BOSTON BIOMEDICAL RESEARCH INSTITUTE

Faculty Book Summaries

Andrew Bohm, Ph.D.

Scientist, Boston Biomedical Research Institute

Adjunct Assistant Professor of Biochemistry, Tufts University

Ph.D. University of California, Berkeley, CA, Biophysics, 1992

B.S. State University of New York at Binghamton, Biochemistry, 1987

Our laboratory uses X-ray crystallography and biochemical methods to determine the molecular structure and functional dynamics of proteins. In 2000, we solved the structure of Poly(A) polymerase, the protein at the core of the multi-protein complex which modifies the end of messenger RNA. This modification occurs in all organisms, and in humans, defects in RNA modification cause thalassemias, arylsufatase A pseudodeficiency, and potentially also sporadic amytrophic lateral sclerosis (Lou Gehrig's disease). More recently, we determined the structure of "edema factor," one of three toxins produced by the anthrax bacillus. Edema factor helps anthrax suppress the natural immune response to the attacking bacteria, and severely disrupts the cells of anthrax victims. We are currently working to design drugs that will inhibit edema factor. Such drugs might prove useful not only against anthrax, but also against other bacteria such as *Bordetella pertussis*, which causes whooping cough.

Keywords: arylsufatase A pseudodeficiency, thalassemia, anthrax, whooping cough

Dr. Bohm is married to BBRI Scientist Celia Harrison, and these days he is too busy with his young daughters to keep up with the lawn, much less do anything really interesting outside of work. Before becoming a family man, Andrew was an avid sailor who lived for three years aboard his 33 foot sailboat, the "Cafe Mildew."

Lynne M. Coluccio, Ph.D.

Senior Scientist, Boston Biomedical Research Institute

B.S. State University of New York at Albany, Biology, 1978

M.S. Rensselaer Polytechnic Institute, Biology, 1980

Ph.D. Rensselaer Polytechnic Institute, Biology, 1982

Our laboratory is interested in how cells move, a process important in a number of cell biological processes such as wound healing and development. Aberrant cell movement is associated with the metastasis of tumors. Myosin proteins mediate cell movement. The study of myosin might culminate in design of a rational approach to inhibit the spread of cancer.

Keywords: cancer, wound healing

Roberto Dominguez, Ph.D.

Scientist, Boston Biomedical Research Institute

M.S. Odessa University, ex-USSR, Theoretical Physics and Mathematics, 1987

Ph.D. Institute Pasteur and Paris-Sud University, Crystallography of Biological Macromolecules and Biochemistry, 1996

We use protein X-ray crystallography and molecular biology to investigate the relationship between structure and function of proteins involved in cellular motility such as actin, myosin, and regulatory proteins. Thus, for instance, we recently solved the crystal structure of monomeric actin, which is the most abundant protein in the human body. This new knowledge is relevant to the study of disease processes, such as the movement of metastasizing cancer cells.

Keywords: cardiovascular disease, cancer, cell movement

Peter Erhardt, M.D., Ph.D.

Scientist, Boston Biomedical Research Institute

M.D., Medical School of Pecs, Pecs, Hungary, General Medicine, 1982

Ph.D., Medical School of Pecs, Pecs, Hungary, Molecular Biology, 1992

Our laboratory's research interest focuses on the mechanism of programmed cell death, or apoptosis. Apoptosis is a highly regulated process that eliminates unwanted cells during normal development as well as plays a role in the pathomechanism of human diseases. In ischemic heart disease the decreased blood supply leads to cell loss at least partially by apoptosis. Cancer cells lose the ability to die by apoptosis which contributes to their uncontrolled growth. We are studying the signal transduction pathways which regulate apoptosis in cardiac and cancer cells and use the newly acquired knowledge to develop gene therapy approaches to cure diseases whose development is based on increased or deregulated apoptosis.

Keywords: cancer, ischemic heart diseases

Dr. Erhardt lives in Natick, MA with his wife Gyongyi and son Peter, who is in first grade. On weekends the family frequents the ski trails of New Hampshire and Vermont.

John Gergely, M.D., Ph.D.

Senior Scientist, Boston Biomedical Research Institute

Associate Professor, Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School

Biochemist, Department of Neurology, Massachusetts General Hospital

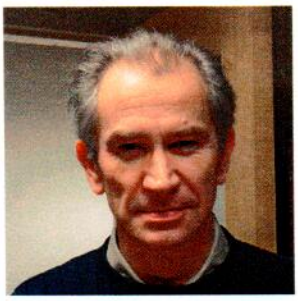
M.D. University of Budapest, 1942

Ph.D. University of Leeds, Physical Chemistry, 1948

D.M.Sc. (hon) Semmelweis University, 1987

My interest in unraveling the molecular basis of muscle contraction and its regulation started more than fifty years ago. Our biochemical and biophysical work on myosin and actin, two key protein components of the contractile machinery, has helped in arriving at the current picture of the so-called sliding filament mechanism of contraction. Regulation of skeletal and cardiac muscle contraction depends on calcium that binds to one of the three components of the protein complex troponin attached to actin filaments. We have characterized these proteins, making it possible to carry out detailed studies on their structure and function. Our current work benefits from earlier X-ray studies on the calcium binding protein and from more recent work establishing a partial structure of the troponin complex opening up new avenues for investigation. Basic work focused on developing an understanding of normal mechanisms is likely to produce results of diagnostic and therapeutic interest, in our case diseases of striated or cardiac muscle.

Keywords: cardiovascular disease, muscle diseases



Zenon Grabarek, Ph.D.

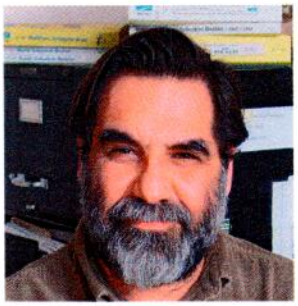
Principal Scientist, Boston Biomedical Research Institute

M.S. Warsaw University, Organic Chemistry, 1972

Ph.D. Nencki Institute of Experimental Biology, Warsaw, Natural Sciences, 1979

Being a chemist at heart, I believe that all or nearly all aspects of life can be explained by the formation or breaking of bonds between atoms. In my lab, we apply this rule to address the question of how calcium ions regulate intracellular processes. We attempt to decipher at atomic and molecular levels the chain of events that is initiated by the interaction of calcium ions with specific regulatory proteins and leads to physiological responses such as contraction of skeletal or smooth muscle, cell division or gene expression. For that, we use a variety of biochemical and physicochemical techniques such as site directed mutagenesis, fluorescence spectroscopy, X-ray crystallography, etc.

Keywords: muscle-related diseases, protein structure, calcium ions



Philip Graceffa, Ph.D.

Senior Scientist, Boston Biomedical Research Institute

B.A. Northeastern University, Chemistry, 1965

Ph.D. Brandeis University, Physical Chemistry, 1972

Muscle contraction involves the sliding of two sets of parallel filaments, thick and thin, past each other, thereby causing the muscle to shorten and produce force. Smooth muscle surrounds hollow organs, like blood vessels, in order to control their shape and allow fluid to flow through them. The smooth muscle thin filament is primarily comprised of the protein actin, along with two actin-binding proteins, tropomyosin and caldesmon. Our results suggest that the arrangement and movement of these latter two proteins is key to their role in the regulation of smooth muscle contraction. We have also recently contributed to the solution of the atomic structure of actin, in collaboration with Roberto Dominguez's laboratory. All of this structural information is essential to gaining an understanding of the molecular basis of the thin filament's function and may help to explain the unique properties of smooth muscle, including its ability to maintain organ shape and force at the expense of little energy.

Keywords: smooth-muscle related diseases, e.g. cardiovascular disease, asthma and stroke

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Steen H. Hansen, M.D., Ph.D.

Scientist, Boston Biomedical Research Institute

Full Registration, Danish Health Authorities/EEC, 1997

D.M.Sc. University of Copenhagen, Copenhagen, Denmark, 1994

M.D. University of Copenhagen, Copenhagen, Denmark, 1990

My lab studies "RND" proteins. RND is an acronym for RouND because these proteins cause some cells to become rounded. We are studying the molecular mechanisms by which RND proteins function in cells. Although the precise significance of RND proteins is not known, there is suggestive evidence that they are important in development of the embryo and, as we have recently shown, in processes associated with cancer.

Keywords: embryonic development, cancer

Celia Harrison, Ph.D.

Principal Scientist, Boston Biomedical Research Institute

B.S. Pacific Lutheran University, Biology, 1988

Ph.D. University of California, Berkeley, Molecular and Cell Biology, 1994

Signal transduction is the process by which information is conveyed to and from cells by molecules on their surfaces. Part of our research is to determine the structure and function of these signaling molecules using X-ray crystallography. We recently solved the structure of a protein (ephrin-B2) that plays a critical role in the formation and organization of blood vessels, a process known as angiogenesis, which is currently the focus of intense research by cancer biologists. Our other research interests include crystallographic analyses of complexes involving proteins that act as chaperones to help other proteins to fold correctly. Detailed structural studies allow us to better understand how these molecular chaperones work.

Keywords: cancer

Noriaki Ikemoto, Ph.D.

Senior Scientist, Boston Biomedical Research Institute

Principal Associate in Neuropathology, Harvard University

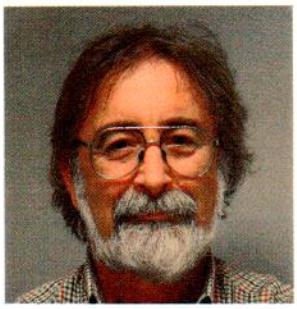
B.S. Okayama University, Japan, Biology, 1954

Ph.D. Tokyo University, Japan, Biology, 1964

The activation signal received at the muscle cell surface (plasma membrane and T-tubule) is sent to the internal calcium store (sarcoplasmic reticulum). This opens the floodgate located in the foot protein to release calcium ions from the calcium store to the cell-space (cytoplasm), and muscle contraction ensues. Re-accumulation of the calcium back into the calcium store by the calcium pump causes muscle relaxation. In many diseases of both skeletal and heart muscles, the calcium floodgate becomes leaky, which makes the cellular calcium concentration abnormally high even in the relaxed muscle and causes various problems as seen in the diseased tissues. Our research goal is to understand how the opening/closing action of the calcium floodgate is controlled and what causes the abnormal action of the calcium floodgate in disease.

Keywords: malignant hyperthermia (skeletal muscle), central core disease (skeletal muscle), arrhythmogenic right ventricular dysplasia (heart muscle), polymorphic ventricular tachycardia (heart muscle), etc.

In his spare time, Dr. Ikemoto enjoys oil painting and playing classic guitar.



Paul C. Leavis, Ph.D.

Senior Scientist, Boston Biomedical Research Institute

Associate Professor, Tufts University Schools of Medicine, Dental Medicine and Veterinary Medicine, Sackler School of Graduate Biomedical Science

Director, Analytical Biotechnology Services

Research Associate in Neurology, Harvard Medical School

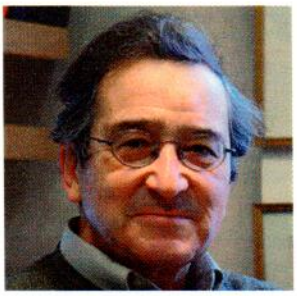
B.S. University of Notre Dame, Biology, 1966

Ph.D. Tufts University Graduate School of Arts and Sciences, Physiology, 1971

In recent years our laboratory has been interested in how embryonic cells communicate with each other to control growth and development of embryonic tissues and to assure the embryo's viability in its earliest stages of existence. We have been able to isolate and identify several compounds that are secreted by the embryo within the first days following fertilization. Our studies suggest that these chemical messengers are able to signal the embryo's existence to the mother and to modulate the maternal immune response to prevent the mother from rejecting it. In related studies, other compounds isolated from tissues of later stage embryos inhibit the growth of a number of human cancers. We are currently working to characterize these compounds and to study their mode of action on cancer cells.

Keywords: cancer, embryo, chemical messengers, immune response

When not at BBRI, Dr. Leavis teaches physiology at Tufts University Medical and Dental Schools and helps his wife, Judy, run a commercial greenhouse/garden center in Epping, NH.



Sherwin S. Lehrer, Ph.D.

Senior Scientist, Boston Biomedical Research Institute

Principal Associate in Neurology, Harvard Medical School

B.S. University of Pittsburgh, Chemistry, 1956

Ph.D. University of California, Berkeley, Chemistry, 1961

Tropomyosin (Tm) is an essential component of the actin thin filament of skeletal, cardiac and smooth muscle which together with calcium ions, troponin and myosin, regulates the contractile on/off switch. It is a rod-like coiled-coil helical molecule located along the actin filament and it interacts with the troponin complex (in cardiac and skeletal muscle) or caldesmon (in smooth muscle). Mutations of Tm cause a variety of diseases such as skeletal nemaline myopathy and cardiac hypertrophic myopathy. The long-range goal of the research in my lab is to understand the molecular basis of the Tm interactions that are involved in muscle regulation so that the diseased state can be better understood.

Keywords: skeletal nemaline myopathy, cardiac hypertrophic myopathy

Dr. Lehrer lives in Lexington with his wife, Liane Reif-Lehrer. He enjoys photography, ballroom dancing and biking.

Renne Chen Lu, Ph.D.

Senior Scientist, Boston Biomedical Research Institute

Research Associate, Harvard Medical School

B.S. National Taiwan University, Taiwan, Republic of China, Biochemistry, 1966

Ph.D. University of California at San Diego, La Jolla, CA, Biochemistry, 1970

Myosin V is one of the proteins that moves around in the cell and works as a transporter like a cable car. One end of the myosin V can grab a package that may contain pigments or other important stuff and the other end of myosin V can attach to the cable, or actin filaments. Thus, pigments and other organelles are shipped by myosin V to various parts of the cell from where they are made. My research is trying to identify the helpers which select the right kind of packages for myosin V to transport and facilitate the loading of the packages onto myosin V. Abnormality in myosin V will result in the decoloration of the skin or neurological disorder with a marked delay in motor development, hypotonia and mental retardation. For example, patients with Griscelli syndrome are found to have defective myosin V.

Keywords: neurological disorders, hypotonia, mental retardation

In spare time, Dr. Lu enjoys reading, traveling and doing community or charity related work.

Jeffrey Boone Miller, Ph.D.

Senior Scientist, Boston Biomedical Research Institute

Associate Professor of Neurology, Harvard Medical School

B.S. Washington State University, Biochemistry, 1973

Ph.D. University of California, Berkeley, Biochemistry, 1977

Our research focuses on three areas of neuromuscular biology and disease. First, we are testing possible ways to inhibit the muscle wasting and loss of muscle function that is found during normal aging and in neuromuscular diseases such as muscular dystrophy. Second, we are examining how the small number of stem cells in adult muscle normally function and might be used in cell replacement therapies. Third, we are using new gene analysis methods to examine how environmental contaminants (e.g. PCBs, pesticides) cause adverse effects on the nervous system during pregnancy and throughout life. Our goals are to understand how certain neuromuscular problems arise and might be ameliorated.

Keywords: aging, developmental disorders, muscular dystrophy, Parkinson's disease

Kathleen G. Morgan, Ph.D.

Senior Scientist, Boston Biomedical Research Institute

Associate Professor of Physiology in Medicine, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School

B.S. College of Mount St. Joseph, Cincinnati, Chemistry, 1972

Ph.D. University of Cincinnati, College of Medicine, Pharmacology, 1976

The main focus of the lab is the differentiated smooth muscle cell, which forms the walls of most of the hollow organs in the body. Inappropriate contraction or relaxation of smooth muscle is responsible for a number of diseases including stroke, hypertension, heart failure, asthma and premature labor. The precise mechanism by which smooth muscle contracts is, to a large extent, currently unknown. We are currently investigating the cell communication pathways leading to the contraction and relaxation of the smooth muscle cell. We are able to knock out putative signaling molecules in model systems to test their suitability as target molecules for future therapeutic approaches.

Keywords: hypertension, coronary artery spasm, premature labor, asthma

In her spare time, Dr. Morgan enjoys birdwatching, and is an avid walker and aspiring rower.

Henry Paulus, Ph.D.

Director and Senior Scientist, Boston Biomedical Research Institute

Associate Professor, Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School

B.A., B.S. University of Chicago, Biochemistry, 1957

Ph.D. University of Chicago, Biochemistry, 1959

Inteins are foreign pieces of DNA that interrupt certain genes and must be excised by a process known as protein splicing for such genes to function. My research group has studied protein splicing for the last eight years and has done much to elucidate its mechanism. We are currently studying an intein in a gene of the TB bacillus that plays an important role in pathogenesis. This gene cannot function without protein splicing, and we are therefore searching for protein splicing inhibitors in the hope that these will attenuate the virulence of the TB bacillus. Such inhibitors would constitute a new class of antibiotics that are badly needed to combat tuberculosis, which affects 100 million individuals world-wide, kills 3 million people a year, and is rapidly becoming resistant to treatment with existing antibiotics. Besides its use as a potential target for anti-tuberculosis drugs, protein splicing has become an important protein engineering tool, which is finding applications in many biomedical fields and even in agriculture.

Keywords: tuberculosis, protein engineering

Dr. Paulus lives on the Boston waterfront at about 300 feet above sea level. Whenever he cannot be found at BBRI for more than a week, he is probably away hiking in some high places in the Himalaya or Papua New Guinea.

Lucia Rameh, Ph.D.

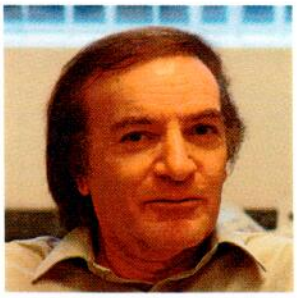
Scientist, Boston Biomedical Research Institute

B.S. Universidade de Sao Paulo, Brazil, Biological Sciences, 1987

Ph.D. Universidade de Sao Paulo, Brazil, Biochemistry, 1992

In contrast to simple unicellular forms of life, such as bacteria and yeast, cells in complex, multi-cellular organisms differentiate to perform specialized functions and utterly depend on each other. This interdependence necessitates intercellular communication to drive development and to assure the well being of the whole organism. We study how normal cells communicate with each other, and how a breakdown in communication leads to disease at the organism level, such as cancer or diabetes. My lab is investigating a class of molecules, collectively known as phosphoinositides, that participate in this basic process of cell-cell communication. As the Ctrl key in a computer keyboard, phosphoinositides serve a broad range of functions in cells, but need to work in concert with other signals to cause a specific outcome. By systematically disrupting the normal functions of phosphoinositides in cells, we seek to better understand their role in health and to design strategies to interfere with the disease process.

Keywords: cancer, diabetes, hormones, obesity



Victor A. Raso, Ph.D.

Senior Scientist, Boston Biomedical Research Institute

B.S. Fordham University, Biology, 1967

Ph.D. Tufts University, Immunochemistry, Biochemistry, 1973

Our laboratory is developing a novel therapy to control Alzheimer's disease that holds great promise for conquering this presently incurable condition. The strategy involves using a unique antibody-based vaccine that targets a peptide thought to be responsible for Alzheimer's disease. That peptide, known as beta-amyloid, forms harmful aggregates in the brain called plaques, which are the most likely cause of the memory loss and dementia that make Alzheimer's such a devastating disease. We currently have a patent application pending for this innovative and potentially high impact approach to treating and preventing Alzheimer's disease.

Keyword: Alzheimer's disease

Nilima Sarkar, Ph.D.

Senior Scientist, Boston Biomedical Research Institute

Lecturer, Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School

B.S. University of Calcutta, Chemistry, 1953

M.S. University of Calcutta, Chemistry, 1955

Ph.D. Northwestern University, Biochemistry, 1961

Gene expression involves transcription of the genetic information into messenger RNA (mRNA), followed by translation into proteins. This process is highly regulated, both at the transcriptional and translational level. One of the control mechanisms in higher organisms involves the addition of adenylate chains to the ends of mRNA molecules, a process known as polyadenylation. In animal cells, it is known that polyadenylation controls both the stability of mRNA and the efficiency of its translation. Moreover, high levels of poly(A) polymerase, the enzyme that catalyzes mRNA polyadenylation, have been found to be associated with certain forms of breast, ovarian, pancreatic, and colon cancers. Owing to their complexity, control mechanisms involving polyadenylation have been difficult to study in animal cells. However, we discovered that mRNA polyadenylation also occurs in bacteria such as *E. coli* and have identified the gene for poly(A) polymerase. We are therefore using *E. coli* as a simple model system to study the mechanism and function of mRNA polyadenylation.

Keyword: cancer

In her spare time, Dr. Sarkar enjoys indoor and outdoor gardening, growing hundreds of Hemarocallis (daylilies), and flowering perrenials. She also enjoys cooking gourmet Indian food, creative sewing, and reading Indian literature in the Bengali language.

Janet L. Smith, Ph.D.

Scientist, Boston Biomedical Research Institute

A.B. Smith College, Biochemistry, 1984

Ph.D. University of California, Berkeley, Biochemistry, 1989

We wish to understand how cells coordinate changes in their architecture, or cytoskeleton, so that they can migrate toward a chemical attractant, a process known as chemotaxis. Chemotaxis is an important cellular phenomenon that occurs in embryonic development, metastatic cancer and defense against infection. Many of our experiments focus on how the activity of a molecular motor (myosin II) is controlled during chemotaxis. We use *Dictyostelium* as a model organism, since it is simple and amenable to many techniques, yet is remarkably similar to many mammalian cells.

Keywords: embryonic development, cancer, defense against infection

Dr. Smith lives in Newton and enjoys hiking, camping, and spending time with her husband and two young children.

Walter F. Stafford, III, Ph.D.

Senior Scientist & Director of Computer Science, Boston Biomedical Research Institute

Associate, Department of Neurology, Harvard Medical School

B.A. Lake Forest College, Chemistry, 1966

Ph.D. University of Connecticut, Biophysics, 1973

Understanding the nature of interactions between different proteins or between proteins and other molecules or ions is central to understanding the vital processes in life. My main interests are in the application of physical methods to the study of such interactions. I was involved in a project called The National Cooperative Drug Discovery Group funded by the National Cancer Institute, in which single chain antibodies to breast cancer cells are engineered and used as vehicles for the targeted delivery of therapeutic agents to kill cancer cells. To assess the strength of binding to targets on the surface of breast cancer cells, physical methods of analytical ultracentrifugation are applied. New optical systems with high sensitivity and mathematical means to analyze the ultracentrifugation data that I developed at BBRI are key to obtaining information about the nature and strengths of the interactions between various biological molecules.

Keywords: breast cancer, Huntington's Disease, basic cellular functions

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Terence C. Tao, Ph.D.

Senior Scientist, Boston Biomedical Research Institute

Research Associate, Department of Neurology, Harvard Medical School

Adjunct Associate Professor, Dept. of Biochemistry, Tufts University School of Medicine

B.S. University of California, Berkeley, Physical Chemistry, 1964

Ph.D. Columbia University, Chemical Physics, 1969

The long-term goal of my research is to understand the regulation of mammalian muscle contraction. There are three types of muscles in the human body: skeletal muscle in the limbs, cardiac muscle in the heart and smooth muscle in a wide variety of tissues including blood vessels, stomach, intestines, uterus etc. The contraction of skeletal and cardiac muscles is regulated by calcium ions, the troponin complex and tropomyosin. Using recombinant DNA techniques, my research creates mutants of the various proteins that are involved in regulation. I then study the interactions between them and how these interactions are affected by calcium using crosslinking and spectroscopic techniques. Smooth muscle is also regulated by calcium, but utilizes the enzymes myosin light chain kinase and phosphatase. I am studying the phosphatase which, like troponin, is composed of three subunits. My laboratory has begun to study the interactions of these subunits among themselves and with myosin using a variety of biophysical techniques. Crosslinking and spectroscopic techniques will soon follow. It is not difficult to imagine that malfunctioning in these regulatory processes can lead to serious health problems. By studying how regulation functions normally, we hope to understand and then correct when disease-causing abnormalities occur.

Keywords: muscle related diseases: heart failure, arteriosclerosis, hypertension, stroke, asthma etc.

Chih-Lueh Albert Wang, Ph.D.

Deputy Director and Senior Scientist, Boston Biomedical Research Institute

Adjunct Associate Professor, Department of Physiology, Tufts University of Medicine

B.S. National Taiwan University, Taipei, Taiwan, Chemistry, 1971

Ph.D. Ohio State University, Chemistry, 1978

The regulatory process of smooth muscle, which is present in the walls of hollow organs in our body, has not been clearly understood. Caldesmon, a major actin-binding protein in smooth muscle cells, is a candidate for conferring a novel regulatory pathway. As a part of the Program Project Grant, my lab is trying to define the role of caldesmon in smooth muscle by a number of biophysical approaches, and ultimately, by genetic methods to eliminate this protein in mice. Our overall goal is to understand the thin filament-based regulation of the smooth muscle system. Such an understanding is essential for developing cures of smooth muscle related diseases.

Keywords: hypertension, asthma, indigestion, miscarriages

Dr. Wang lives in Lexington and enjoys traveling and reading history.

Hartmut Wohlrab, Ph.D.

Senior Scientist, Boston Biomedical Research Institute

Adjunct Professor, Institute of General Pathology, Catholic University Medical School, Rome, Italy

Research Associate, Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School

B.S. Rensselaer Polytechnic Institute, Physics, 1962

Ph.D. Stanford University, Biophysics and Chemistry, 1967

About 25% of the proteins coded for by the human genome are embedded within the various membranes of the cell. This kind of protein transmits signals across membranes, e.g. insulin receptor, or determines what kind of molecule may cross a membrane, e.g. mitochondrial phosphate transport protein. My laboratory has developed a great interest in such transport proteins. Their molecular structures - due to their location in membranes - are not yet known and even their functions are mostly unknown. When these proteins do not function properly, primarily due to inherited mutations and/or mutations induced by environmental factors, diseases of many kinds result. Among them and most closely related to our work are glycogen storage disease / type II diabetes, obesity, and adult-onset type II citrullinaemia. These transport proteins may also underlie toxic side effects of drugs used in the treatment of AIDS and in cancer therapy.

I also have a keen interest in science education. I teach first year medical students at Harvard Medical School, am a judge at the Annual State Science Fair at MIT, and am a mentor for mostly minority students in biotechnology programs and medical careers in the Biomedical Science Career Program sponsored by Harvard Medical School.

Keywords: diabetes, type II diabetes, obesity, adult-onset type II citrullinaemia.

Dr. Wohlrab and his wife reside on the South Shore. Their two children, University of Michigan and Stanford University graduates, have left for homes of their own.

Janice Dominov, Ph.D.

Instructor, Boston Biomedical Research Institute

B.S. University of Rhode Island, Kingston, RI, Microbiology, 1980

Ph.D. Case Western Reserve University, Cleveland, Ohio, Biology, 1986

Skeletal muscles are responsible for all the movements of the body, including breathing, and hence are essential for survival. Normal muscle fibers can live for many years, but when damaged by physical stress or disease (such as Duchenne muscular dystrophy), they are replaced by the growth of precursor cells intermingled among the fibers. Some of these cells act as muscle "stem cells". Our recent studies indicated that Bcl-2, a protein that inhibits the normal process of cell death, may be expressed in muscle stem cells and play a role in their function. Current work is designed to better understand the biology of muscle stem cells, the role of Bcl-2 in muscle survival, the mechanisms involved in muscle repair, and the potential use of muscle stem cells for treatment of muscle diseases.

Keywords: skeletal muscle, muscle stem cells, regeneration, muscular dystrophy

Dr. Dominov enjoys her spare time at home in North Reading, MA with her husband and two children, and is kept perpetually busy in her role as Girl Scout troop leader.

Jonathan M. Goldberg, Ph.D.

Instructor, Boston Biomedical Research Institute

B.A. Hunter College, New York, NY, Chemistry, 1985

Ph.D. University of California, Berkeley, CA, Comparative Biochemistry, 1992

Research Interests: Protein folding, stability, and function

William C. Hatch, Ph.D.

Instructor, Boston Biomedical Research Institute

B.A. Clark University, Worcester, MA, Biology, 1983

Ph.D. Albert Einstein College of Medicine of Yeshiva University, Experimental Pathology, 1993

Research Interests: Cell biology and biochemistry of novel anti-proliferative liver proteins (APLEs)

Vladimir Kolenko, Ph.D.

Senior Research Associate, Boston Biomedical Research Institute

M.D. Academy of Medicine, Moscow, Russia, 1986

Ph.D. Immunology Institute for Vaccines and Sera, Moscow, Russia, 1989

Our studies revealed that the family of mammalian-derived Developmental Peptides (DPs) appears to act as local controller of abnormal cell proliferation. DPs inhibit proliferation and induce programmed cell death in cancer cells of different origin and this effect is independent on signaling through well-known death receptors. Now we are studying intracellular pathways involved in DPs signaling. Taking into account its unique effectiveness and cytotoxicity profile, DPs might represent an attractive new model for anti-cancer drug development.

Keyword: cancer

Knut Langsetmo, Ph.D.

Instructor, Boston Biomedical Research Institute

B.S. University of Minnesota, Biology, 1983

Ph.D. University of Minnesota, Cell and Developmental Biology, 1991

Research Interests: Understanding the nature of energetic contributions to protein stability and to protein-protein, protein-DNA and protein-ligand interactions

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Katsuhide Mabuchi, Ph.D.

Senior Research Associate, Boston Biomedical Research Institute

B.S. Kagoshima University, Kagoshima, Japan, Biology, 1969

M.S. Okayama University, Okayama, Japan, Biology, 1970

Ph.D. Eotvos Lorand University, Budapest, Hungary, Biochemistry, 1979

Living animals, including human beings, are made of millions of different elements, interacting and reacting each other in such way that the state of being alive is created. We, the biologists, are trying to find out what going on inside our bodies. But because these elements exist in vast numbers and are not readily accessible, many biologists, various tools, good and sometimes crazy ideas, and patience are needed to study them. My interest is to see the shapes of some elements. The underlying logic is that it is often possible to deduce a function of a gadget by looking its parts. Unlike a gadget, the elements are microscopic in size and very fragile, and therefore, the work is a challenging one that I enjoy.

Dr. Mabuchi and his wife, Yasuko, live in Stoneham. His hobbies are to assemble computers, and to watch stars. He also enjoys hiking.