

From the Chair

As my tenure as Chair of the Biology Department at MIT comes to a close, I am pleased to report in this, the inaugural issue our new semiannual newsletter, **BIOLOG**, that the technological revolution in the life sciences has given the study of biology ever more prominence in scientific, societal, and economic arenas. The rapid pace at which discoveries are being made — those that drive fundamental changes in our understanding of biology — has given us a sense that we are at the frontier of discovery in research laboratories and our classrooms.



TOP: Different stages of skeletal muscle differentiation. Photo: Zuzana Keckesova
BOTTOM: Chris Kaiser, Chair, Biology Department

I am also pleased to report that our faculty is committed to maintaining its position of leadership in advancing biology research and education, as well as building on our strength in using the tools of informatics, genomics and computational biology. Over the last five years, we have hired several faculty members with significant research interests in these areas, a trend that is likely to continue. Over the same period of time we have increased graduate student diversity from 5 to 18 percent over 6 years — an accomplishment I am personally very proud to report and a trend I am confident will continue.

The challenge we now face is how best to extend the reach of the Department and achieve our ambitious goals. These goals include continuing to recruit new faculty, as well as retaining senior members, securing adequate funding for our renowned graduate program, increasing the diversity of our graduate and faculty populations, and building on our position of strength at the interface of life sciences and engineering. It is our hope that with

the creation of this new biannual newsletter, you the members of our extended community will help us achieve our critical goals.

On the following pages, and in future editions, you will learn more about our stellar faculty and students, our exemplary diversity and outreach programs, our most recent research accomplishments, and our faculty and students awards and honors.

In my new role as director of the National Institute of General Medical Sciences, I intend to be an advocate for the basic research enterprise; one that I believe the Department of Biology at MIT exemplifies and has indeed helped to define. It has been my honor to be a member of the Biology Department's faculty since 1991, and its Chair since 2004, and I will continue take a pride in the Department's ongoing success.

Chris Kaiser, Chair, Biology Department ◉

Simply stated, the pre-eminence of the Biology Department is because of its faculty

Featured in this inaugural edition of BIOLOG are three members of the faculty, each one representing different phases in their academic careers: **Adam Martin**, who joined the department this year; **Amy Keating**, who has been a member of the faculty since 2002; and **Leonard Guarante**, who has been a member of the department of biology faculty since 1981. In this edition, we will provide brief summaries of their research, which will, in subsequent editions, be discussed in much greater detail.



Photo: Kent Dayton

Adam Martin

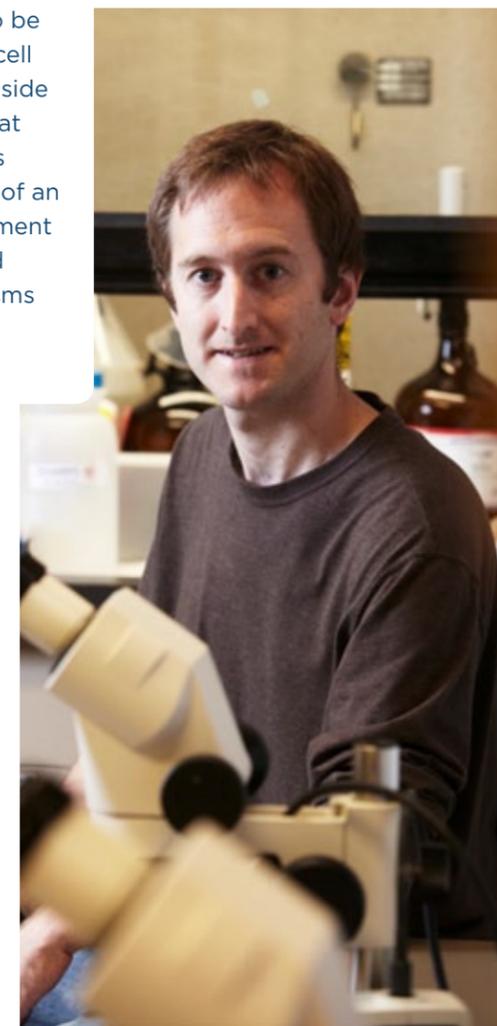
Thomas D. and Virginia W. Cabot Career Development Assistant Professor of Biology

In all developing organisms, cells must move and change shape to be organized into distinct organs and tissues. Early in development, cell constriction allows cells on the exterior of an organism to move inside in a process called gastrulation. This gives rise to layers of cells that differentiate into different sets of organs and cell types. While this developmental process is essential for establishing the body plan of an organism, the equivalent process later in life can be deadly. Movement of cancer cells from their site of origin allows these cells to spread throughout the body. Therefore, studying the molecular mechanisms that drive cell shape change during development is critical to understand both development and tumor progression.

A structure called the actin cytoskeleton plays a key role in inducing cell shape change. Like the skeleton of an animal, the actin cytoskeleton consists of filaments that lend structure and support to the cell. However, actin filaments also interact with molecular motors, myosins, that can cross-link filaments in a network and contract the network to generate pulling forces in cells.

Adam Martin's lab studies how the actin cytoskeleton drives cell constriction. His laboratory uses the fruit fly, *Drosophila melanogaster*, to address this problem, since genetic approaches can be combined with live imaging of cell shape changes and computational image analysis during development. Using this integrated approach, Professor Martin previously found that cell constriction during *Drosophila* gastrulation is dynamic, being driven by pulses of actin-myosin contraction that are uncoordinated in neighboring cells. Between pulses, cell shape is stabilized via a currently unknown mechanism such that cells do not relax back to their original shape. Thus, these cells constrict like a ratchet. The Martin lab is investigating the mechanism of both contraction and stabilization and how this force generation is regulated by transcription factors whose expression is required for constriction.

Amazingly, even though individual cell shape change is incremental, the collective contraction of the tissue is continuous. This suggests the exciting possibility that cells sense mechanical forces transmitted between cells and respond in a way that maintains force balance across the tissue. To test this hypothesis, Professor Martin's lab is investigating the coordination of constriction pulses and the dynamic movements of cells in the tissue to determine how forces are balanced. In addition, we can disrupt attachments between cells and examine how cells respond in the absence of external force. ○



ABOVE: Adam C. Martin, B.S. Cornell University, 2000, Ph.D. University of California, Berkeley, 2006, Post-doctoral training, Princeton University 2006-2010. Photo: Kent Dayton

Amy E. Keating

Associate Professor of Biology

A recent recipient of a NIH Transformative R01 grant designed to support innovative, high-risk and unconventional research projects, Associate Professor, Amy Keating studies the problem of protein-interaction specificity, or how proteins select just one or a few interaction partners from what can be a large number of closely related possibilities.

Interactions between proteins underlie all biological processes and are central to the organization, structure and function of the cell. Proper cellular function requires formation of the appropriate macromolecular complexes. But how are the correct complexes specified, given the enormous number of possible interactions that can occur in a cell?

One class of proteins studied in the Keating lab is the bZIP transcription factors. These proteins regulate gene expression by forming homo- or hetero-dimers that bind to DNA. Which proteins interact can determine which genes are activated or repressed. Intriguingly, there are 53 bZIP proteins encoded in the

human genome, which can potentially form more than 1,400 different pairs. Which of these pairs actually form? And what are the consequences of these interactions for DNA binding?

The Keating group measures bZIP interactions experimentally and uses the resulting data to develop computational models that describe how bZIP protein sequence determines binding. Then, because many bZIP transcription factors are implicated in diseases including cancer, the group uses the resulting models to design new molecules that can block the interaction of certain transcription factors with their partners and with DNA. Similar projects target



ABOVE: Amy E. Keating, B.A. Harvard, 1992, Ph.D. UCLA 1998, Postdoctoral training with Peter S. Kim and Bruce Tidor MIT. Photo: Kent Dayton

other proteins important for resistance to chemotherapy. A long-term goal is to develop rational methods for predicting and re-engineering protein-protein interactions, which would enhance biologists' understanding of natural systems and provide tools for biotechnological and therapeutic applications. ○

Leonard Guarente

The Novartis Professor in the Department of Biology and Director of the Paul F. Glenn Laboratory at MIT. He is an editor of *Cell*, *Genes and Development*, *Cell Metabolism*, *Developmental Cell*, *TIG*, *EMBO Reports*, author of *Ageless Quest* (CSH Press), and editor of *Molecular Biology of Aging* (CSH Press).

Why do living things age? What genes influence longevity? Is it possible to extend youthfulness by means of genetic manipulation? Professor Leonard Guarente analyzes these tantalizing questions and others in molecular detail.

Professor Guarente discovered the central role of sirtuins in slowing aging, and found the biochemical function of this class of proteins – NAD-dependent protein deacetylation, which links metabolism, protein acetylation and aging.

His recent research has focused on mammalian SIRT1, which deacetylates and regulates scores of transcription factors and cofactors in the nucleus. SIRT1 can be activated by calorie restriction (CR) to alter many physiological pathways that govern cell metabolism and stress resistance.

SIRT1 can also mitigate diseases of aging, such as diabetes, neurodegenerative diseases, cardiovascular diseases, cancer, inflammatory diseases and osteoporosis, in a manner similar to CR. SIRT3 has emerged as another very exciting sirtuin, because it is activated by CR in mitochondria and functions to suppress reactive oxygen species (ROS).

Recent data from many labs shows that SIRT3 links sirtuins, aging, CR, ROS and mitochondria, and also plays an important role in tumor



ABOVE: Leonard Guarente, B.S. MIT, 1974, Ph.D. Harvard University 1978, Jane Coffin Childs Postdoctoral Fellow, Harvard 1978-1981. Photo: Kent Dayton

suppression. Sirtuin based therapies may therefore offer new approaches to human diseases. ○

The biology department offers the most brilliant scientists an opportunity to conduct curiosity driven basic research – something that sets us apart from many other molecular biology departments. Our department is fortunate to be imbedded in MIT's highly collaborative academic environment where we are already seeing the rewards of work with colleagues in engineering and physical science departments. The following research highlights exemplify achievements that have occurred over the past year.

Michael Hemann and his colleagues, in a study of mice with lymphoma, have discovered that a small number of cancer cells escape chemotherapy by hiding out in the thymus, an organ where immune cells mature. Within the thymus, the cancer cells are bathed in growth factors that protect them from the drugs' effects. Professor Hemann conjectures that these cells are likely the source of relapsed tumors. In addition, **Michael Hemann** and **Graham Walker** are senior authors of two papers that elucidate how two key DNA replication enzymes play roles in tumor cells' response to DNA damage. This work has opened the possibility that molecules that would disrupt the action of these enzymes may be used in combination with traditional chemotherapy, to provide a better way to treat cancers that don't respond well to the usual treatments.

Tyler Jack's lab is working to understand why lung cancer spreads. His work and that of other MIT biologists have pinpointed a genetic change that helps tumors move to other parts of the body. They have also identified a genetic change that makes lung tumors more likely to spread to other parts of the body. These findings offer new insights into how lung cancers metastasize and could help identify drug targets to combat metastatic tumors – which account for 90 percent of cancer deaths.

Rudolf Jaenisch and collaborators have identified a protein called Musashi 2 that is predictive of prognosis in acute myeloid leukemia (AML) and chronic myeloid leukemia (CML) patients. High levels of Musashi 2 protein is associated with increased cell proliferation, decreased cell maturation, and multiple cancer-related cellular pathways in human leukemias. The protein and the cellular functions it affects could potentially represent therapeutic targets in certain types of leukemia, according to the researchers' article in *Nature Medicine*.

Susan Lindquist and her colleagues have determined that heat shock protein 90 (Hsp90) can create heritable traits in brewer's yeast by affecting a large portion of the yeast genome. The finding has led to the conclusion that Hsp90 has played a key role in genome evolution. This work provides a new way of thinking about how organisms could rapidly evolve new traits.

Hidde Ploegh's group has created a method that site-specifically modifies proteins to exert control over their properties when administered therapeutically. The technique should be useful to increase potency, slow metabolism, and improve thermal stability of therapeutically useful proteins, such as interferon alpha 2 (IFN-alpha 2), which is used to treat variety of diseases, including leukemia, melanoma, and chronic hepatitis C.

Peter Reddien's lab has found that pluripotent adult stem cells power planarian regeneration. Reddien's group has identified a single, pluripotent cell type that gives rise to the planarian's amazing ability to regenerate body parts.

David Sabatini and collaborating Whitehead Institute researchers have found that depriving human melanoma cells of the essential amino acid leucine can be lethal to the cells. This may be a possible strategy for therapeutic intervention. Sabatini's research team also used a new *in vivo* screening system to identify a protein in the serine biosynthesis pathway that is essential in estrogen receptor (ER)-negative breast cancer – a notoriously difficult disease to treat that's associated with low five-year survival rates. According to the researchers, when expression of the gene that codes for this protein – phosphoglycerate dehydrogenase or PHGDH – is suppressed in tumors and cell lines with an overabundance of the protein, the rate of cellular growth declines markedly.

Jeroen Saeij is investigating a the question of why certain strains of the *Toxoplasma* parasite (there are at least a dozen) are more dangerous to humans than others have discovered a new *Toxoplasma* protein that may help explain why the type II strain is more virulent than others. The Saeij lab also showed that *Toxoplasma* infection in mice results causes intestinal inflammation that strongly resembles the intestinal inflammation seen in Crohn's disease in humans. It is unknown if any of these cases are actually caused by *Toxoplasma* but Saeij reports some studies show a higher incidence of *Toxoplasma* in Crohn's patients compared with the general population.

Phil Sharp worked on paper with colleagues to harness power of 'convergence' for revolutionary advances in biomedicine and other fields. Convergence is a broad rethinking of how scientific research can be conducted to capitalize on a broad range of knowledge – from microbiology to computer science to engineering design.

Bob Weinberg and his group discovered that a differentiated cell type found in breast tissue could spontaneously convert to a stem-cell-like state – the first time such behavior has been observed in mammalian cells. These results refute scientific dogma that states that differentiation is a one-way path. Once cells specialize they cannot return to the flexible stem-cell state on their own. This surprising finding may have implications for the development of cancer therapeutics, particularly those aimed at eradicating cancer stem cells. Cancer stem cells are uniquely capable of reseeding tumors at both primary and distant sites in the body. ○

Musings on the department's new web site

A thing of beauty is a joy forever: its loveliness increases; it will never pass into nothingness — John Keats

When I first set my sights on revamping the department's web site my goal was simple – to create something easy to navigate and visually appealing.

Over the past year my vision and charge broadened to translating a 50+-year legacy of leadership in academic biology into a resource that is representative, functional, and beautiful. Producing the web site required me to assemble a team of professionals to refine its architecture, create an identity, define the department's voice, unify the site's messages, engage internal and external stakeholders to build consensus for new ideas, embrace technology and MORE to showcase the department's quality, excellence and richness while preserving time honored traditions.

At times it was a nail-biting experience to bear this responsibility but we did it! I'm pleased and proud of the work of what our team created. Simply put, the web site is awesome and does the department justice.



ABOVE: Michelle Coleman, Administrative Officer for the Biology Department. Photo: Chareese Allen

I was privileged to partner with several key individuals to produce this site. Many thanks to Tom Pixton aka our web godfather from MIT's Publishing Services Bureau. We literally could not have done this without him. Many thanks to Janice Chang, Laurie Ledeen, Luke McNeill, and Nick Polizzi. My biology colleagues went above and beyond the call of duty by bringing their creativity, intellect and institutional memory to this project. I am eternally grateful. Finally, thanks to our team of web-development-professionals: Nimble Partners, Stolze Design, Indigo Digital and Robert and Kathleen Thurston-Lighty.

Please explore and enjoy our new site at: www.biology.mit.edu ○

MIT Biology Department Facts and Figures:

- This past year the National Research Council (NRC) ranked the biology doctoral program as the top PhD program in molecular biology
- Including emeritus faculty, the department has 4 Nobel Laureates, 29 members of the National Academy of Sciences, 10 Howard Hughes Medical Institute (HHMI) Investigators and 3 HHMI Early Career Investigators.
- Joint faculty appointments provide important connections to other departments, including Brain and Cognitive Sciences (5), Chemistry (3), Physics (1), Biological Engineering (5), and Civil and Environmental Engineering (1).
- The biology department has 56 primary faculty members, located in 5 buildings: 23 in the Koch Biology Building, 16 in the Whitehead Institute, 13 in the David H. Koch Institute for Integrative Cancer Research and 2 each at the Broad and Picower Institutes
- In 2010-2011 the Department awarded 33 PhD degrees in biology, 5 PhD degrees and 3SM degrees in the joint program in biological oceanography with the Woods Hole Oceanographic Institute (WHOI). The department registered 213 graduate students and another 28 in the joint WHOI program. ○

Biology's Innovative B3 Program Expands with Two New Students

In the fall of 2010, we introduced the inaugural members of the Biology Department's innovative initiative, the Biology and Biotechnology Bridge Program (B3), a two-year post-baccalaureate program based on collaboration between the biology department and our local biotech partners. Brigitta Tadmor, Vice President and Global Head, Diversity/ Inclusion and Health Policy, at Novartis, notes that "for us this is a great opportunity to open our labs to scientific talent from places we typically don't recruit from and to offer our researchers the opportunity to host and mentor a B3 student."

This fall, the Biology and Biotechnology Bridge Program welcomed two new students to B3 — German Velez and Ana Berglind, who bring the total number of students to six. German and Ana now join Jonathan Baffoe, Shekela Baccus, Tavina Claiborne and Monika Avello, the continuing participants in the program.

The goal of the B3 program is to provide additional research and academic preparation to talented individuals from minority groups and economically disadvantaged backgrounds to prepare them for the country's most competitive biological and biomedical PhD programs. ○



ABOVE: Pictured left to right: German Velez, Jonathan Baffoe, Shekela Baccus, Ana Berglind, Tavina Claiborne, and Monika Avello. Photo: Mandana Sassanfar



ABOVE: Rudolf Jaenisch receives his Medal of Science from President Barack Obama. Photo: Chuck Kennedy/White House

David Bartel was elected to the National Academy of Sciences in the spring of 2011.

Ian Cheeseman received the 2011 R.R. Bensley Award — one of four young investigator awards bestowed by the American Association of Anatomists (AAA). The Bensley award honors a cell biologist who has completed his or her highest degree in the past ten years, advanced the field of anatomy, and published papers that substantially impacted his or her field.

Penny Chisholm was awarded the Petersen Award: IFM-GEOMAR Kiel, Germany.

Gerald Fink was awarded the 2010 Gruber Genetics Prize of The Peter and Patricia Gruber Foundation for his groundbreaking research in yeast genetics.

Mary Gehring was named a 2011 Pew Scholar in the Biomedical Sciences.

Nancy Hopkins, Susan Lindquist, Hazel Sive and Joann Stubbe were among the faculty that participated in a two day celebration of Leaders in Science and Engineering: The Women of MIT that took place March 28 - 29, 2011. The symposium highlighted the work and accomplishments of women at MIT and beyond. In addition, Nancy delivered the University of Chicago's inaugural colloquium on 'How to Advance Women in Science and Engineering' on May 12, 2011.

Richard O. Hynes received the 2010 Earl Benditt Award from the North American Vascular Biology Organization.

Chris Kaiser was elected a fellow of the American Association for the Advancement of Science and has been selected as the new director of the National Institute of General Medical Sciences (NIGMS). As NIGMS director, Kaiser will oversee a \$2 billion budget, which primarily funds basic research in the areas of cell biology, biophysics, genetics, developmental biology, pharmacology, physiology, biological chemistry, bioinformatics and computational biology.

Amy Keating received an NIH Transformative R01 grant. She plans to develop new DNA sequencing technologies to study protein-protein interactions. She expects this will lead to new models that speed annotation of protein functions and dramatically advance protein-engineering capabilities.

Rudolf Jaenisch was named one of the seven winners of the 2011 National Medal of Science, the nation's highest scientific. In addition, he has been named a recipient of the 2011 Warren Triennial Prize of Massachusetts General Hospital (MGH). Created in 1871, the Warren Prize was named for Dr. John Collins Warren, a co-founder of the MGH who played a leading role in establishing what would become The New England Journal of Medicine.

Michael Laub received the Presidential Early Career Award for Scientists and Engineers

Susan Lindquist was the recipient of the 2010 National Medal of Science. Lindquist was cited "for her studies of protein folding, demonstrating that alternative protein conformations and aggregations can have profound and unexpected biological influences, facilitating insights in fields as wide-ranging as human disease, evolution, and biomaterials". She also received Mendel Medal, Genetics Society UK Max Delbrück Medal, Berlin.

Terry Orr-Weaver was elected a fellow of the American Association for the Advancement of Science. She was selected for "distinguished contributions to the field of yeast genetics, specifically protein sorting and secretion".

David Page has been named a recipient of the 2011 March of Dimes Prize in Developmental Biology. The prize honors David's groundbreaking body of research on the human Y chromosome. David was also elected as a member of the American Academy of Arts And Sciences.

In January 2011, the American Association of Immunologists named Whitehead Member **Hidde Ploegh** the recipient of its Meritorious Career Award. The award recognizes a mid-career scientist for outstanding research contributions to the field of immunology.

Jeroen Saeij was named a 2010 Pew Scholar in the Biomedical Sciences.

Matthew Vander Heiden has been named a 2011 recipient of the Damon Runyon-Rachleff Innovation Award and a junior faculty award from the Smith Family Award for Excellence in Biomedical Research.

Robert A. Weinberg PhD *honoris causa*, Helsinki University, 2010 Associate Member, European Molecular Biology Organization. The scientist credited with discovering the first human oncogene, Professor Weinberg won the 2011 American Society of Clinical Oncology (ASCO) Science of Oncology Award. According to ASCO, Professor Weinberg won the award for "for furthering the understanding of cancer through his innovative and groundbreaking research". ○



The Alexander Rich Lecture

On Tuesday, April 12th the department hosted the “The Alexander Rich Lecture” as part of its for Biology colloquium series. The special lecture honored Dr. Alexander Rich, William Thompson Sedgwick Professor of Biophysics at MIT.

The lecture was given by Dr. Alexander Varshavsky from the Department of Biology at the California Institute of Technology. Dr. Varshavsky, who was at MIT briefly in the late 1970’s, lectured on: “Recent Discoveries About the Ubiquitin System and the N-End Rule Pathway.” Dr. Rich, who has been with the department since 1958, has focused on the molecular structure and the biological function of the nucleic acids with some additional emphasis on protein structure, and the author of over 550 papers.

Prof. Rich has been awarded Honorary Doctor of Science degrees from several universities, including the Eidgenössische Technische Hochschule, Zurich; Freie University, Berlin; and the Weizmann Institute of Science, Rehovot, Israel. He is also a member of the Institute of Medicine, Washington; the American Academy of Arts and Sciences; the American Philosophical Society; and the Pontifical Academy of Sciences, Rome.

InnoWorks’ Second Year at MIT

InnoWorks held its second annual program at MIT this year from August 15th - 19th with the help of over 12 undergraduate students, hosting 14 middle school students. The program was held in the Koch Center, where students worked, experimented, and explored science. The students were also lucky enough to get the opportunity to work in a basics science laboratory for an entire day!

MIT InnoWorks is a free one-week science and engineering program for middle school students in Cambridge, MA. The program targets students who are registered in the federal free or reduced lunch programs and have limited resources and exposure to science outside of their schools. The goal of InnoWorks is to increase student interest in STEM (Science, Technology, Engineering and Math) fields and encourage them to pursue careers in these areas.

Paul Schimmel Gives 3rd Annual Dean’s Colloquium Lecture

Paul Schimmel, Ernest and Jean Hahn Professor, Skaggs Institute for Chemical Biology, The Scripps Research Institute

On Tuesday, September 22, Professor Paul Schimmel was the honored

speaker at the 3rd annual Dean’s Colloquium lecture series. The title of his talk was “What Was Learned for the Academic Life And The Darwinian World of Biotechnology.” In his lecture, Professor Schimmel spoke about his experience in bringing basic scientific discoveries to the market.

Having served for many years as a member of the Biology Department, Professor Schimmel acknowledged his debt to Professors Alex Rich and Tom RajBhandary, and reminded the audience that it is MIT’s unique culture that encourages responsibility not only for the creation of new knowledge but also to make the world a better place.

Department of Biology Annual Retreat

The Biology Department held its annual retreat on June 16th and 17th at the Sea Crest Hotel in Falmouth, MA. The 197 attendees included faculty, graduate and postdoctoral students, as well administrators. The retreat included 3 poster sessions lead by faculty members Chris Burge, Adam Martin, and Tom RajBhandary. ○

Photo: Juhee Bae

Photo: Bryce Vickmark

Photo: Luke McNeill

Tell us what you think!

What would you like see featured in BIOLOG? Send all comments and suggestions to ledeen@mit.edu

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