

SAVE THE DATE...

The 7th Annual Evening of Hope – May 12, 2011

Please save the date for the 7th Annual Evening of Hope to be held on Thursday, May 12, 2011 at the Sheldon Concert Hall. The evening will begin with cocktails, dinner and the concert followed by a dessert reception with the artists.

The Evening of Hope will feature a performance by the Eroica Trio. The most sought-after trio in the world, the Grammy-nominated Eroica Trio will thrill our audience with flawless virtuosity, irresistible enthusiasm and sensual elegance. Whether playing the great standards of the piano trio repertoire or daring contemporary works, the three young women who make up this celebrated ensemble electrify the concert stage with their passionate performances. The Trio won the prestigious Naumburg Award, resulting in a highly successful Lincoln Center debut and has since toured the United States, Europe, and Asia. They have also performed at Carnegie Hall and released eight critically lauded recordings and garnered multiple Grammy nominations.

The Eroica Trio will be performing songs from their most recent album, *An American Journey*, which was acclaimed by NPR as “One of the Best CD’s of 2008.” It features new arrangements of music from Gershwin’s “Porgy and Bess” and Bernstein’s “West Side Story” commissioned by the Eroica Trio to Mark O’Connor’s “Poets and Prophets,” written for Eroica and inspired by the music of Johnny Cash.

The women who make up the Eroica Trio, Sara Sant’Ambrogio, cellist; Erika Nickrenz, pianist; and Susie Park, violinist, are all top-ranked, award-winning soloists and have performed on many of the world’s greatest stages. They share many personal and musical connections and their paths have crossed at many artistic junctions. Sara and Erika studied both piano and chamber music with Isabelle Sant’Ambrogio, Sara’s grandmother, and coached chamber music with Sara’s father and first teacher, John Sant’Ambrogio, former principal cellist of the St. Louis Symphony. Sara was a second generation student at The Julliard School, following in the musical footsteps of her father. Sara and Susie both attended Curtis Institute of Music and all three women performed at the Marlboro Music Festival.

The Eroica Trio appeared on numerous television programs, including ABC’s *The View*, CNN’s *Showbiz Today*, CBS and ABC News, the CBS *Morning Show* and *Saturday Morning*, A&E’s

Breakfast with the Arts. They will be featured in the international broadcast of *The Artists’ Way At Work*, an in-depth exploration of artistic creativity. *Eroica!*, a special documentary about the Trio and its commissioning of a new triple



The Eroica Trio will perform *An American Journey* at the 7th Annual Evening of Hope

concerto by Kevin Kaska, premiered on PBS series *Independent Lens* and has had multiple airings worldwide as well as performed at the St. Louis Symphony. For further information, visit the Eroica Trio website: www.eroicatrio.com.

Tickets for this enchanted musical evening are \$250 per person. Sponsorships are available at various levels, beginning with Patrons at \$1,000 per couple up to Principal Sponsors at \$20,000 and over. If you were a sponsor or patron for last year’s Annual Evening of Hope, we thank you for your generous support and are looking forward to your continued support as a Patron or Sponsor for the 7th Annual Evening of Hope.

In order to reach our goal and allocate necessary funding to the Hope Center for Neurological Disorders at Washington University School of Medicine, we need your participation once again. The Hope Center is making significant progress in many important areas that affect the brain and nervous system. The Evening of Hope supports this collaborative and translational research – which one day will lead to cures that afflict thousands of people who are diagnosed with a neurological disorder every day.

We will be sending out sponsorship information with various levels of giving. If you or your company would like to become a new sponsor, please contact Sandy Kaplan, Director of Development, at (314) 725-3889 or e-mail sandy@hopehappens.org.

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A Message from the Board President

Dear Friends of Hope Happens:

I wish first to thank Josephine and Richard Weil for hosting a Hope Happens cultivation party at their home on October 7. Their beautiful garden and the delightful autumn evening provided the perfect setting to welcome some new Hope Happens supporters. Nearly one hundred guests heard from eight Hope Center scientists, who strive daily to find treatments and cures for neurological disorders.



Many thanks to Alison Goate, DPhil, Hope Center Director, to David Holtzman, MD, Chairman of the Department of Neurology, and to all the Hope Center scientists at Washington University School of Medicine for giving their time to discuss their work and to meet the people who play such a vital role in funding the work being done at the Hope Center. This unique collaboration and partnership between Hope Happens and the Hope Center offers hope to so many patients, their families, and their loved ones afflicted with a neurodegenerative disease.

As we approach the holiday season, we are most thankful for our loved ones' good health and well being. At this grateful time of year, we also think about charitable giving and hope that you will respond to our forthcoming holiday letter by making a tax-deductible donation to Hope Happens. Please see the article in the newsletter with details about becoming a member of the Hope Society, our donors who are recognized for contributions of \$1,000 or more annually, and various other ways to make your gift.

As 2010 nears its close, we continue to prepare for our spring event, the "Evening of Hope," and for a new event next fall, the "Hike for Hope Happens." Both activities are generating a great deal of interest and anticipation in the St. Louis community and beyond. You can read more about the 2011 Evening of Hope in this issue's cover story.

The Danforth Foundation Challenge remains a priority for our partnership with Washington University School of Medicine. Thus far, the challenge has raised \$3.8 million, reminding all of us that a good deal more needs to be done to reach the \$10 million goal by 2013. Please keep that challenge in mind when discussing the Hope Center with your friends.

Those of us at Hope Happens and the Hope Center look forward to a bright year in 2011. No matter what the pace of economic recovery, dollars used to fund research will continue to be scarce, as in the past. We encourage all of you to support us and talk about the important work that is done at the Hope Center for Neurological Disorders.

A handwritten signature in black ink, which appears to read "Toby Martin".

Toby Martin
Board President



Bob Kindle Hope Happens' New Executive Director

Hope Happens for Neurological Disorders welcomes Bob Kindle as its new Executive Director. Bob brings nearly thirty years of management experience, both in the private and the non-profit sector.

Bob attended Southeast Missouri University, and following his military service, began working for what is called now Enterprise Rent-A-Car. During most of his tenure he worked for the non-automotive division. His experience in all aspects of operating and managing a business provides unique perspectives. Throughout that time, Bob's responsibilities included accounting, human resources, and property management.

Bob, who lost his father to ALS, had been an active board member of the local ALS chapter for seven years, including being the interim CEO during the search process. He feels his passion for finding cures and treatments for all neurological diseases will provide the energy to help spread the word about Hope Happens and its mission.

Cynthia Meiners Hope Happens' New Board Member

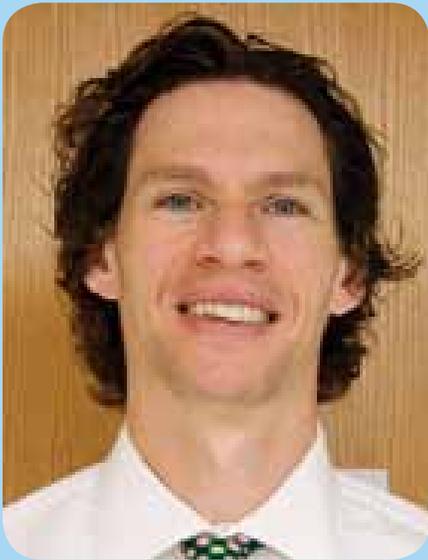
Cynthia Meiners, Vice President, Express Scripts, Account Management and Operations, Pharma and Retail Strategy, has been with Express Scripts since 2000 and has served in a variety of corporate and site roles during her 10+ years of service. Cynthia is currently responsible for leading the Account Management and Operations teams within the Pharma and Retail Strategy group. In this capacity she leads both internally and externally facing teams that managed Supply Chain and Trade Relations for a Fortune 100 Pharmacy Benefit Management organization.

Prior to her current role, Cynthia was responsible for designing and improving Operational Strategies to ensure that Express Scripts' service model remained innovative and fostered a premier service offering. Cynthia has also served as Vice President, Patient Savings and Advocacy leading teams of pharmacists, nurses and technicians focused on customer alignment through the increased use of generics, home delivery and formulary compliance. In this role, Cynthia led the operational implementation of a URAC award winning Bronze Best Practice in Consumer Empowerment and Protection for "Generics Today."

Cynthia has 20+ years of experience in healthcare. Prior to joining Express Scripts, Cynthia was Senior Vice President for Magellan Health, a behavioral health organization where she oversaw the provider relations and management efforts and then led account management for the employer division. Cynthia has also worked as a consultant in the medical HMO and Medicaid environment and has held positions in the areas of finance, human resources, information systems, and quality control.

Cynthia holds a Master of Business Administration from Washington University in St. Louis, Missouri, as well as Bachelor of Arts degrees in Psychology and German.





David Brody, MD, PhD

Dr. David Brody completed undergraduate studies in Biological Sciences at Stanford University in 1992. He received both MD and PhD degrees from the Johns Hopkins University in 2000 as part of the NIH Medical Scientist Training Program and was awarded the Hans Prohaska Young Investigator Award at Johns Hopkins in the same year.

He completed an internship in Internal Medicine in 2001 and a residency in Neurology in 2004, both at Barnes-Jewish Hospital. In 2004, he received the Leonard Berg Prize for Research Conducted During Residency and the Medical Student Teaching Award.

As a post-doctoral fellow at Washington University in the laboratory of Dr. David Holtzman, his research focused on the role of the amyloid- β peptide in traumatic brain injury. Currently Dr. Brody is an Assistant Professor in the Department of Neurology at Washington University School of Medicine.

Faces of Hope:

David Brody, MD, PhD Raising awareness about traumatic brain injuries

Dr. David Brody treats patients with subacute and chronic sequelae of traumatic brain injury in the Traumatic Brain Injury Clinic located at the Rehabilitation Institute of St. Louis. Dr. Brody is also the organizer of the Neurotrauma Research Interest Group at the Hope Center for Neurological Disorders and is a member of the Division of Biology and Biomedical Sciences in the Neurosciences Program. He was interviewed by Gabriela Inderwies.

How long have you been with the Hope Center?

I have been involved with the Hope Center since 2004 when I was a postdoctoral fellow in Dr. David Holtzman's lab. I joined the faculty and became a Hope Center investigator in 2007. It has been a wonderful collaborative environment; intense, but not excessively competitive, and very warm and welcoming.

Have you always been a clinician and a researcher?

I have been doing about 80% research and 20% clinical care since I joined the faculty. That has always been my goal, to have a mixture of clinical and research interests that are closely linked. Most of the patients that I see have traumatic or other brain injuries, and all of my research is focused on brain injuries and the patients' long-term quality of life.

Can you talk more about your research lab?

The laboratory work involves two main lines of investigation. The first involves understanding the mechanisms by which traumatic brain injury increases the risk of Alzheimer's Disease. Either a single severe injury or multiple concussive type injuries increase the long-term risk of Alzheimer's Disease but no one knows why. Likewise, no one knows how to prevent this increased risk, or even if it is possible to prevent it. We have focused on the hypothesis that changes in amyloid- β protein (and more recently in tau protein) are set in motion immediately at the time of injury and continue to lead to neurodegeneration over time. We have been working on

characterizing the amyloid- β related and tau related processes in transgenic mice, using experimental models of traumatic brain injuries.

We have also done human studies focusing on amyloid- β . In human studies, we used a method called microdialysis which involves a neurosurgeon placing thin catheters into the brain at the time of another surgical procedure. Severe brain injury patients often have to have a intracranial pressure monitor placed into the brain and the microdialysis catheters can be put in at the same time with little added risk. We then sample fluid from the microdialysis catheter and make measurements of amyloid- β every hour for three days or longer. We have done this here in the intensive care unit at Washington University Medical Center and also in collaboration with a major trauma center in Milan, Italy.

We found that the dynamics of amyloid- β are very interesting and very different from what we expected. We were expecting that there would be a great elevation in amyloid- β early on after brain injury, but in fact, we found just the opposite. We found that the levels were low initially but as the patients recovered from the brain injuries, the amyloid- β levels rose. In Dr. Holtzman's lab, it was shown in mice that reduced synaptic activity leads to reduced amyloid- β production. Our studies indicated that this was likely the case in humans as well. This was published in 2008 in *Science*, and that was the first time that this sort of measurements had been performed in the human brain.

The second line of investigation involves axonal injury. In traumatic brain injury, it is becoming increasingly clear that injury to axons plays a key role in adverse outcomes. Axons are like the wires that connect the nerve cells to each other. The human brain is about half white matter, made up primarily of axons, and axons seem to be the structures that are most vulnerable to traumatic injury. There are several exciting new methods to assess the injuries to axons, which has been tricky because traditional scans like MRI and CT scans do not detect injured axons very well at all. With the investigators here at the Mallinckrodt Institute of Radiology, we have employed some of these new methods that are more sensitive to injury to axons. One method

called diffusion tensor imaging, or DTI. DTI involves measurement of the diffusion of water in many directions. In healthy axons, most of the axons are running in the same direction, so water diffuses faster in this direction but more slowly perpendicular to the axons. When axons are injured, the diffusion of water becomes slower in the main direction and faster in perpendicular directions.

The Department of Defense has been very interested in this question of axonal injury. As many as 320,000 U.S. military service members have returned from the wars in Iraq and Afghanistan with clinical histories that are consistent with traumatic brain injury. However, many of them have conventional brain scans that are completely normal. It is not clear exactly what has happened to these people, nor is it clear who will have a good outcome and make a good recovery, or who is likely to have various problems.

We have applied DTI to US military personnel as part of a collaboration with a U.S. military hospital in Germany, Landstuhl Regional Medical Center. Just about every injured U.S. military service member coming from Iraq or Afghanistan comes through Landstuhl Regional Medical Center and gets assessed there. At Landstuhl, they make the decision whether to send them back to Iraq or Afghanistan or to send them home to the United States for definitive treatment. These triage decisions are very important. If someone is sent back into a combat situation when they are cognitively impaired, and they make an error, it can have serious consequences. On the other hand, it isn't practical to send everyone back to the US. It is a hard problem, and nobody knows exactly the right way to do this. We hope that DTI assessments will help.

One big challenge is that the brain is not homogeneous. In some ways, it is a little bit like the board from the game of Monopoly. There are high rent districts and low rent districts; some parts that when injured cause critical deficits, while other parts that when injured do not seem to cause many long-term problems. For example, some regions are very important for memory, while others are important for attention, and others for emotional reactivity. Less is known about the regions for emotional stability, and post-traumatic stress disorder

is a major problem in injured US military personnel, so that is an area we are especially interested in.

I would like to ask you about the program you direct that involves treating retired NFL football players.

It is becoming increasingly clear that retired athletes who have sustained many concussive traumatic brain injuries have cognitive changes which are similar to, but in many respects distinct from Alzheimer's Disease. Clinically, the disorder involves memory impairments like AD, but also more erratic behavior and more emotional instability than it is typically seen in AD. The symptoms also can occur at younger ages.

Last year, the NFL put together five centers to care for former football players with neurological problems, one of which is the program that I direct at Washington University School of Medicine.

Do you think that these findings might change the future of contact sports?

It is too soon to say. Football is already changing, even before our centers make any findings. The NFL is already taking this issue much more seriously than they have in the past. Importantly, these brain injuries also affect college, high school and even younger football players, and most of them will make a living doing something other than playing football, likely something that requires good cognitive function and emotional stability. If they have brain injuries, this could be a major disadvantage in their lives.

I would like to point out that the most common cause of concussive brain injury is not sports, but motor vehicle accidents, especially in young people. In older people, falls are the major cause of brain injuries. The NFL has highlighted these issues, but they have much wider implications. I hope to raise awareness of the importance of brain injuries not just in NFL football players, but from the broader society perspective.

There are an estimated 1.5 million people a year who have traumatic brain injuries in the United States alone and an estimated 5 million people who are living with traumatic brain injuries, and yet the topic receives comparatively little attention.

Can you tell us about the treatment of traumatic brain injuries and how it might change in the future?

There are no specific treatments that improve the actual injury itself, but there is a lot that we can do to improve the symptoms and help people function better. For example, patients who have severe injuries often would die if it were not for the excellent care provided in major trauma centers. Many people surviving traumatic brain injuries have memory loss, attention deficit, mood disorders, and chronic headaches afterwards. We can augment memory function using the same medicines that are used in Alzheimer's disease. We can improve attention deficit disorder using stimulants. We can treat mood disorders and migraine headaches.

In the future, I think we are going to need a clearer understanding of injury to axons in order to develop effective therapeutics that treat the actual injury. In the past, the scientific community focused extensively on the causes of nerve cell death in animal models, and at least a dozen very interesting therapeutics have been developed that worked beautifully in animal models to prevent cell death but then failed in human trials. The problem in my view is that the primary determinant of outcomes in humans is the extent of axonal injury, and yet axonal injury is difficult to model in animals. There are lots of ideas, and we and others around the world are looking carefully for strategies that would produce results, and therapeutics that might protect the brain from the effects of subsequent concussions.

Do you have any final thoughts you would like to share?

I think the Hope Center is a great environment for collaborative studies. There have been some synergistic interactions between Hope Center investigators that would have been unlikely to happen without this mechanism. One leading researcher recently called this "the golden age" for traumatic brain injury research, and I am optimistic that we will make great progress.

Thank you very much!

Garden of Hope Gathering

Hosted By Josephine and Richard Weil

Guests were invited to the Weil's home to discover how they can help Hope Happens grow a Garden of Hope. After meandering in the Weil's magical garden, attendees were cultivating their knowledge of neurodegenerative and neuromuscular diseases by hearing from scientists from the Hope Center for Neurological Disorders at Washington University School of Medicine.

Prior to a beautiful buffet dinner, Josephine Weil welcomed everyone and spoke about her involvement with Hope Happens and the Hope Center. Toby Martin, Board President, gave a brief update on Hope Happens' mission and partnership with the Hope Center.

He introduced Bob Kindle, newly appointed Executive Director of Hope Happens, and Alison Goate, DPhil, Director of the Hope Center, who presented her research along with other featured researchers, Anneliese Schaefer, JD, PhD, Executive Director, Hope Center; David Holtzman, MD, Chair, Department of Neurology; Karen O'Malley, PhD; Jeff Millbrandt, MD, PhD, Chair, Department of Genetics; Tim Miller, MD, PhD; Chris Gurnett, MD, PhD; Anne Cross, MD, Faculty, Hope Center; Valeria Cavalli, PhD, Faculty, Hope Center; Chris Weihi, MD, Faculty, Hope Center.

This successful event cultivated many new friends and supporters of Hope Happens thanks to the Weil's generous hospitality.



Anne Key and Maria Desloge



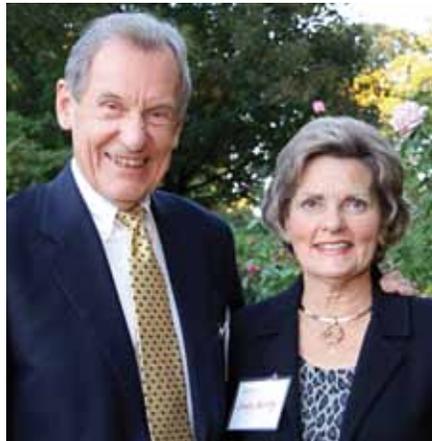
Toby Martin, Nardi Hobler and Harry Orchard



Sandy Kaplan, Dr. Bill Danforth, Guy and Peggy McClellan



Jean Hobler, Josephine Weil and Nardi Hobler



Ken and Cindy Hartley



Peter Hobler and Jane Bryan

Opportunities for Giving to Hope Happens

The Hope Society

The Hope Society is our special group of donors who are recognized for their annual contributions of \$1,000 or more. Any donation in a calendar year including the Evening of Hope tickets, patron and sponsorship levels are recognized as part of your Hope Society membership.

The Hope Society members are listed in our annual publication of donors, invited to a special event thanking our donors at this level as well as educational programs and tours of the Hope Center for Neurological Disorders.

Please join The Hope Society and support our annual giving program at one of the following levels:

Hope Society Member	\$ 1,000-\$ 2,499
Hope Society Fellow	\$ 2,500-\$ 4,999
Hope Society Patron	\$ 5,000-\$ 9,999
Hope Society Benefactor	\$10,000-\$24,999
Hope Society President's Circle	\$25,000 and over

We hope to get many new members of The Hope Society and increase our donor involvement and participation in our programs and events. It is an exciting time for growth, and we look forward to having you join The Hope Society if you are not already a member. For further information, contact Sandy Kaplan, Director of Development, at (314) 725-3889 or sandy@hopehappens.org.



Jean Hobler, Frank Jacob, Marylen Mann, and Jeff Millbrandt, MD, PhD



Karen O'Malley, PhD, Alison Goate, DPhil, and Christina Gurnett, MD, PhD



Jim and Kay Connaughton with Vicki and Roger Altvater



Prue Gershman, Josephine Weil, and Jill Petzall

Cash or stock gifts may be made to Hope Happens for Neurological Disorders through various giving instruments.

Pledges

Pledges can be made over a period of three to five years payable annually with a billing month of choice.

Stocks and Securities

Please obtain instructions to transfer stock or other equities to Hope Happens at (314) 725-3888 or info@hopehappens.org.

Tribute Gifts

Tributes are made in honor or memory. Notification is promptly mailed to inform honorees and families of the tribute made.

Planned Gifts

Contributions of significant assets may be made during a donor's lifetime or posthumously through planned giving. Hope Happens accepts gift annuities, charitable lead trusts and charitable remainder trusts along with estate documents such as wills and bequests.

Matching Gifts

If your company has a Matching Gift Program, please send Hope Happens your employer's form to process the match.

hope happens

for neurological disorders

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OUR MISSION

At Hope Happens our mission is to improve the lives of people with neurodegenerative disorders by funding collaborative, translational research that has the potential to fast-track new treatments and cures.

How You Can Help Hope Happens

You can help shape the future of devastating neurological disorders by donating to Hope Happens. Your generous donations will allow doctors and scientists to do the research necessary to find cures for neurological disorders such as ALS, Alzheimer's, multiple sclerosis, Parkinson's disease, Huntington's disease, epilepsy, brain and spinal cord injury and stroke. We hope you will become a member of the Hope Society, our annual giving program with levels beginning at \$1,000, so you can help us meet our \$1 million goal. Please see the envelope inside for details or contact Hope Happens for more information.

Your donation can make a difference.

Sandy Kaplan

Director of Development

Hope Happens for Neurological Disorders

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Ellen S. Clark Hope Plaza at the BJC Institute of Health.

photo by: Robert Boston,
Washington University in St. Louis,
Medical Public Affairs

Hope

Hope is the thing with feathers
That perches in the soul,
And sings the tune — without the words,
And never stops at all,
And sweetest in the gale is heard;
And sore must be the storm
That could abash the little bird
That kept so many warm.
I've heard it in the chilliest land,
And on the strangest sea;
Yet, never, in extremity,
It asked a crumb of me.

— Emily Dickinson