



SAFAR CENTER
FOR RESUSCITATION RESEARCH



ANNUAL REPORT

2014-2015

MISSION STATEMENT

The mission of the Safar Center for Resuscitation Research 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.”

The Safar Center for Resuscitation Research at the University of Pittsburgh School of Medicine was founded by the late Dr. Peter Safar in 1979, initially as the International Resuscitation Research Center. In recognition of Dr. Safar’s innumerable contributions to the field of resuscitation medicine, it was renamed the Safar Center for Resuscitation Research in 1994. The Safar Center’s current research programs include Traumatic Brain Injury, Child Abuse, Cardiac Arrest, Emergency Preservation and Resuscitation, Hemorrhagic Shock, Combat Casualty Care, and Rehabilitation of CNS Injury. Center investigators work closely with the depts. of Critical Care Medicine, Surgery, Neurological Surgery, Anesthesiology, Emergency Medicine, and Physical Medicine and Rehabilitation at both the University of Pittsburgh Medical Center and Children’s Hospital of Pittsburgh. In addition to conducting basic research, the Safar Center also provides training to the next generation of resuscitation researchers. The Center is a 20,000 square-foot freestanding research facility that houses the laboratories of scientists and clinician-scientists working across a broad spectrum of fields important to resuscitation medicine.

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LETTER FROM THE DIRECTOR

It is an honor to update you with this report on the Safar Center for Resuscitation Research. Our Center continues to grow and serve the University of Pittsburgh School of Medicine (SOM) as a world renowned research facility in the area of cerebral resuscitation. Our programs in traumatic brain injury (TBI) and cardiopulmonary arrest are internationally recognized and are leading their respective

fields on a number of facets of both pre-clinical and clinical investigation. 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 develop-

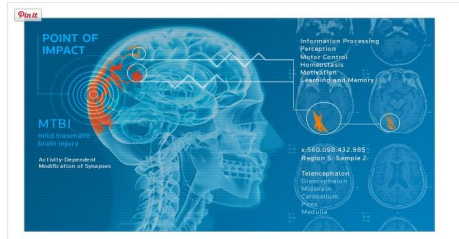
ment of novel therapies and interventions that can be implemented from the field through to rehabilitation. We feature several additional special programs addressing 1) research training, along with research in both 2) combat casualty care and 3) pediatric and adult neurocritical care. Research training is multi-departmental and includes a long-standing T32 in pediatric neurointensive care and resuscitation research. Our combat casualty care related research features Operation Brain Trauma Therapy (OBTT) and other important collaborations with investigators in the Department of Defense (DoD). Our work in pediatric neurocritical care is linked to translational investigations at Children's Hospital of Pittsburgh (CHP). Our faculty members and trainees come from many departments in the SOM including Critical Care Medicine (CCM), Pediatrics, Neurological Surgery, Physical Medicine and Rehabilitation (PM&R), Emergency Medicine, and Anesthesiology, and also from the Schools of Pharmacy and Nursing.

SCIENCEWATCH

HOME SCI-BYTES CITATION LAUREATES GLOBAL RESEARCH REPORTS ABOUT SCIENCEWATCH

SPECIAL TOPIC: TRAUMATIC BRAIN INJURY

OCTOBER 2014



OVERVIEW AUTHORS INSTITUTIONS NATIONS JOURNALS PAPERS
FIELD DISTRIBUTION

Recent years, particularly in the United States, have seen a new awareness of the dangers and consequences of traumatic brain injury (TBI). Unfortunately, although not unexpectedly, this trend has been driven by grim developments. America's long wars in Iraq and Afghanistan, and their toll of veterans dealing with lingering brain injuries caused by improvised explosive devices and other ordnance, have provided one impetus. And a supposedly lighter sphere of activity—the world of sports—has also deepened the sense of

ScienceWatch.com

Our programs in traumatic brain injury (TBI) and cardiopulmonary arrest are internationally recognized and are leading their respective fields on a number of fronts in both pre-clinical and clinical investigation.

In FY 2015, Thompson Reuters *Science Watch* released a special topic report on TBI which surveyed bibliometric citation data aggregated by *Web of Science* in the field of TBI over the past 15 years. I was pleased and surprised to have been identified as the most prolific and most highly cited author in the field of TBI, having authored or co-authored >300 papers on TBI which have been collectively cited >3800 times. My long-time colleague Dr. Robert Clark, Chief of CCM at CHP was identified as having co-authored >100 of those publications with me. This development is a testament to the herculean team effort of the Safar Center family of investigators and trainees with whom I have had the honor of working with as center director for 21 years. Also notable was the fact that the University of Pittsburgh was identified as the leading institution in the nation for publications in the field of TBI with >900 in the past 15 years.

This was another banner year for the acquisition of new grants by Safar Center investigators—for both junior and senior investigators. Two highly successful young investigators received national grants. Dr. Ericka Fink, Associate Professor of CCM and Pediatrics received a \$1.87M grant from PCORI to lead a multicenter study of the imple-

mentation of early rehabilitation for children after acute brain injury. Her work on this project is helping to launch an exciting collaboration with Dr. Amy Houtrow, Associate Professor and Vice Chair of PM&R at CHP. Also, Dr. Travis Jackson, Assistant Professor of CCM received an R21 from NINDS to study RNA binding protein 5 (RBM5) in TBI and a

New federal funding specifically in FY 15 totaled \$8.6M (total costs) and reflects the tremendous work effort and innovation of the Safar Center faculty.

Scientist Development Grant from the American Heart Association to study the role of PH domain and leucine rich repeat protein phosphatase 1 (PHLPP1) in pre-clinical models of cardiac arrest. Travis is a talented young neuroscientist who we recruited as a post-doctoral fellow and is now a rising star on our faculty. Several senior faculty members also received new grants, including a remarkable four new R01 awards from NINDS. Dr. Anthony Kline in the Dept. of PM&R received an R01 to study enriched environment as a pre-clinical model of rehabilitation after TBI. Dr. Hülya Bayır Professor of CCM received an R01 from NINDS to study the role of oxidized phospholipids in mediating neuronal death after TBI in pre-clinical models. Dr. Bayır, collaborating with Dr. Valerian Kagan in the Pittsburgh Center for Free Radical

and Antioxidant Health, has been a prolific investigator in our center. Dr. C. Edward Dixon in the Dept. of Neurological Surgery received an R01 to study Alpha-Synuclein and Synaptic Vesicle Dysfunction after TBI. Finally, Dr. Edwin Jackson, Professor of Pharmacology and Chemical Biology and I received a new dual PI R01 from NINDS to study the 2,3 cAMP pathway in TBI. The Safar Center also has a substantial amount of funding for investigations in TBI from the



Safar Center Associate Director Dr. Rachel Berger is serving on President Obama's Commission on Child Abuse. Rachel's work on the development of novel diagnostic approaches to reduce the number of cases of misdiagnosis of abusive head trauma is nationally recognized.



In FY 15, four fellows were funded by the National Institutes of Child Health and Human Development via our long-standing T32 grant in Pediatric Neurointensive Care and Resuscitation Research, including Drs. Erik Brockman, Shaun Carlson, Diana Pang, and Dennis Simon. In addition to other awards and accomplishments previously discussed, Dr. Brockman (pictured) has just been named the Director of Neurocritical Care for Children's Hospitals and Clinics of Minnesota, and Dr. Carlson was just awarded an F32 grant to continue his research under the mentorship of Dr. C. Edward Dixon at the Safar Center.

U.S. Army. Related to this at the end of FY 14 I received a \$2.99M grant to expand the highly acclaimed Operation Brain Trauma Therapy (OBTT) pre-clinical multi-center drug screening consortium that seeks to identify the most promising therapies to be considered for clinical trials in severe TBI. New federal funding specifically in FY 15 totaled \$8.6M (total costs) and reflects the tremendous work effort and innovation of the Safar Center faculty. Several of our trainees also received special honors this year. Dr. Diana Pang one of the CCM fellows supported by our T32 grant received the 2015 Shock Society Research Investigator's Award for Early Scientists. Diana is working on septic encephalopathy in children under the guidance of Dr. Raj Aneja. Matt Diamond, a recent Pitt BPhil graduate won the 2014 *Epilepsia* Prize. The award recognizes the best article in the journal as selected by the editors. His work titled "IL-1B Associations with Post-Traumatic Epilepsy Development: A Genetics and Biomarker Cohort Study" was carried out under the mentorship of Dr. Amy Wagner, Professor and Vice Chair of PM&R. Dr. Thomas Uray, a visiting fellow from the University of Vienna, was named the

Young Investigator of the Year by the European Resuscitation Council for his research comparing ventricular fibrillation and asphyxial cardiac arrest. He was mentored by Dr. Cameron Dezfulian in CCM. Dr. Dennis Simon, a pediatric CCM fellow funded by our T32 and mentored by Dr. Robert Clark was named the 2015 Nancy Caroline Fellow as the top trainee at our center. I am pleased that Dennis is joining our Pediatric CCM faculty. Dr. Ruchira Jha, a T32 fellow in adult neurocritical care working on novel therapies for brain edema under the mentorship of Dr. Kochanek was awarded a KL2 position in the prestigious Multi-

risk for that condition.

Safar Center Associate Director Dr. Michael Bell, Director of Neurocritical Care at CHP is leading the highly successful multi-center ADAPT comparative effectiveness trial in pediatric TBI. This year, this remarkable study reached the milestone of becoming the largest trial in the history of severe pediatric TBI having entered >350 children with severe injury. On its way to studying 1000 patients, Mike is leading a trial that is being viewed as the poster child for successful clinical pediatric TBI research by NINDS. Safar Center Associate Director Dr. Anthony Kline was re-elected to the position of Secretary Treasurer of the National Neurotrauma Society (NNTS) for 2016 and 2017. Dr. Kline is one of the leaders in the field of PM&R in the NNTS and an important representative of both the Safar Center and the University to that Society.

Former Associate Director Dr. Samuel Tisherman accepted a position as Professor and Director of the Institute for Critical Care and Trauma Education and Director of the Surgical ICU at the University of Maryland Medical Center. Sam is a fantastic physician-scientist and friend and colleague to many of us at the Safar Center and will be greatly missed.

The Safar Center has been looking for a new home for the past few years and I am pleased that as this report is going to press, Senior Vice Chancellor Dr. Arthur Levine just informed me that plans are being developed to relocate the Safar Center to within the Rangos Research Center at Children's Hospital of Pittsburgh. We are excited by this development and are looking toward a 9-12 month timetable for renovations and relocation.

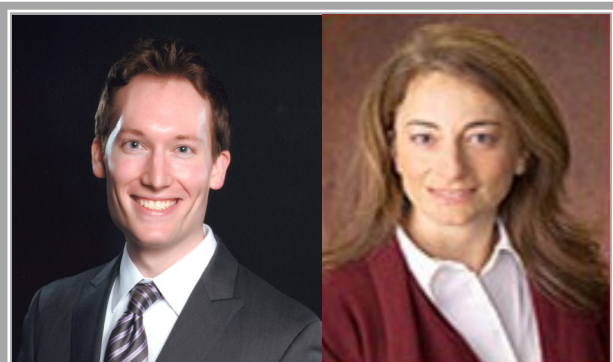
Finally, I was honored this year to be named the Ake N. Grenvik Professor of CCM. As a faculty member in CCM, Dr. Grenvik was a pioneer in the field, an important part of the amazing legacy in CCM at Pitt, and has been a long-time friend of the Safar Center.

I look forward to new successes and discoveries in FY 2016.

Sincerely,



Patrick M. Kochanek, MD, MCCM
Director, Safar Center for Resuscitation Research



Two young faculty investigators received their first national funding as principal investigators in FY 15. Ericka Fink, MD, MS received a large grant from the Patient-Centered Outcomes Research Institute (PCORI) for a clinical trial of early rehabilitation after brain injury in infants and children receiving neurocritical care and Travis Jackson, PhD received both an R21 from NINDS/NIH and a Scientist Development Grant from the American Heart Association for his work on novel neuroprotective approaches in traumatic brain injury and cardiac arrest.

disciplinary Clinical Research Scholars Program directed by Dr. Wishwa Kapoor. Ruchira was recruited from MGH to the adult neurocritical care program by Dr. Lori Shutter and is an exceptional talent. Dr. Corina Bondi, a post-doctoral fellow in the laboratory of Dr. Anthony Kline was recently promoted to Assistant Professor of PM&R and joined our Center. Corina is a talented young investigator studying frontal lobe function using innovative approaches in pre-clinical models of TBI.

Safar Center Associate Director Dr. Rachel Berger is serving on President Obama's Commission on Child Abuse. In addition to her important work on that commission, she just completed a landmark multi-center study on the use of a clinical decision rule and serum biomarkers to aid in alerting physicians to the possible diagnosis of abusive head trauma in infants at

FUNDING

In FY 15, a total of 13 Safar Center investigators were funded by 23 federal grants. There has been tremendous growth in grant support acquired by Safar Center investigators over the past twenty years. As shown in the bar graph on the following page, as of July 1, 2014, Safar Center investigators had over \$45M in extramural grant support in total and direct costs for the full funding period.

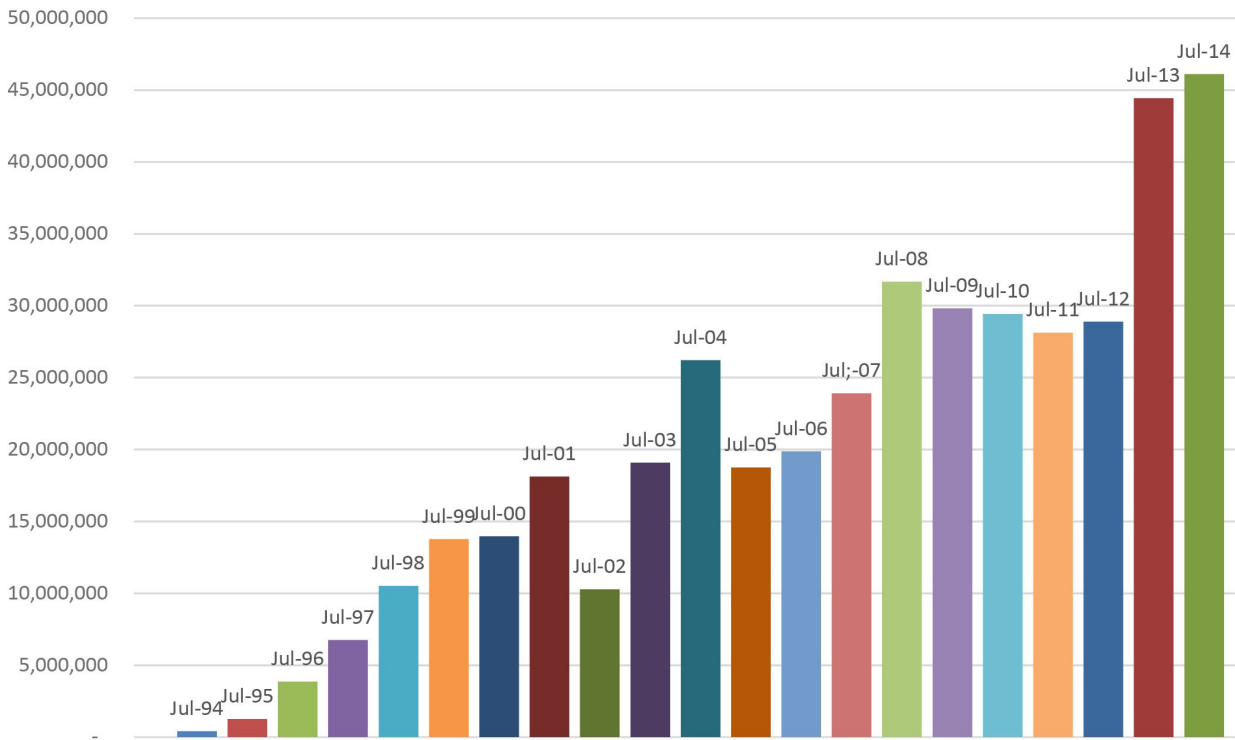
Successful acquisition of several large multi-center programmatic awards have been instrumental in this success. Three examples include the National Institutes Health/National Institute of Neurological Disorders and Stroke (NIH/NINDS)-funded Approaches and Decisions in Acute Pediatric TBI (ADAPT) trial by Dr. Michael Bell, the U.S. Department of Defense (DoD) funded Operation Brain Trauma Therapy (OBTT), and our T-32 from the National Institute of Child Health and Development focused on training in pediatric neurocritical care held by Dr. Kochanek. The growth of funding support by our center investigators over the past 20 years has been truly remarkable and is a testament to the hard work, dedication, and expertise of our faculty and trainees.

The specific sources of grant support are shown in the pie chart. Support from the NIH continues to represent the greatest source of funding and we also continue to have considerable support from the DoD. We also have federal support from the Department of Veteran's Affairs and the National Institute on Disability and Rehabilitation Research in the Department of Education. It is also noteworthy that three of our junior faculty members are funded by K awards from the NIH. Several new funding sources this year include the Patient-Centered Outcomes Research Institute (PCORI), and the American Heart Association.

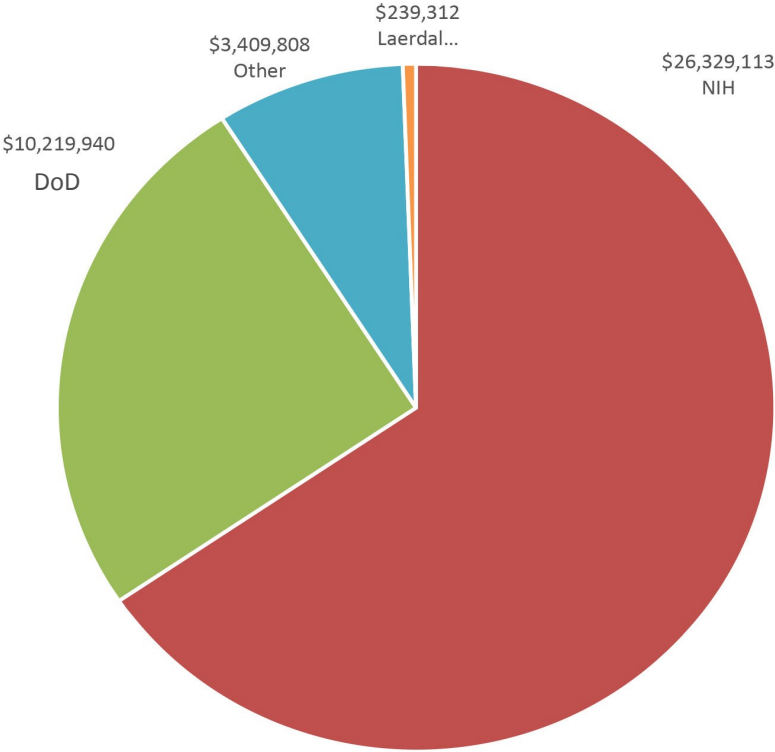
We continue to receive generous support from the Laerdal Foundation, which has been a supporter of our center since its inception in 1980. We are grateful to all of the funding agencies for support. One of the abiding missions of the Safar Center is to support training for young investigators, to that end, we would like to extend our thanks to all of the individuals who have donated to the Safar Legacy Fund.

As of July 1, 2014, Safar Center investigators had over \$45M in extramural grant support in total and direct costs for the full funding period.

Direct and Indirect Costs for the Full Award Period of Safar Center Grants



Specific Sources of Grant Support 2010 - 2015



RESEARCH

Safar Center investigators were highly productive in FY 15 publishing 55 peer reviewed manuscripts, with 15 additional manuscripts currently published ahead of print, 26 editorials, letters, and chapters, and over 40 abstracts. Many of these publications were authored by trainees. Details on the specific programs in our center are described below.

TRAUMATIC BRAIN INJURY (TBI)

The Safar Center is one of the leading centers in the world for the investigation of TBI. Research in TBI by Safar Center investigators includes 1) both pre-clinical and clinical investigations, 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 combat casualty care. Although our work is predominantly focused on severe TBI, several projects addressing the topic of mild TBI are also ongoing. This academic year, Safar Center investigators published a remarkable 31 peer reviewed manuscripts on TBI and have 11 additional manuscripts currently published ahead of print. A brief update of developments in FY 15 for each laboratory is presented below.

Patrick M. Kochanek, MD, MCCM

(CCM, Pediatrics, Anesthesiology, Clinical and Translational Science, and Bioengineering)

Dr. Kochanek's laboratory is currently focused in three areas of investigation, namely: 1) Operation Brain Trauma Therapy (OBTT): a multi-center drug screening consortium to identify promising therapies to advance to clinical trials for severe TBI, 2) development of novel therapies for TBI resuscitation, and 3) study of the role of the 2, 3 cAMP pathway in TBI. Dr. Kochanek is leading OBTT funded by the U.S. DoD with the goal of identifying the most promising therapies to advance to clinical trials for severe TBI. OBTT is a \$10M program comprised of two grants that are supporting rigorous therapeutic screening across multiple TBI models and in multiple species. Novel serum biomarkers of brain injury are also being evaluated across the models. In addition to the Safar Center, participants include the University of Miami School of Medicine, Walter Reed Army Institute of Research, Virginia Commonwealth University, The University of Florida, Messina University, and Banyan Biomarkers, LLC. This

work is being viewed as having special importance in the field related to the "reproducibility crisis" in pre-clinical research that has been a topic of considerable recent discussion.

Secondary insults such as shock are important contributors to poor outcome after TBI and the resuscitation required exacerbates the development of cerebral edema. Dr. Kochanek's laboratory has developed a unique mouse model of TBI plus



hemorrhagic shock that is being used to test novel therapies targeting the development of cerebral edema. Current work funded by a U44 from NINDS and the U.S. DoD focuses on the development of new therapies including the ultra-small volume resuscitation agent polynitroxylated pegylated hemoglobin, inhibitors of the Sur-1 pathway, and novel aquaporin-4 channel antagonists. Finally, based on the recent discovery by University of Pittsburgh Professor Dr. Edwin Jackson of the 2, 3 cAMP adenosine pathway in both kidney and brain Drs. Jackson and Kochanek, funded by a dual PI R01 are carrying out investigations of this pathway in TBI. Given the fact that 2, 3 cAMP is neurotoxic while its metabolite adenosine is neuroprotective, the pathway may play an important role in governing secondary injury vs. protection after TBI. A number of publications in FY 15, including several reports by post-doctoral fellow Jon Verrier, indicate that this pathway is readily detectable after TBI in murine models and in humans with severe injury.

Hülya Bayır, MD (CCM, Pediatrics, and Environmental and Occupational Health)

Dr. Bayır's laboratory is funded by multiple R01 awards from NINDS and addresses novel mass spectrometric imaging of lipids after TBI in rat brain, oxidative lipidomics after pediat-

ric TBI, development of mitochondrial targeting therapies for oxidative injury and neuronal death, and identifying and testing of novel therapies for mild repetitive TBI in the brain. This work is being carried out in collaboration with Dr. Valerian Kagan in the Pittsburgh Center for Free Radical and Antioxidant Health.

A major and exciting accomplishment in Dr. Bayır's laboratory in FY15 has been the establishment and characterization of a unique pediatric pre-clinical model of mild repetitive TBI in developing (post-natal day 17 [PND 17]) rats. That work was carried out by Dr. Emin Fidan, a young investigator from Turkey working with Dr. Bayır, and suggests important roles for both axonal injury and neuro-inflammation after repetitive insults. Given the importance of mild repetitive TBI in both sports concussion in children, and abusive head trauma in infants, and the paucity of preclinical work in this area, this new model could provide unique insight into these conditions and help define optimal therapies.



Rachel P. Berger, MD, MPH (Pediatrics)

Dr. Berger is Chief of the Child Advocacy Center at CHP, Safar Center Associate Director, and a leading investigator in the field of abusive head trauma (AHT) in infants. This year she completed patient entry on a multi-center study on the use of both a clinical decision rule and a panel of serum biomarkers to aid in alerting physicians to the possible diagnosis of AHT in infants at risk for that condition. It is well known that AHT is a diagnosis that is often missed by physicians resulting in return of the infant to an abusive environment with high risk for repeated injury and/or death. The study was carried out at three sites, CHP, Lurie Children's Hospital in Chicago, and Primary Children's Hospital in Salt Lake City, enrolled >1040 infants at risk for AHT, and the initial results are being submitted for publication. Dr. Berger is also funded by a grant from PCORI to study the use of the electronic medical record to improve screening for child abuse.

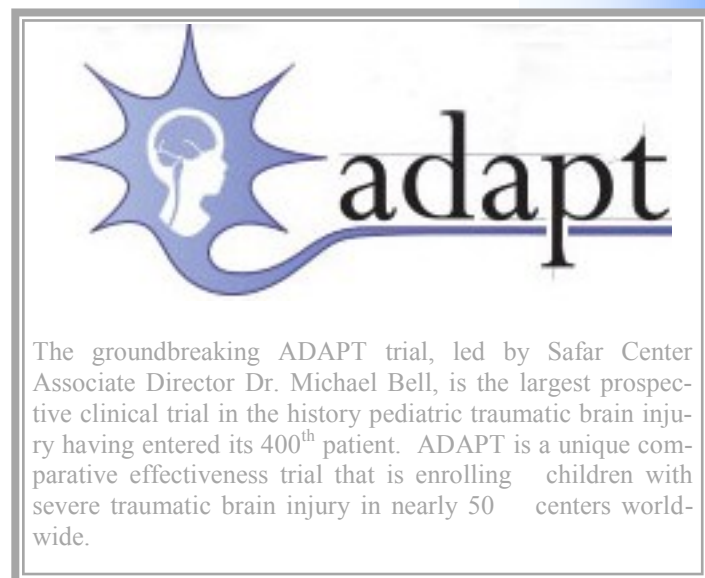


Michael J. Bell, MD (CCM, Pediatrics and Neurosurgery)



Dr. Bell is Director of Neurocritical Care at Children's Hospital of Pittsburgh (CHP) and his work in TBI focuses on the optimization of therapy for severe TBI in infants and children. Dr. Bell is the PI of the ADAPT trial funded by a \$17M grant from NINDS. This is a groundbreaking study in the field of pediatric TBI, represents the first comparative effectiveness trial of key aspects of standard care in the field (such as osmolar

therapy, hyperventilation, and nutrition, among others) and is already the largest clinical trial in the history of pediatric severe TBI having entered >400 children. On its way to studying 1000 patients, the study includes nearly 50 sites worldwide. Dr. Stephen Wisniewski, Associate Vice Provost for Planning, Office of the Provost and Professor in the School of Public Health is the Co-PI of the project. Dr. Bell is also carrying out a number of clinical investigations on pediatric TBI management at CHP and published numerous manuscripts this year on pediatric TBI with trainees from multiple departments including CCM, pediatrics, and neurological surgery.



Robert S. B. Clark, MD (CCM and Pediatrics)

Dr. Clark, Chief of CCM at CHP leads a bench to bedside program on TBI in his laboratory, with a special focus on translational investigation in combination therapy development for pediatric TBI. He is currently co-mentoring Dr. Philip Empey, a young investigator in the School of Pharmacy (supported by a KL2 in the Multidisciplinary Clinical Research Scholars Program in the CTSI) on a unique single center trial funded by NINDS called PRONAC. The investiga-

tions in PRONAC are exploring the combination of the antioxidant N-acetylcysteine (NAC) with the transport inhibitor probenecid. Blood brain barrier penetration of NAC is well known to be limited by transporters that can be inhibited by probenecid. This innovative strategy is being explored in both pre-clinical models and in children with severe TBI at CHP. Dr. Empey is a young investigator with expertise in the area of drug transporters and thus this represents an exciting collaboration between the Safar Center and the School of Pharmacy. Dr. Clark's laboratory is also pursuing a second line of investigation in TBI and in FY 15 submitted a new R01 application in collaboration with Dr. Simon Watkins and others focused on effects of raised intracranial pressure on the injured brain independent of effects on perfusion.

Robert Clark, MD



C. Edward Dixon, PhD (Neurological Surgery)

Dr. Dixon's laboratory is pursuing multiple preclinical lines of investigation in TBI with two R01 awards from NINDS and support from the Veteran's Administration. One of the major areas of focus in FY15 was on how disturbances in SNARE



proteins contribute to synaptic dysfunction after controlled cortical impact TBI in rats. Post-doctoral T32 fellow Shaun Carlson, working under the mentorship of Dr. Dixon has focused on this emerging area of investigation in TBI and notably has five recent publications including three currently ahead of print. Dr. Dixon is also studying lithium as a potential therapy for TBI in work funded by the Veteran's Administration.

Dr. Dixon is also the Co-PI of OBTT and is performing all of the pre-clinical drug screening in the controlled cortical impact model in rats for the OBTT consortium at the Pittsburgh site. Dr. Dixon is a Safar Center Associate Director and as director of functional outcome testing in pre-clinical research at the Safar Center is also a key resource on many funded projects at the Center that include behavioral assessment of rats and mice after TBI in experimental models. This includes work by investigators across multiple departments in the School of Medicine. Finally, Dr. Dixon is also collaborating with Dr. Milos

Ikonomic in the Dept. of Neurology on additional TBI investigations funded by the Veterans Administration. That work addresses studies on the link between TBI and Alzheimer's Disease and therapeutic testing of memantine in pre-clinical models of TBI. Dr. Ikonomic has a long track record of collaboration with the Safar Center and is one of the leading investigators examining the link between TBI and neurodegenerative disease.

Travis C. Jackson, PhD (CCM)

Dr. Jackson, Assistant Professor of CCM is carrying out novel studies of RNA binding protein 5 (RBM-5) in TBI funded by a new R21 from NINDS. He has recently shown both *in vitro* in neuronal culture and *in vivo* studies in a murine model of

Drs. Jackson and Kochanek are co-inventors on a filed USPTO patent application titled, "Small Molecule Inhibitors of RBM Proteins for the Treatment of Acute Cellular Injury" (USPTO Application #14/401,088).

TBI that RBM-5 plays an important role in exacerbating neuronal death. Dr. Jackson was a highly prolific author in FY 15 with 5 manuscripts and it is also notable that his innovative work with RBM-5 has identified a novel inhibitor. Related to this work Drs. Jackson and Kochanek are co-inventors on a filed USPTO patent application titled, "Small Molecule Inhibitors of RBM Proteins for the Treatment of Acute Cellular Injury" (USPTO Application #14/401,088). The IP is based on their discovery that anthraquinone-2-sulfonic acid sodium salt (AQ2S) is a potent neuroprotective compound. AQ2S is also a known inhibitor of RBM5 which promotes RNA splicing of cell death/survival genes which causes increased apoptosis. RBM5 is increased after brain injury and may be an important novel therapeutic target. Finally, Dr. Jackson is also studying the role of PH domain and leucine rich repeat protein phosphatase 1 (PHLPP1) inhibitors as potential neuroprotectants in TBI.



Travis Jackson, PhD

Anthony E. Kline, PhD (PM&R)

Dr. Kline's laboratory is focused on work on two R01 awards, one from NICHD titled "Understanding the Impact of Antipsychotic Drugs after TBI" and a second new R01 from NINDS titled "Optimizing Environmental Enrichment to Model Preclinical Neurorehabilitation." His investigative



team uses the controlled cortical impact model in rats and mice for these pre-clinical investigations. His work on antipsychotics in TBI has raised concern over the clinical use of drugs such as haloperidol after TBI—having demonstrated marked exacerbation of posttraumatic cognitive impairment with its use. In addition, he is currently exploring the impact of enriched environment (as a pre-

clinical rehabilitation analog) both to optimize its efficacy and study its mechanics underpinnings—including its impact on plasticity, neuroprotection and neurogenesis. This year Dr. Corina Bondi completed her work as a postdoctoral fellow in Dr. Kline's laboratory in the important yet vastly understudied area of assessment of frontal lobe dysfunction in rodents after TBI. Dr. Bondi has joined the faculty in the Dept. of PM&R and will serve as a new Safar Center investigator. Finally, Dr. Kline's group published an impressive 7 manuscripts on TBI in FY 15.

Amy K. Wagner, MD (PM&R)

Dr. Wagner's laboratory has focused on three major lines of investigation in TBI: 1) pre-clinical research on disturbances in dopamine systems, and experimental models of cognitive rehabilitation, 2) clinical studies of *Rehabilomics*—including the investigation of a variety of biomarkers and bio-mediators in the acute, sub-acute, and chronic phases after TBI, and 3) clinical studies of genetic polymorphisms and their relationship to depression and behavior, posttraumatic seizures and epilepsy, and cognitive disfunction after TBI. Her clinical research is funded through a center grant sponsored by the National Institute of Disability and Rehabilitation Research. In FY 15 Dr. Wagner's laboratory has been exceptionally pro-

ductive with 15 published manuscripts and an additional 3 reports published ahead of print. It is notable that almost all of these manuscripts have trainees working in the Wagner laboratory as a first author. This year under Dr. Wagner's mentorship, Matt Diamond received his BPhil and as indicated earlier in this report, for his work he also received the *Epilepsia* prize for best paper published by a young scientist.



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 models—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 and children, with a focus on investigation of hypothermia, and biomarkers of brain injury—both serum and imaging. Notable in this area of investigation at the Safar Center in FY 15 is that there are currently three K funded faculty working in this area, Drs. Cameron Dezfulian, Ericka Fink, and Nahmah Kim-Campbell and two of these investigations have first R01

applications in re-submission, both of which were scored on first submission. This academic year, Safar Center investigators had 12 peer reviewed manuscripts published or ahead of print on cardiac arrest. A brief update of developments in FY 15 for each laboratory is presented below.

Hülya Bayır, MD (CCM, Pediatrics, and Environmental and Occupational Health) and Robert S. B. Clark, MD (CCM and Pediatrics)

Drs. Bayır and Clark are dual PIs on an R01 from NINDS titled "Mitochondria-Targeted Redox Therapy for Cerebral Ischemia in the Developing Brain" supporting investigation of

the application of novel mitochondrial nitroxides in the treatment of pediatric cardiac arrest using an established model of asphyxial cardiopulmonary arrest in PND 17 rats. In FY 15, Drs. Bayır and Clark published a report in the *Journal of Cerebral Blood Flow and Metabolism* demonstrating beneficial effects of this novel resuscitative strategy in their developmental model. This novel therapeutic approach was developed at the University of Pittsburgh and a library of mitochondrial nitroxides has been synthesized. This targeted approach is also showing promise for therapeutic development in TBI and radiation injury.

Cameron Dezfulian, MD (CCM)

Dr. Dezfulian, supported by a K08 award from NINDS is carrying out bench-to-bedside investigations of the use of nitrite therapy in cardiopulmonary arrest. He is jointly mentored by Drs. Bayır, Clark, Gladwin, Kochanek, published exciting findings in pre-clinical models of cardiac arrest in mice and rats showing neuroprotection from nitrite therapy, and has carried out parallel studies of nitrite pharmacokinetics and nitrosylation in platelet mitochondria. His R01 application outlines an impressive translational set of studies to define an optimized precision medicine nitrite therapy approach for cardiac arrest in humans.



Dr. Thomas Uray, a visiting fellow from the university of Vienna, was named young investigator of the year by the European Resuscitation Council. He was mentored by Dr. Cameron Dezfulian and supported by grants from the Laerdal Foundation and the Max Kade Foundation. Dr. Uray also received an MPH degree from the University of Pittsburgh School of Public Health during his fellowship in Pittsburgh. Dr. Dezfulian, as a practicing intensivist in both the adult and pediatric programs, also uniquely serves as a liaison between the Safar Center's cardiac arrest program and the adult cardiac arrest service directed by Dr. Clifton Callaway, Vice Chair in the Dept. of Emergency Medicine. Dr. Callaway trained at the Safar Center, is a long-time collaborator, and is a Safar Center Associate Director. Clif's cardiac arrest clinical service is a

Dr. Fink, a graduate of our T32 program is also serving as the site PI for the THAPCA trial of mild hypothermia after cardiac arrest in children and co-authored a paper this year in the New England Journal of Medicine from one of the completed trials in that program.

fantastic platform for clinical investigations in cardiac arrest in adults that is being collaboratively used by Dr. Dezfulian.

Tomas Drabek, MD, PhD (Anesthesiology)

Dr. Drabek is an Associate Professor in the Dept. of Anesthesiology who is studying

new therapeutic approaches to cardiopulmonary arrest and is currently focused on two lines of investigation, 1) the neuroinflammatory response and use of extracorporeal cytokine removal to mitigate secondary systemic and cerebral injury after cardiac arrest in rats, and 2) joint investigations in collaboration with Dr. Amy Wagner in the Dept. of PM&R, evaluating derangements of dopamine signaling via assessment of evoked dopamine release using cyclic voltammetry after asphyxia and ventricular fibrillation cardiac arrest in rats. We are pleased to report that in FY 15 Dr. Drabek also received his PhD from Charles University, Prague, in the Czech Republic.



Ericka L. Fink, MD, MS (CCM and Pediatrics)

Dr. Fink is a Safar Center Associate Director and heads the clinical research program in the pediatric ICU on pediatric cardiac arrest at CHP. Funded by a K23 award from NINDS, she is studying the use of both serum biomarkers of brain injury to predict outcome and guide therapy and, in collaboration with Dr. Ashok Panigraphy at CHP, the parallel use of magnetic resonance spectroscopic and imaging biomarkers. Ericka has submitted a revised R01 application on her work and we are hopeful that she will be able to continue to expand her exciting studies in this area. Dr. Fink, a graduate of our T32 program is also serving as the site PI for the THAPCA trial of mild hypothermia after cardiac arrest in children and co-authored a paper



this year in the *New England Journal of Medicine* from one of the completed trials in that program. Dr. Fink is also leading two other major research programs in the field of pediatric neurocritical care at CHP which will be discussed later in the section in this report on pediatric neurocritical care.

Nahmah Kim-Campbell (CCM, Pediatrics, and Emergency Medicine)

Dr. Kim-Campbell is a new young investigator in pediatric CCM who currently is funded by Dr. Clifton Callaway's K12 award in the field of Emergency Medicine. Nahmah was also



a graduate of our T32, is now on the pediatric CCM faculty, and is studying the role of hemolysis in the development of multiple organ dysfunction and failure after extracorporeal resuscitation. She has also been funded by a grant from the Vascular Medicine Institute and has been guided and is collaborating with Drs. Hülya Bayır and Mark Gladwin. Her

research spans bench to bedside and takes advantage of the unique resources at the Safar Center for pre-clinical investigations of extracorporeal support of rats.

Mioara D. Manole, MD (Pediatrics, Emergency Medicine)

Dr. Manole is a Safar Center Associate Director and a Pediatric Emergency Medicine faculty member at CHP. She is studying the role of cytochrome P450 metabolites of arachidonic acid in the development of cerebrovascular failure after cardiopulmonary arrest in pre-clinical investigations in our pediatric asphyxial cardiac arrest rat model. Dr. Manole is PI of an R01 from NINDS that is supporting these investigations and the work is being carried out in collaboration with Samuel Poloyac, PharmD, PhD, an expert in cytochrome P450 metabolites in the cerebral circulation. Her work has also included important collaboration with Dr. Kevin Hitchens and his investigative team at the Pittsburgh NMR Center in the Mellon Insti-



tute at Carnegie Mellon University. Dr. Manole has also launched two exciting new initiatives this year including *in vivo* microscopic assessment of the cerebral microcirculation after pediatric cardiac arrest in rats, in novel studies using 2-photon imaging done in collaboration with Drs. Simon Watkins and Robert Clark. In addition, in collaboration with Drs. Tomas Drabek and Joan Sanchez-de Toledo in the cardiac ICU at CHP she is launching the development of a pediatric rat model of cardiac arrest and extracorporeal resuscitation—using a miniaturized ECMO circuit—to our knowledge, the pediatric rat model of ECMO is the first of its kind ever reported.

Travis C. Jackson, PhD (CCM)

Dr. Jackson, Associate Director of Molecular Biology at the Safar Center is pursuing two lines of investigation in cardiac arrest at the Safar Center. In studies funded by a newly awarded Scientist Development Grant from the American Heart Association, he is investigating the potential neuroprotective role of inhibition of PHLPP1 in pre-clinical models of cardiac arrest in adult models of ventricular fibrillation and asphyxia. In addition, in our pediatric cardiac arrest model and TBI models, and in *in vitro* models of neuronal death, Travis is studying the cytoprotective role of RNA binding motif 3 (RBM3)—namely its novel role as a mediator of neuroprotection during ultra-mild hypothermia. Related to his work on RBM3, Drs. Jackson and Kochanek are co-innovators on a submitted provisional patent application titled, “Method to Improve Neurologic Outcomes in Temperature Managed Patients” (Application #62164205). The IP is based on the discovery that fibroblast growth factor 21 (FGF 21) increases cold shock protein RBM3 in neurons very mildly cooled just a single degree to 36°C. RBM3 is a well-known neuroprotective protein. Drugs designed to augment hypothermia-induced neuroprotection may have great utility in cardiac arrest and other types of brain injuries.

SPECIAL PROGRAMS

RESEARCH TRAINING

The Safar Center is an important training site in the Schools of Medicine, Pharmacy, and Nursing for students, medical students, residents, pre-doctoral candidates, post-doctoral fellows, and junior faculty—specifically those interested in research related to resuscitation medicine in its broadest sense. The environment at the Safar Center is a highly collaborative and nurturing one that is perfect for trainees across the spectrum of experience. Our long-standing T32 serves as a key infrastructure for research training and supports a weekly neurocritical care journal club at the Safar Center and weekly “Safar Rounds” in the pediatric ICU at CHP—where the most challenging neurocritical care cases are presented. In addition to training in pediatric neurocritical care, the Safar Center plays a major role in resident and both pre-and post-doctoral training in the Dept. of PM&R led by two outstanding mentors—Drs. Amy Wagner and Anthony Kline. Drs. Wagner and Kline are both devoted to cultivating young investigator development across the full spectrum of trainee levels. They have had a high level of success in mentoring undergraduates interested in PM&R and neuroscience. The Safar Center also serves as a key training environment for pre-doctoral students in the

School of Pharmacy, led by Samuel Poloyac, PharmD, PhD, a talented investigator and mentor. The PharmD/PhD program in the School of Pharmacy features substantial investigative links between projects in the laboratories of Drs. Poloyac and Empey and the Safar Center. These projects have served as an outstanding platform for investigation by many trainees in the School of Pharmacy. As discussed in the introductory letter from the director in this report, Safar Center trainees had a tremendous number of successes in FY 15 winning numerous research awards.



Fanuel Hagos is one of four PhD candidates in the School of Pharmacy, along with trainees Solomon Adams, Kacey Anderson, and Lingjue Li, who are working collaboratively with Safar Center investigators on research related to neurocritical care. This exemplifies the strong inter-disciplinary bond between the Safar Center and the University of Pittsburgh School of Pharmacy that was originated through collaboration between Drs. Samuel Poloyac and Patrick Kochanek.



The 2014 Safar Center Trainee's Research Day featured trainees from the Departments of Critical Care Medicine, Neurosurgery, Physical Medicine and Rehabilitation, Anesthesia. Ranging from undergraduate to graduate/medical student, each trainee gave a 20 minute presentation outlining his or her work this summer to the faculty of the Safar Center, and other trainees. Each participant was mentored by a Safar Center Associate Director or Scientist.

PEDIATRIC AND ADULT NEUROCRITICAL CARE

The Safar Center is closely linked to the pediatric neurocritical care program at CHP, led by Dr. Michael Bell, through its role in the ongoing clinical investigations, mentoring of junior faculty, and training of fellows supported by our unique and long-standing T32 program from NINDS titled “Training in pediatric neurointensive care and resuscitation research” that is now in its 15th year of NIH funding. In addition to the aforementioned clinical and translational research in

pediatric TBI and cardiopulmonary arrest, there are several other noteworthy initiatives that are ongoing. Two of these are led by Dr. Ericka Fink. As discussed in the opening letter from the center director, Dr. Fink, in collaboration with Dr. Amy Houtrow, Vice Chair of PM&R, has launched a multi-center study of the im-



Ruchira Jha, MD is one of several young clinician scientists from Dr. Lori Shutter's burgeoning new Adult Neurocritical Care program at Presbyterian Hospital that is carrying out research at the Safar Center. Dr. Jha was just awarded a position in the prestigious KL2 program within the University of Pittsburgh Clinical and Translational Science Institute (CTSI). She is working on novel approaches to mitigate brain edema after traumatic brain injury.

plementation of early rehabilitation protocol for children after acute brain injury across the spectrum of pediatric neurocritical care disorders (the ERP study). That work is funded by a \$1.87M grant from PCORI. In addition, Dr. Fink is leading a unique international multi-center point prevalence study in pediatric neurocritical care (PANGEA). That work is being funded by the Laerdal Foundation and is the first of its kind in the emerging field of pediatric neurointensive care. A number of other projects are also ongoing in pediatric neurocritical care that are linked to the Safar Center, particularly related to clinical investigations on neurocritical care management of children with severe TBI or after cardiac arrest, and this work generated 6 publications under the guidance of Dr. Michael Bell in FY 15, including first author reports by residents and fellows working at CHP. Dr. Alicia Au, another young investigator on the pediatric CCM faculty is also working with Dr. Robert Clark on the development of a biomarker panel to aid in the detection of early brain injury across the entire pediatric ICU. Finally, with the recruitment of Dr. Lori Shutter to lead the adult neurocritical care program at Presbyterian Hospital, several of the adult fellows and junior faculty have

begun investigations at or linked to the Safar Center. As noted in the opening letter from the Safar Center director, Dr. Ruchira Jha working with Dr. Kochanek was just awarded a KL2 grant. Dr. Sherry Chou is also working on a K23 mentored by Drs. Kochanek, Derek Angus and Sachin Yende. We look forward to new developments in this parallel neurocritical care research arena in adults.

COMBAT CASUALTY CARE

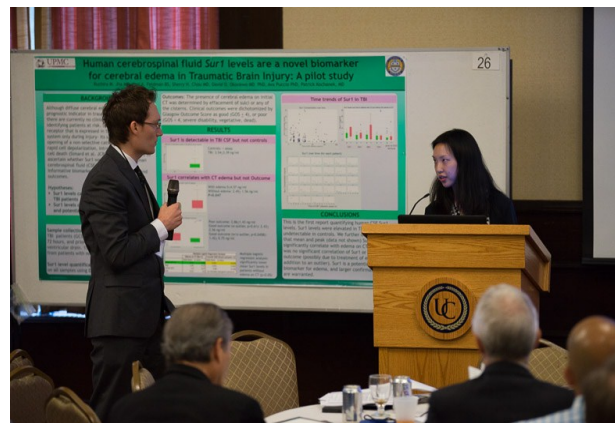
Given its strengths in resuscitation, the Safar Center has a long history of research in the area of combat casualty care, has many active and close collaborations with investigators in the U.S. Army including Drs. Frank Tortella, Deborah Shear and Joseph Long at Walter Reed Army Institute for Research (WRAIR). The \$10M multi-center OBTT program in pre-clinical TBI investigations, funded by the U.S. Army, is being led by Dr. Kochanek at the Safar Center. In FY 15, Dr. Kochanek led an invited panel presentation on OBTT at the annual meeting of the National Neurotrauma Society, and OBTT investigators just submitted 8 manuscripts as part of an invited special issue in the *Journal of Neurotrauma* devoted to this important program. Dr. Kochanek, along with other Safar Center investigators, has close ties to the University of Pittsburgh Center for Military Medicine led by Dr. Ronald Poropatich. In addition, Dr. Kochanek also has a

The Safar Center has a long history of research in the area of combat casualty care, has many close collaborations with investigators in the U.S. Army including OBTT investigators Drs. Frank Tortella, Deborah Shear at Walter Reed Army Institute for Research (WRAIR).

number of other collaborations with WRAIR investigators and has carried out numerous investigations of novel resuscitation approaches germane to combat casualty care, emergency resuscitation, emergency preservation for delayed resuscitation, blast injury and hemorrhagic shock funded by the U.S. Army, the U.S. Navy, and DARPA.

SAFAR SYMPOSIUM 2015

Presented jointly by the Safar Center for Resuscitation Research and the Peter M. Winter Institute for Simulation, Education, and Research (WISER), the 13th Safar Symposium was held May 22nd and 23rd, 2015, and was met with record attendance and wide acclaim. The May 22nd morning session, titled “Cerebral Resuscitation: Hypothermia and Beyond,” featured plenary presentations by national authorities in the field of hypothermia and was held at the University Club in Oakland. Highlights included lectures by Dr. W. Dalton Dietrich, Scientific Director of the Miami Project to Cure Paralysis and editor-in-chief of the journal *Therapeutic Hypothermia and Temperature Management*, who gave an overview of the current understanding of the mechanisms of action of hypothermia in acute brain injury, and Dr. Javier Provencio from the Cleveland Clinic who presented on the impact of hypothermia on neuro-inflammation in intracranial hemorrhage. The morning session also featured a special case presentation and panel discussion titled “Resuscitation at UPMC 2015: from the Field through to Rehabilitation,” which featured experts from the departments of Emergency Medicine, Neurosurgery, Critical Care, and PM&R. The session described a remarkable case



Safar Center Associate Director Dr. Travis Jackson co-moderated the platform presentation during trainee’s research day and is shown here questioning pediatric critical care medicine fellow Dr. Diana Pang. Of note, as discussed earlier, Dr. Pang received the 2015 Young Investigator Award from the Shock Society for her bench to bedside work on septic encephalopathy in the developing brain.

which showcased the collaborative and state-of-the-art nature of the continuum of care at UPMC which included targeted temperature management and helped produce an outstanding result for the patient.

The morning session featured a special case presentation and panel discussion... which showcased the collaborative and state-of-the-art nature of the continuum of care at UPMC which included targeted temperature management and helped produce an outstanding result for the patient.



The 35th Peter and Eva Safar Lecture in Medical Sciences and Humanities was held as part of the Safar Symposium and was presented by Hans Friberg MD, PhD, Associate Professor in the Department of Anesthesiology at Lund University in Sweden. His lecture was titled “Cardiac Arrest, Temperature Management, and Return to a Good Life.” Dr. Friberg is the senior author of the landmark Targeted Temperature Management after Cardiac Arrest Trial (TTM-trial) published in December 2013 in the *New England Journal of Medicine*.

The program also included a Trainees Research Day session, which drew participants from the Departments of Anesthesiology, Critical Care Medicine, Emergency Medicine, and PM&R. Over 50 platform and poster presentations were made by trainees. The top overall platform presentation was awarded to Allison Koller, BS who presented her work titled “Comparison of three cognitive exams in cardiac arrest survivors.” She was mentored by Drs. James



Each year at the Safar Symposium, one outstanding trainee from the Safar Center is given the Nancy Caroline Award in recognition of academic excellence in research. The recipient is chosen by the Safar Center Associate directors and the award was created in honor of Dr. Nancy Caroline, a pioneer in paramedic services development and one of Dr. Peter Safar's first fellows. This year, Safar Center T32 Fellow Dr. Dennis Simon won the award. Dennis was mentored by Dr. Robert Clark.

key role for game-based education. Dr. Eric B. Bauman, Assistant Dean for the DeVry Medical International Institute at the University of Wisconsin, highlighted the key role of mobile technology in the future of simulation-based education.

We would like to thank the Ake Grenvik Endowment, the Laerdal Foundation, and the Departments of Anesthesiology, Critical Care Medicine, Emergency Medicine, and PM&R for their continued support.

Menegazzi, Jon Rittenberger and Clifton Calloway in the department of Emergency Medicine. The top poster presentation was made by Lisa McIlvried, BS for her work titled "Sex-, stress-, and sympathetic post-ganglionic neuron-dependent changes in the expression of pro- and anti-inflammatory molecules in dural immune cells." She was mentored by Dr. Michael Gold in the department of Anesthesiology.

We would like to thank the Ake Grenvik Endowment, the Laerdal Foundation, and the Departments of Anesthesiology, Critical Care Medicine, Emergency Medicine, and PM&R for their continued support.

The second day of the Safar Symposium took place at WISER. The session was titled "Simulation Now and into the Future," and featured demonstrations and lectures on technologies at the forefront of simulation education, including a profile of the advances expected in coming years. Noteworthy lectures included two guest speakers. Dr. Jeffrey Taekman, Assistant Dean for Educational Technology at Duke University, gave a captivating presentation focused on the future of simulation as an education tool and emphasized a

ACKNOWLEDGEMENTS

I would like to thank everyone working at the Safar Center for an outstanding job in FY 15. The hard work and dedication of the faculty, staff, technicians, and trainees is impressive. I would like to thank each of the Safar Center Associate Directors for their help and support in navigating what has been an exceptionally successful albeit challenging year. This includes Drs. Hülya Bayır, Michael Bell, Rachel Berger, Clifton Callaway, Robert Clark, C. Edward Dixon, Ericka Fink, Travis Jackson, Anthony Kline, Mioara Manole, Samuel Poloyac, and Amy Wagner. Their devotion to our center along with the efforts of their staff members is greatly appreciated. As many of you know, we were incapacitated for over four months as the result of a chlorine dioxide fumigation of the center and it is truly astounding how much work we were able to accomplish during this period. Many collaborators opened their laboratories to us and we are thankful for the outpouring of support that we received from many faculty members. We are also grateful to Nick Vizzoca and all of faculty and staff on the sixth floor of Scaife Hall in the Department of Critical Care Medicine for sharing available space with us during a difficult time.

Thanks to Drs. Derek Angus, Michael Boninger, Robert Friedlander, and Donald Yealy, Department Chairmen in CCM, PM&R, Neurological Surgery, and Emergency Medicine respectively for their help and support.

I would like to personally thank the administrative staff members who work at the Safar Center for their expertise, professionalism, assistance, and genuine kindness. Linda Ryan, Fran Mistrick, Marci Provins, Jackie Pantazes, and Natalie Nieman are amazing people and I could not be more pleased that such an incredibly talented administrative staff works at our Center. That sentiment is shared by the countless number of people who they help. They are truly special. I would also like to personally thank the many technicians working in our center. Many of them have an unparalleled level of experience and talent working in very complex pre-clinical model systems. This in-

cludes Henry Alexander, Vincent Vagni, Keri Feldman, Jason Stezoski, Jeffrey Cheng, Xiecheng Ma, Jeremy Henchir, Sherman Culver, Nicole Toney, Yaming Chen, Elizabeth Brough, Amalea Misse, Lee Ann New, Lesley Foley, Lori Beck, and Emad Madha.

Thanks also to many faculty members who have helped us this year including Drs. Derek Angus, Michael Boninger, Robert Friedlander, and Donald Yealy, as Department Chairmen in CCM, PM&R, Neurological Surgery, and Emergency Medicine respectively for their help and support. Thanks are also in order to several faculty members this year who are colleagues and/or friends of the Safar Center that helped me and/or other faculty in our center immensely, namely, Drs. Yvette Conley, Cameron Dezfulian, Tomas Drabek, Lina Du, Philip Empey, Robert Gorman, Edwin Jackson, Valerian Kagan, John Kellum, David Okonkwo, Paul Phrampus, Ron Poropatich, Lori Shutter, Jon Verrier, Hong Yan, Steven Wisniewski, and Ashok Panigrahy. Thanks also to Megan Piplica for her tireless work on post-award grant accounting.

In addition, there were many other faculty members who helped us this year including Drs. Sheila Alexander, Raj Aneja, Alicia Au, Timothy Billiar, Sherry Chou, Emin Fidan, Mark Gladwin, Ann Gleeson, Steven Graham, Chien Ho, Kevin Hitchens, Milos Ikonovic, Jing Ji, Nahmah Kim-Campbell, Bradley Molyneaux, Ava Puccio, Simon Watkins, and Qin Yan.

Thanks also to the many fellows, residents, medical students, and undergraduates who contributed enormously to the work accomplished in FY 15. Special congratulations to three T32 fellows this year, Drs. Ruchira Jha and Dennis Simon, who will be staying on as part of the Safar Center family as new faculty members in the Department of Critical Care Medicine. And to Dr. Erik Brockman who will be the new Director of Neurocritical Care for Children's Hospitals and Clinics of Minnesota. I am expecting great things from these three talented young investigators.

I want to also send special thanks to a number of faculty members outside of the University of Pittsburgh who I would like to thank for their help and/or collaboration this year including Drs. Frank Tortella, Deborah Shear, and Joseph Long from WRAIR, W. Dalton

Dietrich and Helen Bramlett from the University of Miami, John Povlishock and Audrey Lafrenaye at Virginia Commonwealth University, Kevin Wang, at the University of Florida, Ronald Hayes at Banyan Biomarkers, LLC, Stefania Mondello at Messina University, COL Dallas Hack, Ken Curley and Brenda Bart-Knauer at Ft. Detrick, Nancy Carney at the University of Oregon Health and Science University, Ramon Diaz-Arrastia and Denes Agoston at Uniformed Services University for the Health Sciences, Steve Parks at ORA, Inc, David Ritzel at Dyn-FX Consulting, LTD, Carleton Hsia at Synzyme Technologies, LLC, and Li Ma at Georgia Southern University.

We continue to be appreciative of the support of Mr. Tore Laredal and the Laerdal Foundation for Acute Medicine for their support of our work and the Annual Safar Symposium, and to Mrs. Eva Safar and to the Safar family for their continued interest and support of our work.

For the past few years we have used our Newsletter as a tool to update our faculty, fellows and friends, but generation of a formal annual report was long overdue and I am grateful to my staff and the Associate Directors for their assistance in assembling this report. I also would like to thank Max Glider from Media Development in Critical Care Medicine for his help both with the annual Safar Symposium and with the preparation of this report.

We continue to be appreciative of the support of Mr. Tore Laredal and the Laerdal Foundation for Acute Medicine for their support of our work and the Annual Safar Symposium, and to Mrs. Eva Safar and to the Safar family for their continued interest and support of our work.

Finally, I know that I speak for everyone at our Center that we are looking forward to a new home for the Safar Center within the Rangos Research Center at Children's Hospital. Children's has always had a special place in my heart having served as a faculty member in its intensive care unit for nearly two decades. It will thus be great personally to be returning to where I began my faculty career. Sincere thanks to Senior Vice Chancellor Dr. Arthur Levine and Vice

Dean Dr. Ann Thompson for helping make this possible. Nevertheless, the Hill Building has held significance to all of us who knew and worked beside Dr. Peter Safar and has been the Safar Center's home since 1980. Dr. Safar's boundless enthusiasm, spirit, and passion will continue to be an inspiration to all of us in our new home.

Sincerely,



Patrick M. Kochanek, MD, MCCM
Director, Safar Center for Resuscitation Research

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