McGovern Institute for Brain Research

The McGovern Institute for Brain Research at MIT is led by a team of world-renowned neuroscientists committed to meeting two great challenges of modern science: understanding how the brain works and discovering new ways to prevent or treat brain disorders. Patrick J. McGovern and Lore Harp McGovern, committed to improving human welfare, communication, and understanding through their support for neuroscience research, established the McGovern Institute in 2000. Patrick McGovern passed away in March 2014.

Faculty Changes

Our faculty decreased by one as Ki Ann Goosens did not receive tenure at MIT. We currently have 17 faculty and two associate members.

Resource Development

Fundraising from individuals and private foundations remains a priority at the McGovern Institute. McGovern Institute staff hosted multiple donor cultivation events during the fiscal year, and faculty and staff met with more than 70 donors and prospects in Cambridge, New York, Florida, and California.

We raised over $1.9 million in outright cash gifts and $6.2 million in new pledges from individuals, companies, and small family foundations in FY2016; $4 million of this total was a pledge from Jim and Pat Poitras to create the new Poitras Professorship.

McGovern Institute Spring Symposium

The McGovern Institute held its spring symposium on May 9, 2016. The symposium was organized by Assistant Professor Mark Harnett and featured 10 talks. The symposium's theme was "Computations: From Synapses to Systems."

Other Major Events

The McGovern Institute Scientific Advisory Board met on November 13, 2015. The current board members are John Duncan, Gerry Fishbach, Eve Marder, Josh Sanes, Terry Sejnowski, Carla Shatz, Chuck Stevens, Torsten Wiesel, and Bob Wurtz. Faculty members Mark Harnett and Feng Zhang presented their research to the board, and many labs presented posters during a lively poster session. The meeting culminated with a report from the board to Lore McGovern, Liz McGovern, and Dean Mike Sipser.

Alan Jasanoff and Edward Boyden hosted the Neurotech 2015 symposium on November 17. The symposium featured talks by neurotechnology pioneers whose cutting-edge innovations are changing the face of neurobiological research. Speakers included Eric Betzig (Howard Hughes Medical Institute, Janelia Farm campus), Kristin Branson (Howard Hughes Medical Institute, Janelia Farm campus), Viviana Gradinaru (California Institute of Technology), Elizabeth Hillman (Columbia University), John Rogers (University of Illinois at Urbana-Champaign), Bryan Roth (University of North Carolina at Chapel Hill), and Chandra Tucker (University of Colorado at Denver).

The annual Phillip A. Sharp Lecture in Neural Circuits (endowed by Biogen Idec in honor of the McGovern Institute's founding director, Phillip Sharp) was given by Markus Meister from the California Institute of Technology on March 8, 2016, and was titled "Neural Computations in the Retina: From Photons to Behavior."

The 2016 Scolnick Prize was awarded to Dr. Cornelia Bargmann of The Rockefeller University and the Howard Hughes Medical Institute. Her lecture, given on March 30, 2016, was titled "Genes, Neurons, Circuits and Behavior."

The Poitras Center and Stanley Center jointly sponsored a monthly seminar series held in our building that featured leading researchers in the area of psychiatric disorders. Speakers were as follows: Steve Hyman (Harvard Department of Stem Cell and Regenerative Biology), Christopher A. Walsh (Harvard Medical School), Amy Arnsten (Yale University), Lee Rubin (Harvard Stem Cell Institute), Stewart Anderson (University of Pennsylvania/Children's Hospital of Philadelphia), and Kerry Ressler (Harvard Medical School). All talks were held in Singleton Auditorium and followed by a reception.

Annual Retreat

The McGovern Institute, along with the Picower Institute and the Department of Brain and Cognitive Sciences, held its biannual retreat at the Newport Marriott Hotel in Newport, RI. The two-day event, held on June 6 and June 7, 2016, was attended by over 300 people studying brain science. It provided a tremendous opportunity for scientists to share highlights of their work and get to know fellow researchers they may not have met before. There were nine talks, a very large poster session, and many opportunities to interact.

McGovern Institutes in China

The McGovern Institute at MIT continues to collaborate and interact with the three International Data Group/McGovern Institutes in China at Tsinghua University, Beijing Normal University, and Peking University.

Board of Directors

The McGovern Board of Directors meets quarterly, in July, October, January, and April. Membership of the board for FY2016 was as follows: Lore McGovern; Elizabeth McGovern; Michelle Bethel; Michael Sipser, MIT; Robert Langer, MIT; Sheila Widnall, MIT; and James Poitras, Avalon Mining Inc. Pat McGovern's seat was filled by his stepdaughter, Michelle Bethel. Ed Scolnick of the Broad Institute rotated off the board and will become a member of our Scientific Advisory Board, which meets every other year.

McGovern Institute Leadership Board

The McGovern Institute Leadership Board meets once per year. The board participates in programming at the McGovern Institute and interacts with the director and faculty members throughout the year, providing critical funding and strategic advice to the institute.

Core Facilities

The McGovern Institute operates several core laboratories that serve the local neuroscience community, including but not confined to members of the institute.

Martinos Imaging Center at MIT

The Martinos Center provides access to neuroimaging technologies, including two 3T magnetic resonance imaging (MRI) scanners for human brain imaging, a 9.4T MRI scanner for small animal imaging, a magnetoencephalography scanner, and an electroencephalography system. There is also a coil fabrication lab and a mock MRI scanner to help subjects (especially children) adapt to the scanning environment.

Viral Gene Transfer Core

The viral core is a joint project of the McGovern and Picower Institutes. It operates on a fee-for-service basis to provide viral vector technologies to neuroscience researchers inside and outside MIT.

Two-Photon Microscopy Core

This core features a sophisticated two-photon system with four lasers to support two-color imaging and uncaging. The system includes two workstations, configured for slice physiology and whole animal work. It has recently been upgraded to include an electrophysiology system.

OpenMind Computing Cluster

This cluster was established in 2014 to provide the MIT brain research community with access to state-of-art computing resources. The cluster is housed at the theMassachusetts Green High Performance Computing Centerin Holyoke, MA, with a 10 G link to the MIT campus.

McGovern Institute Neurotechnology Program

The McGovern Institute Neurotechnology Program (MINT) provides seed funding for collaborations between McGovern labs and researchers from other disciplines within and beyond MIT, with a focus on developing new technologies for brain research. Since its establishment in 2006, MINT has supported nearly 40 projects. Collaborating principal investigators are from multiple departments and schools at MIT and from other institutions, including the Broad Institute, Massachusetts General Hospital, and McLean Hospital.

Awards and Honors

Mehrdad Jazayeri was named the Robert A. Swanson Career Development Professor in the Life Sciences at MIT. This professorship recognizes junior faculty who show exceptional promise of making important contributions to the field of life sciences throughout their career. Jazayeri also received the Klingenstein-Simons Fellowship Award in the Neurosciences, which funds young investigators engaged in basic or clinical research that may lead to a better understanding of neurological and psychiatric disorders.

Rebecca Saxe was promoted to the rank of full professor in the Department of Brain and Cognitive Sciences.

Gloria Choi was named the Samuel A. Goldblith Career Development Professor in the Department of Brain and Cognitive Sciences.

Ed Boyden was presented the Young Investigator Award by the Society for Neuroscience. In addition, Boyden won the 2016 Breakthrough Prize in Life Sciences for his role in the development of optogenetics, a technique for controlling brain activity with light. Boyden received the $3 million award at a live ceremony televised by the National Geographic Channel on November 8. Boyden also won the BBVA Foundation Frontiers of Knowledge Award in Biomedicine for his work in optogenetics.

Robert Desimone was one of the keynote speakers at the Society for Neuroscience annual meeting in Chicago, among the largest of all scientific meetings with almost 30,000 attendees. In his lecture, Desimone discussed how attention controls the flow of information within the brain.

John Gabrieli was among the speakers at an MIT forum on STEM education that included Congressman Joe Kennedy. Also, Gabrieli was one of six MIT faculty members elected to the American Academy of Arts and Sciences.

H. Robert Horvitz was one of four MIT faculty members named a 2015 fellow of the National Academy of Inventors.

James DiCarlo was named the Peter De Florez Professor of Neuroscience in the Department of Brain and Cognitive Sciences.

Harbaljit Sohal, a postdoc in Bob Desimone's lab, was named one of *Forbes* magazine's "30 Under 30" in the science category.

McGovern investigator Feng Zhang, who joined MIT and the Broad Institute in January 2011, was awarded tenure at MIT. Zhang has pioneered the development of the CRISPR genome editing tools. These tools, which he has made widely available, are accelerating biomedical research around the world. Zhang received an honorable mention on the Bostonians of the Year list, and CRISPR was named *Science*'s Breakthrough of the Year. In addition, Zhang was named a 2016 Tang Prize Laureate in Biopharmaceutical Science and won the 2016 Canada Gairdner International Award—Canada's most prestigious scientific prize—for his role in developing the CRISPR-Cas9 system and demonstrating pioneering uses in eukaryotic cells.

Nancy Kanwisher received the 2016 Distinguished Woman in Science Award from Yale University.

Ann Graybiel was elected to the American Philosophical Society.

Research Highlights

Researchers find that brain scans predict the success of treatment for social anxiety disorder

For patients with social anxiety disorder (SAD), current behavioral and pharmaceutical treatments work about half of the time. But a new study from Susan Whitfield-Gabrieli, John Gabrieli, and colleagues suggests that it may be possible to do better than a coin toss when choosing psychiatric therapies for patients. By performing brain scans on patients with SAD, the researchers were able to predict with about 80% accuracy which patients would do well in cognitive behavioral therapy, an intervention designed to help patients change thinking patterns.

Researchers discover neurons in the brain that weigh costs and benefits to drive formation of habits

Research from Ann Graybiel's lab shows that habit formation is driven by neurons that represent the cost of a habit as well as the reward. This study is the first to show that cost considerations are wired into the learning of habits. The findings could also provide insights into neuropsychiatric disorders that involve problems with repetitive behavior, such as Parkinson's disease, Huntington's disease, obsessive-compulsive disorder, Tourette syndrome, and autism spectrum disorder.

Visual cortex of blind children can be remodeled to process language

In 2011, Rebecca Saxe and colleagues reported that, among blind adults, brain regions normally dedicated to vision processing instead participate in language tasks such as speech and comprehension. In a new study of blind children, Saxe's lab found that this transformation occurs very early in life, before the age of four. The study, published in the *Journal of Neuroscience*, suggests that the brains of young children are highly plastic, meaning that regions usually specialized for one task can adapt to new and very different roles.

Possible new weapon against posttraumatic stress disorder

Ki Ann Goosens, Ed Boyden, and colleagues examined the role of serotonin in the stress-induced enhancement of fear memory in a rat model of posttraumatic stress disorder (PTSD). Their findings suggest a potential new approach to the treatment of human PTSD.

New system for human genome editing has potential to increase power and precision of DNA editing

Feng Zhang, along with collaborators at the National Institutes of Health and Wageningen University, described a new CRISPR system that can be adapted for genome editing. The new system is based on a DNA-cutting enzyme called Cpf1, which has a number of potential advantages over the more familiar Cas9-based system. In a separate study led by graduate student Silvana Konermann, the Zhang lab described a further increase in the versatility of the CRISPR toolbox. Their new paper shows that

Cas9 nuclease can be directed to cut the DNA of one gene while activating transcription of a second gene, depending on the design of the short guide RNA.

More flexible machine learning

Research from the Center for Brains, Minds and Machines identified a machine-learning algorithm that enables semantically related objects to reinforce each other.

Neuroscientists find evidence that the brain's inferotemporal cortex can identify objects

James DiCarlo and colleagues found that patterns of neural activity in the inferotemporal cortex can encode object representations detailed enough to allow the brain to distinguish different objects.

How the brain keeps time

Keeping track of time is critical for many tasks, such as playing the piano, swinging a tennis racket, or holding a conversation. Mehrdad Jazayeri and his collaborator Michael Shadlen of Columbia University have now figured out how neurons in one part of the brain measure time intervals and accurately reproduce them. The researchers found that the lateral intraparietal cortex (LIP), which plays a role in sensorimotor function, represents elapsed time. They also demonstrated how the firing patterns of neurons in the LIP could coordinate sensory and motor aspects of timing.

Search and find

Imagine you are looking for your wallet on a cluttered desk. As you scan the area, you hold in your mind a mental picture of what your wallet looks like. McGovern Institute director Robert Desimone has identified a brain region that stores this type of visual representation during a search. The researchers also found that this region sends signals to the parts of the brain that control eye movements, telling individuals where to look next.

Engineers design magnetic cell sensors

Engineers in Alan Jasanoff's lab have designed magnetic protein nanoparticles that can be used to track cells or to monitor interactions within cells. The particles are an enhanced version of a naturally occurring, weakly magnetic protein called ferritin. The new "hypermagnetic" protein nanoparticles can be produced within cells, allowing the cells to be imaged or sorted using magnetic techniques. This eliminates the need to tag cells with synthetic particles and allows the particles to sense other molecules inside cells.

Neuroscientists identify neural patterns birds use to learn their songs

Male zebra finches, small songbirds native to central Australia, learn their songs by copying what they hear from their fathers. These songs, often used as mating calls, develop early in life as juvenile birds experiment with mimicking the sounds they hear. McGovern neuroscientists in Michale Fee's lab have now uncovered the brain activity that supports this learning process. Sequences of neural activity that encode the birds' first song syllable are duplicated and altered slightly, allowing the birds to produce several variations of the original syllable. Eventually these syllables are strung together into the bird's signature song, which remains constant for life.

Improved gene editing

Feng Zhang has engineered changes to the revolutionary CRISPR-Cas9 genome editing system that significantly cut down on "off-target" editing errors. The refined technique addresses one of the major technical issues in the use of genome editing.

One gene, two brain disorders

Although it is known that psychiatric disorders have a strong genetic component, untangling the web of genes contributing to each disease is a daunting task. Neuroscientists in Guoping Feng's lab have now shed light on how a single gene can play a role in more than one disease. In a study appearing in the December 10, 2015, online edition of *Neuron*, they revealed that two different mutations of the Shank3 gene produce distinct molecular and behavioral effects associated with autism and schizophrenia.

Music in the brain

MIT neuroscientists have identified a neural population in the human auditory cortex that responds selectively to music. The finding was enabled by a new method designed to identify neural populations from functional magnetic resonance imaging data. "The music result is notable because people had not been able to clearly see highly selective responses to music before," said Sam Norman-Haignere, a postdoc with Nancy Kanwisher and Josh McDermott, and the lead author of the paper.

Altered brain chemistry in autism

Researchers in Nancy Kanwisher's lab have found a link between a behavioral symptom of autism and reduced activity of a neurotransmitter whose function is to dampen neuron excitation. According to the researchers, the findings suggest that drugs that boost the action of this neurotransmitter, known as GABA, may improve some of the symptoms of autism. This work was led by Caroline Robertson, a postdoc in the Kanwisher lab.

Machines that learn like people

Although object-recognition systems are becoming relatively effective, they are typically trained on millions of visual examples, which is a far cry from how humans learn. Four years ago, Tomaso Poggio's group at the McGovern Institute began developing a new computational model of visual representation intended to reflect what the brain actually does. In a new study, the researchers proved that a machine-learning system based on their model could indeed make highly reliable object discriminations on the basis of just a few examples.

Diagnosing depression before it starts

A new brain imaging study from MIT and Harvard Medical School may lead to a screen that can identify children at high risk of developing depression later in life. In the study, the researchers found distinctive brain differences in children known to be at high risk because of a family history of depression. According to John Gabrieli, who led the study, these results suggest that this type of scan can be used to identify children whose risk was previously unknown, allowing them to undergo treatment before developing depression.

How maternal infection might lead to autism

In 2010, a large study in Denmark showed that women who suffered an infection severe enough to require hospitalization while pregnant were much more likely to have a child with autism. Now research from Gloria Choi's lab reveals a possible mechanism for how this may occur. In a study of mice published in *Science*, the researchers found that immune cells activated in the mother during severe inflammation produce an immune effector molecule called IL-17 that appears to interfere with brain development. The researchers also found that blocking this signal could restore normal behavior and brain structure.

Reversing autism symptoms in mice

Guoping Feng has previously developed a mouse model of autism based on a mutation in the Shank3 gene, which is linked to autism in humans. His team has now shown that many of the mutation's effects on the brain and on behavior can be reversed by restoring Shank3 gene activity in adult mice. The findings offer hope that it will eventually be possible to reverse some of the effects of autism in human patients.

How the brain recognizes objects

We can easily recognize objects independent of their size or viewing angle, but we also perceive these variables and use them to interpret complex visual scenes. Jim DiCarlo and colleagues have developed a computational model that mimics the brain's visual recognition capabilities and explains how the visual system can achieve both of these tasks in parallel.

Gene controls worms' behavioral state; may be linked to autism

In a study of worms, researchers from the Robert Horvitz and Martha Constantine-Paton labs have discovered a gene that plays a critical role in controlling the switch between alternative behavioral states, which for humans include hunger and fullness and sleep and wakefulness. This gene, which the researchers dubbed vps-50, helps regulate neuropeptides, tiny proteins that carry messages between neurons or from neurons to other cells. This kind of signaling is important for controlling physiology and behavior in animals, including humans. Deletions of the human counterpart of the vps-50 gene have been found in some people with autism.

Study reveals a basis for attention deficits

More than three million Americans suffer from attention-deficit hyperactivity disorder (ADHD), a condition that usually emerges in childhood and can lead to difficulties at school or work. A new study out of Guoping Feng's lab links ADHD and other attention difficulties to the brain's thalamic reticular nucleus (TRN), which is responsible for blocking out distracting sensory input. In a study of mice, the researchers discovered that a gene mutation found in some patients with ADHD produces a defect in the TRN that leads to attention impairments. These findings suggest that drugs boosting TRN activity could improve ADHD symptoms and possibly help treat other disorders that affect attention, including autism.

Controlling RNA in living cells

Ed Boyden and colleagues have devised a new set of proteins that can be customized to bind arbitrary RNA sequences, making it possible to image RNA inside living cells, monitor what a particular RNA strand is doing, and even control RNA activity. The new strategy is based on human RNA-binding proteins that normally help guide embryonic development. The research team adapted the proteins so that they can be easily targeted to desired RNA sequences.

New CRISPR system for targeting RNA

Feng Zhang and colleagues at the Broad Institute, the National Institutes of Health, Rutgers University, and the Skolkovo Institute of Science and Technology have characterized a new CRISPR system that targets RNA rather than DNA. In a study published in *Science*, the team reported the identification and functional characterization of C2c2, an RNA-guided enzyme capable of targeting and degrading RNA. Whereas DNA editing makes permanent changes to the genome of a cell, the CRISPR-based RNA targeting approach may allow researchers to make temporary changes that can be adjusted up or down and with greater specificity and functionality than existing methods for RNA interference.

Press Mentions

A Bloomberg Business article about how poverty can impact brain development in children highlights research by John Gabrieli examining how family income can affect academic achievement. "It's only in the last few years that there's been any systematic research asking about the biological side of the story," explains Gabrieli. (Bloomberg, July 20, 2015)

According to the *Boston Globe*, "A memory researcher, MIT professor Ki Ann Goosens decided she could refocus her own work to be more useful to people and families dealing with mental illness. Now she studies the intersection of stress and mental illness." (*Boston Globe*, September 11, 2015)

Science News surveyed 30 Nobel Prize winners to learn whose work has caught their attention. Feng Zhang was among 10 early-career scientists selected for this list. (*Science News*, September 23, 2014)

Gene editing scientists, including Feng Zhang, discovered a CRISPR system involving a different protein that also edits human DNA, and in some cases it may work even better than Cas9. (*WIRED*, September 25, 2015)

Scientists led by Feng Zhang reported that they discovered enzymes "that cut more precisely than those now in use in CRISPR, a technique with an uncanny ability to make a beeline for a targeted stretch of DNA, snip it out, and replace it. If the finding holds up, CRISPR…could become an even more powerful tool to reveal the genetic defects underlying diseases and to perhaps repair them." (*Boston Globe*, September 25, 2015)

MIT researchers have found a molecule that could make the CRISPR gene editing technique more precise. (*Popular Science*, September 28, 2015)

According to *WIRED*, Feng Zhang's lab reported finding another CRISPR system "that uses a different protein to cut DNA, which not only gives his lab its own free-and-clear discovery but, more importantly, suggests researchers might be able to find a whole library of editing proteins." (*WIRED*, October 4, 2015)

Professors Karl Deisseroth of Stanford University and Edward S. Boyden of MIT each received $3 million for their roles in the development of optogenetics, a technique that allows scientists to use light to turn neurons and groups of neurons on and off. (*New York Times*, November 8, 2015)

In an article published in *Smithsonian* magazine, Rebecca Saxe explained why she made an MRI of herself and her young son: "The Mother and Child is a powerful symbol of love and innocence, beauty and fertility. Although these maternal values, and the women who embody them, may be venerated, they are usually viewed in opposition to other values: inquiry and intellect, progress and power. But I am a neuroscientist, and I worked to create this image; and I am also the mother in it, curled up inside the tube with my infant son." (*Smithsonian* magazine, December 2015)

McGovern Institute director Bob Desimone and Picower Institute professor Earl Miller described what is happening in the brain when we try to multitask. (*Today Show*, January 27, 2016)

(Reuters, Harbaljit Sohal was interviewed by BBC Coventry/Warwick about being named one of *Forbes* magazine's "30 Under 30." Sohal, a postdoc in the Boyden and Desimone labs, is developing new brain technologies for circuit analysis and control. (February 8, 2016)

Nancy Kanwisher posed the following questions in an article published in the *New York Times*: "Why do we have music? Why do we enjoy it so much and want to dance when we hear it? How early in development can we see this sensitivity to music, and is it tunable with experience? These are the really cool first-order questions we can begin to address." (*New York Times*, February 8, 2016)

According to Ed Boyden, "I've been thinking a lot over the last decade primarily about the technology that helped us figure out what we need to understand about the brain in terms of circuits and how they work together. But now that those tools are maturing, I'm thinking a lot about how we use these tools to understand what we all care about." (*Edge*, February 12, 2016)

MIT researchers have found that they can reverse some of the behavioral symptoms associated with autism. "The discovery may open the door to developing more universal approaches to treating autism, like identifying and targeting the specific circuits that cause each patient's behavioral gaps." (*Boston* magazine, February 18, 2016)

MIT researchers found that genetic engineering could be used to reverse some of the symptoms of autism. The researchers showed that turning on the Shank3 gene "could reverse symptoms associated with autism, such as repetitive behaviors and social avoidance." (*Huffington Post*, February 19, 2016)

Genome editing pioneer Feng Zhang hopes his work will shed light on neurological disorders. (*MIT News*, March 22, 2016)

The *Globe and Mail* spotlighted Feng Zhang and his role in developing the CRISPR-Cas9 gene editing system. "CRISPR genome editing technology is a really powerful platform," said Zhang. "I think it will advance both our ability to understand disease and to develop treatments." (*Globe and Mail*, March 23, 2016)

Researchers from MIT have identified how sensory overload occurs among people with neurodevelopmental disorders. The researchers hope they can use their findings to "classify these disorders in a better way, but also develop therapies that alleviate or diminish the symptoms." (*Popular Science*, March 23, 2016)

MIT researchers have found a possible link between attention-deficit disorders and autism. "One of the long term goals is gene therapy where we can actually introduce genetic material that might be missing from the human," explains graduate student Michael Wells. (*Boston Herald*, March 24, 2016)

On May 12, the McGovern Institute hosted a visiting delegation from China headed by Hu Chunhua, the party secretary of Guangdong province. The delegation also included Xu Qin, the mayor of Shenzhen; Cui Tiankai, the Chinese ambassador to the United States; and Zhang Qiyue, the consul-general to New York. (*MIT News*, May 12, 2016)

According to Nancy Kanwisher, in an article published in *New York* magazine, "It's not crazy to…hypothesize that some aspects of face perception may be evolved." (*New York* magazine, June 2, 2016)

With Feng Zhang's latest CRISPR study, some say that the field of genetic engineering is now moving in "dog years—it feels like seven times faster than real time." (*New York Times*, June 3, 2016)

Rebecca Saxe studies human brain development in order to understand how the human mind is built. The challenges and rewards of this research connect her experiences as a scientist and as a mother. (TEDx Cambridge, June 9, 2016)

Parkinson's disease, blindness, chronic pain, and more could all be cured using optogenetics, a revolutionary therapy that has just begun its first trial in humans. (*New Scientist*, June 22, 2016)

Feng Zhang "successfully harnessed CRISPR with Cas9 to edit a gene in a eukaryotic cell—that is, a cell with a nucleus. In the eyes of some, that distinction vaulted him ahead of Doudna and Charpentier. To edit a bacterial gene was one thing; to actually monkey with the building blocks of humanity was another." (Bloomberg, June 29, 2016)

Robert Desimone
Director
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