Petersburg, FL

Continuing Fellow
Wonshill Koh, MD, PhD
Medical School: Texas A&M Health Science Center College of Medicine; University of Missouri School of Medicine
Residency: Pediatrics, Cohen Children’s Medical Center, New York, NY
Fellowship: Pediatric Cardiology, Cleveland Clinic Children’s Hospital, Cleveland, OH
Abstract Presented: PCCIS Annual Conference

Incoming Fellow
Catherine Gretchen, MD, MS
Medical School: LSU Health New Orleans School of Medicine, New Orleans, LA
Residency: Pediatrics, Johns Hopkins Children Center, Baltimore, MD
Fellowship: Pediatric Cardiac Critical Care Medicine, Children’s Hospital of Pittsburgh of UPMC

Curriculum

All Pediatric Fellows participate in multiple educational conferences, as described below.

<table>
<thead>
<tr>
<th>Conference</th>
<th>Frequency</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Journal Club</td>
<td>Weekly</td>
<td>With faculty mentors, fellows select, present, and organize discussions on recent, classic, or otherwise relevant papers from the biomedical literature.</td>
</tr>
<tr>
<td>Professor Rounds</td>
<td>Weekly</td>
<td>Discussion of interesting or controversial cases within the PICU or CICU with faculty, fellows and residents.</td>
</tr>
<tr>
<td>Neurocritical Care Safar Rounds</td>
<td>Weekly</td>
<td>Fellow presents interesting or controversial neurocritical care cases from the PICU to faculty, usually Dr. Kochanek, who teach and facilitate discussion.</td>
</tr>
<tr>
<td>Safar Journal Club</td>
<td>Weekly</td>
<td>Fellows select, present, and organize discussion regarding research articles and projects to review (single subject, recent review, etc.).</td>
</tr>
<tr>
<td>PICU Morbidity &amp; Mortality Conference</td>
<td>Monthly</td>
<td>Fellows organize and present cases, participate in discussion, and help identify needed system or policy changes.</td>
</tr>
<tr>
<td>PCCM Ethics Conference</td>
<td>Monthly</td>
<td>Fellows present cases and participate in discussion of ethical, legal, and psycho-social aspects of care with ethicists, faculty, nursing staff, social workers, chaplains, and others.</td>
</tr>
<tr>
<td>CICU Conferences</td>
<td>Monthly</td>
<td>Discussion about congenital heart disease diagnosis and management.</td>
</tr>
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</tr>
<tr>
<td>CRRT/ECMO</td>
<td>Monthly</td>
<td>Multidisciplinary conference discussing CRRT and ECMO, including educational sessions and review of problems occurring during individual CRRT and ECMO treatment courses.</td>
</tr>
<tr>
<td>Fellow Core Curriculum</td>
<td>4 hours monthly</td>
<td>Continuing education for PCCM fellows on different topics relevant to pediatric critical care. Specific topics are presented by faculty from PCCM and outside departments.</td>
</tr>
<tr>
<td>Performance, Quality, Research, and Safety (PQRS) Conference</td>
<td>Bi-Monthly</td>
<td>The objective is to teach methods of QI, to generate QI projects, and to determine results of QI efforts, with an overall goal of improving the safe and effective care of patients in pediatric critical care.</td>
</tr>
<tr>
<td>Introduction to PCCM</td>
<td>Annually</td>
<td>Intensive 4-week educational program with didactics by faculty from PCCM and other subspecialties, simulation sessions led by Dr. Hamilton and senior fellows, and includes workshops.</td>
</tr>
<tr>
<td>Faculty Research Day</td>
<td>Annually</td>
<td>Presentations by all PCCM faculty and some faculty from Adult CCM on fellow-related research activities. Fellows ask questions after each presentation; the meeting serves to help fellow focus their scholarly activity direction.</td>
</tr>
<tr>
<td>CICU Educational Rounds</td>
<td>Weekly</td>
<td>Continuing education for PCCM fellows on cardiac critical care topics relevant to the CICU. Specific topics are presented by faculty from PCCM and outside departments.</td>
</tr>
<tr>
<td>CICU Core Lecture</td>
<td>Bi-Monthly</td>
<td>Discussion of interesting or controversial cases within the CICU with faculty, and fellows</td>
</tr>
</tbody>
</table>

In addition to the above core conferences, we conducted the following additional educational activities in FY17:

**High-fidelity Simulation Sessions for Pediatric Residents**

Throughout fellowship, PICU fellows facilitate high-fidelity simulation sessions for Pediatric residents with Dr. Hamilton during the resident PICU rotation. Sessions include recognition and management of respiratory distress, shock, and seizures. PICU fellows take an active role in conducting and debriefing the simulation sessions, affording them unique opportunities to teach cognitive principles and psychomotor skills, and to utilize adult education principles and debriefing techniques. Fellows co-facilitated this course with Dr. Hamilton.

**MCCTP Professionalism and Communication Course**

PCCM fellows attend the professionalism series, coordinated by the Adult Division. Didactics and workshops center on adult education principles, how to negotiate for faculty positions, and academic career advancement among other topics.

**Research**

PCCM fellows conduct scholarly research under the guidance and mentorship of faculty members within the Safar Center for Resuscitation Research and the Clinical Research, Investigation and Systems Modeling of Acute Illness (CRISMA) Center. Scholarly activities and research includes such topics as sedation protocols in the PICU, costs of healthcare, and using the medical record to predict acute change in patient status as well as educational curriculum design, simulation studies, and quality initiatives.
The Safar Center for Resuscitation Research

Directed by Dr. Patrick Kochanek, MD, MCCM, the Ake N. Grenvik Professor and Vice Chairman of Critical Care Medicine, the Safar Center is the primary research facility of the PCCM Division. This was a special year for the Safar Center. Having been located in the Hill building on the main campus in Oakland since 1979, the Safar Center moved into spectacular newly renovated space on the Children’s Hospital of Pittsburgh of UPMC campus, within the Rangos Research Center. The center features multiple pre-clinical surgical suites, a post-operative ICU, and a state of the art long-term behavioral outcome facility. It houses the laboratories of faculty across multiple departments including CCM, neurological surgery, physical medicine and rehabilitation, pediatrics, and others, and serves collaborators in numerous departments and schools across the medical center. Safar Center investigators focus on studies in traumatic brain injury (TBI) and cardiopulmonary arrest (CA), and offers additional unique pre-clinical modeling in rodent models such as ECMO. It also houses a number of important resources for clinical research in the field of pediatric brain injury.

Pediatric Neurointensive Care and Resuscitation Research T32
Director: Patrick Kochanek, MD, MCCM
Our T32 program is in its 16th year. The program is directed by Dr. Kochanek and co-directed by Robert S.B. Clark, MD, Chief or Critical Care Medicine at Children’s Hospital of Pittsburgh at the University of Pittsburgh Medical Center, and Anthony Kline, PhD, professor in the Department of Physical Medicine and Rehabilitation. The T32 training program’s aim is to train clinicians, specifically, pediatric critical care medicine, child neurology, pediatric neurosurgery, physical medicine and rehabilitation, pediatric emergency medicine, newborn medicine, and pediatric radiology fellows. We also train selected other fellow-level clinician-scientists or scientists with related research interests targeting investigations into two key insults: TBI and CA, which are central to the field of pediatric neurointensive care and resuscitation. Indeed, these are the two conditions that contribute the greatest morbidity and mortality to children across the field of pediatric neurocritical care. Our T-32 program offers research opportunities in these two areas with 21 outstanding and highly experienced NIH-funded senior mentors—each of whom has successfully guided many trainees to academic careers and/or independent funding. The research program runs in conjunction with ACGME accredited training programs in Pediatric Critical Care Medicine, Neurological Surgery and Physical Medicine and Rehabilitation, at Children’s Hospital of Pittsburgh and University of Pittsburgh Medical Center.

More information about the Pediatric T32 program can be found in the Research section of this Annual Report.
## Faculty Data

Promotions for Faculty in the Department of Critical Care Medicine

### July 1, 2016 through June 30, 2017

<table>
<thead>
<tr>
<th>Name</th>
<th>Date Promotion Approved</th>
<th>Academic Rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ali Al-Kafaji</td>
<td>October 1, 2016</td>
<td>Professor</td>
</tr>
<tr>
<td>Hülya Bayır</td>
<td>November 1, 2016</td>
<td>Endowed Chair in Pediatric Research</td>
</tr>
<tr>
<td>Sherry H-Y Chou</td>
<td>October 1, 2016</td>
<td>Associate Professor</td>
</tr>
<tr>
<td>Jeremy Kahn</td>
<td>October 1, 2016</td>
<td>Endowed Chair in Critical Care Organization and Management</td>
</tr>
<tr>
<td>Sachin Yende</td>
<td>February 15, 2017</td>
<td>Professor</td>
</tr>
</tbody>
</table>

### Faculty New Hires

#### July 1, 2016 through June 30, 2017

<table>
<thead>
<tr>
<th>Name</th>
<th>Previous Location</th>
<th>Previous Rank</th>
<th>Current Rank</th>
</tr>
</thead>
<tbody>
<tr>
<td>Robert Bart</td>
<td>Department of Health Services for Los Angeles County</td>
<td>Chief Medical Information Officer</td>
<td>Associate Professor</td>
</tr>
<tr>
<td>Yolandee Bell-Cheddar</td>
<td>St. Christopher’s Hospital for Children, Philadelphia</td>
<td>Assistant Professor</td>
<td>Clinical Assistant Professor, Pediatrics</td>
</tr>
<tr>
<td>Timothy Girard</td>
<td>Vanderbilt University Medical Center</td>
<td>Assistant Professor</td>
<td>Visiting Associate Professor</td>
</tr>
<tr>
<td>Christopher Horvat</td>
<td>UPMC</td>
<td>T32 Scholar, Safar Center</td>
<td>Assistant Professor</td>
</tr>
<tr>
<td>Wonshill Koh</td>
<td>UPMC</td>
<td>Pediatric Cardiac CC Fellow</td>
<td>Clinical Instructor</td>
</tr>
<tr>
<td>LaTasha Lewis</td>
<td>UPMC</td>
<td>Pediatric Cardiac CC Fellow</td>
<td>Pediatric Intensivist St. Joseph’s Children’s Hospital</td>
</tr>
<tr>
<td>Matthew Siedsma</td>
<td>University of Pittsburgh</td>
<td>T32 Scholar, NRSA</td>
<td>Clinical Assistant Professor</td>
</tr>
</tbody>
</table>

Adult Division

Ali H. Al-Khafaji, MD, MPH, FACP, FCCP


Derek C. Angus, MD, MPH, FRCP


Christopher Brackney, MD

Brad Butcher, MD


Sherry H-Y Chou, MD, MSc, FNCS


Gilles Clermont, MD, MSc


Joseph M. Darby, MD


Cameron Dezfulian, MD


Chenell Donadee, MD


Jonathan Elmer, MD, MS

- Peer Reviewed Articles

Chennel Donadee, MD


David Emlet, PhD


Lillian Liang Emlet, MD, MS, FACEP


Timothy D Girard, MD, MSCL

Scott Gunn, MD


David T. Huang, MD, MPH, FACEP, FCCM


Seymour CW, Martin-Gill C, Callaway C, Yealy D, Scales D, Kahn JM, Angus DC. Delays from first medical contact to antibiotic administration in sepsis. Critical Care Medicine 2017 May;45(5):759-765. PMID: 28234754.


Barbash IJ, Kuza CC, Rak KJ, Kahn JM. Hospital perceptions of Medicare’s sepsis quality reporting initiative. Journal of Hospital Medicine 2017 [Epub ahead of print].

A. Murat Kaynar, MD, MPH


Surg. 2016 Feb; 80(2):243


Florian Mayr, MD
- Mayr FB, Talisa VB, Balakumar V, Chang CH, Fine M, Yende S. Proportion and Cost of Unplanned 30-Day Readmissions After Sepsis Compared With Other Medical Conditions. JAMA 2017;317(5):530-531. PMID:28114505

Deepika Mohan, MD

Bradley Molyneaux, MD, PhD

Jason Moore, MD, MS
Francis Pike, PhD


Michael Pinsky, MD

- Pinsky MR. The Right Ventricle: Interaction with the Pulmonary Circulation. Crit Care 10; 20, 266, 2016. (PMID: 27613549)
- Pinsky MR. The right ventricle: interaction with the pulmonary circulation. Crit Care. 2016 Sep 10;20:266.. PMID: 27613549
- Pinsky MR, Broachard L, Kellum JA. Ten recent advances that could not have come about without applying physiology. Intensive Care Med. 2016 Feb;42(2):258-60. PMID: 25805653

Patients with Respiratory Distress. Becker TK, Martin o, oxygenation support

Intervention for Suicidal Veterans with Major Depression. Community Ment Health J. 2016; 440

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Penny Sappington, MD


Christopher K. Schott, MD, MS, RDMS, FACEP


Critical Care Medicine

Annual Report FY17 | 129


Matthew Siedsma, MD

- Siedsma MP, Emlet LL. Physician burnout: can we make a difference together? Crit Care 2015 July 2;19:273. PMID 26134266

David J. Wallace, MD, MPH, RDMS


- Seymour CW, Aotaik M, Wallace DJ, Elhabasy AE, Chhatwa J, Rea TD, Angus DC and Kahn JM. County-Level Effects of Prehospital Regionalization of Critically Ill Patients: A Simulation Study. Critical care medicine (2015); 43;1807-1815


- Wallace DJ, Seymour CW & Kahn JM. Hospital-level changes in adult ICU bed supply in the United States. Critical Care Medicine (2017).

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- Lapsis MH, Yo M, Przybysz ME and Wallace DJ. What Is Causing a Man’s Severe Abdominal Pain and Yellow Blood? Consultant; (2017)


### Xiaoyan Wen, MD, MSc


### Douglas White, MD, MAS


Fermentable fiber alters the gut microbiota and confers protection in a murine model. 


**Pediatric Division**

**Rajesh Aneja, MD**


- Au AK, Chen Y, Du L, Smith CM, Manole MD, Baltagi SA, Chu CT, Aneja RK, Bayir H, Kochanek PM, Clark RS. Ischemia-induced autophagy contributes to neurodegeneration in cerebellar Purkinje cells in the developing rat brain and in primary cortical neurons in vitro. Biochim Biophys Acta. 2015 Sep;1852(9):1902-11. PMID: 26071643


Alicia K. Au, MD


- Au AK, Chen Y, Du L, Smith CM, Manole MD, Baltagi SA, Chu CT, Aneja RK, Bayir H, Kochanek PM, Clark RS. Ischemia-induced autophagy contributes to neurodegeneration in cerebellar Purkinje cells in the developing rat brain and in primary cortical neurons in vitro. Biochim Biophys Acta. 2015 Sep;1852(9):1902-11. PMID: 26071643

Hülya Bayır, MD

- Wallisch JS, Simon DW, Bayir H, Bell MJ, Kochanek PM, Clark RS. Cerebrospinal Fluid NLRP3 is Increased After Severe Traumatic Brain Injury in Infants and Children. Neurocrit Care. 2017 Feb 8. [Epub ahead of print]


Association of bleeding and thrombosis with outcome in extracorporeal life support.


Shaun Carlson, PhD


Robert S. B. Clark, MD


Yulia Domnina, MD

- Wolf MS, Mahesh SS, Domnina YA In-Line CRRT via Centrifugal Flow RVAD for Management of AKI During Mechanical Circulatory Support of End-Stage Heart Disease. Artificial Organs submitted and accepted for publications doi:10.1111/AOR.12957

Ericka L. Fink, MD, MS

- Au AK, Bell MJ, Fink EL, Aneya RK, Kochanek PM, Clark RSB. Brain-Specific Serum Biomarkers Predict Neurological Morbidity in Diagnostically Diverse Pediatric Intensive Care Unit Patients. Neurocritical Care, Epub ahead of print.


Dana Y. Fuhrman, DO, MS


Melinda Hamilton, MD, MSc


- Jackson TC, Manole MD, Kotermanski SE, Jackson EK, Clark RS, Kochanek PM. Cold stress protein RBM3 responds to temperature change in an ultra-sensitive manner in young neurons. Neuroscience. 2015 Oct 1;310:268-78. PMID: 26265550
- Au AK, Chen Y, Du L, Smith CM, Manole MD, Baltagi SA, Chu CT, Aneja RK, Bayır H, Kochanek PM, Clark RS. Ischemia-induced autophagy contributes to neurodegeneration in cerebellar Purkinje cells in the developing rat brain and in primary cortical neurons in vitro. Biochim Biophys Acta. 2015 Sep;1852(9):1902-11. PMID: 26071643
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Jiunn-Huey Ivy Lin, MD, PhD
- Lin JH, Kean AC and Cordes TM. The Risk of Thromboembolic Complications in Fontan Patients with Atrial Flutter/Fibrillation Treated with Electrical Cardioversion. Pediatr Cardiol. 2016 Oct;37(7):1351-60

Alejandro Lopez-Magallon, MD

Joan Sanchez De Toledo, MD, PhD
- Rodríguez-Fanjul J, Moreno J, Sanchez-de-Toledo J; Lung Ultrasound for Cardiogenic Shock on VA-ECMO; Accepted; Rev Esp Cardiol. 2017; http://dx.doi.org/10.1016/j.recesp.2017.07.015

Dennis W. Simon, MD


Ann E. Thompson, MD, MHCPM


Shekhar T. Venkataraman, MD
