

spring 2009

bc^s news



Massachusetts
Institute of
Technology



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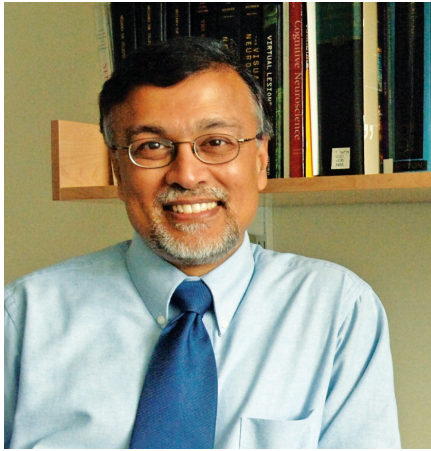
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Marcus Family Leads Campaign
for Brain Disorders Research



brain+cognitive sciences



A Message from the Department Head Mriganka Sur

It is difficult these days to talk about BCS without also talking about the economy. MIT, like most other institutions of higher education, has seen a significant impact from the developments of the last year, with all sources of income affected in one way or another. Due to cuts in the MIT budget, BCS has been asked to work within a constrained fiscal environment at the same time that public and private funding for research is increasingly hard to come by.

I remain, however, unreservedly optimistic about the fields of cognitive science and neuroscience, and specifically about their role and practice in BCS. I view the current constraints as an opportunity to better understand what is important in what we do and to direct our energies where they will be most fruitful. Education, of course, is core to our overall mission and will not be deprived of our best efforts or our best ideas. And with respect to research, we will continue to invest in the areas of investigation that draw on the unique strengths of BCS and of MIT as a whole.

The BCS Education Committee led by Matt Wilson has made specific recommendations for tiering our undergraduate courses, for reorganization of specific classes, and for adding more rigor to the curriculum. These recommendations were approved by the faculty at a recent meeting, and will be rolled out in the next academic year—though we have already started implementing specific ideas.

In research, it is increasingly obvious that many of today's most interesting questions are too complex to be fully explained by any one discipline or investigative approach. It is also obvious that many of the challenges of interdisciplinary research are as much organizational as they are scientific. In these respects, BCS benefits tremendously from being part of MIT. Not only is there a rich tradition of collaboration here on campus, but President Susan Hockfield also continually emphasizes the strategic importance of working across traditional boundaries—a theme that BCS epitomizes.

In the last issue of this newsletter, you learned of the Intelligence Initiative, an interdisciplinary research effort organized by BCS faculty that reaches across the Institute to unite researchers from a number of departments in common purpose to understand biological intelligence and how it might be captured in machines. In this issue, I am pleased to bring news of the Brain Disorders Initiative, and in particular its embodiment in the Simons Initiative on Autism and the Brain. Established recently with a generous grant from the Simons Foundation, this program builds on a continuing multi-year effort to establish BCS as the leader in basic science approaches to studying diseases and disorders of the brain. Taken together, these initiatives reflect the tremendous intellectual ferment of the Department and demonstrate that even in these difficult times, BCS does not lack for ideas or the means to execute them—and that is certainly worth being optimistic about.

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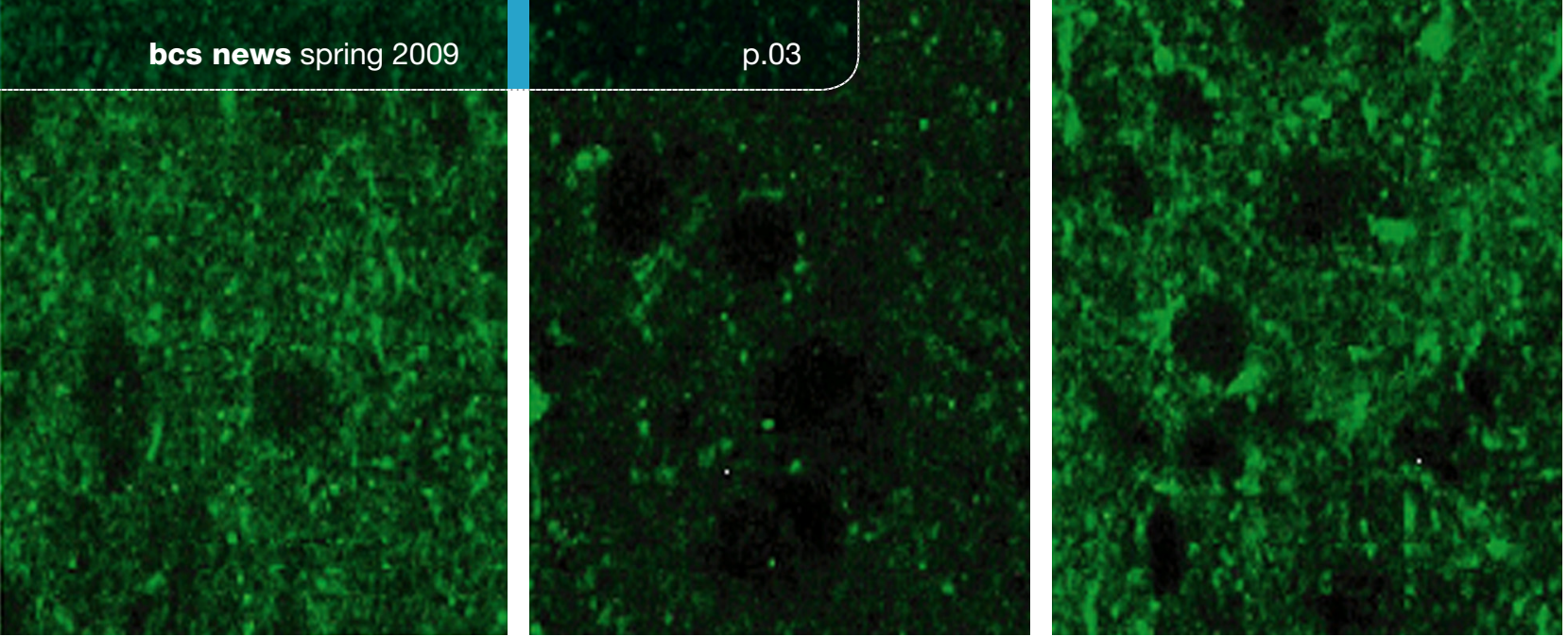
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On the Cover

In everyday learning, people routinely make successful generalizations from very limited evidence. Even young children can infer the meanings of words, the hidden properties of objects, or the existence of causal relations from just one or a few relevant observations, far outstripping the capabilities of conventional learning machines. How do they do it? And how can we bring machines closer to these human-like learning abilities? These are the questions that Josh Tenenbaum's lab studies. The cover image illustrates one experiment conducted by Tenenbaum and graduate student Lauren Schmidt, testing people's ability to learn words labeling object categories from very few examples. Subjects are first introduced to a world of unfamiliar but natural looking objects, and then shown several examples of objects that belong to a particular category: for instance, the three objects enclosed in boxes are examples of "tufas." The task is to pick out all of the other tufas. Given just a few examples, people can confidently judge which other objects belong to this category. The generalization judgments of both adults and children in such tasks can be modeled quantitatively as Bayesian inferences over a tree-structured hypothesis space, with objects organized into a tree based on their similarity along relevant perceptual dimensions.



Flourescence microscopy images showing levels of the synaptic protein PSD-95 in (*left*) control and (*center*) MeCP2 knockout mice which are a widely used animal model for Rett syndrome. Treating MeCP2 mice with Insulin-like Growth Factor 1 (*right*) restores PSD-95 to control levels. Images by Daniela Tropea, Sur Lab

Simons Foundation Grant to Anchor Autism Research in BCS

A new \$4.5 million grant from the Simons Foundation will underwrite the recently established Simons Initiative on Autism and the Brain at MIT. The initiative is intended to provide a common infrastructure and technical resources that will support autism research in BCS and across the MIT campus. “This is an important acceleration of our efforts over the last five years to bring MIT to the forefront of basic research into diseases and disorders of the brain,” says Department Head Mriganka Sur. “We are grateful to the Simons Foundation for this support and we also thank MIT President Susan Hockfield for her continuing efforts on behalf of this initiative.”

The provisions of the grant call for a fellowship program for post-doctoral scholars who will work in the BCS labs of current and future Simons Investigators. In addition, the funding will support a core equipment facility to be shared by autism researchers at the Institute and to support a colloquium series that aims to raise awareness in the community. Finally, the initiative will seed further research by funding a number of pilot projects throughout MIT.

According to Mriganka Sur, MIT is an ideal place for such an effort. “Autism is clearly a complex disorder which needs to be approached simultaneously at a number of levels and across a number of disciplines. Genes, synapses, networks of neurons, and modules of the brain and mind are all implicated – and BCS is among the only places in the world that has both presence and core strengths in all of these areas.”

Autism has been an increasingly important area of investigation within BCS for more than five years. What began in 2003 as the Brain Diseases and Disorders Project with generous seed funding from the Anne and Paul Marcus Family Foundation has

quickly grown and evolved. With further funding from the Marcus Foundation, significant early grants from the Simons Foundation and, increasingly, Federal and private support, no fewer than 10 BCS faculty and an equal number in departments throughout MIT are now involved.

And the research is beginning to pay dividends. BCS Professor Mark Bear has discovered a potential therapeutic solution for fragile X syndrome, a type of mental retardation that is typically accompanied by autism. And in recently published research supported by the Simons and Marcus Foundations,

Mriganka Sur and Rudolph Jaenisch from the Whitehead Institute demonstrated a promising therapy for Rett syndrome, a leading cause of autism in girls.

Current Simons Investigators in BCS include Mriganka Sur and Mark Bear as well as Li-Huei Tsai, Susumu Tonegawa, Ann Graybiel, John Gabrieli, Rebecca Saxe, Morgan Sheng, and Pawan Sinha. Biology and Whitehead Institute member Hazel Sive is also a Simons Investigator. And BCS faculty members Nancy Kanwisher and John Gabrieli recently received a significant grant from the Ellison Foundation for their research into autism and dyslexia. ■



THE SIMONS INITIATIVE
ON AUTISM & THE BRAIN
AT MIT

55 Years of Amnesia Remembered: The Story of H.M.



H.M. in front of his family's home 20 years after the operation

Henry's tragedy gave memory an address in the brain

whole brain. While that is true to a certain extent, scientists did not know that damage to a specific part of the brain, the medial temporal lobe structures, would render an individual incapable of laying down new long-term memories. Henry's

In 1953, at the age of 27, Henry Gustav Molaison, known in the scientific literature as "the amnesic patient H.M.," underwent an experimental brain operation to treat his intractable epilepsy. In one regard, the surgery was a success because it dramatically reduced the frequency of his seizures. Unfortunately, this success was overshadowed by a tragedy of immense proportions: From the moment Henry awoke from anesthesia, he was unable to form new long-term memories. We now know, however, based on the pioneering work of Brenda Milner and Suzanne Corkin, that Henry's story was not that simple.

It is true that Henry could not form new long term memories in the sense that most people think about them. For example, Dr. Corkin met H.M. in 1962 and tested him hundreds of times in the subsequent decades. Each time she asked whether they had ever met before, and each time he responded that they met in high school. At the same time, Dr. Corkin and her colleagues determined, through careful study, that there were specific, often remarkable, things that Henry was able to remember.

H.M.'s case revolutionized the field of memory research in several ways. Before H.M., scientists didn't realize that memory could be localized to a discrete part of the brain. They thought that when you remembered something, you used your

tragedy gave memory an address in the brain.

H.M.'s case also led to an understanding that short-term memory and long-term memory are separable processes. We know this because Henry's short-term memory was preserved. He could remember information for about 20-30 seconds. Beyond that, unless he consciously rehearsed something, he could not retain that information.

That H.M. did not lose all types of his memory told neuroscientists that different types of memory were encoded by different parts of the brain. In her studies at the Montréal Neurological Institute, and later at the MIT Clinical Research Center and the Department of Brain and Cognitive Sciences, Dr. Corkin showed that H.M.'s ability to learn new skills remained intact. That is, while his explicit, or declarative, memory was impaired, his implicit, or nondeclarative, memory was spared.

Henry was remarkable not only because of his profound amnesia, but also because of his endearing personality. Even after losing the ability to form new memories, he remained a courteous, intelligent, and humorous individual. He was also benevolent. He truly hoped that the research performed with him would someday help other people. Henry and his court-appointed guardian always agreed to research studies over the years and they felt it was important to donate his brain for further scientific study after his death. Henry died on December 2, 2008 at the age of 82. While Henry was unable to form new long-term memories for the last 55 years of his life, our memory of him will live on for ages, through the papers and books that have already been inscribed in the scientific literature, and through the studies that are yet to be published. Henry's tragedy has left a lasting mark on the field of systems neuroscience. The knowledge gained through his misfortune will most certainly pave the way to new therapies that will help countless future generations. ■

Dedicating the Singleton Auditorium

In recognition of an extraordinary gift given in support of BCS graduate fellowships, the BCS auditorium was renamed to honor the Singleton family that made the gift.



President Susan Hockfield addresses the MIT Corporation and guests at the dedication



Above: Vice President for Research Claude Canizares, Susan Lester, Dean Marc Kastner
Left: Past and present Singleton Fellows

Ann Graybiel Named Institute Professor



Department Head Mriganka Sur, Ann Graybiel, and Professor Robert Desimone celebrate Ann's induction as Institute Professor.

On November 3rd, BCS faculty member Ann Graybiel was named Institute Professor, the highest honor MIT can bestow on a member of the faculty. She joins Emilio Bizzi as one of only 14 Institute Professors. In presenting the honor, MIT President Susan Hockfield noted that "Professor Graybiel's research has provided new insights to the neurobiological basis of a range of disorders, from Parkinson's disease to major depression."

Ann is a pioneer in the study of brain organization and circuitry and has revolutionized scientists' understanding of the functional anatomy and physiology of the brain and, more specifically, of the large forebrain region known as the basal ganglia. Her insights have helped further researchers' understanding of disorders such as Tourette Syndrome, obsessive-compulsive disorder and attention deficit disorder.

"Ann embodies the extraordinary creativity and interdisciplinary strength of MIT neuroscience. Her work spans an unusually broad range of approaches and levels of analysis including structural and chemical anatomy, molecular biology, electrophysiology, and behavior," said Department Head Mriganka Sur. "Her discoveries have shaped the field, and earned her worldwide recognition not only from basic scientists but also from neurologists and psychiatrists. She is also an enthusiastic and dedicated teacher and mentor to numerous graduate students and postdoctoral fellows."

Graybiel received her PhD in 1971 from MIT and has been on the faculty since 1973. She is a member of the National Academy of Sciences, the Institute of Medicine, and the American Academy of Arts and Sciences. Graybiel was named a recipient of the 2001 National Medal of Science, the nation's highest science and technology honor. In 2002, Graybiel was awarded the James R. Killian Faculty Achievement Award, which recognizes extraordinary professional accomplishment by full-time members of the MIT faculty. In 2004, Graybiel received the Woman Leader of Parkinson's Science award from the Parkinson's Disease Foundation, and in 2006, she was named the Harold S. Diamond Professor by the National Parkinson Foundation in recognition of her contributions to the understanding and treatment of Parkinson's disease. In 2008, she received the Vanderbilt Prize in Biomedical Science in recognition of her scientific achievements and for mentorship of women in science. ■

Noteworthy

FACULTY

Discover Magazine selected **Ed Boyden** as one of their "20 Best Scientists Under Age 40." Ed also received the MIT Alumni Class Funds Award for Excellence in Educational Innovation for his new series of courses about neuroengineering and neurotechnology.

John Gabrieli, Mriganka Sur, and Li-Huei Tsai were named American Association for the Advancement of Science fellows.

Neville Hogan was accorded the Henry M. Paynter Outstanding Investigator Award by the American Society of Mechanical Engineers Dynamic Systems and Control Division, 2008

Popular Science magazine has named MIT BCS faculty member **Rebecca Saxe** to its annual "Brilliant 10" list of the country's top young scientists to watch.

Richard Wurtman was invited to be a guest lecturer by the Porcellati Foundation and the European Society for Neurochemistry (ESN) at the 4th Biennial Conference on "Advances on Molecular Aspects of Neurological Diseases" to be held in Leipzig in July. Dick was also named William E. M. Landis Lecturer in Nutritional Biochemistry at the University of Michigan.

STAFF

Research Scientist **Akira Yoshii** is the recipient of a DoD Tuberculous Sclerosis Complex Research Program Career Transition Award to study protein synthesis-dependent synaptic changes in Tuberculous Sclerosis.

Postdoctoral Fellow **Wasim Malik** was elected a Senior Member of the IEEE in October 2008.

STUDENTS

BCS graduate alumna **Elizabeth Kensinger** ('03) received a Searle Scholar Award, the Boston College Distinguished Research Award, and was granted early tenure by Boston College where she serves on the faculty of the Department of Psychology.

Five BCS seniors have been elected 2009 Phi Beta Kappa members: **Sha-har Admoni, Abby Clark, Jamie Mehringer, Kim Reinhold, and Matt Serna**. They will be inducted on June 4, immediately before commencement.

Faculty Profile: Troy Littleton



Troy with his son, Ryan



Troy Littleton's first venture into neuroscience can be described as serendipitous or even accidental.

Upon graduating from high school, Troy was awarded a scholarship to Louisiana State University, where he planned to study either medicine or law. But when faced with a choice of work/study positions ranging from dishing out cafeteria food or mowing the campus lawns to lab research, his interest in neuroscience began to blossom. "It was a hot, humid climate," he jokes. "The lab assistant position seemed like a nice, indoor, air-conditioned job."

The lab was studying the catfish olfactory and gustatory systems, and specialized in electrophysiological recordings from brain regions involved in olfaction or gustation and how sensory percepts were coded into electrical signals in the brain. Troy began his time there washing dishes, but in year or two he graduated to performing his own experiments doing electrophysiology on fish, and thereby developed a long-lasting affinity for neuroscience.

Troy's interests in studying how the nervous system responds to external cues and mediates appropriate responses were further shaped by a summer doing research at the Whitney Marine Biology lab at the University of Florida. There, Troy spent his time characterizing purinergic chemosensation in the gustatory and olfactory systems of the Spiny Lobster. "It was really interesting work," he says, "plus, we got to eat the leftover lobsters."

When Troy finished his undergraduate studies, he chose to move on to the Medical Scientist Training Program at Baylor College of Medicine (MSTP), where he achieved the distinction of top student after his first year and was provided special funding. Troy was attracted to the program because it would allow him to pursue studies in both research and medicine, but after the first year he focused more on his research studies. He joined Hugo Bellen's lab, where they were studying *Drosophila* synapses and how they transmit chemical signals from the presynaptic terminal. After four successful years at MSTP, it was obvious that he would pursue a career in research and, after finishing the PhD portion of his program, he took time off to do a postdoc year in Hugo's lab. He received his MD in 1997.

The University of Wisconsin was the next step in Troy's career, where he went to work in Barry Ganetzky's lab. There he continued to study the mechanisms of synaptic transmission, and began large-scale screens for conditional temperature-sensitive *Drosophila* mutants that could be used to alter neural activity or synaptic transmission in the fly brain. This position was also a test for Troy, who wanted to find out if he could stand a Northern winter. At the end of three years of what were the warmest winters in Wisconsin history (due to the El Niño effect), he began looking for professorships. The Picower Institute was just getting up and running at the time and the center was seeking someone doing synaptic plasticity in a model system. Troy felt MIT was nearby family ties. Fortunately for MIT, Duke declined to offer season tickets for the Duke Blue Devils basketball team as part of a start-up package, and Troy started his position as Assistant Professor here at MIT in Spring 2000, where he hit the ground running. By the end of his first year he had four graduate students and several postdocs. A Wisconsin undergraduate who had worked with him during his postdoctoral research joined the group as the lab technician. He had also written an NIH grant proposal in anticipation of his start at MIT, and it began upon his arrival.

Today, Troy is still using *Drosophila* as a model system to determine how synapses work and how they can be modified, including how they communicate with each other and how behavioral experiences and changes in neuronal firing patterns can alter synapses to store information. The general consensus is that many of the mechanisms underlying the plasticity of fly synapses will be similar to those in our own brain. The foundation of understanding how synapses normally work also allows the lab to try and figure out how disease proteins interrupt those basic processes. There is a great deal of research involving the interface of disease mechanisms with their standard work on synapses. The lab is currently developing and studying models for Huntington's Disease, epilepsy and autism in *Drosophila*. For example, flies expressing a disease-causing human allele of Huntington's become ataxic and die quickly

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"It was really interesting work - plus we got to eat the leftover lobsters"

Marcus Family Leads Campaign for Brain Disorders Research

Ask Paul Marcus '81 and he'll tell you it's a natural transition from civil engineering to real estate development.

His company, Marcus Partners, a real estate investment and development firm with offices in Boston, Connecticut and south Florida, focuses on commercial office, light industrial, biomedical and medical office properties and select residential and retail projects. Marcus Partners is known for its integrity, insight, creativity, and ability to execute complex acquisition and development projects. Paul readily admits that he honed many of these attributes at MIT. Just as his MIT training was a natural fit for his current profession, he'll also tell you it was perfectly natural for him and his wife Anne to begin working together with



Anne and Paul Marcus with their sons, Chris and Robbie

the Department of Brain and Cognitive Sciences.

When their seven-month-old son was diagnosed with cerebral palsy, Anne and Paul Marcus were devastated. They wrestled with the difficult question of how to cope with the diagnosis. And, like so many other families faced with a developmental diagnosis, they were frustrated with the lack of research-driven treatments available for their son. They had to navigate their way through numerous institutions in order to develop an optimal treatment plan for him while racing against the clock, knowing time is

the most critical factor in obtaining quality of life for children with brain disorders or brain damage.

What began as a personal journey also became a mission for their family's philanthropic efforts. For Paul and Anne, the answer was to get involved and give of their time, energy and pocketbook. "We found philanthropy very therapeutic", says Paul. The couple began with fundraising efforts for the Developmental Medicine Center at Children's Hospital Boston, where they were instrumental in recruiting a volunteer board and leading a campaign to raise over \$12 million. Paul has learned that "as individuals, we can have a massive impact by opening our checkbooks and devoting just a little bit of our time."

Predictably, Paul's philanthropic vision to help children with developmental disorders and their families did not end at Children's Hospital Boston. Paul felt that more could be done, and started to look for broader solutions. He came to MIT in 2003 and knocked on the door of Mriganka Sur, BCS Department Head. Paul saw the Institution as "the place where scientists and

engineers work together to understand a problem and then fix it." Building on that spirit of collaboration, he wanted to help BCS faculty work with physicians and clinicians in order to think about new ways to attack brain disorders. The result was a \$250,000 gift that established the Brain Development and Disorders Project. This gift and the research it inspired was the catalyst that ultimately seeded the Autism Consortium.

In 2006, Paul and Anne helped to found the Autism Consortium, a Boston based multi-institutional collaboration which funds clinical innovation and research in Autism and other brain disorders. Paul personally recruited the lay leadership for the Board of Directors. He reached out to leadership of 14

"If you are interested in unlocking the mysteries of the mind, MIT is the place to come for results"

institutions, bringing MIT together with Harvard, Boston University, the Broad Institute, MGH and Children's Hospital Boston, to build the Consortium. Paul also provided the important seed funding for the initial clinical and research projects. Bringing the message of partnering to this important area of brain research, he assembled a group of donors to invest in the enhanced clinical care and genetic diagnostic expertise at five clinical sites across Boston. He asked friends with expertise in genetics and drug discovery to help entice biotech firms to provide cutting edge technology to new transformative projects. These efforts have resulted in tangible progress, improving the lives of patients and families and generating new knowledge and treatments for those with Autism Spectrum Disorders. In January 2008, The New England Journal of Medicine published the first significant results of the Autism Genome Scan, funded by the Anne and Paul Marcus Family Foundation. The new finding of a missing or duplicated piece of chromosome containing 30 genes caught the attention of the scientific community, as well as the general population.

Paul's persistence motivated the BCS faculty to see the possibilities of intensive collaboration. This cooperation and collaboration among various researchers from different institutions enables discovery to proceed at a pace unlike anything seen before for brain disorders. Moreover, the results have encouraged other alumni to support the research and MIT has received additional gifts in support of this project. It makes sense the work takes place here at the Institute, according to Paul. "If you are interested in the brain and unlocking the mysteries of the mind, MIT is the place to come for results."

According to Mriganka Sur, "Paul is somewhat unusual. Perhaps it is the strength of his MIT engineering training, but Paul is able to envision the roadmap. He embraces risk and finds the people and resources needed to increase the pace of change. He and Anne are committed to changing this landscape and improving the care and treatment for children and their families everywhere. 'No' is simply not in his vocabulary. He never asks for recognition, just results." ■

For more information about giving opportunities, please contact Martha Ruest, BCS Director of Development 617-253-5563 mruest@mit.edu

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as adults, allowing the lab to characterize the underlying disease pathology and work to find cures in the fly model. The fact that they can rapidly breed many generations of these animals, coupled with the sophisticated genetic approaches in the fly, make *Drosophila* an attractive system for studying hereditary disorders like Huntington's. They hope the molecular pathways they find that regulate disease pathology in these models will be applicable to humans.

Among the discoveries in the Huntington field they have made is the observation that defects in axonal transport caused by aggregated mutant Huntington proteins can lead to neurodegenerative disorders. Troy is collaborating with scientists at Harvard and the Broad Institute to screen small molecule libraries for drugs that can prevent toxicity in the fly caused by the Huntington genes. They want to know how drugs work and affect axonal transport. They hope to then apply this to mammalian models (via collaborations) and ultimately to humans. Epilepsy is another disease they are looking at in this way. Drugs are needed to reduce membrane excitability, so they are using genetic approaches in the fly to find genes that cause epilepsy and to screen for new drugs that can inhibit seizure phenotypes. In addition, the recent discovery of several genes linked to rare forms of autism has provided new tools to model these diseases in the fly. Many of the known candidate loci for autism are implicated in synapse development or plasticity, tying in to the strength of the Littleton lab's studies on synaptic plasticity. These genes, when mutated, may alter the ability of synapses to change appropriately during early childhood development, when a lot of plasticity takes place. Although the exact function for many autism linked genes is unknown, most are homologous to proteins found in *Drosophila*, where they can be more easily studied. He anticipates that the next decade in his lab will involve more research into molecular and cellular bases of diseases such as autism, schizophrenia, and depression.

Troy's contributions to the MIT community also include working to put together a new program scheduled to begin in the Fall of 2009 in which biology and BCS students can freely rotate through labs in either department. Troy's work depends on being able to interface with both his Biology colleagues who are using cutting edge molecular techniques, and the BCS neuroscientists. He considers this kind of collaboration key to the success of

individual labs and to the scientific community.

When not in the lab, Troy tries to spend most of his free time with his family: his wife, a former teacher and currently a stay-at-home mom, and their 10 year old son, Ryan, who enjoys sports, especially skiing, little league baseball, and video games. Troy's other major outside distraction and favorite "sport" is poker (and the associated gossip sessions), and he engages in both at a regular Friday night game. As a bona-fide sports nut, Troy also is a big fan of the Celtics, Red Sox and Patriots. ■

New Beginnings

In December, graduate student **Livia King** became engaged to Jeff Blackburne, a graduate student in the physics department. He proposed by tying pig balloons by the train tracks outside her office, in reference to a comment he once made about the likelihood of his ever proposing. They will be married in August.

Graduate student **Michael Frank** became engaged to Alison Kamhi on September 20th, and they will be getting married in spring 2010.

3rd year graduate student **Lauren Barr** and post-doc **Derek Buhl** will be getting married on Oct. 11, 2009, at the Normal Rockwell Museum in Stockbridge.

Postdoctoral Associate **Won Mok Shim** and husband Sang-Hyun welcomed their first child, a daughter, Yoon Kim, on February 15. Both mom and baby are doing very well.

Administrative Assistant **J.C. Howard** and his wife Jenny welcomed their 2nd child, a baby girl named Juliet Maris Howard.

Postdoctoral Associate **Ming Meng** and his wife Juan Azhang welcomed Aniu Meng on August 16, 2008.

Postdoctoral Fellow **Natasha Hussain** and husband Marshall Shuler (assistant professor Johns Hopkins University) are expecting their first child in May.