

Reaching forward through innovation



**Boston Biomedical
Research Institute**



Boston Biomedical Research Institute

MISSION STATEMENT

Boston Biomedical Research Institute is an independent not-for-profit institution dedicated to basic biomedical research to promote the understanding, treatment and prevention of specific human diseases, and to the training of research scientists. Investigations focus on structure and function of proteins that control cellular communication, muscle contractility, cell movement, growth and differentiation and on the underlying causes of human disease from the study of disease models and development of novel therapeutics. In a uniquely collaborative environment that fosters innovative multidisciplinary research, our mission is to advance the frontiers of human knowledge in the biomedical sciences and to develop cures for a wide range of diseases such as cancer, cardiovascular disease and degenerative diseases including muscular dystrophy and Alzheimer's disease.



Boston Biomedical Research Institute's state of the art laboratory at 64 Grove Street, Watertown won an architectural award for innovative design. The building's open lab structure enhances the collaborative, collegial environment that has always characterized the Institute. Together 37 laboratories, in disciplines ranging from physics to physiology, are focused on illuminating the roots of human disease.

"The Board offers its deep gratitude to each and every donor for their part in helping BBRI reach a higher plane of scientific excellence and achievement."



Of all human activity, gardening is one of the oldest and most widely practiced. We know from carbon-14 dating that humans in Mesopotamia raised crops as far back as 8500 B.C. For them, it was essential for survival. These days, few Americans rely on their farming or gardening capabilities for sustenance. Yet, they spend billions of dollars each year on gardening goods and services – plants, seeds, fertilizer and mulch, tools and equipment and how-to books. Why is that?

Noted gardening author, Marina Schinz, provides the following insight: "To create a garden is to search for a better world. In our effort to improve on nature, we are guided by a vision of paradise. Whether the result is a horticultural masterpiece or only a modest vegetable garden, it is based on the expectation of a glorious future. This hope for the future is at the heart of all gardening." Gardening, however, is not some bucolic activity for the frail or faint of heart. True gardeners are passionate, hard-working, curious, innovative and extremely dedicated.

There is no better description about what is at the heart of Boston Biomedical Research Institute than providing "hope for the future." Our

scientists are continually in pursuit of a better world, guided by their own visions of a paradise in which deadly diseases no longer menace human society.

This past year, we have begun to enlarge and reconfigure BBRI's garden, so it can yield an even greater bounty. By grouping the Institute's research programs into four strategic areas – Cancer, Cardiovascular Biology, Degenerative Disease and Regenerative Biology and Proteomics – cross-fertilization of research ideas is enhanced, introducing hybrid vigor and generating even greater progress in developing new therapeutics and treatments. A significant early benefit has been in our recruitment of new BBRI investigators. Our scientists were able to recognize specific areas in these research programs needing enrichment, which enabled more targeted recruiting. In addition, candidates were better able to see how their research interests would fit within the Institute. We anticipate that our seven newly recruited scientists will stimulate thinking in new ways and directions, leading to further research success.

BBRI's garden is thriving because of the hard work and dedication of its many caretakers. I

offer my deepest appreciation to BBRI's Board of Trustees, members of the Corporation, donors, scientists and staff for all the time, energy, money and sweat they have poured into our special garden over the past year – cultivating new ground, rearranging and transplanting individual plants to make room for new additions, fertilizing, watering and weeding. We have made extraordinary progress, and the future is bright. However, a larger and more fruitful garden requires additional effort. Fulfilling the Institute's increased promise will require broader and deeper commitment from our existing caretakers, as well as many new ones. I encourage you to roll up your sleeves and sink your hands into this fertile soil, and introduce us to other willing gardeners. Together we can ensure a bountiful harvest for the benefit of human health.

JOHN R. LAYTON

John R. Layton
President



"I am fully confident that the discoveries made by BBRI scientists in the next year and the coming years will be the basis for innovative therapies...."

Seeking novel innovations in the fight against disease is our most valued goal at Boston Biomedical Research Institute. This year, since the launch of our strategic plan, our scientists have developed research initiatives which have put into motion four new disease-based programs: Cancer, Cardiovascular Biology, Degenerative Disease and Regenerative Biology and Proteomics. To support these initiatives, the Institute has acquired an impressive array of cutting-edge instrumentation and technologies, as highlighted in this Annual Report. As eloquently noted by Dr. Eric Sundberg, one of our talented new investigators, "Instrumentation is a platform for collaboration at BBRI." I extend my personal thanks to Drs. Lynne Coluccio, Janice Dominov, Henry Paulus, Eric Sundberg and Sarah Wilcox-Adelman, who committed their time and energy to the critically important effort to acquire this new instrumentation. Thanks also to our Trustees, who have had the vision to commit their own resources to help build our research infrastructure as a key first step in ensuring ongoing biomedical innovations at BBRI for the betterment of human health.

A second major accomplishment has been the recruitment of seven talented scientists. These scientists, also highlighted in this Report, include both established and new investigators, all of whom conduct exciting research programs and add new expertise and collaborations to existing research programs in areas of muscle disease and heart damage (Dr. Shinichi Takayama, Dr. Sachiko Homma), developmental signaling

and stem cell cancers (Dr. Kent Nybakken), neurodegenerative diseases (Dr. Moonkyoung Um and Dr. Martin L. Duennwald), stem cell biology, aging and tissue regeneration (Dr. James L. Sherley), and mathematics/computational biology, (Dr. Oliver King) whose research and analysis of large data sets uniquely complements our ongoing work in areas of genomics, proteomics and neurodegenerative diseases.

With all of the intense work of the past year, a recent personal incident has provided me a poignant but energizing reminder of the importance of BBRI and the research we do. My mother and I were in the radiation oncology unit of a local hospital, where she was undergoing radiation treatments for cancer. For two weeks, we had come together in the waiting room with about eight other patients, all scheduled for treatment at about the same time. We were becoming familiar, nodding hello to one another as we waited for the roll call, but did not speak much until the last day of my mother's treatment plan. Then began an arrestingly honest sharing of personal therapy experiences among several of the group, followed by an animated and remarkably informed discussion about whether "research" was producing any successful new cancer therapies, with decidedly mixed opinions.

I was listening with rapt attention, both as a scientist who is working to develop new therapeutics for cancer, and as a caregiver of a cancer patient. These patients were not only thinking about their treatments; they also fully

and personally understood the importance of research in their treatments. The conversation was brief, and ended with a spontaneous comment by the same woman who began. She simply said she was hopeful for research progress, and had agreed to take part in experimental treatments so that her daughters and granddaughters would not have to go through what she has experienced. She then went back to reading her magazine, leaving me with my thoughts, as Director, scientist and cancer caregiver, about the high hopes and real expectations of patients and the public in their support of biomedical research.

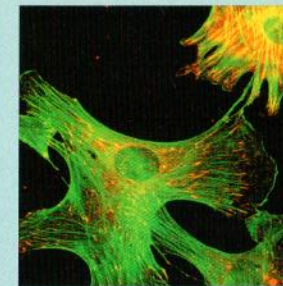
I am fully confident that the discoveries made by BBRI scientists in the next year and the coming years will be the basis for innovative therapies for many of the debilitating and untreatable human diseases that are the focus of our strategic initiatives, including stem cell cancers, muscular dystrophies and neurodegenerative and cardiovascular diseases. On behalf of our scientists, I am enormously thankful for the generous support and encouragement of BBRI's trustees and many friends for our new disease research initiatives. I look forward to working with you all in the coming year to continue to realize the promise of our shared vision of the brightest research future for BBRI.

Charles P. Emerson, Jr., Ph.D.
Director and Senior Scientist

innovation

With five new pieces of equipment in hand and seven newly recruited scientists on board, Boston Biomedical Research Institute is reaching forward in its quest to advance innovative disease-based research.

Since setting our strategic plan in motion, BBRI is continuing to define and expand our four programmatic areas of Cancer, Cardiovascular Biology, Degenerative Disease and Regenerative Biology and Proteomics. With the purchase of these five new pieces of equipment, and seven outstanding new scientific colleagues, BBRI scientists, working collaboratively with each other and with researchers in the greater Boston biomedical complex, will now be able to reach higher levels of innovative research with the hope of one day eradicating the world's most deadly diseases, including cancer, cardiovascular disease, Alzheimer's, Parkinson's and Huntington's diseases, muscular dystrophies as well as many other diseases and conditions.



BBRI welcomed seven outstanding new faculty members to the Institute in 2007.

James L. Sherley, M.D., Ph.D.
Senior Scientist

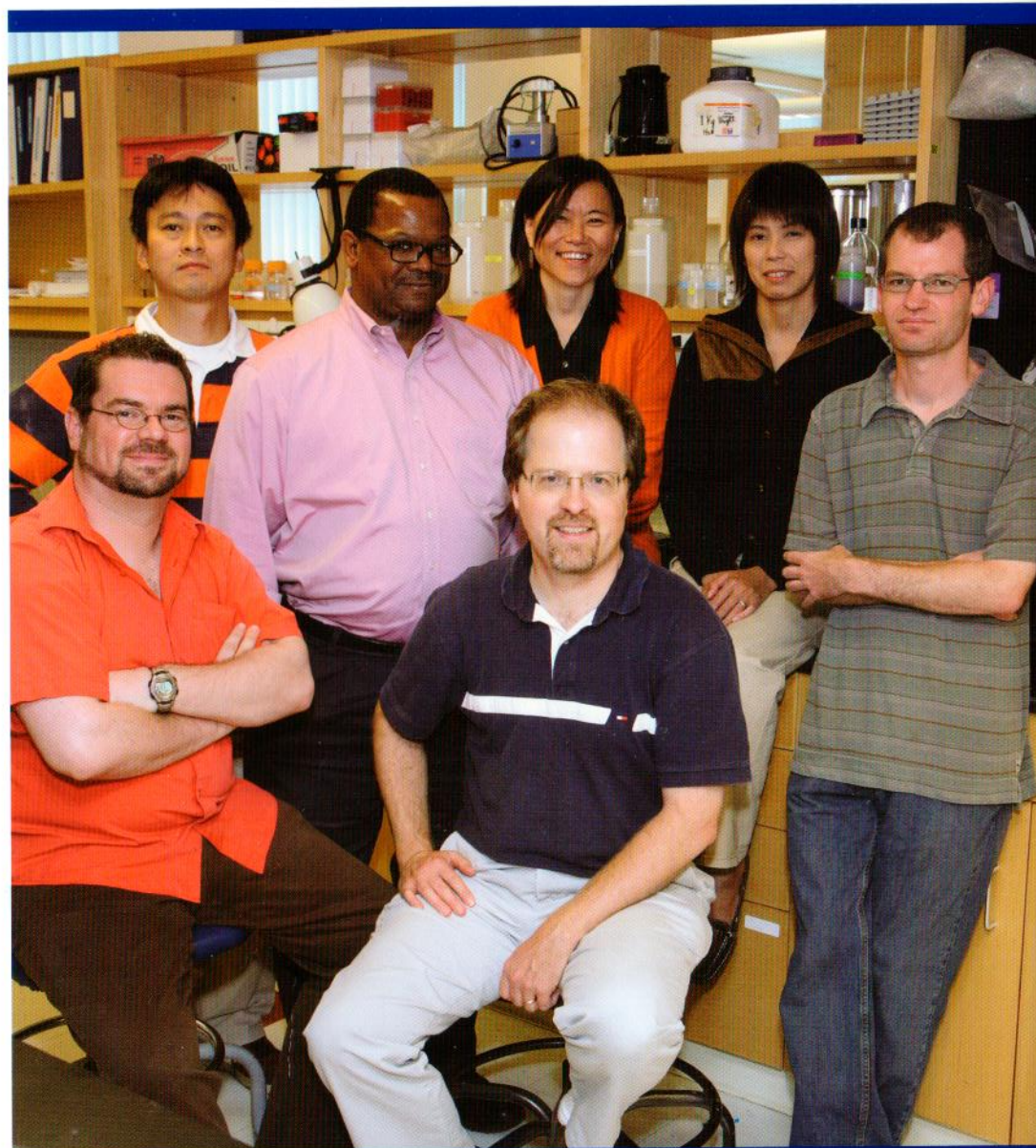
Dr. Sherley graduated from Harvard College with a B.A. in biology in 1980. He completed his M.D. and Ph.D. degrees from Johns Hopkins University School of Medicine in 1988. After post-doctoral studies at Princeton University, he joined the Fox Chase Cancer Center in Philadelphia as principal investigator in 1991. In 1998, he joined the future Biological Engineering Department at Massachusetts Institute of Technology. Dr. Sherley is a 1993 Pew Scholar, 2003 Ellison Medical Foundation Senior Scholar, and 2006 NIH Director's Pioneer Award recipient.

Dr. Sherley notes, "We are investigating normal molecular and biochemical processes in adult stem cells that are involved in cancer initiation and that contribute to aging. Adult stem cells are rare tissue cells that continuously replace expired tissue cells. Investigations of their specialized properties will yield new therapies for injured, diseased, and aging tissue cells. We employ an integrated approach, incorporating both basic and applied research strategies, to elucidate novel mechanisms of adult stem cell-specific functions and apply the knowledge to improve methods for identifying adult stem cells and producing them in large number for therapeutic development."

Shinichi Takayama, M.D., Ph.D.
Principal Scientist

Shinichi Takayama, M.D., Ph.D., comes to Boston Biomedical Research Institute from the Medical College of Georgia, where he was Assistant Professor at the Center for Molecular Chaperone Biology and also the Department of Radiology. He was a Research Assistant Professor as well as a Staff Scientist, Instructor and Postdoctoral Associate at The Burnham Institute from 1992 to 2004. In 1992 Dr. Takayama was a Fellow of Clinical Pathology at Sapporo Medical University. He received his Ph.D. in Pathology/Immunology and M.D. at Sapporo Medical University Graduate School and School of Medicine respectively.

Dr. Takayama describes his research: "We are investigating the biological function of molecular chaperone regulators, BAG family proteins. BAG family proteins interact to 70Kd family of molecular chaperones (Hsp70) and regulate their protein-folding activity. Molecular chaperones and their regulators (co-chaperones) maintain cellular homeostasis against environmental stress. Recently, we generated BAG3 gene deletion mice, which showed early lethality with massive muscle degeneration. BAG3 over-expression has been observed in human cancers and regulates cell motility in vitro and in vivo. One of our major goals is to find the mechanisms of how BAG3 regulates muscle integrity and cell motility."



New Scientists

Standing: (L-R) Shinichi Takayama, M.D., Ph.D., James L. Sherley, M.D., Ph.D., Moonkyoung Um, Ph.D., Sachiko Homma, Ph.D., Oliver King, Ph.D.
Seated: Martin L. Duennwald, Ph.D., Kent Nybakken, Ph.D.

Martin L. Duennwald, Ph.D. Scientist

Prior to arriving at Boston Biomedical Research Institute, Martin L. Duennwald, Ph.D. was a Postdoctoral Fellow with Dr. Susan Lindquist at the Whitehead Institute for Biomedical Research in Cambridge, MA. Dr. Duennwald received his Diploma in Biological Sciences at Albertus Magnus University in Cologne, Germany in 1997. He began his graduate work at the Max Delbrueck Laboratory, Max Planck Institute for Breeding Research, Cologne, Germany, before receiving his Ph.D. at Albertus Magnus University in 2001.

As Dr. Duennwald notes: "Proteins only function properly after folding into their specific three-dimensional conformation. Consequently, the misfolding of proteins can have catastrophic effects as exemplified by neurodegenerative diseases such as Alzheimer's, Parkinson's and Huntington's diseases (HD). To date, there are no effective therapies for these disorders and our understanding of their molecular pathology is limited. Focusing on HD, we aim to decipher how protein misfolding causes toxicity and devise new therapeutic approaches. To this end, we use diverse experimental models including yeast, cultured neurons, and mice along with a combination of genetic, biochemical, and cell biological experimental approaches."

Sachiko Homma, Ph.D. Research Scientist

Sachiko Homma, Ph.D. joins Boston Biomedical Research Institute having most recently served as Assistant Research Scientist at the Center for Molecular Chaperone/Radiology and Cancer Virology at the Medical College of Georgia. Dr. Homma was a Research Fellow at The Burnham Institute, and a Research Fellow in the Department of Medicine, Division of Physiology at the University of California, San Diego. She received her B.S. in Applied Physiology in 1989 and M.S. in Health Science in 1992 from the University of Tsukuba. Dr. Homma completed her Ph.D. in Physiology at Otsu Women's University in 1996.

Dr. Homma describes her research: "We are investigating the molecular mechanism of sarcopenia. Sarcopenia is the loss of muscle mass with aging and one of the most severe problems in geriatric medicine. Recently, it has been suggested that several muscle atrophy specific protein degradation pathways were activated in sarcopenia. Additionally, activation of apoptosis (cell-death)-related proteases have been observed in sarcopenia. Therefore, using mouse models with gene deletions and over expression of apoptosis-related genes, I will be investigating the role of apoptosis signaling pathways to understand the cellular and physiological processes that lead to sarcopenia. This research could give us clues to develop medical treatment or prevention of sarcopenia."

Oliver King, Ph.D. Scientist

Oliver King, Ph.D. comes to Boston Biomedical Research Institute from the Whitehead Institute in Cambridge, MA, where he was a Postdoctoral Associate. Dr. King received his Ph.D. in Mathematics at the University of California, Berkeley in 2001. Upon completion, Dr. King moved to Dr. Fritz Roth's laboratory in the Department of Biological Chemistry and Molecular Pharmacology at Harvard Medical School. In 2004, Dr. King moved to Dr. Susan Lindquist's laboratory at the Whitehead Institute to extend his work on applying mathematical models to quantitative phenotyping and functional genomics, phenotypic switching and evolutionary dynamics, protein evolution and co-evolution, and prion identification.

Dr. King's laboratory uses computational approaches to illuminate biological systems. Current research interests include modeling the evolution of proteins involved in neurodegenerative disorders, and analyzing high-throughput experimental data to understand how genetics and the environment interact to influence the phenotype of an organism.

Kent Nybakken, Ph.D. Scientist

Kent Nybakken, Ph.D. completed his Postdoctoral Fellowships in the laboratories of Dr. Norbert Perrimon at Harvard Medical School, and Dr. Michael Rosbash at Brandeis. He received his Ph.D. in Biochemistry from the University of California, San Francisco in 1999, working on signaling pathways in the lab of Dr. Michael Bishop.

Dr. Nybakken discusses the work of his laboratory: "We are investigating the function of the Hedgehog (Hh) pathway, a signaling pathway important in normal development, stem cell regulation, and cancer. We use the fruit fly, *Drosophila melanogaster*, and vertebrate cell lines as models in which to discover new components of Hh signaling and to dissect their roles in the pathway. A genome-wide screen we recently conducted in *Drosophila* cells using RNA interference revealed a host of new Hh signaling factors, and we are presently in the process of ordering these new components in the pathway. Among the new regulators we identified are intracellular trafficking regulators, RNA regulatory genes, and a phosphatase. By elucidating the Hh signaling pathway, this research will identify new therapeutic targets in both Hh-related cancers and in stem cell regulation."

Moonkyoung Um, Ph.D. Scientist

Since receiving her Ph.D. from Columbia University in 2000 with Dr. James Manley, Moonkyoung Um, Ph.D. has been a Postdoctoral Associate/Fellow at the Whitehead Institute for Biomedical Research in Cambridge, MA, with Dr. Harvey F. Lodish. Dr. Um completed both her B.S. and M.S. at Seoul National University, College of Pharmacy, and was Clinical Pharmacist at Seoul National University Hospital in the Republic of Korea until she began her graduate work at Columbia.

Dr. Um notes: "The major interest of my laboratory is to determine the role of hormones in preventing neuronal loss during the progression of neurodegenerative diseases. In particular, we are investigating neuroprotection conferred by the hematopoietic cytokine, erythropoietin, in Parkinson's and Huntington's diseases, and elucidating the molecular mechanism underlying this activity. The goal of our research is to understand how neurons are protected by cytokines under the devastating pathological conditions of neurodegenerative diseases. Additionally, these studies will provide an important basis for the therapeutic application of erythropoietin in neurodegenerative diseases and for developing therapeutic strategies for their treatments."

HIGH-THROUGHPUT INSTRUMENTATION

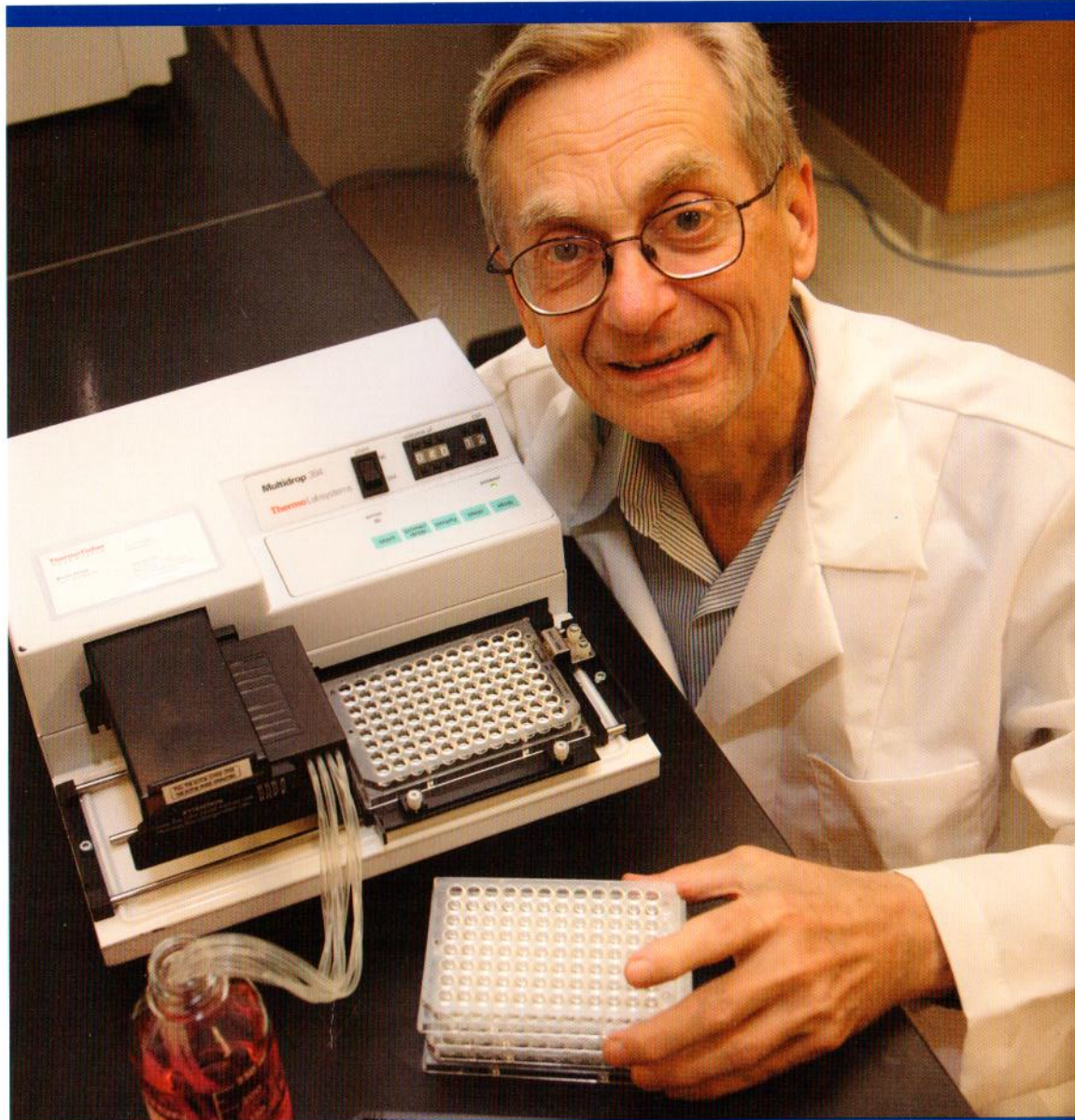
The availability of this powerful instrumentation will stimulate many new projects and innovative approaches to understanding and treating human disease.



BBRI's new liquid dispenser can transfer micro-liter volumes of fluids with high accuracy in fewer than 15 seconds.

In the past decade, there have been important changes in the way biomedical research is conducted in order to address ever more complex questions: can one identify a chemical substance that prevents cancer cells from growing without affecting normal cells? Whereas most experiments used to involve at most a few dozen test tubes, today's research is often carried out in a high-

throughput mode, involving many thousands of samples, which, instead of test tubes, use microwell plates that each can accommodate hundreds of very small samples in tiny volumes corresponding to a small drop of water. These plates have to be filled robotically; BBRI's new liquid dispenser can transfer micro-liter volumes of fluids to the wells of a 384-well microplate with high accuracy in fewer than 15 seconds. After filling a series of such plates with the appropriate combination of components, they are incubated and then analyzed for the biochemical changes that have occurred. This involves measurement of changes in color, fluorescence, or luminescence, which can be conducted automatically with high accuracy and speed using BBRI's new Safire microplate reader.



Henry Paulus, Ph.D., Senior Scientist

BBRI's high-throughput instrumentation will find immediate use in a number of projects, from identifying the genes required for hedgehog signaling in the fruit fly and in pancreatic cancer to the screening for chemicals that can compensate for the folding defect in the protein that causes Huntington's disease.

Lynne Coluccio, Ph.D., Senior Scientist

Dr. Lynne Coluccio is studying the protein myosin-1, which is key to cell movement. Myosin-1 has a specialized function in the inner ear and its study may shed light on the causes of deafness.



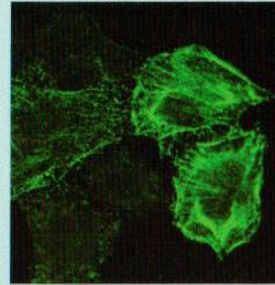
SPINNING DISK CONFOCAL MICROSCOPE

Live-cell imaging is a powerful experimental tool that enables researchers to view live cells, allowing real-time, multidimensional mapping of biological events as they occur.

BBRI's new spinning disk confocal microscope offers the highest spatial resolution that is available today. This comes at a cost, for scanning an entire cell with a single laser beam limits the time resolution. The spinning disk confocal microscope compensates for this problem by scanning a cell using hundreds of light beams, generated by passing light through a rapidly rotating disk perforated with hundreds of pin-holes, a technology that was used for the first television transmission in the 1920s.

Live-cell imaging is a powerful experimental tool that enables researchers to view live cells, allowing real-time, multidimensional mapping of biological events as they occur. This type of dynamic cellular analysis will be indispensable to several very promising, disease-based research programs currently underway at Boston Biomedical.

Many laboratories at BBRI will benefit from the new live-cell imaging capability. This includes Dr. Peter Erhardt, who is investigating programmed cell death with the aim of preventing the tissue damage that occurs after a heart attack and Dr. Lucia Rameh, who is studying the cellular function of a novel phosphoinositide molecule and its role in cancer and diabetes.



An image of a cluster of human cancer cells engineered to express fluorescently labeled non-muscle myosin II, a filamentous protein required for cell movement, cell division and cell-cell adhesion. Myosin II, which appears green, can be seen at the cell periphery and throughout the cell interior especially in the cells on the right, which are expressing myosin II at high levels.

FLOW CYTOMETER

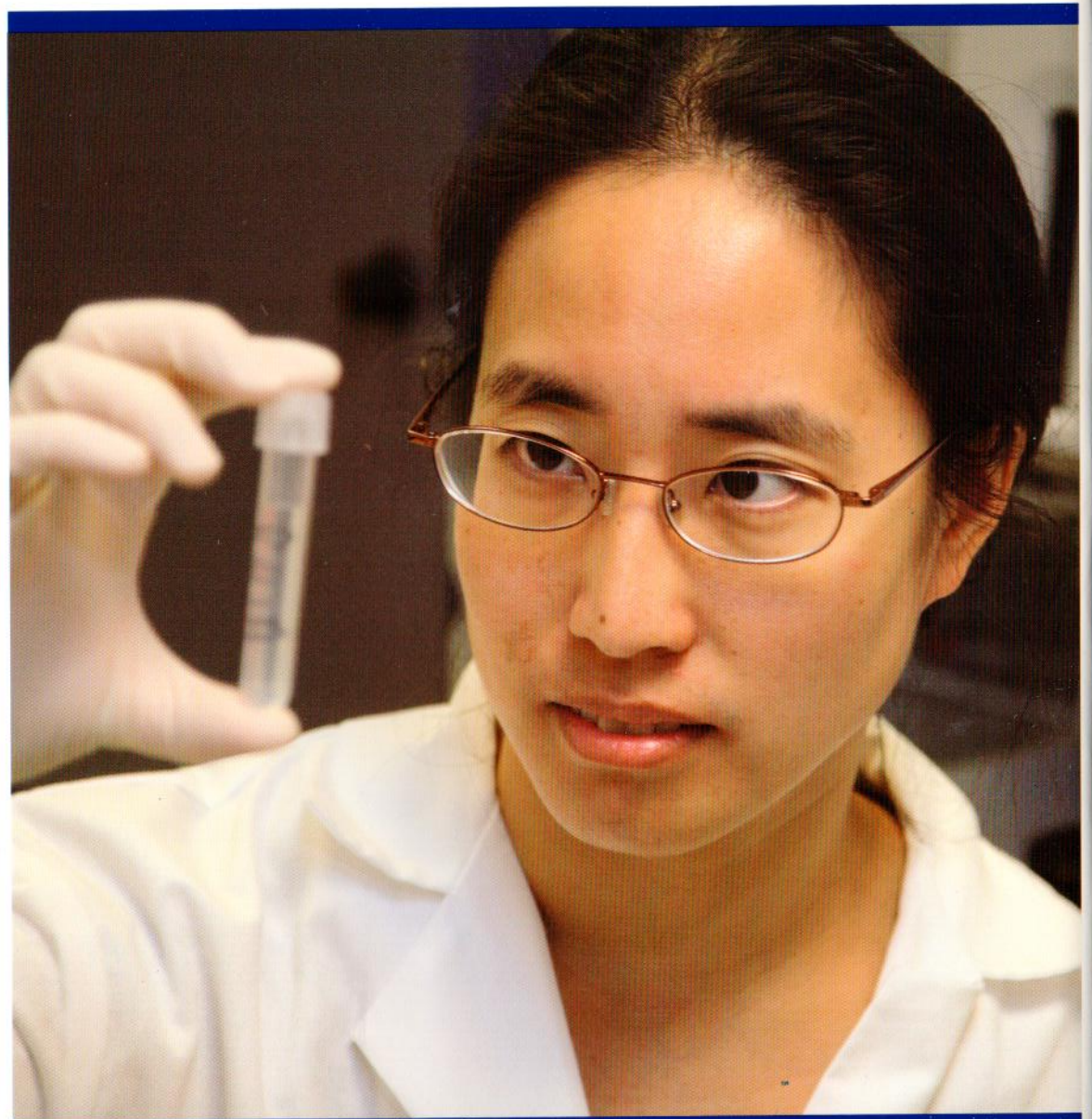
BBRI scientists are now able to reach the required high-speed sorting capacity (20,000-30,000 cells per second) and multicolor analysis producing an exceptional degree of sensitivity and accuracy.



Special sensors monitor how a cell scatters light in order to determine properties such as size and cell complexity.

Scientists at Boston Biomedical Research Institute studying cancer, regenerative and stem cell biology, proteomics, immunology and cardiovascular disease depend on the ability to rapidly and accurately distinguish, count, and sort specific types of cells at the single cell level from a mixed population. This “high throughput analysis” is achieved using a flow cytometer, which feeds the

mixed population through a beam of light; special sensors monitor how a cell scatters light in order to determine properties such as size and cell complexity. Additionally, a series of fluorescent light detectors can recognize cells expressing proteins of interest that are bound by specific fluorescence-tagged antibodies, providing added power to the technique. The previously existing flow cytometry needs at Boston Biomedical were able to achieve both data collection and analysis, at a sorting rate of up to 300 cells per second. Now, with this new piece of equipment BBRI scientists are able to reach the required high-speed sorting capacity (20,000-30,000 cells per second) and multicolor analysis producing an exceptional degree of sensitivity and accuracy.



Jennifer Chen, Ph.D., Postdoctoral Research Fellow

Dr. Jennifer Chen and scientists at BBRI will use this new technology to further their studies in multiple avenues including identifying and analyzing cancerous cells so that novel therapies can be tested, and isolating and characterizing tissue-specific stem cells for functional testing in cardiovascular, muscle and neural regeneration models.

Eric Sundberg, Ph.D., Scientist

Dr. Sundberg is elucidating the molecular mechanisms by which bacterial toxins, known as superantigens, cause disease. Superantigens over-stimulate the immune system, which can lead to autoimmune disorders and numerous diseases including toxic shock syndrome. Dr. Sundberg's research has led to the development of peptides that can reverse the effect of toxic shock syndrome in a rabbit model.



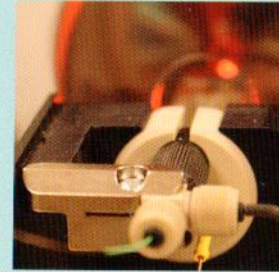
MASS SPECTROMETER

The new mass spectrometer will benefit all BBRI scientists who study the control of cell growth and development, cell signaling pathways, and tissue regeneration.

The study of proteins, in which mass spectrometry has become an essential tool, is critically important to disease-based research because proteins carry out most of life's functions and as such are targets of therapeutics for disease.

Proteins can be fragmented into peptides, each of which has a unique molecular mass. If the molecular mass of peptides could be determined with high accuracy, it would be possible to identify the protein from which they are derived. Modern mass spectrometers not only determine molecular masses with great precision but can further fragment peptides to elucidate the sequence of their amino acid to allow unambiguous identification.

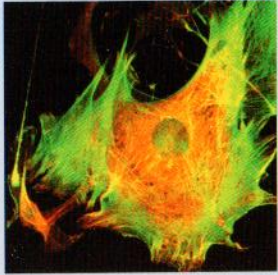
BBRI is a recognized leader in the area of protein structure and in what is now called proteomics. The new state-of-the-art mass spectrometer will benefit all BBRI scientists whose research is focused directly on proteins and also the growing number of our scientists who study the control of cell growth and development, cell signaling pathways, and tissue regeneration as well as the changes that occur in cancer, cardiovascular disease, muscular dystrophy, and degenerative diseases.



Modern mass spectrometers determine molecular masses with great precision.

LASER SCANNING CONFOCAL MICROSCOPE

Confocal microscopy can be applied to living cells and provides valuable information about how specific molecules are distributed and migrate between various parts of a cell.

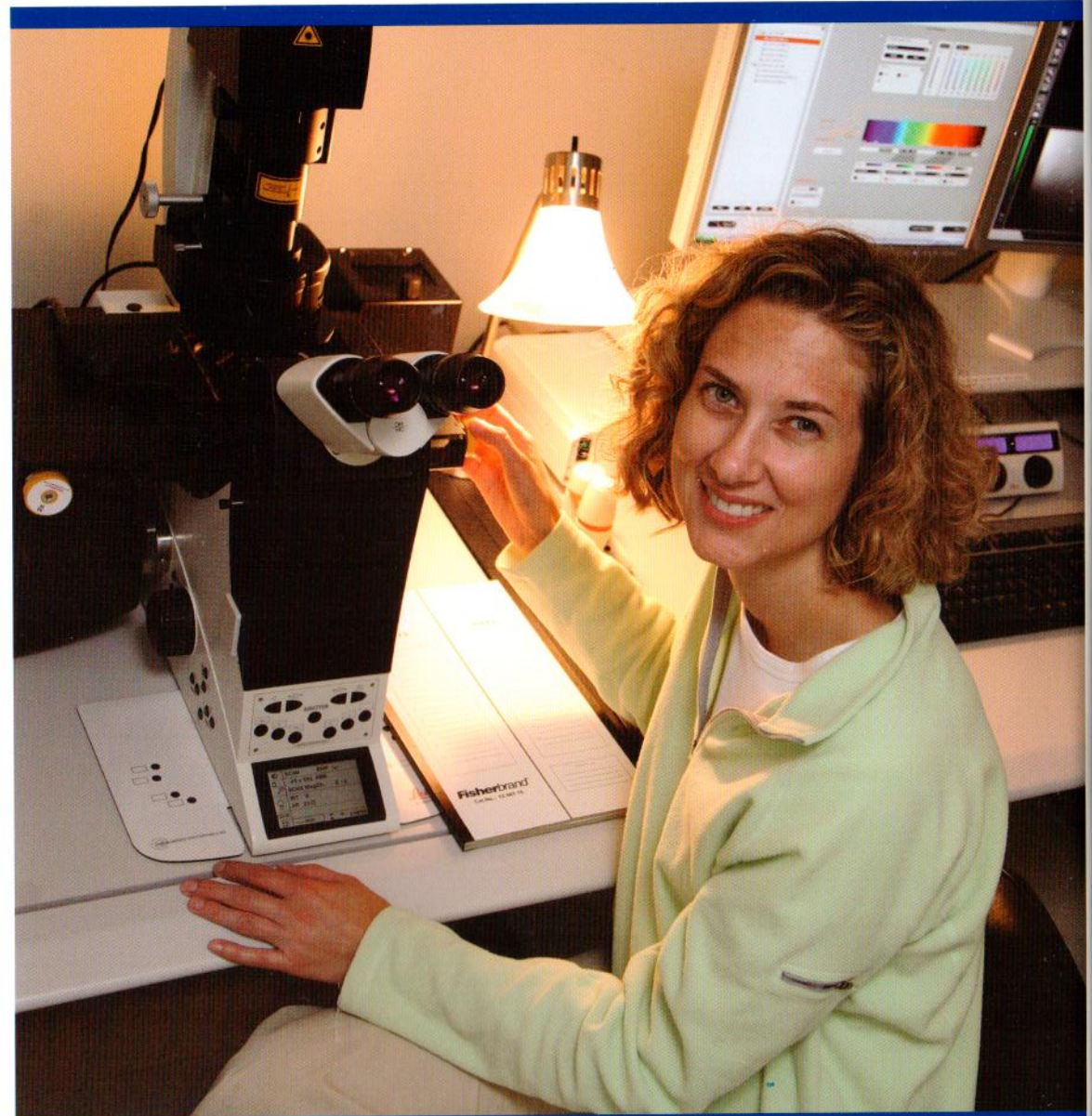


A dermal fibroblast cell is stained by a marker protein (shown in red) to show where the focal adhesions are located, which are points where cells are attached to matrix proteins.

Microscopy has always been an important medical research tool; indeed, in 1839, Theodor Schwann, upon examining tissue samples in the light microscope, concluded that cells are the basic building blocks of living organisms. Today, we know that a human being is composed of 100 trillion cells, all of which derive by the repeated divisions of a single fertilized egg.

Laser-scanning confocal microscopy, which was invented 50 years ago by Marvin Minsky at MIT, is an ingenious method for analyzing the distribution of fluorescently labeled molecules within a cell. It involves scanning a cell at different planes with a laser beam, narrowed by passage through a pin-hole, and then reconstructing a 3D image of the cell from the planar cross-sections analogous to the reconstruction of the image of a human body after a CAT scan.

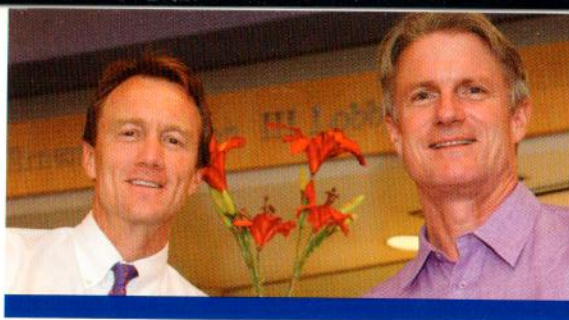
Unlike conventional light microscopy, which requires fixing and sectioning a tissue, confocal microscopy can be applied to living cells and provides valuable information about how specific molecules are distributed and migrate among various parts of a cell. This provides important insights into the functioning and dynamics of cells and how these processes are altered by cancer and other disease states.



Sarah Wilcox-Adelman, Ph.D., Research Scientist

Dr. Sarah Wilcox-Adelman and her fellow scientists look to understand protein interaction which promotes cell movement, causes cells to divide, or modifies higher-order processes such as muscle contraction and nerve firing in the brain. These studies have relevance to cancer, muscular dystrophy and Alzheimer's disease.

"As we move into 2008, we aim to expand our efforts with the goal of introducing many new faces to the Institute."



Two thousand and seven brought many new challenges to the Advancement Committee. Our committee has grown as new Trustees and Corporators joined us to raise important funds for the newly identified programmatic initiatives. We also launched new efforts to help Boston Biomedical obtain essential pieces of equipment, including a successful challenge campaign completed this year.

The Institute's new mass spectrometer, acquired through this challenge campaign, will be a tremendous boost to the basic research programs at Boston Biomedical. Many thanks to all of the dedicated donors and friends who supported us in reaching this goal, as well as to the Thoracic Foundation which made a substantial gift in helping us complete this challenge. Several corporation members also made substantial gifts to the challenge campaign, to whom we are especially grateful.

In September, and again in May, Corporator Kitty Flather, with the help of Trustee Allie Flather Blodgett, graciously opened her home to more than twenty-five women friends who are new to the Institute, for the *West Cedar Street Series, Women of Science* events. These exciting gatherings gave us the opportunity to introduce several of Boston Biomedical's women scientists and showcase their continued efforts in research-

ing some of the most deadly diseases with the aim of one day eradicating them and providing innovative new therapeutics.

The Advancement Committee's Vice Chair Stuart Watson and his wife Karen, opened their home to more than fifty friends who are new to Boston Biomedical, in March. Although the power went out for a brief time, the lack of light could not detract from the enthusiasm generated by Dr. Eric Sundberg and Dr. Sarah Wilcox-Adelman as they shared details of their current work and explained the functions of the newly purchased mass spectrometer.

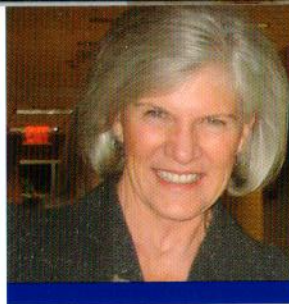
In May, we held our very successful 2nd Annual *Walk for Science Education*, with the invaluable support of our Presenting Sponsor Enanta Pharmaceuticals, Inc., State Representative Rachel Kaprielian, Trustee Paul Airasian and the other dedicated members of the Science Education Outreach Committee. For this popular event, Boston Biomedical's faculty and staff joined students and teachers from Watertown and Belmont High Schools, along with community members, for a five kilometer walk around the Charles River. We are happy to report that with the help of more than fifty walkers and several corporate sponsors we were able to raise more than \$23,000 for our Science Education Outreach Program.

As we move into 2008, we aim to expand our efforts with the goal of introducing many new faces to the Institute. With the formation of the four new programs, the recruitment of brilliant new scientists, and the purchasing of advanced pieces of equipment will come many exciting innovations and collaborations, all of which we hope to share with you. We invite all of our donors and friends to join us in helping to raise funds and awareness for the disease-based research underway at Boston Biomedical Research Institute with the goal of achieving a healthier future for us all.

Nathaniel S. Howe, Jr.
Chair

Stuart H. Watson
Vice Chair

PARTNERS IN DISCOVERY



"What a pleasure to be hosting the West Cedar Street Series featuring our own Women of Science at BBRI. This series has developed quite a following, and our new friends are eagerly awaiting the next conversations with these brilliant scientists to learn more about ground-breaking research."

— Kate Sides Flather, Corporator

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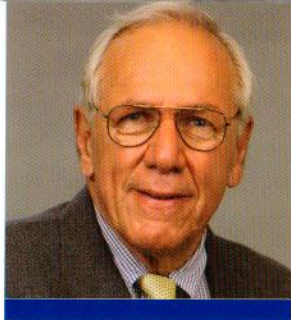
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"BBRI improved its financial strengths as measured by an increase in unrestricted net assets for the fiscal year ended June 30, 2007, while meeting its financial bond requirements."

BBBRI identified four programmatic initiatives in its strategic planning process during fiscal year 2006. These initiatives include the areas of Cancer, Cardiovascular Biology, Degenerative Disease and Regenerative Biology and Proteomics. BBRI successfully recruited seven extremely talented faculty members during fiscal year 2007 which will help solidify each of the four programs. BBRI is confident that these new scientists will enable the Institute to become a leader in cutting-edge biomedical research.

BBRI improved its financial strength as measured by an increase in unrestricted net assets of \$805,000 for the fiscal year ended June 30, 2007, while meeting its financial bond requirements. The Statements of Financial Position reflect total assets at June 30, 2007, of approximately \$43,285,000. Investments, including investments in limited partnerships, approximated \$18,992,000 as of June 30, 2007, an increase of approximately \$1,413,000 over the prior year. The investment portfolio had another strong year with an annual total return of 14.2%. Grants receivable approximated \$6,925,000 as of June 30, 2007, a decrease of approximately \$3,185,000 over the prior year. This decline was due to the anticipated departure of two investigators, who left for leadership positions elsewhere, coupled with the highly competitive environment for securing federal funds.

The Statements of Activities show total

unrestricted support approximated \$13,797,000 for the year ended June 30, 2007, an increase of \$201,000 over the year ended June 30, 2006. BBRI revenues from grants and contracts approximated \$10,998,000 for the year ended June 30, 2007, a decrease of \$806,000 over the prior year. Revenue from federal agencies represents approximately 95% of such revenue. BBRI has been impacted by the increasingly competitive environment in securing federal funds shared with the experience of its peer institutions. During the last fiscal year the Institute continued to diversify its grant revenue sources and was awarded two new grants from the National Institutes of Health, one new grant from the Muscular Dystrophy Association, four new foundation awards and two new biotech company awards.

Charitable giving is an increasingly important revenue source for BBRI. Total contributions approximated \$783,000 during fiscal year 2007. Unrestricted, temporarily restricted and permanently restricted contributions approximated \$339,000, \$373,000 and \$71,000, respectively. These contributions help support important activities not covered by grants from federal agencies and not-for-profit foundations and associations. They also support Principal Investigator research programs, the purchase of scientific equipment and educational initiatives. BBRI is extremely grateful for each donor's generous support. We look forward to continue working with our loyal donors to help BBRI identify and

expand its network of friends, advocates and supporters. This effort is essential to the success of BBRI over the next few years as it implements the strategic initiatives and vision of Dr. Emerson and his scientific colleagues which will strengthen its position of excellence in basic research.

Unrestricted investment income of \$1,994,000 for the year ended June 30, 2007, reflected strong stock market performance.

Total expenses of \$12,992,000 decreased approximately \$751,000 or 5.5% over the prior year due to a decline in research funding as well as a continued commitment to cost containment and purchasing efficiencies.

BBRI exceeded its debt service coverage ratio requirement of 110% for the fiscal year and increased its liquidity ratio (a measure of unrestricted cash and investments available to satisfy outstanding bond debt) to 125% as of June 30, 2007, from 118% as of June 30, 2006.

Once again, I would like to thank Tom DiBenedetto for his expert leadership of the Investment Committee as well as the other members for their thoughtful guidance and insight.

Respectfully submitted,

Geoffrey Nunes, Esq.
Treasurer

STATEMENTS OF FINANCIAL POSITION

	2007	2006
ASSETS:		
Cash	\$1,496,890	\$1,677,438
Grants receivable	6,924,948	10,110,175
Unconditional promises to give	55,917	463,291
Investments	18,282,534	17,307,354
Prepayments, deposits and other receivables	153,295	155,106
Trustee-held funds	1,245,752	1,245,704
Property and equipment	13,576,129	13,570,195
Investments in limited partnerships	709,014	270,828
Deferred compensation investments	840,524	749,796
Total assets	\$43,285,003	\$45,549,887
LIABILITIES AND NET ASSETS:		
Accounts payable and accrued expenses	\$608,294	\$562,106
Accrued interest expense	358,535	365,723
Deferred income	7,104,771	10,222,093
Note payable	1,259	3,660
Obligation under capital lease	108,392	150,387
Bonds payable	14,910,000	15,255,000
Deferred compensation payable	840,524	749,796
Total liabilities	23,931,775	27,308,765
NET ASSETS:		
Unrestricted	16,061,719	15,256,875
Temporarily restricted	1,038,427	802,848
Permanently restricted	2,253,082	2,181,399
Total net assets	19,353,228	18,241,122
Total liabilities and net assets	\$43,285,003	\$45,549,887

STATEMENTS OF ACTIVITIES

	2007	2006
CHANGES IN UNRESTRICTED NET ASSETS:		
Revenues:		
Grants and contracts	\$10,997,688	\$11,803,438
Contributions	338,898	342,560
Investment income	1,994,042	1,354,718
Other income including licensing fees, net	3,168	41,725
Total unrestricted revenues	13,333,796	13,542,441
Net assets released from restrictions	462,911	53,191
Total unrestricted support	13,796,707	13,595,632
Expenses:		
Salaries and benefits	7,968,659	8,411,630
General support and services	1,734,457	2,031,139
Occupancy costs	1,384,655	1,402,108
Interest expense	865,164	884,621
Depreciation	1,038,928	1,013,707
Total expenses	12,991,863	13,743,205
Increase (Decrease) in unrestricted net assets	804,844	(147,573)
CHANGES IN TEMPORARILY RESTRICTED NET ASSETS:		
Contributions	372,700	—
Investment income	325,790	212,486
Net assets released from restrictions	(462,911)	(53,191)
Increase in temporarily restricted net assets	235,579	159,295
CHANGES IN PERMANENTLY RESTRICTED NET ASSETS:		
Contributions	71,683	12,361
Increase in permanently restricted net assets	71,683	12,361
Increase in net assets	1,112,106	24,083
Net assets at beginning of year	18,241,122	18,217,039
NET ASSETS AT END OF YEAR	\$19,353,228	\$18,241,122

EDUCATION PROGRAMS

Through a range of Education Programs, BBRI shows its commitment to building the public's awareness of the excitement and promise of basic biomedical research.

WALK FOR SCIENCE EDUCATION

The Walk for Science Education presented by Enanta Pharmaceuticals and held on Friday, May 11, 2007, at Artesani Park in Watertown, raised over \$23,000 for Boston Biomedical Research Institute's Science Education Outreach Program.

Presenting Sponsor of this year's Walk for Science Education, Enanta Pharmaceuticals, Inc.



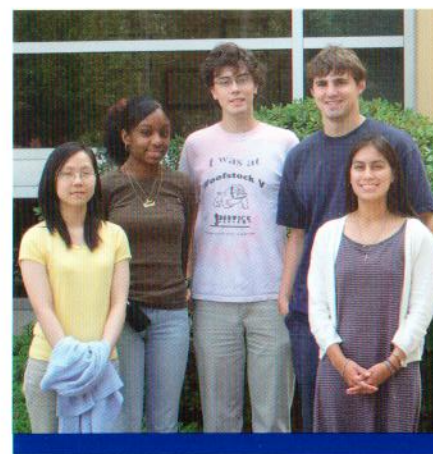
Honorary Chairperson, State Representative Rachel Kaprielian along with (L-R) Boston Biomedical Trustees, Paul M. Airasian, Nathaniel Howe, Jr. and Jillian Hosford Darling helped kick off the 2nd Annual Walk for Science Education at Watertown's Artesani Park.



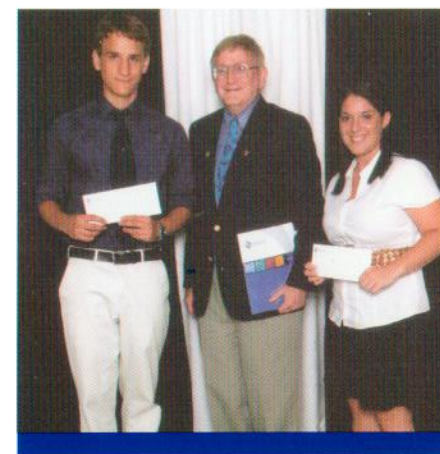
2007 Student Science Expo presenters representing Watertown High School and Belmont High School.

SCIENCE EDUCATION OUTREACH PROGRAM

Boston Biomedical Research Institute is committed to bringing the excitement of discovery science to young people and introducing them to careers in scientific research. Our Science Education Outreach Program includes summer internships for students as well as teachers, scientist visits to local classrooms and college scholarships for high school seniors pursuing a degree in science. Boston Biomedical Research Institute's Outreach Program was launched in 2000 and is conducted in collaboration with local schools in the metropolitan Boston area.



Summer interns (L-R) Eleanor Wu, Nikki Louis, David Lapham, Zachary Ethind and Lauren Sarson.



Scholarship winners Adam Clark and Christine Sideris with Boston Biomedical Corporation, George Buckley (center).



(L-R) Mr. and Mrs. Dan Perez of FSHD Society, Dr. John Gergely, and Dr. Charles Emerson, Jr.

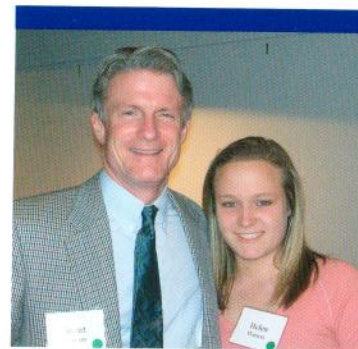
DR. ELKAN R. BLOUT DISTINGUISHED ISRAELI BIOMEDICAL RESEARCH PROGRAM

Boston Biomedical Research Institute launched the Distinguished Israeli Biomedical Research Program on Tuesday, June 12. Speakers at the event included Rony Yedidia, Consul of Israel, New England; Jonathan Fleming, Managing General Partner, Oxford Bioscience Partners, Robin Blatt, Director of Combined Jewish Philanthropies' Boston Haifa Life Science Initiative, and Boston Biomedical's Director Dr. Charles P. Emerson, a leader in cancer research.



The new program, the first of its kind, will provide selected Israeli postdoctoral fellows from leading Israeli research institutions a three-year fellowship at Boston Biomedical Research Institute in post-genomic research including stem cell research and proteomics.

Trustee Janie Stephenson with Robin Blatt of Boston Haifa Life Science Initiative.



Trustee Stuart H. Watson and daughter Helen.

THE NEXT GENERATION OF DISCOVERY

Boston Biomedical Research Institute's next generation of scientists, our postdoctoral fellows, invited our family and friends to explore their labs and look into their microscopes to learn first hand about the discoveries that will bring forth the cures for tomorrow.

Event presenter and Boston Biomedical Research Institute Postdoctoral Fellow, Adel Mandl, M.D.



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NATIONAL INSTITUTES OF HEALTH

Dr. Coluccio

Molecular Mechanism of a Mammalian
Class I Myosin Motor 2/04-1/08 \$1,668,000
NCRR Shared Instrumentation Grant (SIG) Program 4/07-3/08 \$457,000*

Dr. Dominguez

Structural Basis of Actin Cytoskeleton Dynamics 4/05-3/09 \$1,632,000
Structure of the Smooth Muscle
Myosin Phosphatase 9/03-11/08 \$2,465,000

Dr. Dominov

Apoptosis in Laminin-Alpha2 Deficiency 4/05-3/10 \$2,148,000

Dr. Erhardt

Prevention of Myocardial Ischemic Injury by RAF/ERK 4/03-3/08 \$1,471,000

Dr. Emerson

Control of Muscle Protein Synthesis
during Myogenesis 7/05-6/10 \$4,258,000
Sonic Hedgehog Target Genes in Development
and Cancer 12/03-11/07 \$1,900,000

Dr. Fessenden

Molecular Mechanisms of RyR Activation by 4-CmC 8/05-4/08 \$389,000

Dr. Gangopadhyay

CaMK II Variants and Vascular
Smooth Muscle Function 4/04-3/07 \$156,000

Dr. Goetnick and Dr. Wilcox-Adelman

Syndecan-4 Signaling in Cell-matrix Interactions 3/06-2/09 \$1,285,000

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Smooth Muscle Thin Filament 8/01-7/06 \$1,892,000

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Structure and Function of Sarcoplasmic Reticulum 4/02-3/08 \$3,030,000
Regulation of Normal and Diseased Cardiac
Ca²⁺ Channels 4/03-3/08 \$1,682,000

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Mechanism of Ca²⁺ Sensitization in Smooth Muscle 6/02-5/08 \$2,876,000

Dr. Lehrer

Tropomyosin and the Regulation of Muscle Contraction 7/05-6/09 \$1,950,000

Dr. Lieto

Role of Unconventional Myosin Myo1c in Cell Motility 9/04-8/07 \$139,000

Dr. Miller

Neurotoxicogenomics and Child Health 11/01-8/06 \$1,506,000
Pathogenesis of Laminin-Alpha2 Deficiency 9/02-8/07 \$1,291,000
Molecular Physiology of Respiratory Muscles 4/06-2/11 \$2,669,000

Dr. Morgan

Subcellular Organization of Signaling in
Striated Muscle 8/06-7/10 \$1,950,000*
Signaling & Uterine Contractility during Pregnancy 8/03-6/08 \$1,696,000
Regulation of Contraction of Blood Vessels 7/05-6/10 \$2,194,000

Dr. Rameh Plant

The Role of PtdIns-5-P in Cell Function and Signaling 6/03-3/08 \$1,752,000

Dr. Raso

Immunotherapeutic Agents to Treat
Alzheimer's Disease 9/00-8/06 \$1,958,000

Dr. Smith

Cell Development and Function 3 11/03-12/07 \$1,343,000

Dr. Stafford

Structure-Function Study of Angiogenic
Protein, Ephrin 7/01-6/07 \$1,261,000

Dr. Tao

Mechanism of Calcium Regulation in Striated Muscle 6/03-5/08 \$3,205,000

Dr. Wang (Pro. Proj.)

Molecular Mechanism of Smooth Muscle Regulation 12/02-11/07 \$10,356,000

UNITED STATES DEPARTMENT OF AGRICULTURE**Dr. Miller**

Poultry Muscle Development: Molecular & Cellular Biology 1/06-9/09 \$360,000

JOHN W. ALDEN TRUST**Dr. Dominov**

Cell Death Mechanisms in a Congenital Muscular Dystrophy Model 6/07-5/08 \$25,000*

AMERICAN HEART ASSOCIATION**Dr. Khalina**

Evaluation of Regulatory Properties of Smooth Muscle Thin Filaments using a Caldesmon Knockout Model 7/06-6/08 \$76,000*

Dr. Vetterkind

Characterization of a Novel Branch of the Signaling Network that Controls Vascular Muscle Contraction 7/06-6/08 \$76,000*

CONCERN FOUNDATION**Dr. Ai**

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Regulation of Satellite Cell Development and Muscle Regeneration by Two Extracellular Herparan Sulfate 6-O Endosulfatases 1/06-12/08 \$135,000

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Sulfs Function as Regulators of Extracellular HS-mediated Signaling 6/07-6/08 \$163,000*

**New grants in fiscal 2007*

PUBLICATIONS

Boston Biomedical Research Institute's Art Program, centered in our lobby gallery, provides exhibits of local emerging artists and was recently expanded to include an artist-in-residence program with the School of the Museum of Fine Arts. The first BBRI-SMFA Artist in Residence was Julie Miller. The 2006-2007 art exhibits also included a show by six of BBRI's own faculty members, entitled "Our World Through Scientists' Eyes," which was organized by Dr. Sam Lehrer.

PERIOD: JULY 2006 – JUNE 2007

Adjunct Scientist publications are not included.

Ahn, D. S., Choi, S. K., Kim, Y. H., Cho, Y. E., Shin, H. M., Morgan, K. G. & Lee, Y. H. (2007). Enhanced stretch-induced myogenic tone in the basilar artery of spontaneously hypertensive rats. *J Vasc Res* 44, 182-91.

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Our World Through Scientists' Eyes
December 18, 2006 – February 26, 2007
Dr. Sherwin S. Lehrer
"Axle"

New Work

Julie Miller, BBRI SMFA 2006-2007

Artist in Residence

May 24 - August 31, 2007

"Study for $\alpha(16)$ "



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PENDING U.S. PATENTS

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Compositions and methods for binding or inactivating Grehlin, Victor Raso, filed 11/6/06

Methods for identifying modulators or Hedgehog autoprocessing, Henry Paulus, Charles Emerson, Xingbin Ai, filed 12/5/05

Methods and compositions for specific inhibition of protein splicing by small molecules for the treatment of tuberculosis, Henry Paulus, filed 1/24/05

Development and biological effects of leptin peptide antagonists (LPAs), Ruben Rene Gonzalez, Paul Leavis, filed 5/7/2004

Methods for preventing or reducing ischemia/reperfusion induced myocardial cell death, Peter Erhardt, filed 4/13/2004

Inhibition of FGF signaling, Charles Emerson, Xingbin Ai, filed 2/13/2004

Methods for screening chemical compounds and genes that reverse polyglutamine toxicity, Michael Sherman (with Massachusetts Institute of Technology)



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Methods and compositions relating to anthrax pathogenesis, Andrew Bohm (with University of Chicago), filed 11/1/02

Use of Sulf Proteins and Heparan Sulfate in GDNF-Dependent Neural Innervation and Protection, Charles Emerson, Xingbin Ai, filed 7/17/07

ISSUED U.S. PATENTS

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US 6,872,554: Immunological control of β -amyloid levels in vivo, Victor Raso, Issued 3/29/2005

US 6,140,091: Anti-idiotypic vaccines to elicit catalytic antibodies, Victor Raso and Henry Paulus, Issued 10/31/2000

US 6,096,711: Heat shock protein induction and applications, Michael Sherman, Issued 8/1/2000

US 6,858,775: Methods for generating split, non-transferable genes that are able to express and active protein product, Henry Paulus (with New England Biolabs), Issued 2/22/2005

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