



# SAFAR CENTER FOR RESUSCITATION RESEARCH

2008/2009 & 2009/2010  
Annual Report



[www.safar.pitt.edu](http://www.safar.pitt.edu)

**T**he 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, Perinatal Brain Injury, and Rehabilitation of CNS Injury. Center investigators work closely with the clinical 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 of UPMC. 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.

## SAFAR CENTER

### FOR RESUSCITATION RESEARCH

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**Featured on the cover:** Selected pictures of events, people, and other items that have been an important part of the history of the Safar Center on the occasion of the 50<sup>th</sup> anniversary of the birth of CPR. This montage, created by Christopher Edwards, was used as the cover for the program to the 8<sup>th</sup> annual Safar Symposium.

# LETTER FROM THE DIRECTOR...



**T**his “Annual” report addresses two academic years at the Safar Center for Resuscitation Research, 2008-09 and 2009-10, representing the 30<sup>th</sup> and 31<sup>st</sup> years of operation for the Safar Center, and my 14<sup>th</sup> and 15<sup>th</sup> years as director. The need to combine these reports resulted from demands put on me and my staff to launch several new programs, and the related efforts that were put forth to submit the proposals to support those programs that, fortunately, were ultimately funded.

## *Highlights from the 2008-09 and 2009-10 academic years*

With over 100 new manuscripts published in the 2008-09 and 2009-10 academic years by Safar Center investigators, new federal grants, and a host of significant awards, it is a challenge for me to select some of the most important highlights for the opening of this letter. These successes have spanned the gamut of research interests in the center from traumatic brain injury (TBI) to cardiac arrest—and have included investigators at all levels—from students to professors. I am very proud of our trainees and faculty for these successes, and of our remarkable staff, who worked tirelessly to help in the realization of these achievements.

**A major development in the Center has been the growth in our research on blast TBI.**

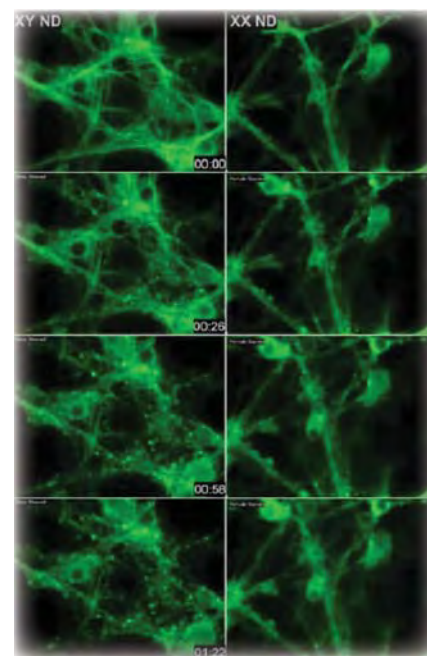
A major development in the center has been the growth in our research on blast TBI. This topic has emerged as a critical target in the field of TBI as a result of terrorist attacks with improvised explosive devices in military and civilian settings. Our research on this topic stems from our longstanding work and reputation in the field of TBI and is supported by several grants from the U.S. Department of Defense (DOD). Safar Center investigators are carrying out studies as part of the DARPA PREVENT program. These important studies, launched early in 2008 are focused on the neuropathology, molecular biology,

In the field of TBI resuscitation, pediatric critical care fellow Dr. David Shellington, under the mentorship of Dr. Kochanek and in collaboration with SynZyme Technologies, reported on promising studies using the novel blood substitute polynitroxylated pegylated hemoglobin (PNPH). Surprisingly, unlike other cell free hemoglobins, PNPH was neuroprotective rather than toxic in cell culture, and it could thus represent a paradigm shift in blood substitute development. Dr. Shellington's work is in press in *Critical Care Medicine*. David is currently serving as a medical officer for the U.S. Navy in Afghanistan; the entire Safar Center family wishes him the best in his current assignment.





and biochemistry of experimental blast TBI—with the target being the development of new treatments. We also launched two new albeit related programs supported by the U.S. Army that address TBI resuscitation and therapy, respectively. In the first, we are exploring the impact of resuscitation with 100% oxygen versus room air on outcome in an effort to optimize field management of TBI resuscitation. In the second, we are leading a unique multi-center pre-clinical experimental TBI drug and biomarker development consortium called “Operation Brain Trauma Therapy” that includes research teams at the University of Miami, The Virginia Commonwealth University, Walter Reed Army Institute of Research (WRAIR), and Banyan Biomarkers, Inc. Additional grants from Veterans Administration and the Army to Drs. C. Edward Dixon and Amy Wagner support other aspects of TBI-related research, most notably, biomarker development. Between the 2008-09 and 2009-10 academic years, the DOD-related percent of total extramural grant funding at the Safar Center nearly doubled, increasing from 16 to 27%. I will present more on these programs later in the report. This work on TBI supported by the DOD, dovetails with our many ongoing NIH-funded research initiatives.



Several scientific discoveries were recently reported by Safar Center investigators. An important finding came from the laboratory of Safar Center associate director Dr. Robert Clark. As part of the work on neuronal death in Dr. Clark’s laboratory, scientist Dr. Lina Du and colleagues published a paper in the *Journal of Biological Chemistry* that revealed divergent responses in female versus male neurons when they are exposed to starvation—a key natural trigger of a process called autophagy. This finding could have important implications and suggests that gender-based approaches to neuroprotection and nutrition may be required to improve outcome in critically ill patients with brain injury.

On the topic of developmental brain injury, Dr. Mioara Manole, an Assistant Professor in the division of Pediatric Emergency Medicine collaborating with Dr. Chien Ho’s team at Carnegie Mellon University, published studies in the *Journal of Cerebral Blood Flow and Metabolism* that revealed marked region-dependent derangements in cerebral blood flow after resuscitation from experimental cardiac arrest. This finding builds upon classic work of the late Dr. Safar, and suggests the need for brain-region-specific therapies to maximally improve neurological outcomes from cardiac arrest.

In our child abuse program, Safar Center associate director, Dr. Rachel Berger published a paper in *Pediatric Research* exploring the utility of multiplex approaches of serum biomarkers to aid in making the diagnosis of brain injury in otherwise missed cases of abusive head trauma (AHT). Her important work, discussed in more detail later in this report, is targeting the development of a biomarker or biomarker panel for clinical use in AHT screening by pediatricians.

The pediatric neurocritical care research group at Children’s Hospital of Pittsburgh of UPMC (CHP), led by Dr. Michael Bell, is one of the most productive clinical research components of the Safar Center and investigators in this group published several reports, two

### Neurological sequelae of 2009 influenza A (H1N1) in children: A case series observed during a pandemic\*

Sirine A. Baltagi, MD; Michael Shoykhet, MD, PhD; Kathryn Felmet, MD;  
Patrick M. Kochanek, MD; Michael J. Bell, MD

Pediatric critical care fellow, Dr. Sirine Baltagi, mentored by Dr. Michael Bell, published a unique case series of infants and children with neurological complications of H1N1 influenza infection during the recent pandemic. Neurological complications of influenza are rarely described. That paper was the most highly cited report published in 2010 in the journal *Pediatric Critical Care Medicine* along with being one of the more popular downloads from the journal website.

of which are particularly noteworthy. Dr. Ericka Fink, an Assistant Professor in Critical Care Medicine at CHP described the use of intravenous iced saline to optimize fever control in infants and children with brain injury. Fever can be damaging to the injured brain and Dr. Fink's approach to "targeted temperature management" in the pediatric ICU could help reduce secondary damage early after brain injury in children. Cooling devices that can allow careful control of body temperature are readily available for adults with CNS injury; however, similar devices are not yet available for children. Thus, her approach is of special interest to pediatric neurocritical care.

Many Safar Center investigators received awards in the past two academic years. Notably, Dr. Samuel Tisherman received the 2009 Lifetime Achievement Award in Trauma Resuscitation from the American Heart Association for his work on hypothermia in resuscitation. Congratulations Sam!

I have always said that "it is the people that count" and this year several Safar Center faculty members achieved important career milestones. Dr. Robert Clark was named Chief of the Division of Pediatric Critical Care Medicine at CHP. Bob replaces Dr. Ann Thompson who retired from that position after over 25 years of service. Bob is an accomplished clinician-scientist-educator-and administrator whose devotion to the critically ill kids at CHP, trainees, faculty and the allied professionals that work in the pediatric ICU is absolute; he is the perfect choice to lead the division.

This year, Dr. Anthony Kline, Associate Professor in the Dept. of PM&R, received Tenure. Anthony is a highly respected scientist working on TBI and has carried out some of the most meticulous work on behavioral outcomes in experimental TBI that I have ever seen. He was also recently named to the editorial board of the *Journal of Neurotrauma*. Anthony also received an Alumni Achievement Award for Research from the American Psychological Association/Diversity Program in Neuroscience. This award was presented during the Society for Neuroscience meeting in Washington, DC. Safar Center Associate Director and former trainee, Dr. Hülya Bayır was appointed Director of Pediatric Critical Care Research at CHP. Dr. Bayır is one of the most talented scientists to graduate from our program and is poised to lead the many talented fellows recruited to the pediatric CCM program at CHP to new heights in academics. Finally, my long time collaborator, friend, and former Chair of the Dept. of Neurology, Dr. Steven DeKosky was named Dean of the School of Medicine at the University of Virginia. UVA gained a terrific leader. Everyone at the Safar Center is grateful to Steve for the many successful collaborations that we shared and wishes him the best of luck.

A special development in 2009 was the formal establishment of a Pediatric Neurocritical Care service at CHP.

The service, directed by Dr. Michael Bell has delivered cutting edge care to critically ill infants and children with neurologi-



cal conditions in Pittsburgh. It has also facilitated research on disorders such as brain injury from cardiac arrest, TBI, CNS infections, and seizures, has led to a flurry of new publications, and has enhanced the education of our trainees. That this clinical service is led by four NIH-funded faculty members and is enrolling patients into three NIH-funded randomized clinical trials is unique. Dr. Bell has energized the entire field in this regard and thanks in large part to his efforts, Pediatric Neurocritical Care is emerging as a bona-fide subspecialty of pediatric critical care medicine.



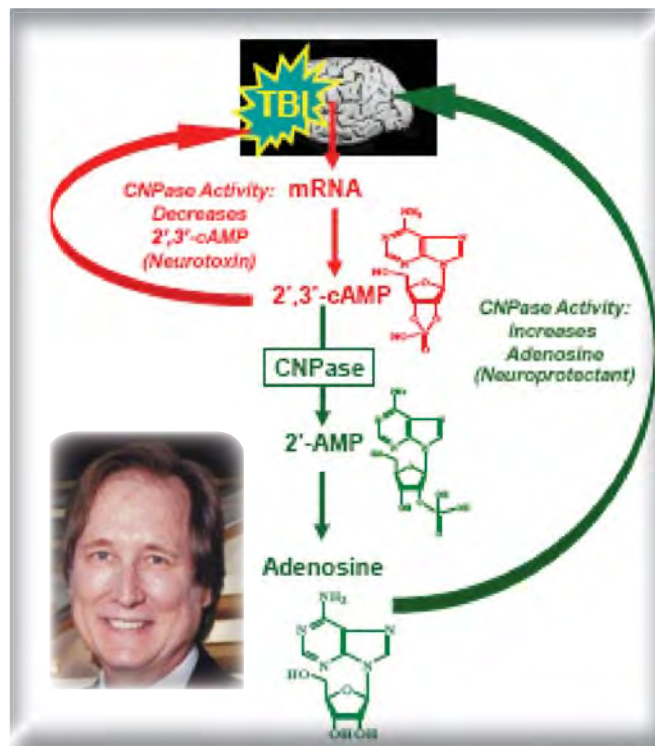
In two separate studies, work from the laboratory of Dr. Anthony Kline (pictured with Jeff Cheng), Associate Professor in the Dept. of Physical Medicine and Rehabilitation (PM&R) and Safar Center Associate Director, demonstrated detrimental effects of the commonly used sedative haloperidol on cognitive outcome after experimental TBI. These studies support the new movement in the field to re-examine how to best sedate all critically ill patients—particularly those with evolving brain injury.

## NEW GRANTS

The number of new grants to our faculty in the 2008-09 and 2009-10 academic years was impressive. We launched several new initiatives supported by the U.S. DOD related to research on TBI. Most notable among these is the new \$7.48 million award from the U.S. Army titled "Operation Brain Trauma Therapy" that was previously discussed. Embellishing our long-standing program project on TBI from the National Institute of Neurological Disorders and Stroke (NINDS)/NIH, Dr. Robert Clark, received a new RO-1 for work on combination therapy. It has long been suspected that multiple therapies will be required to produce meaningful improvements in outcome in brain injured patients and his new research is evaluating the combination of two drugs, probenecid and N-acetyl-cysteine in an attempt to reduce oxidative damage in brain after severe TBI in children. His work is one of several exciting multi-departmental collaborations between our group and the investigative teams at both the Pittsburgh Center for Free Radical and Antioxidant Health (Drs. Valerian Kagan and Hülya Bayır) and the University of Pittsburgh School of Pharmacy (Drs. Samuel Poloyac and Philip Empey). It is fitting that some of the earliest work on combination therapy in CNS injury was carried out by the late Dr. Safar in his pioneering studies of cardiac arrest—thus we continue to build on Dr. Safar's legacy.

I am also pleased to report that Dr. Rachel Berger received her first RO-1 from the National Institute for Child Health and Human Development (NICHD)/NIH titled "Novel approaches to screening for inflicted childhood neurotrauma." Rachel's work on detection of missed cases of AHT is unique and important and it is also great to see another of our K-awardees successfully progress to RO-1 level support. Special thanks to Dr. Carol Nicholson at NICHD/NIH and Dr. Duane Alexander, former director of NICHD for their enthusiastic support of Rachel's work.

Two of our young investigators received "Beginning Investigator Grant in Aid" awards from the American Heart Association. In 2009, Dr. Tomas Drabek received his award to study the effect of deep hypothermic cerebral preservation on the neuroinflammatory response—specifically microglial activation. Dr. Manole Mioara, in 2010 received support for her work in experimental cardiac arrest. Mio is studying brain tissue oxygenation in a developmental rat model in work that is ultimately targeting the clinical use of brain tissue oxygen monitoring in infants and children to improve neurological outcome after cardiac arrest. She is also funded by a KO8 award from NIH. Congratulations to both of these young investigators.



Drs. Edwin Jackson (pictured above) and Kochanek were awarded, as dual PIs, a new two year R21 award from NINDS to study the novel 2, 3 cyclic AMP (2, 3, cAMP) pathway in experimental TBI. Dr. Jackson, Professor in the Dept. of Pharmacology and Chemical Biology, in seminal studies, recently uncovered this pathway. Unlike traditional 3, 5 cAMP, 2, 3 cAMP is generated in tissue injury from the breakdown of the poly adenine tails of messenger RNA in cells and may thus play a particularly important role in the setting of CNS injury. We are very excited at the Safar Center to be able to be participating in these potentially groundbreaking studies.



Dr. Philip Empey received a Clinical Research Scholar Award from the NIH through the University of Pittsburgh Clinical and Translational Science Institute. Dr. Empey, another promising young investigator emanating from Dr. Sam Poloyac's group in the School of Pharmacy, is studying the underexplored area of drug transporters in brain injury with a special focus on its role during the emergence of the use of mild therapeutic hypothermia in clinical care.



Dr. Ericka Fink received a grant from the Laerdal Foundation for her work in cardiac arrest. She is carrying out a single center randomized trial of mild hypothermia comparing 24 hours versus 72 hours of treatment in infants and children after cardiac arrest. She is also K23 funded from NICHD and is collaborating with Dr. Ashok Panigraphy, Chief of the Division of Radiology at CHP. Application of novel magnetic resonance imaging and spectroscopic tools to study cardiac arrest in children is a very exciting opportunity and a great collaboration.



Dr. Andreas Janata, a visiting fellow from the program of Dr. Fritz Sterz in Vienna, Austria, received both the Safar Fellowship grant and an individual project grant from the Laerdal Foundation to support his studies of extracorporeal reperfusion after experimental cardiac arrest. Andreas is using a new ventricular fibrillation model in rats that he established in the Safar Center. He also received support from a FWF Schroedinger grant. We are once again greatly indebted to the Laerdal Foundation for their long-standing support of our young investigators.



Samuel Shin, an MD, PhD student working under the mentorship of Dr. C. Edward Dixon received an NRSA F30 grant from NINDS for his work studying the interaction between alpha synuclein and altered dopaminergic neurotransmission after TBI. Sam, one of the brightest and hardest working trainees at the Safar Center, frequently closes the place down on Sunday nights.



Three of our trainees, Sarah Chlebowska (left) and Amanda Panos (middle), mentored by Dr. Anthony Kline in PM&R and Jing Ji (right), mentored by Dr. Hülya Bayır in pediatric CCM were selected as finalists in the highly competitive student competition at the 2010 National Neurotrauma Society meeting. Sara and Jing also received a travel award to attend the meeting.

## AWARDS AND ACCOMPLISHMENTS OF TRAINEES & FACULTY

Few things are more satisfying than the successes that our trainees have experienced across the partnering departments at the Safar Center during my years as director. The 2008-09 and 2009-10 academic years featured many additional successes in this regard. It was humbling to me that at the 2010 Congress of the Society of Critical Care Medicine (SCCM), six of our pediatric CCM fellows received awards, including Dr. Alicia Au (Neurology Specialty), Dr. Sirine Baltagi (In-Training), Dr. Mark Hall (Scientific), Dr. Yi-Chen Lai (Young Investigator), Dr. Paul Shore (Scientific and Ethics), and Dr. Stephen Robert (Cell Biology). That our current and former trainees received both the In Training and Young Investigator awards at the 2010 Critical Care Congress is special. Congratulations to both Sirine and Yi-Chen.

Benjamin Wells de Witt received the Stephen Phillips award during the Dean's Summer Research Program for Medical Students, and Amanda Panos received a Center for Neuroscience Undergraduate Research Program Fellowship. Kathryn Ehrenberg was awarded a travel fellowship to present her undergraduate research at the 2009 Society for Neuroscience meeting in Chicago, IL. All of these trainees were mentored by Dr. Anthony Kline. In addition, J'mir Cousar, a medical student mentored by Dr. Robert Clark, received a travel award for the Brain '09 meeting. Rachel Kyper, an undergraduate from Ohio University mentored by Dr. Kochanek received third prize for her work at the annual CHP poster day for summer students in 2009. The annual summer student program and poster day at CHP is a wonderful event. A number

of other prestigious awards were received by our trainees and many of these are discussed in relevant sections throughout this report. There were also a countless number of oral and poster presentations by trainees at the Safar Center.

Regarding faculty awards, in addition to Dr. Tisherman's Lifetime Achievement Award that was discussed above, Dr. Kochanek received the 2008 Distinguished Career Award from the Critical Care Section of the American Academy of Pediatrics. He also gave the 4th Integra Lecture at the 2009 Congress of Neurological Surgeons—and was the first intensivist to be selected for that honor.



Pictured from left to right, Dr. Alicia Au (Neurology Specialty), Dr. Sirine Baltagi (In-Training), Dr. Mark Hall (Scientific), Dr. Yi-Chen Lai (Young Investigator), Dr. Paul Shore (Scientific and Ethics), and Dr. Stephen Robert (Cell Biology).



## SPECIAL EVENTS

On January 7<sup>th</sup>, 2010, Congressman Tim Murphy visited the Safar Center. Congressman Murphy toured the center and given that he serves as a Lieutenant Commander in the U.S. Navy Reserve Medical Service Corps, working with wounded warriors with Traumatic Brain Injury and Post Traumatic Stress Disorder, he had a special interest in our work on TBI. We were honored that Congressman Murphy chose to visit our center and review our most recent research.

Dr. Ericka Fink volunteered with project Medishare in a field hospital near Port-au-Prince after Haiti's earthquake on January 12, 2010. She administered care in the first ICU able to provide mechanical ventilation for children in Haiti. I am also pleased to report that a special article about this experience, co-authored by Dr. Fink, is in press in the journal *Pediatric Critical Care Medicine*.

We were pleased to be informed by Mr. Christoph Redelsteiner, Chief of Emergency Medical Services of the Vienna Red Cross, that the Austrian government approved the renaming of the street outside of the EMS Training Center in Vienna "Safargasse" (Safar Lane) in honor of the late Dr. Peter Safar. Dr. Safar was born in Vienna in 1924 (see page 9).

Dr. Safar was also honored at Johns Hopkins Bayview Medical Center (formerly Baltimore City Hospital) on the occasion of the 50th anniversary of his opening of the first multidisciplinary intensive care unit in the USA on July 14, 1958. The celebration, which occurred in September of 2008, featured lectures by pioneers in the field of critical care medicine, including Drs. Max Weil and Joseph Parrillo. A collection of Dr. Safar's papers and works was dedicated in the Bayview Hospital Library collection.





## GUEST PROFESSORS

On March 23-24, 2009, Dr. Jamie Hutchison served as a guest professor to both the Safar Center and the Dept. of CCM. Dr. Hutchison is an Associate Professor in the Dept. of Critical Care and Paediatrics at Toronto Sick Children's Hospital and a leading investigator in the field of pediatric TBI. He was the PI of the recent RCT of therapeutic hypothermia in pediatric TBI—the results of that study were published in the *New England Journal of Medicine*. Dr. Hutchison presented his work on secondary injury in pediatric TBI at the Safar Center and our pediatric fellows and other trainees also presented their work to him in a reverse site visit fashion.



On December 14, 2009, James Atkins, MD, PhD, visited the Safar Center. Jim is Chief of the Closed-Head Injury Branch in the Center for Military Psychiatry and Neuroscience at WRAIR in Rockville, Maryland. He presented research on his work on ferrous iron binding in hemorrhage resuscitation. Jim's visit also facilitated discussions to launch our collaborative work with him studying the optimal approaches to oxygenation and ventilation in combined experimental TBI and hemorrhagic shock. We are currently using a conventional model of TBI in mice combined with hemorrhagic shock to study these important questions and parallel studies are being carried out by Dr. Atkins along with his colleague Dr. Joseph Long also at WRAIR, and Dr. Gary Fiskum and his research team at the University of Maryland.



## ANNUAL SUMMER STUDENT RESEARCH DAY

Each summer, the Safar Center serves as the home base for many students in its various laboratories. They range in experience from advanced high school students to medical students and many of them visit from other universities. In August, the Safar Center holds a student research day where each trainee presents their work in an oral format to a group of senior scientists. In 2009 and 2010, we hosted over 18 talented students, many of whom have also pre-

sented their work at national scientific conferences in the areas of traumatic brain injury, neuroscience, resuscitation, physical medicine and rehabilitation, neurosurgery, and critical care, among others. Two of our leading mentors, Drs. Amy Wagner and Hülya Bayır, are also pictured in the 2010 photo below (2nd and 3rd from right, respectively). Thanks to all the students and mentors for their hard work.

### 2009 Student Research Day



### 2010 Student Research Day





## ACKNOWLEDGEMENT

I would like to once again thank everyone working at the Center for a fantastic job in the 08-09, and 09-10 academic years. I am indebted to Linda Ryan, Marci Provins, Fran Mistrick, Jackie Pantazes, and Cara Boyer for their administrative and secretarial excellence. Marci also serves as my local editorial assistant for the journal *Pediatric Critical Care Medicine*. I also thank Henry Alexander, John Melick, Keri Feldman, Vincent Vagni, Xiecheng Ma, Jeremy Henschir, Sherman Culver, Yaming Chen, Jeffrey Cheng, Ashley Glumac, Christina Hosler, Youming Li, Roya Tehranian, Nicole Toney, Jason Stezoski, and Mu Xu for their technical contributions. Two faculty members/research associates working in the Safar Center deserve special thanks—Lina Du and Hong Yan. Both Lina and Hong have contributed enormously to the success of the Safar Center for many years and continue to do high quality scientific work vital to our mission. I am continually amazed by the work ethic and commitment of everyone.

I thank Drs. Derek Angus, Robert Clark and Ms. Susan Stokes for departmental support and Drs. Bayir, Bell, Berger,

Neurology, Dr. Simon Watkins in the Dept. of Cell Biology and Physiology, Drs. Ava Puccio and Yvette Conley and Sheila Alexander from the School of Nursing, Dr. David Okonkwo in the Dept. of Neurological Surgery and Director of the Neurotrauma Program at UPMC, Dr. Peter Wipf at the Combinatorial Chemistry Center, Dr. Anna Lokshin at the Pittsburgh Cancer Institute, Drs. Joel Greenberger and Michael Epperly in the Dept. of Radiation Oncology, and Dr. Mark Gladwin in the Cerebral Vascular Disease Research Center. The expertise of these individuals greatly raises the level of the research at the Safar Center. Thanks are also in order to Provost, Dr. George Klinzing and Dr. Carey Balaban for discussions on blast TBI.

I also look forward to working with a new faculty member in critical care, Travis Jackson, PhD and a new postdoctoral scientist in the Dept. of Pharmacology and Chemical Biology, John Verrier, PhD. I have already been impressed at the new tools and ideas that they have brought to the Safar Center.

Special thanks also to Dr. Joseph Newsome for helpful veterinary support and his tireless efforts with planning on the many renovation projects in our center.

{ The goal for our Center is an endowment of two million dollars to keep alive Dr. Safar's dream to prevent the premature loss of people with "**hearts and brains too good to die.**" }

Callaway, Clark, Dixon, Jenkins, Kline, Tisherman, and Wagner for their assistance, as associate directors, on a wide variety of matters important to the Safar Center. Thanks are also due to a number of department chairs including Drs. John Williams, Michael Boninger, Timothy Billiar, Robert Friedlander, David Perlmutter, Jonas Johnson, and Donald Yealy.

I am also especially thankful to Dr. Ann Thompson, Associate Dean for Faculty Affairs for her continued support, guidance, and friendship.

I am also grateful to a number of key collaborators affiliated with the University of Pittsburgh including Dr. Edwin Jackson in the Dept. of Pharmacology and Chemical Biology, Dr. Valerian Kagan at the University of Pittsburgh Center for Free Radical and Antioxidant Health, Drs. Chien Ho, Kevin Hitchens, and Eric Aherns, Ms. Lesley Foley, and doctoral student Parker Mills at the Pittsburgh NMR Center for Biomedical Research, Dr. Stephen Wisniewski and his team in the Dept. of Epidemiology, Dr. Robert Garman of Consultants in Veterinary Pathology, Inc., Drs. Samuel Poloyac and Phil Empey and Jocelyn Zhou, PhD candidate, in the School of Pharmacy, Drs. Steven Graham, Milos Ikonovic, and Steven DeKosky in the Dept. of

I also wish to acknowledge many scientific collaborators outside of the University of Pittsburgh who make critical contributions to our mission. These include Drs. Carleton Hsia and Li Ma of SynZyme Technologies, Inc., for collaboration on our US Army and NIH funded work on novel resuscitation fluids, Drs. Frank Tortella, Richard Bauman, James Atkins, and Joseph Long at WRAIR, Steve Parks at ORA, Inc., David Ritzel at Dyn-FX Consulting Ltd and Dr. Denes Agoston at the Uniformed Services University for valuable discussions and collaboration on TBI in combat casualty care and blast TBI, Drs. Dalton Dietrich, Helen Bramlett, John Povlishock, Frank Tortella, Deborah Shear, Ronald Hayes, Kevin Wang, Kenneth Curley, and Major Kara Schmid for their efforts toward the success of Operation Brain Trauma Therapy, and Dr. Jurgen Schnermann at NIDDK for his help with a number of knockout mice in the area of adenosine biology.

Thanks are also in order to Dr. Nancy Carney and her team at the Oregon Health & Science University for their collaboration on the update of the Guidelines for the Management of Severe TBI in Children that is being assembled. I also am pleased that our collaboration with pediatric TBI expert Dr. P. David Adelson has continued, despite his move to Arizona.

Many other individuals were helpful to our Center this year.

I would like to acknowledge Drs. Carol Nicholson, Tamara Jenkins, Ralph Nitkin, Beth Ansel, and Michael Weinrich of the National Center for Medical Rehabilitation Research (NCMRR)/NIH, Dr. Ramona Hicks at the NINDS/NIH, Ken Curley, MD, at US Army Medical Research and Materiel Command (USAMRMC) in Ft. Detrick, Maryland and Colonel Dallas Hack, Director, US Army Combat Casualty Care Research Program at USAMRMC, Colonel Geoff Ling at DARPA, and Mr. Robert Read at TATRC for their efforts on behalf of our work.

Thanks are also in order for Dr. Lyn Yaffe and S. William Stezoski of EPR Technologies, who continue to contribute enormously to our success. We also thank Mr. Gene McGrevin and his team at Medivance for their commitment to hypothermia research and their support of the Safar Symposium.

I also owe a special debt of gratitude to Mr. Tore Laerdal of Laerdal Medical. His generous support of our young investigators, along with the support of the Laerdal Foundation, has been incredible for many years. We were

also pleased to learn about his new “Helping Babies Breathe and Helping Mothers Deliver” initiative targeting an important need in developing countries and the new company to facilitate this work— Laerdal Global Health. Everyone at the Safar Center wishes Tore the best of luck with this vital new effort—it represents a cause that would have similarly inspired the late Dr. Safar.

I would also like to recognize and thank Marci Provins for her efforts on the design and layout for this year’s annual report.

Finally, fundraising efforts continue for the Safar Legacy Fund to provide a core budget for the Center, along with funds to support the Nancy Caroline Fellowship Award and, of course, the Safar Symposium. We have enclosed a pledge card describing those funds in this year’s report and thank you in advance for your support. Thanks to each of you who have donated to these efforts. These funds aid us in keeping alive Dr. Safar’s goal of the resuscitation of “hearts and brains too good to die.” I look forward to success in the 2010-11 academic year and beyond in our efforts to develop new therapies in the field of resuscitation medicine, and thank you for your continued support of our work.



Congratulations to Henry Alexander who was recognized in 2010 for a remarkable 40 years of service to the Safar Center and the University of Pittsburgh School of Medicine. Henry is one of the senior technicians in the Center. He began his career under the direction of the late Peter Safar and worked on a number of pioneering studies in cerebral resuscitation. He has been instrumental to the success of hundreds of studies at the Safar Center and currently oversees work in experimental pediatric models of cardiac arrest and traumatic brain injury in support of the work of Drs. Clark, Bayir, Manole, and Empey.

## ...LATE BREAKING NEWS...

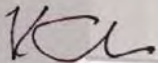
As we go to press with this report, I am pleased to announce that we appear to have successfully renewed our longstanding T-32 grant from the NICHD titled “Training in pediatric neurointensive care and resuscitation research.” It is marvelous news that our competitive renewal received a perfect priority score of 10 in peer review. It epitomizes the highly collaborative approach that we take in fellow and junior faculty development. The T32 program, a cornerstone of our mission, has been instrumental in helping to launch the careers of many of our most successful trainees, and it is comforting to know that we will have that support through 2016. I am grateful to Dr. Carol Nicholson, Director of the Pediatric Critical Care Medicine Program in the NCMRR/NIH for her tireless support of our program and to Drs. Ralph Nitkin and Michael Weinrich at NCMRR and Dr. Duane Alexander, former NICHD director who helped us launch this T32 over 11 years ago.

I am also pleased to announce new funding of a U44 grant from the NINDS that will begin in 2011. It will allow us to build on the promising work with PNPH in TBI resuscitation, in collaboration with principal investigator Dr. Carleton Hsia at SynZyme Technologies—with the hope that this agent will be able to be moved ultimately to a clinical trial in TBI resuscitation. Thanks also to Dr. Li Ma at Georgia Southern University for her help and to Dr. Ramona Hicks for her efforts on behalf of TBI research at NINDS.

On October 19, 2010 we were visited by COL Dallas Hack Director, U.S. Army Combat Casualty Care Research Program at USAMRMC to launch the new Operation Brain Trauma Therapy multicenter pre-clinical drug and biomarker research program for TBI. He provided us with important insight on TBI from the perspective of current U.S. combat casualty care and we are pleased and honored to begin this important program with our many collaborators.

Finally, as I write this letter, construction is well underway for a new laboratory for the PM&R group on the second floor of the Safar Center. It is exciting to see the collaboration with PM&R continue to grow—the PM&R investigators at the Center are an integral part of the Safar family. Thanks once again to Dr. Michael Boninger for his support.

Respectfully submitted,



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Director, Safar Center for Resuscitation Research



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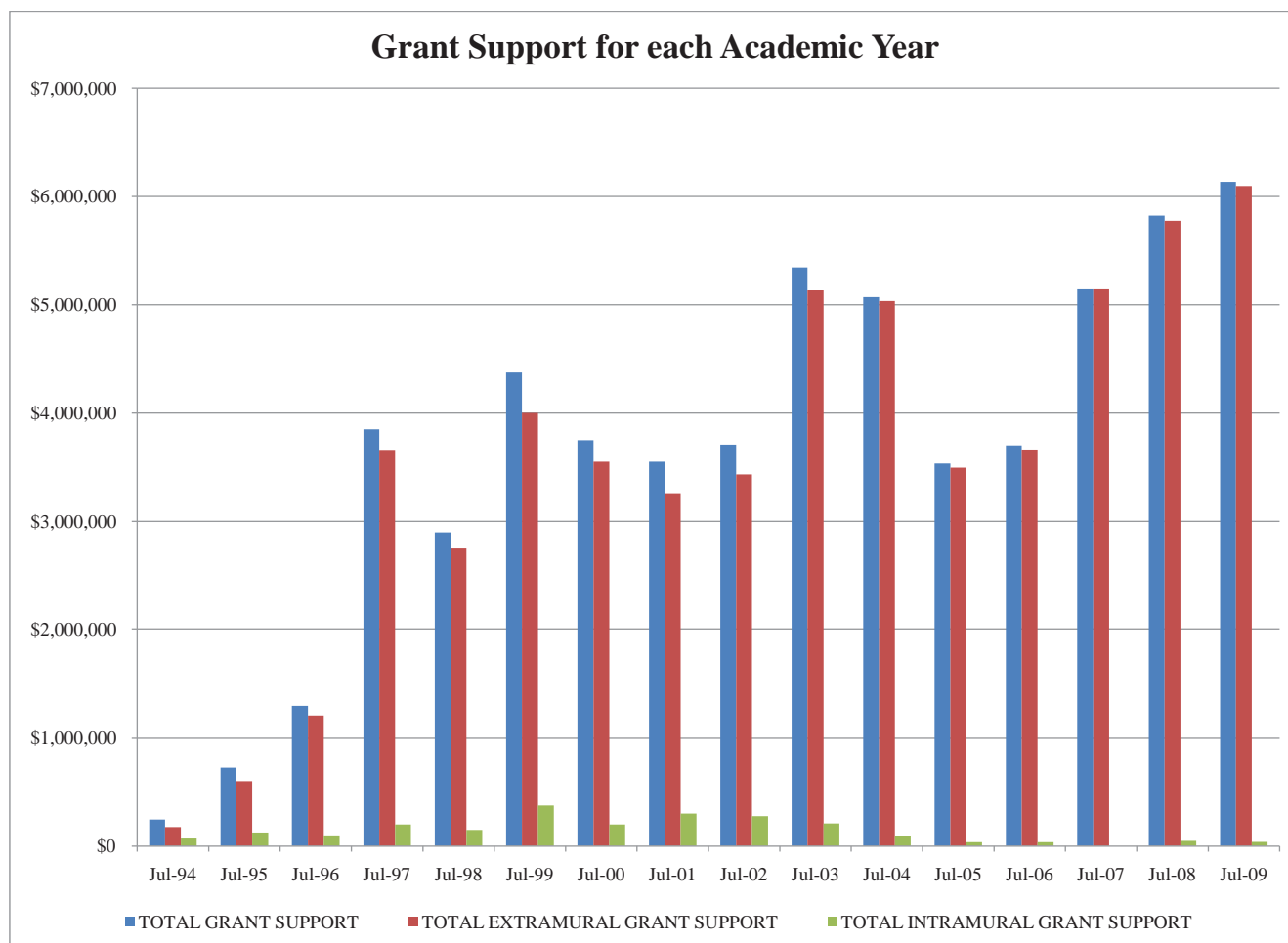
\* Denotes T32 fellow

During the 2008-09 and 2009-10 academic year, Safar Center investigators had a total of 92 and 90 grants, respectively, all of which were extramural. The direct and indirect costs for the full award periods of these grants totaled \$33,047,255 and \$29,415,411, respectively, and these figures are plotted below for the current and preceding fourteen academic years.

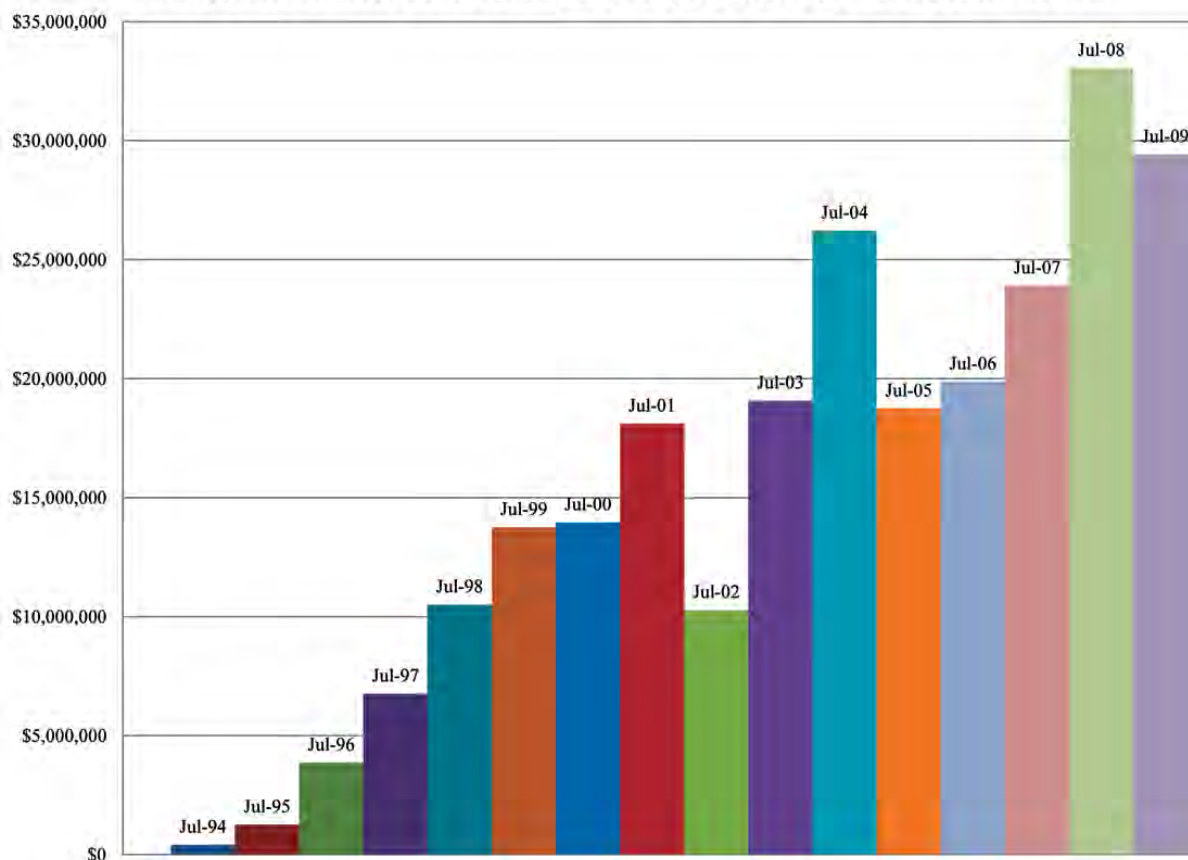
The portion of the budget for use in each academic year (July 1 through June 30) is also plotted for the current and preceding fourteen academic years and similarly reflects continued growth. This represents direct and indirect costs and is shown for total, extramural, and intramural grant support.

The specific sources of support are shown. Extramural funding sources included the NIH, the United States Army, DARPA, the Centers for Disease Control and Prevention, the Laerdal Foundation, the American Heart Association, the Society for Cardiovascular Anesthesiology, and other sources. Intramural support was provided by the Departments of Critical Care Medicine, Anesthesiology, Pediatrics, and PM&R and the Children's Hospital of Pittsburgh of UPMC. As previously discussed, between the 2007-08 and 2009-2010 academic years, the DOD-related percent of total extramural grant funding at the Safar Center nearly doubled, increasing from 16 to 27%. We are deeply grateful for this support.

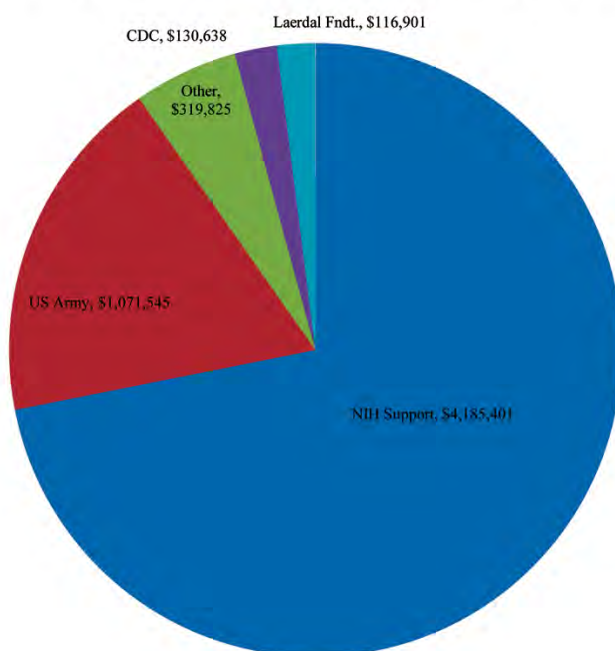
We continued to grow, even given the economic downturn that was encountered during this two academic year period. Both the support of the DOD and funding via President Obama's economic stimulus package were helpful in this regard. Nevertheless, maintaining sustained growth during this challenging period required a monumental effort by our faculty and staff since our support is almost completely derived from extramural grants. Congratulations once again to the faculty for their funding successes.



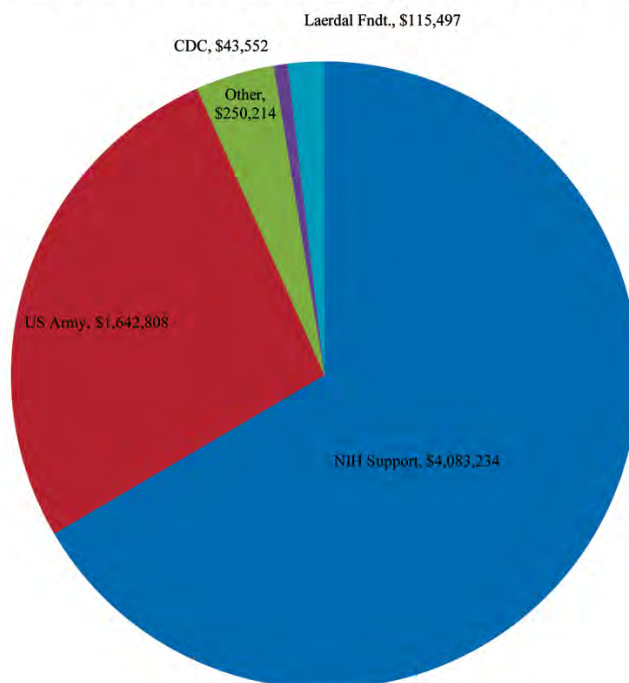
**Direct and Indirect Costs for the Full Award Period of Safar Center Grants**



**Specific Sources of Grant Support 2008 - 2009**



**Specific Sources of Grant Support 2009 - 2010**





In the United States, about two million people incur TBI each year, largely as a result of vehicular accidents, falls, acts of violence, and sports accidents. Over 50,000 people die and 200,000 are hospitalized as a result of TBI, at an annual cost of about \$10 billion for acute care and rehabilitation. Given the role of TBI in combat casualty care (discussed later in this report) and its huge exposure in the mainstream media as a result of enhanced awareness of the potential deleterious consequences of concussion in professional sports, TBI has gained considerable importance worldwide. Current treatment is comprised of supportive care and, in severe cases the control of brain swelling and raised intracranial pressure. New therapies are badly needed across the spectrum of injuries, from mild to severe.

The TBI programs at the Safar Center are funded by a long-standing program project from NINDS that supports the University of Pittsburgh Brain Trauma Research Center (Principal Investigator, Dr. C. Edward Dixon) along with numerous R01 and R21 awards. The TBI program also serves as an interface for clinical TBI research at both Presbyterian and Children's Hospitals and provides an outstanding environment for translational research. Safar Center scientists had a remarkable 42 manuscripts published or in press from work on TBI during these two academic years. The TBI program is also supported by a number of grants from the U.S. DOD including grants from DARPA, the U.S. Army, and the Veterans Administration. Additional information about our DOD-related work on TBI can be found in the section on Combat



Dr. Ikonomic is now leading a team of investigators in collaborative work with the Safar Center that is unraveling the link between TBI and neurodegenerative diseases, such as Alzheimer's disease. New studies have suggested that TBI may trigger a number of neurodegenerative diseases, and thus new treatments for TBI could have major public health benefits across a wide spectrum of neurological and psychiatric disorders.

neurodegenerative pathways linked to Alzheimer's disease by TBI. This work emanated from seminal studies by Drs. DeKosky and Ikonomic on the TBI-Alzheimer's disease link that were carried out at the University of Pittsburgh in collaboration with the Safar Center, prior to Dr. DeKosky's departure to accept the position of Dean of the Medical School at the University of Virginia.

In studies funded by NINDS/NIH, collaborative research between Dr. Kochanek's and Dr. Chien Ho's laboratories at the Pittsburgh NMR Center for Biomedical Research demonstrated that new magnetic resonance imaging techniques can be used to track the migration and accumulation of circulating macrophages in the injured brain after experimental TBI. Using the controlled cortical impact model of TBI in mice and submicron iron oxide (MPIO)

Safar Center investigators are tackling the problem of TBI from the field through to rehabilitation in pursuit of both neuroprotective therapies that will improve the outcome of patients and biomarkers to help make the diagnosis and monitor therapy.

Casualty Care later in this report. Similarly, TBI is important to many programs in the center, and some research highlights on this topic are also featured in other sections of this annual report. A few highlights of our work in TBI are discussed below.

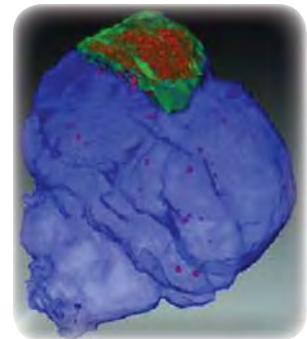
There were many noteworthy reports on TBI by our trainees and faculty in the field of TBI. Some of this work was highlighted in the introductory letter in this annual report, written by Dr. Kochanek. Several others are discussed below.



In a paper published in the journal *Annals of Neurology* by Eric Abrahamson (pictured) working in collaboration with Drs. Milos Ikonomic, C. Edward Dixon, and Steven DeKosky, beneficial effects of the drug simvastatin (Zocor) were observed in experimental TBI in mice. These effects were mediated by blunting of the deleterious consequences of activation of

particles to label macrophages, Lesley Foley published a paper in the *Journal of Neurotrauma* in 2009 describing the feasibility of this approach. Dr. Ho's group at Carnegie Mellon University is a world leader in the development and application of non-invasive macrophage tracking in laboratory studies. Recent work by doctoral student, Parker Mills, mentored by Dr. Eric Aherns, also at the Pittsburgh NMR Center, is using novel PDQ imaging and suggests the possibility of tracking the

Non-invasive inflammatory cell tracking has great potential to the development of optimized anti-inflammatory therapies for TBI and we are pursuing this approach in our current studies funded by both DOD and NIH.



movement of individual macrophages noninvasively in the injured brain.

A number of bench to bedside studies were performed by Safar Center investigators. Several of the most important are discussed below. In a bench to bedside study, Dr. Hülya Bayır led a team of investigators at CHP, the Pittsburgh Center for Free Radical and Antioxidant Health and the Safar Center to carry out a clinical study assessing the impact of mild therapeutic hypothermia on oxidative stress in infants and children with severe TBI. In a report on this work published in the journal *Critical Care Medicine*, she showed that hypothermia attenuated oxidative stress and damage as assessed in samples of cerebrospinal fluid in infants and children that were randomized to treatment with hypothermia versus normothermia. Safar Center investigators, in a series of studies, have revealed that mild hypothermia appears to have differential effects on secondary injury mechanisms after TBI. Oxidative stress appears to be one of its most important clinical targets.



Dr. Hülya Bayır's work on hypothermia and oxidative stress in TBI may help determine what therapies could be combined with mild therapeutic hypothermia to optimize its effectiveness in both TBI and cardiac arrest.

Dr. Ajit Sarnaik, working under the mentorship of Dr. Robert Clark and Dr. Yvette Conley in the School of Nursing, published a manuscript in the *Journal of Neurotrauma*, describing clinically relevant polymorphisms of the poly-ADP ribose polymerase (PARP) gene that were associated with outcome in human TBI. Dr. Clark's laboratory has been studying PARP for several years and has demonstrated that this enzyme is important in contributing to poor TBI outcomes—likely via effects in mitochondria. Dr. Sarnaik graduated from our T-32 program and is now on the faculty of Children's Hospital of Michigan.



In another collaborative study examining genetic polymorphisms in human TBI, Dr. Amy Wagner, in collaboration with Drs. Conley and Kochanek, reported on associations between polymorphisms of the adenosine A<sub>1</sub> receptor and posttraumatic seizures in a study just published in *Epilepsy Research*. That work provides a clinical link to the prior work of Drs. Kochanek and Edwin Jackson which suggested a critical role of adenosine A<sub>1</sub> receptors in preventing posttraumatic status epilepticus after experimental TBI in mice. Manipulation of both the PARP and adenosine pathways may represent important future targets for drug therapy in human TBI.

## FACULTY PRINCIPAL INVESTIGATORS

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Michael J. Bell, MD  
Rachel P. Berger, MD, MPH  
Robert S.B. Clark, MD  
Yvette Conley, PhD  
Steven DeKosky, MD  
Lina Du, MD

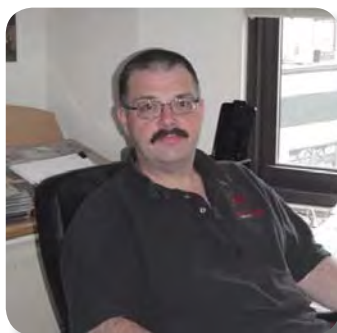
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Steven H. Graham, MD, PhD  
Milos Ikonovic, MD  
Larry W. Jenkins, PhD  
Anthony E. Kline, PhD  
David Okonkwo, MD, PhD  
Samuel Poloyac, PharmD, PhD  
Ava M. Puccio, RN, PhD  
Amy K. Wagner, MD  
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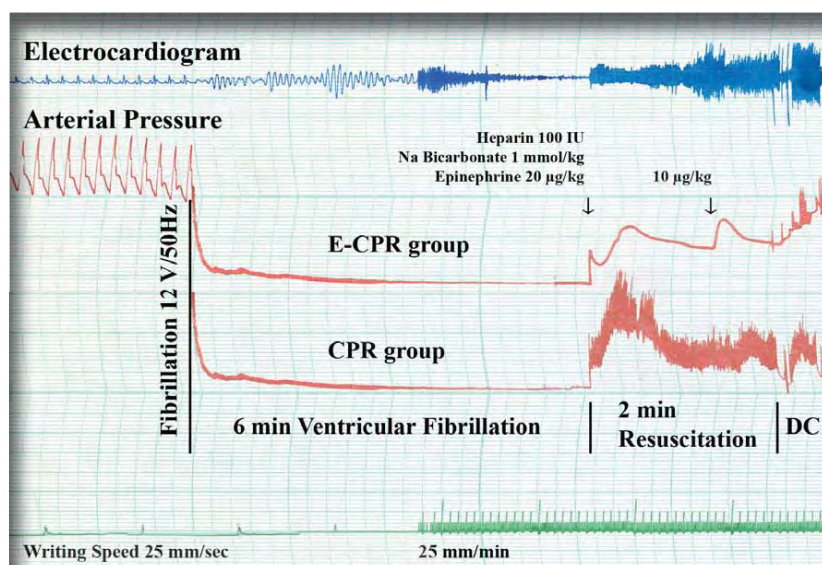
Cardiac arrest in adults and children is an enormous public health problem. There are an estimated 330,000 out-of-hospital cardiac deaths per year in the United States. Overall survival rates from out-of-hospital cardiac arrests are estimated to be as low as 6% in both adults and children. Resuscitation leads to return of spontaneous circulation in less than 40% of arrest victims and traditionally only about 10% ever regain consciousness.

### CARDIAC ARREST AND RESUSCITATION IN ADULTS

Dr. Clifton Callaway (pictured, right), Ronald D. Stewart Endowed Professor and Vice Chairman of Emergency Medicine and Safar Center Associate Director, leads a team of talented investigators at the UPMC Center for Emergency Medicine in generating an impressive portfolio of over 20 publications in journals such as *JAMA*, *Circulation*, and *Resuscitation* targeting the goal of improved outcomes for adults who suffer cardiac arrest. Using the NIH-funded Resuscitation Outcomes Consortium mechanism, and in separate studies, he and his team have played an important role in generating a wealth of new knowledge about the various characteristics of patients and care that are associated with favorable or unfavorable outcomes. Included in this body of work, Dr. John Rittenberger, Assistant Professor of Emergency Medicine and Medical Director of STAT MedEvac, published three reports addressing the topics of the value of the clinical examination after resuscitation, optimized patient transport in out-of-hospital arrest, and the impact of a coordinated hospital-wide plan on patient outcomes after cardiac arrest.



The application of therapeutic mild hypothermia has demonstrated benefit in some cases of cardiac arrest in adults. However, hypothermia has myriad effects that are poorly understood and additional research is needed to optimize its use—particularly in critically ill and highly complex patients after cardiac arrest. Dr. David Hostler (pictured, left), Assistant Professor of Emergency Medicine and Director of the Emergency Responder Human Performance Lab at the University of Pittsburgh carried out a collaborative study between investigators at the UPMC Center for Emergency Medicine, the laboratory of Dr. Samuel Poloyac at the University of Pittsburgh School of Pharmacy, and the Safar Center on the important topic of the effect of mild hypothermia on drug metabolism in normal healthy subjects. His study was recently published in the journal *Drug Metabolism and Disposition*.



Dr. Andreas Janata, a visiting fellow from the Emergency Medicine program of Dr. Fritz Sterz at the Vienna General Hospital, with the assistance of Dr. Erik Popp at the University of Heidelberg, established a new rat model of ventricular fibrillation cardiac arrest. The physiological findings during and immediately after cardiac arrest in this model are shown in the figure on the left. Using this model, Dr. Janata, in studies funded by the Laerdal foundation, has studied the use of extracorporeal reperfusion to improve outcome after cardiac arrest. His work was presented at the 2010 Congress of the American Heart Association.



**CARDIAC ARREST IN INFANTS & CHILDREN**

A team of physician-scientists led by Dr. Robert Clark, and including Drs. Hülya Bayır, Michael Bell, Ericka Fink, Robert Hickey, and Mioara Manole are working to develop new treatments to attenuate the devastating brain injury that can occur in children who suffer cardiac arrest.

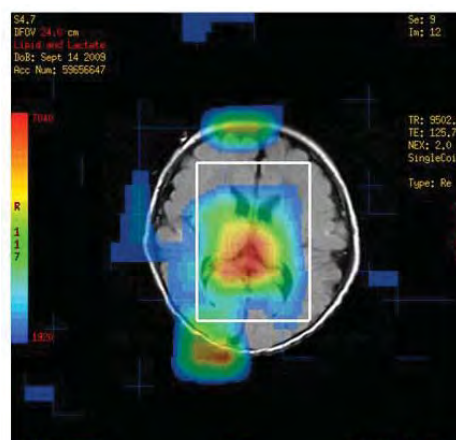
An exciting positive therapeutic trial in an experimental model of asphyxial cardiac arrest was reported in the *Journal of Cerebral Blood Flow and Metabolism* by research associate Minke Tang, working in the laboratory of Dr. Hülya Bayır. Treatment of immature rats with the drug minocycline after cardiac arrest attenuated the inflammatory response in brain, reduced neurological damage, and improved outcome. Minocycline might have special potential as a new therapy to reduce damage in the immature brain after cardiac arrest, particularly since the inflammatory response to brain injury seems to be heightened early in development. It is FDA approved for other uses and should be given consideration for future clinical trials of cardiac arrest in children.

Dr. Ericka Fink, Assistant Professor of Critical Care Medicine published a series of reports addressing hypothermia and its use after cardiac arrest in infants and children. These included manuscripts addressing intravenous cooling with iced saline for fever control published in *Pediatric Critical Care Medicine* and a review on the "Pittsburgh" approach to the use of mild hypothermia that was published in the journal *Neurocritical Care*. Her work is supported by a K23 award from NICHD/NIH and a grant from the Laerdal Foundation.

Dr. Mioara Manole, Assistant Professor of Pediatrics is studying the cerebrovascular response to cardiac arrest in the developing brain. Her work has revealed important regional differences in the blood flow pattern in the developing brain after cardiac arrest. This work was published in the *Journal*

*of Cerebral Blood Flow and Metabolism*. She is testing new therapies in an attempt to improve perfusion and neurological outcomes after cardiac arrest. She is funded by a KO-8 award from NIH and a grant from the American Heart Association.

Dr. Samuel Poloyac and his research team in the School of Pharmacy is collaborating with Dr. Kochanek to study the effect of mild hypothermia on drug metabolism by the cytochrome P450 pathway in experimental asphyxial cardiac arrest in rats. In work funded by an RO-1 to Dr. Poloyac, Dr. Michael Tortorici published a study in *Critical Care Medicine* that defined the interaction between cytokines, hypothermia and the P450 pathway after cardiac arrest. Understanding how hypothermia affects drug metabolism is essential to defining its optimal use in critically ill children and adults after cardiac arrest, because these patients require treatment with drugs that are metabolized by cytochrome P450 isoforms.



Dr. Ericka Fink in collaboration with Dr. Ashok Panigraphy, Chief of Radiology at CHP, is comparing the impact of 24 vs 48 hrs of therapeutic hypothermia on outcomes in children after cardiac arrest. She is using se-

rum biomarkers of brain injury along with novel magnetic resonance spectroscopy (MRS) approaches. Shown is a two-dimensional MRS map of brain lactate levels in a child treated with mild hypothermia after cardiac arrest. This exciting approach has great potential to help children after cardiac arrest.

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Hülya Bayır, MD  
Michael J. Bell, MD  
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Ericka L. Fink, MD  
Robert W. Hickey, MD

David Hostler, PhD  
Patrick M. Kochanek, MD  
Mioara D. Manole, MD  
Samuel M. Poloyac, PharmD, PhD  
John Rittenberger, MD, MS  
Samuel A. Tisherman, MD

**A**busive head trauma (AHT) remains the most important type of injury resulting from child abuse and the most common form of severe TBI in children less than two years of age. Commonly known as the shaken baby syndrome, or inflicted childhood neurotrauma, this form of TBI is the leading cause of death from trauma in infants. Approximately 1 in 3,300 infants

the child abuse and TBI literatures, including a chapter in the new textbook *Frontiers in Pediatric TBI* in collaboration with Drs. Ronald Hayes and Kevin Wang at Banyan Biomarkers.

In 2009, Safar Center associate director, Dr. Rachel Berger published an important paper in *Pediatric Research* exploring the utility of multiplex approaches of serum biomarkers

Dr. Rachel Berger, Associate Director of the Safar Center and Director of the Child Abuse Program, is leading a team of collaborators working toward the goal of developing a blood test to aid clinicians in making this difficult diagnosis, in studies funded initially by the Centers for Disease Control and Prevention (CDC), and now by the NIH and the University of Pittsburgh.

less than 1 year of age are victims of severe or fatal AHT each year in the United States, and the number of more mild cases may be over 100 times greater. Recognition of this condition can be difficult for physicians.

Dr. Berger has built upon the early biomarker work initiated by Dr. Kochanek and others at the Safar Center and has carried out a number of clinical trials that have greatly advanced the potential use of serum biomarkers in pediatric brain injury. She is also carrying out collaborative studies with investigators at the Pittsburgh Cancer Institute who have special expertise with Luminex technology to assess simultaneously multiple biomarkers

The interest in biomarkers in AHT and other forms of TBI at the Safar Center is substantial. Biomarkers in TBI, a topic that has been studied for over 15 years in the Safar Center, has become one of the hottest topics in TBI research. In the spring of 2008, Drs. Kochanek, Berger, Bayır, Wagner, Jenkins, and Clark published a review on biomarkers in traumatic and ischemic brain injury in *Current Opinion in Critical Care*. That article was the most highly cited report in that journal published in 2008, likely reflecting the long-standing collective expertise and seminal contributions of the investigative team at the Safar Center in this area of research. Drs. Berger and Kochanek also published a number of recent reviews and chapters on this topic in both

to aid in making the diagnosis of brain injury in otherwise missed cases of AHT. This work involved collaboration with Dr. Anna Lokshin's outstanding team in the Luminex Core Facility at the University of Pittsburgh Cancer Institute. In that study, using a panel of over 20 biomarkers, several promising candidates were identified when comparing the serum response between infants with known AHT and infants with symptoms that are often associated with AHT—but not having the diagnosis. Neuron specific enolase (NSE) has been one of the more promising biomarkers for TBI in infants and children and in 2009 Dr. Berger published a manuscript in *Pediatric Critical Care Medicine* that addressed the optimization of the NSE assay to adjust for hemolysis if it occurs.

Dr. Berger, with new RO-1 funding from NICHD/NIH, has launched a definitive multi-center clinical trial to evaluate the ability of serum biomarkers to identify brain injury (point to the brain) in infants with AHT – signaling the need for additional diagnostic evaluation such as head CT scan. Infants who present to an emergency department with nonspecific symptoms such as vomiting or irritability, among others, are the target for trial. Over 200 infants have been enrolled with a goal 500. Two new sites, the Children's Memorial Hospital in Chicago and Primary Children's Hospital in Salt Lake City have just been added to this trial. We are anxiously awaiting the result of this important research for the field of AHT.

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P. David Adelson, MD  
Hülya Bayır, MD

Robert S.B. Clark, MD  
Larry W. Jenkins, PhD  
Patrick M. Kochanek, MD



Despite the millions of lives saved through the pioneering development and implementation of CPR, many challenges remain in the field of resuscitation. One scenario that continues to have nearly 100 percent mortality in both the civilian and military settings is exsanguination cardiac arrest. This condition, which generally results from trauma, is a leading cause of death of potentially salvageable trauma victims.

One scenario that continues to have nearly 100 percent mortality in both the civilian and military settings is exsanguination cardiac arrest.

Several EPR-related lines of research were pursued in the laboratory. Dr. Tomas Drabek, Assistant Professor of Anesthesiology is studying the effect of deep hypothermia on the inflammatory response in the brain to exsanguination cardiac arrest. Using a rat model of EPR, he reported in *Anesthesia and Analgesia* that hypothermia is more effective at attenuating the inflammation than preventing neuronal death. At the 2010 congress of the American Heart Association,

In 1984 Dr. Safar with advice from Colonel Ronald Bellamy, an authority on combat casualties during the Vietnam conflict, developed a revolutionary new concept targeting battlefield death from rapid exsanguination. It involved transient “preservation” of the victim—to allow evacuation, transport, and emergency “damage control” surgery, followed by a delayed resuscitation using cardiopulmonary bypass. This concept was first described in the literature by Dr. Samuel Tisherman and co-workers in 1990 in a report in the *Journal of Trauma* where the concept was called “deep hypothermia for preservation and resuscitation.” Shortly thereafter, it was called “Suspended animation for delayed resuscitation” and eventually Emergency Preservation and Resuscitation (EPR). EPR involves the use of a rapid ice-cold aortic flush to induce profound hypothermia (~10°C) and induce a preservation state in injury victims that “buys time” for the trauma surgeon to perform damage control surgery that is followed by a delayed resuscitation using cardiopulmonary bypass. The feasibility of EPR was confirmed in a comprehensive series of experimental studies at the Safar Center and the results were published in numerous manuscripts. Research at Harvard Medical School and the University of Vienna confirmed the feasibility of this novel approach to resuscitation and furthered its development.

The congressional support of the EPR program is being administered by TATRC of the U.S. Army at Fort Detrick, Maryland. This work also led to submission of a provisional patent and facilitated the launching of a spin off company, EPR Technologies, LLC, that is led by Dr. Lyn Yaffe along with S. William Stezoski. For this work, Drs. Tisherman, Kochanek, Xianren Wu, and Mr. Stezoski were honored at the 2008 and 2010 annual University of Pittsburgh Celebration of Innovation.

he also reported major regional differences in neuroinflammation after cardiac arrest. Despite marked neuronal death in the hippocampus, the cytokine response was maximal in the striatum. His work suggests that anti-inflammatory effects of deep hypothermia could contribute to its ability to induce preservation and that a combination of drugs targeting inflammation and neuronal death may limit the depth of hypothermia that is required in EPR. Pediatric cardiac ICU fellow Dr. Manuella Lahoud-Rahme received the Young Investigator Award at the 2008 Resuscitation Science Symposium held during the American Heart Association Congress. She reported that the blood brain barrier was not damaged in EPR—suggesting that drugs serving as potential therapeutic adjuncts to EPR need to be permeable across the blood brain barrier. Her work was subsequently published in *Resuscitation*.





During the 2008-09 and 2009-10 academic years, Dr. Tisherman held an EPR training session that was hosted by internationally renowned trauma surgeon Dr. Thomas Scalea at the University of Maryland R. Adams Cowley Shock Trauma Center. The session was also attended by other trauma surgeons with special expertise in EPR-related applications including Drs. Hasan Alam and Peter Rhee. Dr. Tisherman, supported by congressional funding, and in collaboration with this team developed a protocol to test the clinical feasibility of EPR in civilian trauma. An application for an Investigational Device Exemption was submitted and approved by the U.S. Food and Drug Administration. The clinical protocol has also been approved by the University of Pittsburgh IRB and is under review by the U.S. Army IRB. We are hopeful that the clinical trial will launch in 2011.

## FACULTY

Samuel A. Tisherman, MD  
 Patrick M. Kochanek, MD  
 Tomas Drabek, MD  
 Miroslav Klain, MD, PhD  
 S. William Stezoski

**H**emorrhagic shock is a leading cause of death in civilian and military trauma and the Safar Center has a rich history of resuscitation research in this area of study. Hemorrhagic shock can lead to either acute death from exsanguination or delayed morbidity and/or mortality from multiple organ failure. The program on hemorrhagic shock at the Safar Center is directed by Dr. Samuel Tisherman and has focused on the use of clinically-relevant models of hemorrhagic shock to evaluate novel resuscitation strategies. These models were designed by Dr. Tisherman and the late Dr. Safar, along with a number of research fellows in our center, and have carefully implemented shock/trauma, field resuscitation, and hospital resuscitation phases, to study therapies throughout the continuum of care. Clinically relevant uncontrolled hemorrhage is incorporated into many of these models to simulate the ongoing uncontrolled bleeding during the shock phase.

A number of therapies have been evaluated in experimental models of hemorrhagic shock at the Safar Center in order to improve outcomes of patients suffering hemorrhagic shock. Promising therapies in this regard have included mild hypothermia and intraperitoneal adenosine, among others (please see prior Annual Reports at [www.Safar.Pitt.edu](http://www.Safar.Pitt.edu)).

In 2010, investigators interested in hemorrhagic shock studied a very novel putative therapy. Dr. Tomas Drabek pursued the use of intravenous hydrogen sulfide. This agent, used by inhaled or intravenous routes, has been suggested in several reports by others, in single cell systems and rodent models, to confer benefit in shock states both by inducing hypothermia and via favorable effects on cell signaling and metabolism. In a report in press in the journal *Shock*, Dr. Drabek was not able to demonstrate either a hypothermia inducing effect or a beneficial effect on outcome using a large animal (pig) model of hemorrhagic shock.

#### FACULTY

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Tomas Drabek, MD  
Patrick M. Kochanek, MD

Inclusion of a comprehensive research program in rehabilitation of central nervous system injury is a vital and unique component of the Safar Center. Investigators in our center have been increasingly interested in strategies to improve long-term outcome for CNS insults, such as TBI and cardiopulmonary arrest. Thus, inclusion of investigators in the Dept. of PM&R of the University of Pittsburgh School of Medicine is essential and is allowing Safar Center scientists to evaluate new treatments along the entire continuum of care of brain injury victims—from the field to rehabilitation.

In the 2008-09 and 2009-10 academic years, Safar Center investigators working under the direction of Drs. Anthony Kline and Amy Wagner in the Dept. of PM&R authored or co-authored ten manuscripts in the arena of TBI rehabilitation.

As discussed in Dr. Kochanek's introductory letter, Dr. Anthony Kline's research group published papers in the journals *Life Sciences* and *Neuroscience Letters* that outlined a series of studies revealing detrimental effects of the use of haloperidol in the subacute period after TBI in rats. This finding is important because haloperidol is a commonly used sedative in critically ill adults. Haloperidol has a number of effects, one of which is its antagonism of dopamine  $D_2$  receptors. Given that drugs enhancing dopamine receptor activation are useful in TBI rehabilitation, this finding is logical—and clinical translation is very possible. Dr. Kline's work implies that the critical window for deleterious effects of the use of haloperidol and other sedatives that blunt dopaminergic neurotransmission could include the subacute phase in the ICU and suggests the need for neurocritical care physicians to carry out clinical trials to define optimal sedatives for use in critically ill patients with CNS injury.

Dr. Kline's laboratory is also focused on two other areas of research in TBI therapy and rehabilitation, serotonin-based therapies and enriched environment. In prior studies, Dr. Kline's group described beneficial effects of the serotonin 5-HT<sub>1A</sub> receptor agonist 8-OH-DPAT early after controlled cortical impact in rats. In a report published in *Behavioral Brain Research*, Jeff Cheng, a technician in Dr. Kline's lab, demonstrated beneficial effects of this agent even when therapy was delayed for 24 hours. Serotonin receptor agonist therapy deserves additional exploration in TBI for possible clinical translation. The effect of enriched environment on TBI outcomes has also been a subject of considerable interest at the Safar Center and Christopher Sozda a student mentored by Dr. Kline reported on the effect of various components of typical and atypical enriched environment paradigms on both behavioral and neuropathological outcomes. Chris's work was recently published in the *Journal of Neurotrauma* and he is now in graduate school at the University of Florida.

Dopaminergic supplementation therapy is a mainstay of CNS injury rehabilitation and Dr. Amy Wagner's laboratory has been investigating the biochemical and molecular underpinnings of this therapeutic avenue in rehabilitation. In studies in 2009 published in the *Journal of Neurochemistry* that were carried out in collaboration with Dr. C. Edward Dixon, Dr. Wagner showed

that daily therapy with methylphenidate (Ritalin), an agent empirically used in TBI rehabilitation, restores striatal dopaminergic neurotransmission after experimental TBI.

Dr. Wagner also has a research interest in biomarkers of TBI and is one of the leaders in the field of markers related to the hormonal response to TBI. She recently launched a collaboration with Dr. Dafna Bonneh-Barkay (pictured), and Dr. Clayton Wiley, Chief of Neuropathology at the University of Pittsburgh School of Medicine. In a new publication in the *Journal of Neurotrauma*, Dafna reported on expression after TBI of a novel inflammatory marker – YKL-40—which is induced in neuroinflammatory conditions, such as multiple sclerosis. That translational report included evidence supporting a possible role of this novel inflammatory pathway in both experimental studies in the rat model of controlled cortical impact, and in patients with severe TBI. We look forward to additional collaboration between Safar Center investigators and Dr. Wiley's group in Neuropathology.



Training is also a vital part of the PM&R program. Drs. Wagner and Kline are outstanding mentors for future young investigators in the field of brain injury rehabilitation and they annually attract a large number of students across a wide range of training levels. A number of Dr. Kline's students received awards and honors for their work in TBI. Some of the awards were discussed in the introductory letter. In addition, Rashid Ahmed was recognized for the top abstract presentation by an undergraduate at the annual Institute for Rehabilitation Research Day at the University of Pittsburgh 2010. Similarly, Bhaskar Ganti was recognized for the top presentation by a PM&R trainee at the 1st Annual Multi-Departmental Trainees' Research Day that was held in conjunction with the Safar Symposium in 2010. Lastly, Krishna Yelleswarapu received an Arts & Sciences Undergraduate Research Award for summer 2010 to work on a project evaluating whether the benefits mediated by 8-OH-DPAT are due to activation of 5-HT<sub>1A</sub> or 5-HT<sub>7</sub> receptors.

## FACULTY

C. Edward Dixon, PhD  
Anthony E. Kline, PhD  
Amy K. Wagner, MD



There is a long-standing relationship between the Safar Center for Resuscitation Research and the U.S. DOD. That relationship was initiated in the late 1950s as a result of Dr. Safar's pioneering work on the development and implementation of CPR—which was funded by a grant from the U.S. Army.

Much of our work related to combat casualty care at the Safar Center in the 2008-09 and 2009-10 academic years focused on the topic of blast TBI—which is the focus of this section. Other work at the Safar Center germane to combat casualty care was previously discussed in the sections on TBI, Rehabilitation, EPR and Hemorrhagic Shock.



As part of the DARPA-funded PREVENT program, Dr. Robert Garman carried out a detailed neuropathological evaluation of a rat model of primary blast with body protection using a 'shock tube' insult. His work revealed important evidence of diffuse axonal injury, particularly in the deep white matter structures (cerebellum and brainstem) that mirrored new findings reported by Dr. David Brody in human blast TBI. Dr. Garman's work was presented at the 2009 National Neurotrauma Society meeting. The full manuscript is in submission.

require resuscitation are complex and often involve multiple simultaneous injuries such as TBI, orthopedic and soft tissue injury, eye injury, and burns. The use of body armor by our troops frequently protects the other vital organs, however, hemorrhage produced by these insults can exacerbate brain injury.

Pediatric CCM fellow Dr. Alia Dennis published a report in the *Journal of Neurotrauma* that described a new model of combined TBI plus hemorrhagic shock in mice. The model has served as an excellent tool to evaluate therapies

Blast TBI-related research at the Safar Center in the 2008-09 and 2009-10 academic years included work on four linked programs, 1) a U.S. Army funded program to study novel resuscitation solutions in experimental TBI plus hemorrhagic shock, 2) participation in the DARPA PREVENT blast program, 3) participation in a program directed by Col. James Atkins at Walter Reed Army Institute of Research (WRAIR) focused on defining the optimal approach to oxygenation and ventilation after blast TBI and polytrauma, and 4) leading the previously described new multi-center pre-clinical drug screening TBI consortium "Operation Brain Trauma Therapy (OBTT)." Blast TBI has become critically important in combat casualty care in light of the emergence of terrorist attacks using improvised explosive devices. Blast injuries that

relevant to blast polytrauma. Two additional reports using this model have followed. A second manuscript in the *Journal of Neurotrauma* by pediatric CCM fellow Dr. Jennifer Exo reported failure of conventional resuscitation solutions, such as lactated Ringer's or Hextend, to confer neuroprotection. A new study by Dr. David Shellington reported on neuroprotection using the novel blood substitute polynitroxylated pegylated hemoglobin (PNPH) in this model. Unlike other cell free hemoglobins, PNPH was also neuroprotective rather than toxic in cell culture, and it could represent a paradigm shift in blood substitute development. His work is in press in *Critical Care Medicine*. PNPH, in studies supported by our U.S. Army funded program to study novel resuscitation solutions in experimental TBI plus hemorrhagic shock, have been promising and have led to successful acquisition of a new SBIR award from NINDS to try to bring PNPH to clinical trials in TBI resuscitation.

Dr. Kochanek presented updates of work on the molecular biology of blast TBI from the PREVENT program at the 2009 and 2010 ATACCC conferences. Safar Center investigators Drs. Kochanek, Dixon, and Jenkins were also honored to serve as co-editors of a special issue of *Journal of Neurotrauma* with Drs. Richard Bauman and Joseph Long at WRAIR. Papers by Drs. Ling, Bauman, and Long reported on additional work being carried out on blast TBI in the PREVENT program.

We have initiated studies in collaboration with Dr. Atkins on defining the optimal approach to oxygenation and ventilation after blast TBI and polytrauma. This involves studies at the Safar Center in our mouse model of combined TBI plus hemorrhagic shock, parallel studies in rats by Dr. Gary Fiskum's group at the University of Maryland, and work at WRAIR in a rat blast model. An initial report on findings from the Safar Center will be presented by Anesthesiology resident Dr. Brian Blasiole at the 2011 meeting of the SCCM. This work is also funded by the U.S. Army.

Finally, we have just launched the new U.S. Army funded OBTT program. This program represents a unique multi-center pre-clinical experimental TBI drug and biomarker development consortium that includes research teams at the University of Miami (Drs. W. Dalton Dietrich and Helen Bramlett), The Virginia Commonwealth University (Dr. John Povlishock), WRAIR (Dr. Frank Tortella), and Banyan Biomarkers, Inc. (Drs. Kevin Wang and Ronald Hayes). We hope to be able to update the initial results of this program in next year's report.

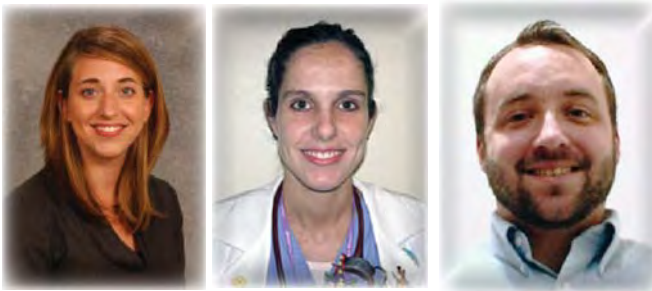
## FACULTY

Patrick M. Kochanek, MD  
Samuel A. Tisherman, MD  
Hülya Bayır, MD  
Robert S.B. Clark, MD  
C. Edward Dixon, PhD  
Larry W. Jenkins, PhD

In 2009, Dr. Michael Bell established a novel Pediatric Neurocritical Care service at Children's Hospital of Pittsburgh (CHP). The service delivers cutting edge care to critically ill infants and children with neurological conditions such as brain injury from cardiac arrest, TBI, CNS infections, and seizures.

This unique clinical service is also closely linked to the Safar Center in that it provides a platform for both clinical research and trainee education in pediatric neurocritical care. Regarding clinical research, the service is led by four NIH-funded faculty members (Drs. Bell, Hülya Bayır, Robert Clark, and Ericka Fink) who are carrying out a number of clinical trials including studies on mild hypothermia, among others. From the perspective of trainee education, Drs. Kochanek and Bell also lead a weekly Pediatric Neurocritical Care Professor Rounds which includes an in-depth fellow level case discussion and literature review. Professor Rounds have also served as an outstanding training opportunity for NIH-funded fellows supported by our T32 that is focused on pediatric neurocritical care and resuscitation research.

Dr. Jennifer Exo carried out a study evaluating the utility of using two intracranial pressure (ICP) monitors when continuous draining of cerebrospinal fluid (CSF) is used to treat infants and children with severe TBI. Her report, currently in press in *Pediatric Critical Care Medicine*, identified unrecognized ICP spikes when only a single monitor was used. Reductions in cerebral blood flow in infants and children are commonly seen after TBI and Dr. Rosanne Salonia, in collaboration with Dr. Samuel Poloyac, assessed CSF levels of the potent vasoconstrictor peptide endothelin-1 (ET-1) in infants and children with severe TBI. Sustained increases in ET-1 levels were seen, suggesting that this mediator may represent a therapeutic target. It was surprising that ET-1 elevations were not blunted by the use of hypothermia. Dr. Craig Smith reported on the value of brain temperature monitoring in critically ill infants and children with severe TBI also in a paper that is in press in *Pediatric Critical Care Medicine*.



The pediatric neurocritical care team published a number of reports in the 2008-09 and 2009-10 academic years and several highlighted publications are discussed below. Many of these reports were published by our Pediatric Critical Care Medicine fellows, including Drs. Jennifer Exo, Rosanne Salonia, and Craig Smith.

Finally, there were several important reports by faculty on the pediatric neurocritical care service. As discussed in the introductory letter in this report by Dr. Kochanek, Dr. Ericka Fink published an article outlining the utility of intravenous iced saline to treat fever in critically ill infants and children with brain injury from cardiac arrest or TBI. Fever is associated with poor outcome in these cases and this aggressive approach to temperature management may minimize secondary brain injury. Dr. Bell published an important report specifically on the development of a pediatric neurocritical care service in the journal *Neurocritical Care*. This new pediatric neurocritical care service is, thus, serving as a role model for the field.

## FACULTY

Michael J. Bell, MD  
Hülya Bayır, MD  
Robert S.B. Clark, MD  
Ericka L. Fink, MD  
Patrick M. Kochanek, MD



The Safar Center for Resuscitation Research has a rich history of training young investigators in resuscitation-related research, particularly in the field of cerebral resuscitation. Research training was a hallmark of Dr. Safar's illustrious career and this tradition continues as a centerpiece in the Safar Center. Many of our trainees have gone on to become independent investigators — including both NIH-funded scientists and clinician-scientists in the United States, and also funded investigators in major medical centers around the globe.

Postdoctoral fellow positions are funded by several means including 1) individual grants to principal investigators in the Center, 2) individual fellowship grants to trainees, 3) a unique T-32 grant from the National Institute of Child Health and Human Development titled "Pediatric Neurointensive Care and Resuscitation Research," and/or 4) support from the Laerdal Foundation. The T-32 program evolved out of a long-standing relationship between the Safar Center and the division of Pediatric Critical Care Medicine at Children's Hospital of Pittsburgh of UPMC. That division, directed by Dr. Robert Clark, has been one of the leading programs in the world for training clinician-scientists in the field. This relationship has brought a number of very talented young pediatric intensive care clinicians to the Safar Center for research training during their three year fellowship. The generous funding of fellow research at our center over the years by the Laerdal Foundation has also been of great importance to our center. We are also pleased that a "Safar Fellowship" stipend has been established by the Laerdal Foundation to support young investigators in Scandinavian countries who are interested in carrying out research training at the Safar Center, and encourage prospective candidates to apply.

On July 15, 2008, Dr. Ramona Hicks, Program Director, Extramural Research Program NIH/NINDS, visited our Center. A number of our trainees had the opportunity to present their recent research findings to her and received a valuable critique and encouragement that was greatly appreciated. From left to right, Eric Abrahamson, PhD, James Bales, PhD, Ramona Hicks, PhD, David Shellington, MD, and Craig Smith, MD.



The Safar Center serves as a resource for research training for interested individuals including residents in medical and surgical training, undergraduates, and high-school students. We actively participate in the medical school and undergraduate summer student programs, and in the minority research programs supported by the University of Pittsburgh. Our annual summer student research day, previously discussed in my letter, occurs each August at the Safar Center. The summer students gave enthusiastic and impressive presentations of their work—and a number of these students have gone on to present at national and international conferences.

In the 2008-09 and 2009-10 academic years, trainees at the Safar Center were first author of over 35 peer reviewed manuscripts—including each of the programs in the center. Similarly, in the last 10 years, 12 trainees at the Safar Center have gone on to achieve RO-Is, K-awards, or other substantial national funding, a testament to the strong commitment to research training in the Center.

This year our trainees made a number of important discoveries in their research and garnered several prestigious awards. Details of these outstanding accomplishments are outlined in the opening letter and throughout the report. Congratulations to our many post-doctoral fellows in training for their many accomplishments. Upon completion of their training, these fellows are highly sought after by other programs throughout the US and abroad.

We are always interested in receiving applications and inquiries from interested young investigators at every level.



A special celebration was held in honor of the 30<sup>th</sup> anniversary of the Safar Center which was celebrated with a toast to Dr. Peter Safar. This was attended by a large number of former and current trainees.



Invited guests, faculty, and both former and current trainees in the Safar Center conference room celebrating a toast to the late Dr. Peter Safar on the occasion of the 30<sup>th</sup> Anniversary of the Safar Center for Resuscitation Research.



Pictured from left to right, former Safar Center fellows Drs. Robert Neumar, Larry Katz, and Uwe Ebmeier.

Pictured from left to right, former Safar Center fellows Drs. Michael Whalen, Ericka Fink, and Mioara Manole.



The 2009 Peter & Eva Safar Lecturer was former fellow Dr. Fritz Sterz, Professor from the Medical University of Vienna and the Emergency Medicine program at Vienna General Hospital. Dr. Sterz' lecture was titled "Peter Safar and Clinical Cooling" and was well-received by the audience, among who were several former fellows of the Safar Center. Dr. Sterz is one of the most successful former Safar Center trainees, and led the European multi-center hypothermia trial, the results of which were published in the *New England Journal of Medicine*. That study was one of two studies which led to the widespread use of mild hypothermia in the treatment of cardiac arrest.



From left to right, Drs. Patrick Kochanek and John Williams, Denise Kochanek, Drs. Fritz Sterz and Peter Winter on the occasion of the 29th Peter and Eva Safar Lecture for the Sciences and Humanities at the University of Pittsburgh School of Medicine. The portraits of University of Pittsburgh medical pioneers, Drs. Peter Safar and Thomas Starzl, which hang in the foyer of the Biomedical Science Tower, are in the background.





Dr. Michael Whalen (left) giving the opening lecture of the morning session of the 7th Safar Symposium, followed by Drs. Robert Neumar (center) and Robert Clark (right).

On May 6, 2009, the Safar Center hosted the 7<sup>th</sup> Safar Symposium at the University of Pittsburgh School of Medicine. It was a special event given that it occurred on the 30<sup>th</sup> anniversary of the Safar Center. The Symposium was held in conjunction with the 29<sup>th</sup> Peter & Eva Safar Annual Lectureship in Medical Sciences and Humanities, in the Starzl Biomedical Science Tower. The *Pittsburgh Post-Gazette* featured this year's symposium in an article published on May 6.

The morning session of the symposium focused on "Resuscitation in the 21<sup>st</sup> Century – from Cells to Systems," and featured presentations by some of the Center's most successful trainees. It included presentations by Drs. Michael Whalen, MD, from the Massachusetts General Hospital, Robert Neumar from the University of Pennsylvania School of Medicine, Amy Wagner, from the Dept. of PM&R at the University of Pittsburgh School of Medicine, Robert Clark, from the Dept. of Critical Care Medicine, at the University of Pittsburgh School of Medicine, and Rachel Berger, from the Dept. of Pediatrics at the University of Pittsburgh School of Medicine. The morning session concluded with a traditional fellow presentation which was given by Dr. David Shellington.

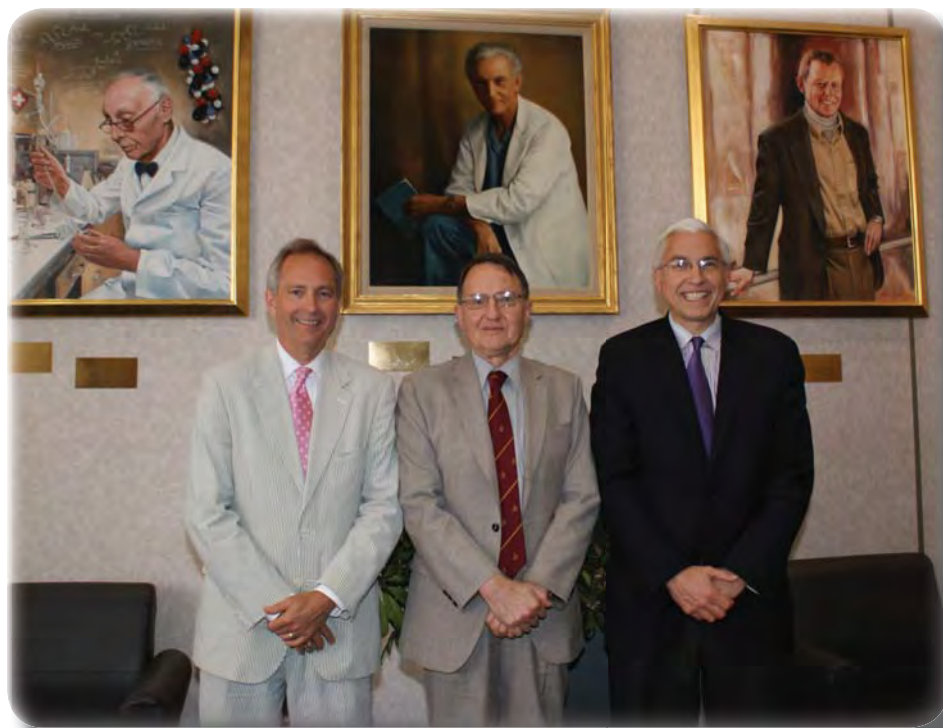
The symposium also included presentation of the annual Nancy Caroline Award—which is traditionally presented to the top fellow trainee at the Safar Center, as selected by the Associate Directors of the Center. In the 2008-09 academic year, the Nancy Caroline fellow award recipient was Dr. David Shellington (pictured right, please see introductory letter of this report for a description of Dr. Shellington's many accomplishments).

The afternoon session of the symposium was held at the Winter Institute for Simulation, Education and Research (WISER) and was crafted by WISER director Dr. Paul Pharmpus. The session addressed "Simulation as a Tool for Education and Assessment of Healthcare Providers." Presentations by Drs. Benjamin Berg from the University of Hawaii, Louis Halamek, from Stanford University, James Gordon, from Harvard Medical School, Mary Patterson from Cincinnati Children's Center for Simulation and Research, and finally, Shushma Aggarwal, from the Department of Anesthesiology at the University of Pittsburgh School of Medicine.



We are grateful to the Laerdal Foundation, Medivance, DARPA, the U.S. Army, TATRC and the USAMRMC for their support of the Safar Symposium. Funding was also provided by the Safar Legacy Fund, as well as the Departments of Anesthesiology and Critical Care Medicine. We are thankful to all supporters of this symposium.

The 2010 Peter & Eva Safar Lecturer was Dr. Frank Shann from the University of Melbourne, Intensive Care Royal Children's Hospital. Dr. Shann's lecture was titled "Critically Ill Children in Developing Countries." The lecture was a powerful, enlightening overview of his work and research over the course of his seven years in Papua, New Guinea.



Drs. John Williams, Frank Shann, and Patrick Kochanek photographed on the occasion of the 2010 Peter and Eva Safar Lecture. Dr. Shann's lecture focused on his remarkable humanitarian work on pediatric intensive care in the third world and was in the spirit of Dr. Safar's 22<sup>nd</sup> law – *"It's up to us to save the world."*



Dr. Ann Thompson, former Chief of Critical Care Medicine at Children's Hospital of Pittsburgh of UPMC and honorary guest, Dr. Frank Shann at the dinner celebration in his honor on Mt. Washington.



The 8<sup>th</sup> Annual Safar Symposium was a two day event held on June 1<sup>st</sup> and 2<sup>nd</sup>, 2010, along with the 30<sup>th</sup> Peter & Eva Safar Annual Lectureship in Medical Sciences and Humanities, in the Starzl Biomedical Science Tower. The symposium was again held in conjunction with a special event, namely the 50<sup>th</sup> anniversary of the birth of CPR.

The first day of the Symposium featured a Multi-Departmental Trainees' Research Day comprised of over 90 students and fellows from the Depts. of Anesthesiology, Critical Care Medicine, Emergency Medicine, PM&R, and WISER giving either poster or oral presentations of submitted abstracts. An esteemed panel of judges of the posters included several speakers from the Symposium and local experts from each department. Awards were given to Lavinia Maria Kolarczyk (Anesthesiology), Mark Donnelly (Critical Care Medicine), Kavitha A. Conti (Emergency Medicine), Bhaskar Ganti (Physical Medicine and Rehabilitation), and Young Min Kim (WISER) for best Poster Presentation from each department. James William Ibinson (Anesthesiology) won the award for best overall poster and Alicia Au (Critical Care Medicine) won the award for the best oral presentation.

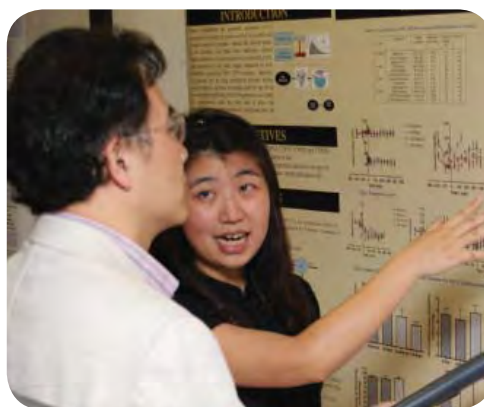
On June 2<sup>nd</sup>, the morning session of the symposium focused on "Resuscitation in the 21<sup>st</sup> Century – From the Field to Rehabilitation," and featured a broad spectrum of speakers across the different departments. The first speaker, Thomas Rea, MD, MPH, from Harborview Medical Center and University of Washington, spoke on the 50<sup>th</sup> Anniversary of CPR about "The Resuscitation Grail: Innovation, Translation, or Tall Tales?"

Other speakers in the morning session of the symposium included Drs. Elizabeth Skidmore, Assistant Professor of Occupational Therapy and PM&R at the University of Pittsburgh, Keith Walley, MD, from the University of British Columbia, and Yan Xu, from the Departments of Anesthesiology, Pharmacology and Chemical Biology, and Structural biology at the University of Pittsburgh School of Medicine. The morning session again concluded with a presentation by a current research fellow at the Safar Center and featured the work of Laerdal Fellow Dr. Andreas Janata.

The afternoon session of the symposium was held at WISER and focused on "Simulation in Healthcare." It featured presentations by Dr. Paul Phrampus, Director of WISER who addressed the topic of "The History of Simulation in CPR Training" in a special lecture on the occasion of the 50<sup>th</sup> anniversary of CPR. The afternoon session also included presentations by Drs. Michael Seropian, Medical Director of Oregon Health and Science University, John Vozenilek, Director of Simulation Technology and Immersive Learning at Northwestern University, James McGee, Associate Professor of Medicine and Assistant Dean



PCCM fellow Alicia Au, MD, received the award for best oral presentation for her work on autophagy in traumatic brain injury at the 1<sup>st</sup> Annual Multi-departmental Trainees Research Day. Dr. Au is the McGrevin Fellow in the Department of Critical Care Medicine.



PhD candidate Jocelyn Zhou (right) discusses her work on cytochrome P450 with Dr. Yan Xu who was a judge for the poster competition. Jocelyn received her PhD this year working in the lab of Dr. Samuel Poloyac. Dr. Xu was also a plenary speaker during the Safar Symposium.



Drs. Rita Patel, Frank Shann, and Paul Phrampus also served as judges for the 1<sup>st</sup> Annual Multi-departmental Trainees Research Day.

for Medical Education Technology at the University of Pittsburgh School of Medicine, John O'Donnell, Director of the University of Pittsburgh Nurse Anesthesia Program, and Connie Lopez, RNC, MSN, CNS, National Leaders for Patient Safety and Risk Management and leader of National Kaiser Permanente Simulation Collaborative.

A special thanks to all of the trainees, speakers, and departments for another successful Symposium. We also are very grateful to the Laerdal Foundation for its support of the Symposium along with support from NICHD/NIH.



Dr. Thomas Rea, Associate Professor of Medicine, Harborview Medical Center, University of Washington, gave a keynote opening presentation on the future of cardiopulmonary resuscitation on the occasion of the 50<sup>th</sup> anniversary of the birth of CPR.



Dr. Rona Gifford, Professor and Vice Chair for Research, Department of Anesthesia and Neurosurgery, Stanford University, gave a special lecture during trainees research day on the novel topic of the role of astrocytes in regulating neuronal death in ischemic brain injury.



From left to right, Drs. Elizabeth Skidmore, Assistant Professor of Occupational Therapy and Physical Medicine & Rehabilitation, University of Pittsburgh and Keith Walley, MD, Professor of Medicine, Heart + Lung Institute, University of British Columbia, gave plenary presentations on novel developments in stroke rehabilitation and resuscitation of patients with septic shock. Laerdal fellow Dr. Andreas Janata, a current research fellow at the Safar Center, concluded the morning session with a presentation on his research addressing extracorporeal resuscitation.





James Bales, a University of Pittsburgh medical student in the Medical Scientist Training Program, was the recipient of the 8th Nancy Caroline Fellowship Award. The Caroline Fellowship Award winner is selected annually by the Associate Directors of the Safar Center for Resuscitation Research. Competition for the award is open to all trainees currently doing research at the Safar Center. James is being mentored by Dr. C. Edward Dixon and is studying secondary injury mechanisms after traumatic brain injury with a special emphasis on dopamine signaling and calcineurin in striatal damage. James recently received his PhD for this work.

Critical Care Medicine pioneer and former Chief at Presbyterian University Hospital, Dr. Ake Grenvik with Dr. Safar's former secretary and current Safar Center administrative secretary, Fran Mistrick, at the 8<sup>th</sup> Safar Symposium. Fran, along with the program committee, is responsible for planning and organizing the event—which was a great success. Thanks to her dedication and tireless efforts.



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*Thank you for your  
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of Peter Safar, M.D.*

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### **Peter Safar Legacy Fund**

Supports clinical and laboratory research in the areas of cardiac arrest, traumatic brain injury, hemorrhagic shock, emergency hypothermia, pediatric neurointensive care and resuscitation, child abuse, and rehabilitation.

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Supports research by trainees in honor of Dr. Nancy Caroline, one of Dr. Safar's first students and the mother of emergency medicine in the country of Israel.

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(over)

**PETER'S LAW #22: "It's up to us to save the world."**

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