MBL Bio Woods Catalyst

FALL 2011
Volume 6, Number 2

IN THIS ISSUE

A Beacon for Science

Inside the Whitman Center for Research and Discovery

Page 2

Fall 2011 Volume

Dear Friends,

I first came to the MBL as a graduate student in 1965, officially to take a course but with the ulterior motive of gleaning information from certain visiting investigators. I knew the world's leading biological scientists gather at the MBL each summer, and I wanted someone to show me how to isolate a component of cells, the mitotic spindle. Once here, I knocked on the doors of senior investigators including Lenny Rebhun and Bob Kane. They were very generous with their time, and they taught me much more than what I had come to learn.

My first MBL experience was key, not least because it was pivotal to our discovery of an important cellular protein, tubulin, which my University of Chicago colleagues and I purified later that year. So, after finishing my Ph.D. and joining the University of Wisconsin, I returned to the MBL as a summer investigator from 1972 to 1976. This was also a significant time in my scientific career, one in which I transitioned from biochemist to cell biologist. Because I wanted to extend my studies of cell division from the test tube to the living cell, I camped on the doorstep of MBL scientist Shinya Inoué so I could observe the living cell using the polarization microscope he had pioneered.

The rewards of those summers at the MBL were great. It was not just my interaction with many of the world's best scientists, or the collaborative atmosphere, or the access to superb microscopy and instrumentation, or the beautiful Woods Hole setting. It was the unique mix of these things that made my years as a visiting investigator so productive and inspiring.

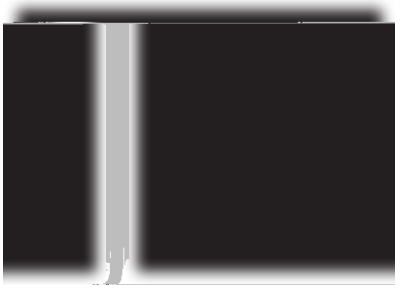
We hope this issue of MBL Catalyst illustrates that my experience was in no way unusual. The summer investigator program began when the MBL opened its doors in 1888, and is now called the Whitman Center for Research and Discovery after the MBL's founding director, C.O. Whitman. The Center has enriched and propelled the research of generations of biological and biomedical scientists, and the dividends to them extend to all of society, in the form of a stellar record of innovation and discovery.

Many thanks to Bob Goldman of Northwestern University for his leadership of the Whitman Center, and for serving as guest science editor of this issue of MBL Catalyst. Bob knows as well as I do that the Whitman Center is a critical component of the MBL's mission and success. To solidify its long-term strength, the MBL has launched a $2 million Whitman Center Endowment fundraising initiative, with an initial $500,000 matching commitment from the MBL. This endowment will support building enhancements to maintain Rowe Laboratory as a state-of-the-art facility for visiting investigators, and fellowship funds to continue to bring the world's best researchers into the Whitman Center fold. By building a solid foundation for the Whitman Center, we will ensure the MBL's continuing stature as the world's crossroads for innovation and discovery in the biological, biomedical, and environmental sciences.

Gary Borisy
President and Director

A Beacon for Science

Every year, hundreds of scientists move their labs researto prthe hson formedic



Departments

“Scientists have different philosophies of why they come to the MBL. Mine is to do experiments that aren’t necessarily in the game plan in my home lab, to do something new. The spirit of MBL is to try things, to be willing to be adventurous, take risks, even if they don’t work out.”

—

Watching a larval lamprey, a jawless fish with an eel-like body, swim around a tank is hardly impressive. But knowing that only 11 weeks prior, the animal sustained a severe spinal cord injury, the lamprey's simple motion seems nothing short of remarkable.

Whitman Center researchers Ona Bloom, Jennifer Morgan, and Joseph Buxbaum are collaborating to chart a timeline of the cellular and molecular changes that occur throughout the lamprey's healing process. "We'd like to know what's happening immediately after the injury, say six or 24 hours after, a week later, two weeks later—to get a really full picture," says Bloom. The hope is that having such a detailed series of molecular "snapshots" could reveal the step-by-step genetic changes that are occurring before their effects are observable in the lamprey's behavior.

Above: Giant nerve fibers in the intact lamprey spinal cord are labeled in red by a fluorescent retrograde tracer.

Right: (L to R) Whitman Investigator Ona Bloom (Feinstein Institute for Medical Research and Hofstra North Shore - LIJ School of Medicine), MBL scientist Joel Smith, Whitman Investigator Jennifer Morgan (University of Texas at A0(duo‹MCIDhe lampr)10(ey can HT1.5MC /. Trely ÓResearch and Ho-Lterey can

Although scientists have reported since the 1950s that the lamprey can regenerate its spinal cord and recover the ability to swim, the prevailing question continues to be: How do they do this? A team of MBL investigators, aided by recent advances in DNA sequencing technology and analysis, is exploring a new approach that may yield crucial insight into how the lamprey's regeneration process unfolds.

his office on his first day," says Bloom. "He was really excited about the

Tinnitus Caused by Too Little Inhibition of Brain Auditory Circuits, Study Finds

Research by two Whitman Investigators has shed new light on tinnitus, a persistent and debilitating ringing in the ears that affects an estimated 250 million people worldwide.

The study, published by Thanos Tzounopoulos (University of Pittsburgh School of Medicine), Gordon Shepherd (Northwestern University) and their colleagues, revealed that tinnitus is the result of under-inhibition of key neuronal pathways in the brain's auditory center. The findings could eventually lead to drugs or therapies for the condition, which currently has no cure. "Prior research has shown that auditory circuits in the brain are more excitable in tinnitus sufferers but until now it has not been clear whether that is due to hyperactivity of excitatory neuronal pathways or reduced activity of inhibitory ones, or both," says Tzounopoulos. He and his collaborators answered this question by using a new imaging technique known as flavoprotein autofluorescence to study auditory circuits in mouse models with tinnitus. Now that the cellular mechanisms are clearer, Tzounopoulos and his team are working to identify drugs that could help treat tinnitus. (*PNAS* 108: 7601–7606,

s

New Microscopy System Illuminates Organization of Key Cellular Protein

Septin proteins play an important role in a number of cellular processes in most organisms, from yeast to humans. Abnormal septin function has been implicated in neurodegenerative disorders such as Alzheimer's and Parkinson's diseases, and in forms of cancer. Discerning the organization of septins in higher-order cell structures such as rings, helices, and fibers is crucial to understanding their assembly and function in normal cells and their malfunction in disease. To determine the organization of septins in live cells, Whitman Investigators Bradley DeMay and Amy Gladfelter of Dartmouth College and MBL Senior Scientist Rudolf Oldenbourg (Cellular Dynamics Program) combined the unique strengths of fluorescence and polarized light imaging to develop the Fluorescence LC-PolScope, a polarized fluorescence microscopy system. Fusing the green fluorescent protein (GFP) to septins in fungal and animal cells, the team found that septin proteins were organized in an identical highly ordered fashion that is conserved from yeast to mammals. "Fluorescence labeling allows us to identify specific proteins and their fate and whereabouts inside the living cell, while polarized light imaging can assess the finer organizational details of protein assemblies, like pairing and alignment of filaments," says Oldenbourg. "Together we can go far." Oldenbourg and Gladfelter are continuing their collaboration with Cellular Dynamics Program scientist Tomomi Tani to use polarized fluorescence of single GFP molecules to determine the orientation and dynamics of single molecules of septins. (*J. Cell Biol.*

s

Scientists Observe New Force During Cell Cycle

Animal cells change in shape and stiffness as they proceed through the cell cycle, the basic life process in which one cell divides into two. Most models posit that the driving force for these shape changes comes from the interaction of actin and myosin (two proteins that power contraction in a muscle fiber and are also present in most cells). Current models suggest that actomyosin at the cell's edges creates tension that regulates the cell's shape, much as surface tension governs the shape of a liquid droplet. These models typically ignore any role the fluid interior of the cell (the bulk cytoplasm) may play in cell shape. However, in a recent study, Whitman Investigators Christine Field, Martin Wühr, and Timothy Mitchison of Harvard Medical School and their colleagues find actomyosin forces at work in the bulk cytoplasm that may modulate cell shape. Working with extract from *Xenopus* (frog) eggs, they found that actomyosin in the bulk cytoplasm undergoes dramatic cell-cycle-regulated changes in organization, suggesting that it too contributes to shaping cells, and/or organizing their internal contents, in a cell-cycle regulated manner. More work is required to test the functions of this interior actomyosin activity. (*J. Cell Sci.* s

Study Provides Insight into Insulin Release from Pancreatic Beta Cells

After a meal is eaten, the sugar (glucose) level in the blood increases. In a non-diabetic person, the pancreatic beta cells respond by secreting insulin, which then moves the glucose from the blood into fat, liver or muscle cells, where it is metabolized or stored for energy. In diabetics, however, the pancreas does not make enough insulin to effectively lower the blood glucose level. At present, the mechanism underlying insulin release in response to elevated blood glucose is not fully understood. In a recent study, Whitman Investigator Joshua Gray (U.S. Coast Guard Academy), MBL scientist Emma Heart (Cellular Dynamics Program) and colleagues identified a novel metabolic pathway in pancreatic beta cells, called PMET (plasma membrane electron transport). While PMET plays an important role in a variety of cell types, this is the first study to demonstrate its presence in insulin-secreting cells. Gray and Heart found that PMET activity in beta cells is dependent on glucose concentration and also identified a protein, NQO1, as part of the beta-cell PMET network. These continuing studies will contribute to the understanding of beta cell function and insulin secretion and help in the design of effective strategies to treat diabetes type 2. (*Am. J. Physiol. Endocrinol. Metab* % % s

What Fish Tell Us About Vocal Communication

Many fish, the most ancient group of vertebrates, vocalize during courtship and territorial defense. Fish social calls are similar in their acoustic structure to vowels and consonants, the most basic units of human vocalization and speech. In 2008, a team of Whitman Investigators discovered a compartment in the developing brain of midshipman fish that produces nerve cells (neurons) that directly control muscles used for sound production. The brains of other vocal vertebrates, including primates, have this same vocal compartment, suggesting that the vocal basis for acoustic communication among all vertebrates, including humans, evolved from an ancestrally shared brain compartment originating with fishes. Following up on their earlier work, Whitman Investigators Andrew Bass of Cornell University and Robert Baker of New York University Langone Medical Center teamed up again, along with Boris Chagnaud of the University of Munich, to show what the neurons in this evolutionarily shared vocal compartment "do for a living" when they grow up. The team recently reported that separate populations of the hindbrain code for frequency and duration, two of the most basic features of vocalizations among all vertebrates. ides a road map for understanding the fundamental working units of the brain that underlie the performance of vocal of the more complex social behaviors that vertebrates have evolved," says Bass. (*Nature Comm.* s

ric Betzig flips on a movie and soon one can hear a pin drop in the Loeb Laboratory room. On his computer screen, a three-dimensional clump of chromosomes is floating in black space. Suddenly the clump starts to pull into halves as the cell divides, and within 20 seconds it is done, the halves disentangled and pushing apart.

What's so exciting is this movie is not a graphic artist's simulation: It is a real (though sped up) process in a dividing cell. Betzig (top, right) made the movie with a microscope he co-developed that collects up to 200 images per second, piles them into 3D stacks, and renders

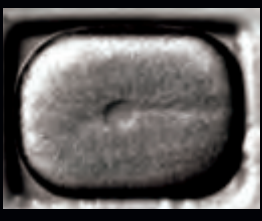
P. Selvin

P. Selvin

E. Betzig

“The MBL is ground zero for super-resolution microscopes this summer. Anything you could possibly want or dream of is here,” says Jim Galbraith. That includes a wide array of instruments on loan from the leading microscope vendors.

Anyone who wants to try a rig out is welcome. In fact, a schedule posted

The Geometry   of Life

MBL Moment

with …

Rodolfo Llinás

Bb3ologytc >>ene(1971-a[new Yi401.66h3f22Dei68 0 diseacided td t2.761 t2.2361-51-51-51C 7.761 t51-1d t2.761 t1idedc t1id2.

MBL: Why is the squid so useful for studying how nerve cells communicate?

RL: If you consider the nervous system, the brain, you find it is a conglomerate of single cells known as neurons, and glia. Neurons contact each other—they "shake hands," if you will—at the synapses. For the most part, a synapse functions by very quickly releasing small molecules, called synaptic transmitters, which then activate the next cell in line. And so, it is a chemical event.

I have spent 45 summers at the MBL basically trying to understand synaptic transmission in the squid mantle, the muscular covering for the animal's vital organs. This is the largest and, to me, the most beautiful synapse ever. While I have also worked with many other synapses, mostly in the mammalian central nervous system, there are very few that are as clear, as large, and as easy to address as that in the squid. We come to the MBL every summer for the squid, and also because the lab is beautiful, the facilities are superb, and the intellectual climate is second to none!

MBL: Over the course of your MBL research, you have literally "written the book" on neurotransmission in the squid. How did this lead to your current research on Alzheimer's disease?

RL: All of our research seemed to suggest that the squid synapse is very similar to the human synapse not just from a biophysical point of view, but more interestingly, from a molecular point of view. So we—Drs. Mutsuyuki Sugimori, Herman Moreno and I—decided to inject molecules known to produce neural diseases in humans into the squid synapse. The advantage is tremendous in the squid because we can inject the substance directly into the presynaptic [nerve] terminal and see where the injection is located, how quickly it moves to a particular terminal and so on. We have perfect control of the location, and a very good idea of concentration. We decided to study two sets of molecules. The first was beta amyloid, a protein that is a necessary step in the generation of Alzheimer's disease. When we injected beta amyloid into the squid synapse, we found that it blocked neurotransmission. But the real horror of Alzheimer's is a protein called tau 42. Because tau 42 can generate Alzheimer's, it is believed to be the mechanism for the neural

degeneration. So we injected human tau 42 into the squid synapse, and it blocked transmission extraordinarily powerfully and very quickly. We realized the squid synapse could, in fact, tell us a lot about the molecular mechanism for Alzheimer's. This is the paper we published last spring. We were quite elated as it promised to be

The **National Science Foundation** awarded

Accolades

MBL Distinguished Scientist and 2008 Nobel Prize Laureate **Osamu Shimomura** was recognized at a ceremony at the State House in Boston for his "significant contribution to biomedical research in Massachusetts." The honor was presented by the Massachusetts Society for Medical Research.

The Biotechnology and Biological Sciences Research Council (UK) named **Jason Swedlow** of the University of Dundee "Innovator of the Year" for his work on the Open Microscopy Environment, a revolutionary venture into open source software. Swedlow co-directs the MBL's Analytical & Quantitative and Light Microscopy course.

Ecosystems Center Distinguished Scientist **Jerry Melillo** was named chairman of a joint public-private sector committee that will produce the next National Climate Assessment report for the United States.

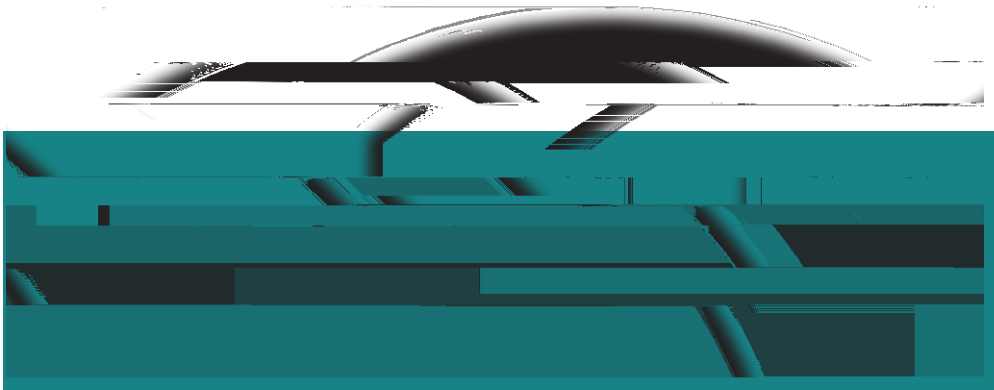
Corporation member **Thoru Pederson** received a European Molecular Biology Organization medal in Prague for "distinction in cell biology" and for "longstanding support of Czech science."

MBL President and Director **Gary Borisy** received the 2011 E.B. Wilson Medal from the American Society for Cell Biology. The medal is awarded for "far-reaching contributions to cell biology over a lifetime in science."

The following members of the MBL community were elected to the National Academy of Sciences: **John Eppig**, faculty, Frontiers in Reproduction; **John Heuser**, faculty, Neurobiology, Biology of Parasitism, Microbial Diversity; **Alexander Johnson**, faculty, Embryology; **Susan McConnell**, faculty, Fundamental Issues in Vision Research; **Carl Nathan**, faculty, Biology of Parasitism; **Michel Nussenzweig**, alumnus, Physiology; **Jisoon Ihm**, alumnus, Computational Neuroscience.

John Valois, longtime specimen collector and naturalist and former manager of the MBL Supply Department, was honored with the dedication of the John J. Valois Tank Room in the MBL Marine Resources Center.

Corporation member **Arthur Pardee** attended the 50th anniversary celebration of the discovery of the operon at Institut Pasteur in Paris. Pardee co-authored (with François Jacob and Jacques Monod) the seminal 1959 "PaJaMo Paper," representing the culmination of findings that illuminated how gene expression could be controlled. Jacob and Monod won the 1965 Nobel Prize in Physiology or Medicine "for their discoveries concerning genetic control of enzyme and virus synthesis."



or a comb jelly, watching the gelatinous creature scoot around a lab tank is a poor approximation of its behavior in the wild. That's why three Whitman Investigators—Sean Colin of Roger Williams University and John Costello of Providence College, both marine ecologists, and John Dabiri, a fluid-dynamics engineer from Caltech—hatched a plan to build a system capable of studying jellies in their natural habitat.

In the lab, you can get a sense for how a jelly propels itself through its surrounding fluid and captures its prey. But what's missing is the influence that ocean currents, nearly impossible to replicate in an artificial setting, exert on these processes. " /T11 1 Tf 10 n g1the wa ve. The what's missing is the 6rly

on the laser spread the beam into a paper-thin sheet, which ensures that only one layer of particles is visible. When a jelly swims through the flattened beam, a high-definition video camera captures footage of what is essentially a cross-section of the animal, displacing the particles as it moves. Back in the lab, a software program uses the change in location of displaced particles over a series of video frames to calculate the animal's speed as it glides through the water.

This past summer, the researchers used the SCUVA to explore the effects that natural turbulence has on the feeding behavior of the warty comb jelly, a predator in plentiful supply off the coast of Woods Hole. The comb jelly, however, is merely a model, serving as a means to address a more basic question of biological oceanography. "All of our exchange rates are based on laboratory work," Costello says. "So, fundamentally, we're asking: Is what we see in our laboratory experiments representative of what we're seeing out in the ocean? If they're not, we'll try and find out how unrepresentative they are and how we might work to correct that."

s— ARM

Placing a Value on the Invaluable

By Robert Goldman
Director, Whitman Center for Research and Discovery

“Summer research” at the MBL, now known as the Whitman Investigators program, is entering its 123rd year. From a historical perspective, the scientific output of the Whitman Center could hardly be more distinguished. Historians have established the crucial role the MBL has played in setting the foundations of the basic biological sciences, from cell and developmental biology to neuroscience, biochemistry, and biophysics. Whitman Investigators have included 30 Nobel Laureates and many more trailblazers, from E.B. Wilson and Nettie Stevens in the 1900s, who first proposed that sex is determined by chromosomes, to Ron Vale and others in the 1990s, who identified a major class of cellular proteins. One could point to hundreds of discoveries at the MBL that have fundamentally shaped the modern life sciences, and provide the conceptual basis for understanding human health and disease and developing medical therapeutics.

Given this record of accomplishment, one might ask what is it that makes the Whitman Center successful and productive. I think there are several factors at play. One is that the MBL provides the space and time for curiosity-driven research. It’s a place where scientists can come and really think about their work and gain an undisturbed period of time to explore new questions. While it may seem disruptive for them to relocate to Woods Hole, they find the great payoff is a focused research period in a highly supportive, stimulating environment.

Another factor is the MBL has always been at the leading edge of microscopy. As a consequence, MBL researchers have pioni 09disease and dev ƀDC 0.0u eoating pan BI

Renewing the Passion for Science

When a scientist invites a student to work in his or her Whitman Center lab, often the student ends up feeling very lucky. She finds herself welcomed into a "family" that is enriched by the culture of Woods Hole, one that often births a new generation of distinguished investigators. One such lab was that of S. Meryl Rose and his wife, Florence. From the 1930s to the 1970s, the Roses studied growth, differentiation, and regeneration at the MBL, and the students Meryl regularly brought into their lab enjoyed rare access to inspirational mentors. One, Elizabeth D. Hay, later became the first female full professor in a Harvard Medical School preclinical department. But while still navigating the challenges of her own medical school training, "what saved me was the summers I went to Meryl and Florence's laboratory in Woods Hole," she later recalled. The Roses often welcomed their students over for dinner and after they would play board games "or just sit around

MBL
7 MBL Street
Woods Hole, MA 02543 USA

www.mbl.edu

Smartphone users: Scan QR code for online content.

NON-PROFIT ORG.
U.S. POSTAGE
PAID
Marshfield, MA
PERMIT NO. 51

Printed with recycled materials.

In the Next *MBL Catalyst*

Biodiversity: Living on Earth

From marine microbes to millions of species in the Encyclopedia of Life, MBL research extends far and wide into the animal and plant kingdoms. In the next issue of MBL Catalyst, we highlight MBL projects that are furthering our understanding of living species and their environments.