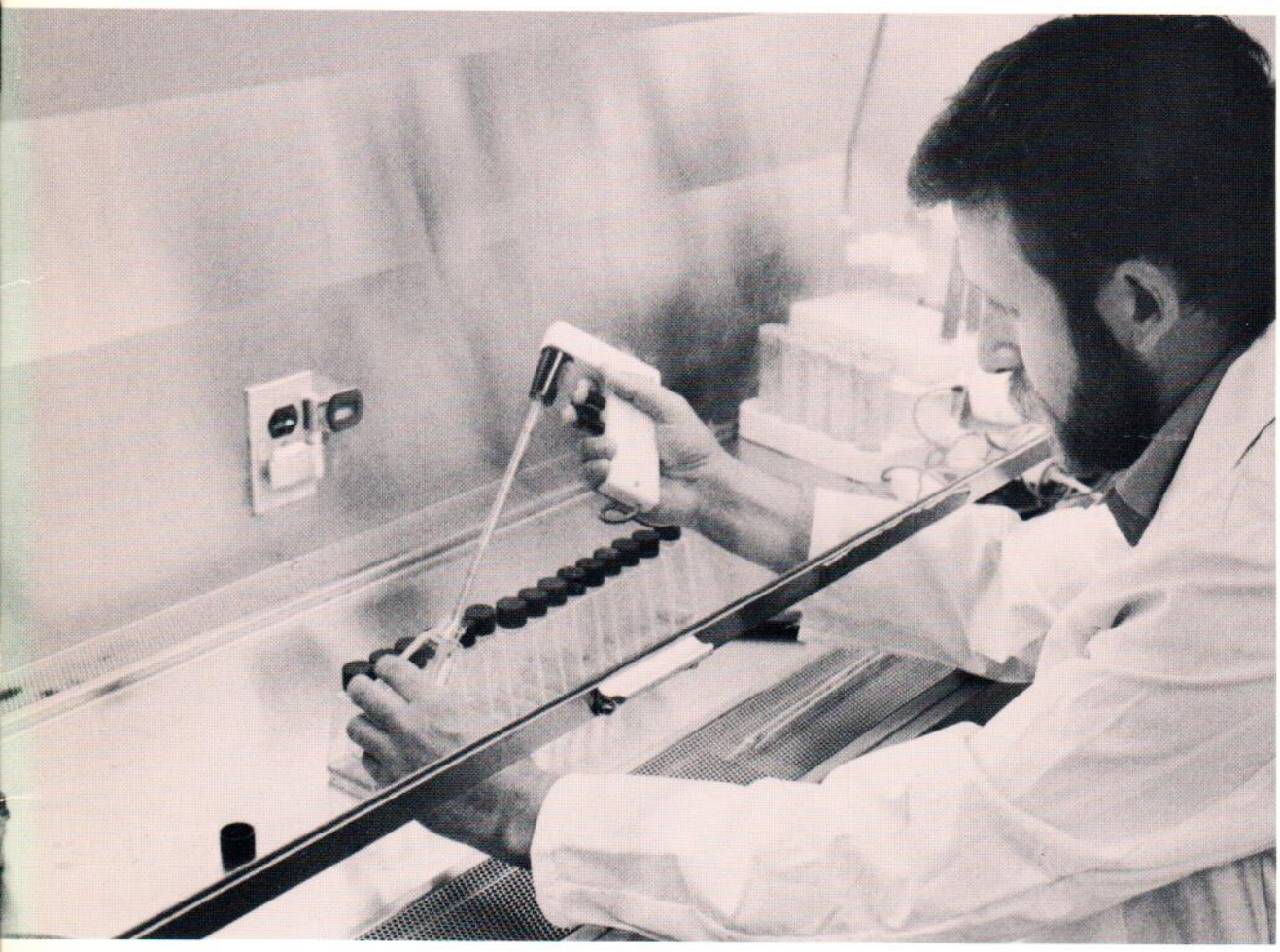
"Discovery consists of seeing what everybody has seen and thinking what nobody has thought"

Albert Szent-Gyorgyi

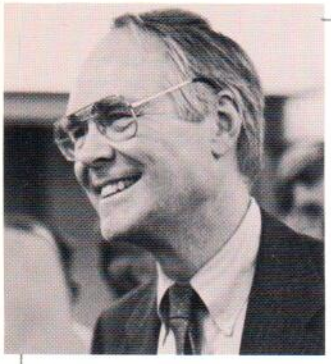


Boston Biomedical Research Institute

Annual Report 1984

CONTENTS

Jack French



Report of The President

The year has been an active and productive one for BBRI. The report of John Gergely, Executive Director, addresses our mission and some standards by which we measure our performance. I will comment on certain other aspects in the life of the Institute.

An inescapable concern of the Institute's Board of Trustees is the private financial support which is critical to BBRI's present and future stature and well-being. This voluntary support is not something which occurs in a haphazard or unplanned way. Rather it is the result of a great deal of hard work by the Trustees, members of the Corporation, and staff, spearheaded by a Development Committee co-chaired this year by Trustees Esther Ewing—whose recent death has saddened all of us—and Peter Sholley. Under their guidance and leadership, ably staffed by our cheerful and indefatigable Director of Development, Jackie Findlay, the story of BBRI has been told with great effect to a wide but selective group of potential donors. The results this year reflect this effort—we received over $150,000 in annual gifts, not only exceeding our goal, but also exceeding the amount received in any prior year by over $40,000. Our thanks and congratulations for the effective work of all involved in the development effort.

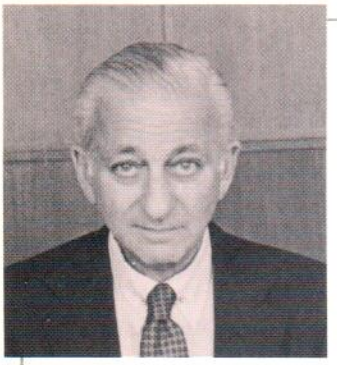
Another concern of BBRI's officers and Trustees is the orderly evolution of the Institute as conditions change and warrant reconsideration of existing policies. During the year two areas of the Institute's activities have been reviewed, leading to some initial changes and the likelihood of additional proposals for further refinement of the procedures under which BBRI operates.

First, in a review of the organization and administration of the Institute, the Committee on Research has proposed a change in the by-laws to make it easier to adapt the Committee to possible changes in the number and size of departments. The change was approved by the Trustees and a revised by-law will be presented to the annual meeting of the Corporation. Also, a committee is being appointed to consider other organizational structures of the Institute, to determine if additional changes are warranted, and, if so, to propose them to the Board of Trustees and, ultimately, to the Corporation.

Second, the problem of the extent of independent outside commercial activities on the part of the staff has received attention of the Board of Trustees. This, of course, is not unique to this institution. It is a difficult issue, which has become more prominent with the recent trend toward commercialization of developments in the field of biotechnology, and it has received a good deal of attention by universities and hospitals, among others. In our case, a committee was set up which in due course suggested that a clearer and tighter standard be applied to any staff member's outside commercial activities. It is expected this will lead to some revisions in the Patent Policy as well as the adoption of a new policy statement on outside activities of staff.

We extend our thanks and best wishes to all who had a part in making this a vigorous and productive year for BBRI. For their support and counsel in my first year as president, I want to thank especially our Officers and Trustees, as well as the Department Directors. I'd like particularly to call attention to those who assumed new responsibilities for the Institute this year: Ernest Henderson, III, as Treasurer and Chairman of the Finance Committee; David Gibbs, Peter Sholley, and Anne Stone as Trustees; Wesley Dixon, Jr., Cornelius McCarthy, and Anne Smith as Corporation members; and William Jencks as Visiting Committee member. Several of our members chose last year to retire from positions they have held with distinction. Happily, most agreed to continue their active participation with BBRI in alternative roles: John Shane, as Trustee; and Daniel Phillips and Carol Nash, as Corporation members. While Carol Means, whose remarkable career in support of medical research was highlighted recently in the *Messenger*, retired as a Trustee this year, we have felt the need of her continued wise counsel; as Trustee Emeritus she is warmly welcomed at Trustees' meetings. Retiring members of the Corporation were Robert Binstock, Shippen Goodhue, and Sidney Slobodkin; and Mahlon Hoagland resigned from the Visiting Committee. All these good and true friends served ably and contributed to making BBRI the fine, vigorous institute it is.

John French
President



Report of The Executive Director

In reviewing a year's activities, different organizations use different criteria. In business, it is often the final line of the profit and loss statement that counts. A hospital may judge itself in terms of the number of patients that have been treated. Other not-for-profit organizations may use the number of members as a yardstick. For a research institute there is no simple way of doing this, and a number of bench marks need to be considered.

Foremost among these is that elusive thing often referred to as excellence. In basic research in the biomedical field it is often difficult to pinpoint this quality. Breakthroughs resulting in spectacular new cures or diagnostic procedures are rare and in many cases may not be good indicators of the steady high quality of work that characterizes an outstanding institution. There are, however, some mundane but reliable tests against which we may want to judge ourselves and be judged by others. In the case of biomedical research there is an established criterion by which the judgment of the scientific community is expressed. This is the evaluation reflected in the "peer review" of applications for the funds by which research is carried out—the research grants, the bulk of which come from the National Institutes of Health. By this standard BBRI has passed the test with flying colors, as shown by the number of research projects that have enjoyed steady support for many years. It also speaks well for BBRI that during the past year several young investigators were awarded their first research grants after having spent a number of years in training at BBRI.

The publications in which the fruits of the research are disseminated provide another measure of an institution's quality. Many scientific journals are well known for the rigorous review the work of would-be authors has to undergo before it is accepted for publication as well as for the high rate—often more than 50%—of rejection. Again, by this standard BBRI has maintained its position in the world-wide scientific community.

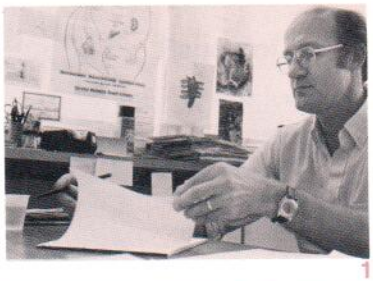
We are proud that during the past year we have been able to attract Dr. Phang-Cheng Tai as Senior Staff Scientist. Dr. Tai joins us from Harvard Medical School, where he retains an appointment as Associate Professor. A profile of Dr. Tai appeared in the recent issue of the BBRI *Messenger*.

While the purpose of basic biomedical research is the development of new knowledge of intrinsic value, new basic insights eventually lead to applications resulting in cure and prevention of disease. BBRI scientists continue to participate in this process, in many instances by collaborating with more clinically oriented colleagues. BBRI is also mindful of the importance of participation in a broader process of technology transfer whenever appropriate. This has resulted in a fruitful research contract with Polaroid Corporation and in the award of several patents while others are pending. The establishment of BBRI of a for-profit corporation—Boston Biotechnology Corporation (BBC)—is another channel for technology transfer. This also indicates BBRI's desire to be prepared to make the fruits of its research available for commercial application where appropriate, but without jeopardizing the character of BBRI as an academic research institute.

The 1984 Annual Report gives, as did the previous ones, a glimpse into BBRI's activities. Last year we looked out from the inside to the world at large—stressing BBRI's interactions with research and teaching institutions in the U.S. and abroad. This year we focus on BBRI's internal affairs, particularly in terms of a look at its individual Departments. Although each Department has its special field of interest, the various research programs have many points of contact and utilize similar techniques.

In closing, I should like to stress that BBRI's research activities could not go on without the support of the members of its Corporation, its Board of Trustees, and many other friends. It is encouraging that during the past year a number of additional charitable foundations as well as business corporations became first time contributors. Beyond the financial support, which is vitally needed for BBRI's ongoing work as well as for its future stability, these representatives of the community at large also provide us with an important channel of communication with the lay public. Such interaction is critical if we are to maintain an atmosphere in which biomedical research, the basis of all important advances in health care and disease prevention, is to flourish.

John Gergely
Executive Director

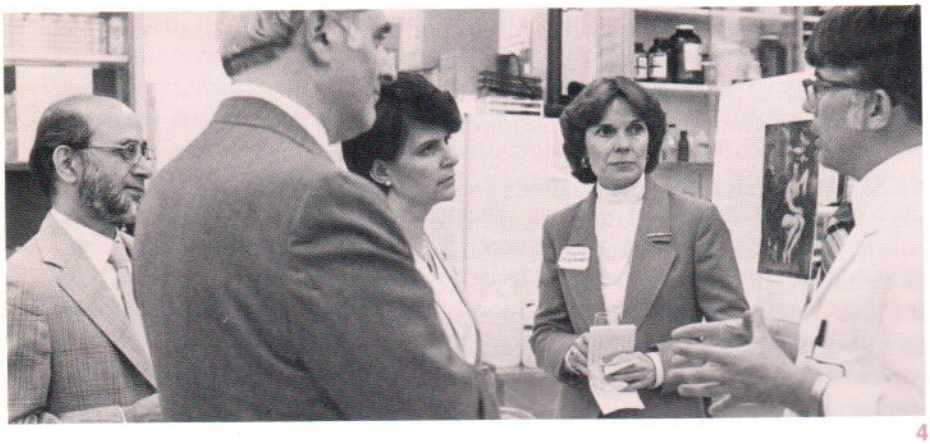


1

2

3

1. Hartmut Wohlrab prepares manuscript for publication.
2. Rao Sanadi and Yuoguo Huang analyze light absorbtion.
3. Rao Sanadi and Suresh Kaplay discuss implications of data.
4. James Hughes explains thermogenesis.



4

Cell Physiology

The research of this Department deals with several aspects of the energy economy of the living cell and the chemical reactions that permit the economy to function to the cell's best advantage. In the overall process, food material is broken down stepwise and finally oxidized (combusted) to carbon dioxide and water in the cell's furnace, which is a collection of sub-cellular organelles called mitochondria. These mitochondria are bags about 1/20,000th of an inch long and are bounded by a membrane which separates the interior of the organelle from the rest of the cell. The combustion takes place in the membrane phase, and the energy released during the combustion process, instead of being lost as heat, generates a microbattery. The inside of the mitochondria acquires a negative charge, and the outside becomes electropositive.

Three of the major projects in the department focus on the question, "How does the electrical charge drive the synthesis of a molecule, ATP, which is the energy currency of the cell?" The energy stored in ATP is necessary for many functions, such as contraction in muscle, motility in sperm, synthesis of fat, protein, and carbohydrate for growth and cell division. The machinery that makes ATP is complex, consisting of several proteins embedded in the membrane. The functions of these proteins, individually and collectively, in the organized structure are being slowly unravelled.

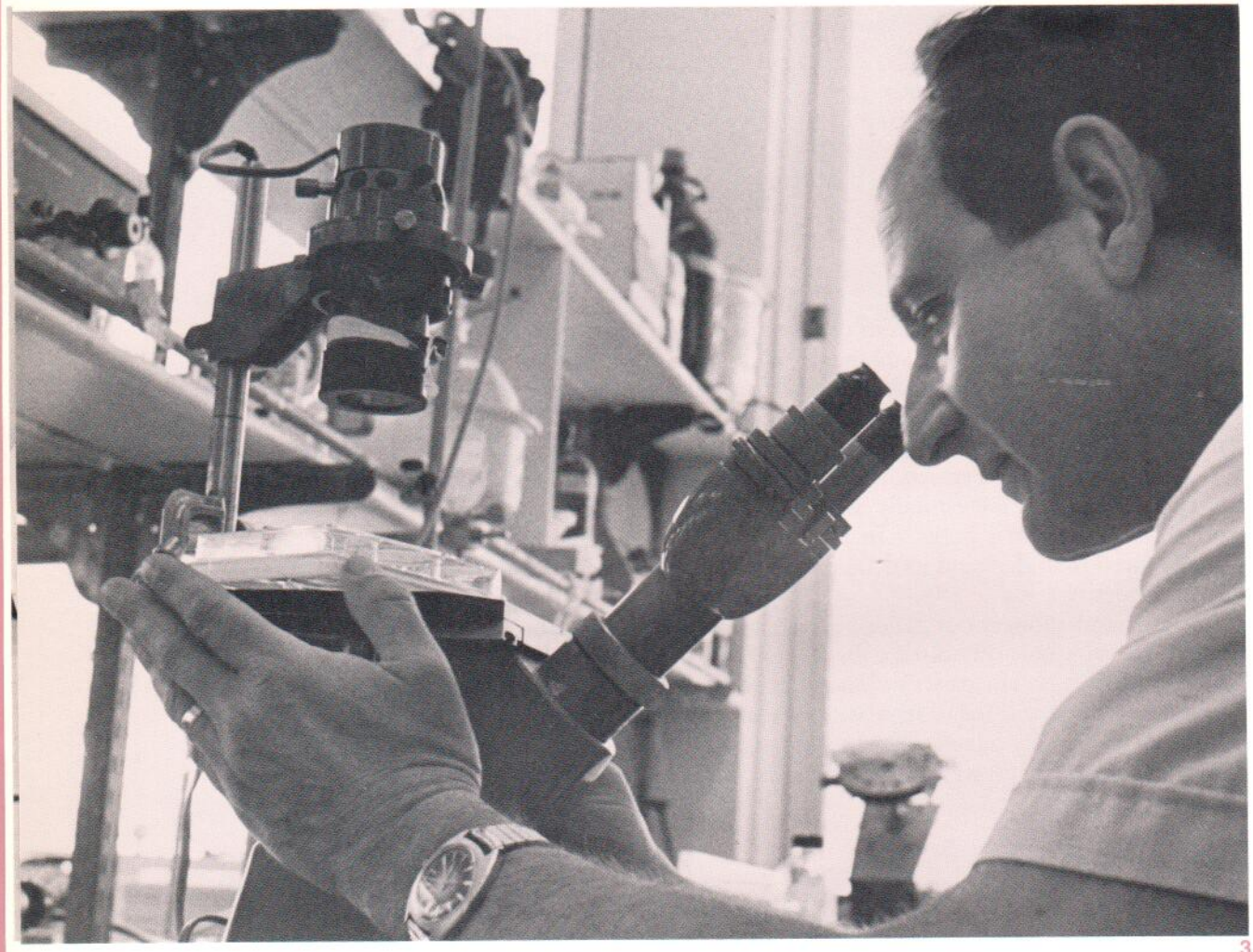
Two other projects are directed to the study of the mechanism by which nutrient and metabolic molecules are selectively carried across the membrane boundary, in and out of mitochondria. The molecular mechanism of these transport processes is currently little understood. The projects are important also for explaining how hormones and drugs enter the cell to produce their effects.

One of the more clinically relevant projects under study concerns the energy metabolism of brown fat cells. Brown fat is different from storage fat, and is present in high amounts in the newborn and in hibernating animals. The mitochondria of these cells are unique in that they have, in addition to the usual metabolic activity, a way of shorting out the electrical charge of the mitochondrial membrane and thus generating heat as needed. It is a physiological mechanism for rapid heat production and is governed by a switch. If the switch is impaired, food combustion produces, instead of heat, more ATP, which is eventually used for buildup of excessive fat. The project aims to take apart the switch to see how it works in maintaining the proper balance between heat and ATP production. We need to understand its detailed operation before we can hope to devise a treatment for human obesity.

Another project, an off-shoot of our major interest, seeks to devise a sound diagnostic test for primary biliary cirrhosis, a chronic liver disease that afflicts mostly women over thirty. In this and a few other chronic liver diseases, the patient's blood has antibodies to a few mitochondrial proteins. Our preliminary studies have led to separation of a mitochondrial protein fraction that reacts with sera from patients of primary biliary cirrhosis but not of other chronic liver diseases. The protein fraction, after further purification, would be suited for a distinctive diagnostic test.

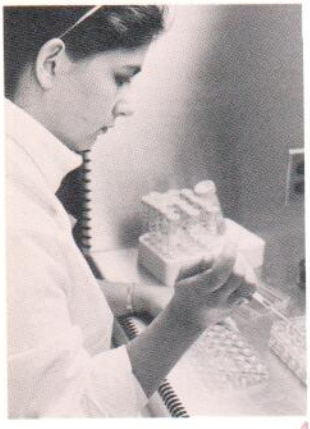
1

2



3

1. Peter Davison prepares presentation for the 6th International Congress of Eye Research.
2. Tatyana Dorfman prepares specialized cells from cow aorta.
3. Bernard Jacobson examines growth of cultured aortic cells.
4. Pamela Tupper tests the inhibitory effect of vitreous on the growth of aortic cells.



4

Fine Structure

The predominant theme of the research in the Fine Structure Department pertains to the chemistry, reactivity and metabolism of components of connective tissue, the material that lies between cells. Connective tissue is a negligible component of many soft tissues, but it forms more than 90% of tendons and ligaments and is a major component of the tissues of the eye. How connective tissue grows and how its growth is controlled as a young animal develops, or as wounds are healing, has been a major subject of study, with the ultimate objective of an understanding of defective growth or healing. Defective control of the building of connective tissue underlies a number of birth defects such as cleft palate, and congenital diseases such as brittle bone disease. Excessive growth of collagen or misplaced growth and deposition is the origin of conditions such as osteoarthritis, emphysema, cirrhosis of the liver, and other fibrotic conditions.

Chemical reactions change the molecules of connective tissue because these molecules may be retained in the body for many years, and they are vulnerable to attack from reactive molecules in the circulation. The role that such changes in connective tissue molecules might play in diseases such as diabetes and cancer is also the subject of present studies.

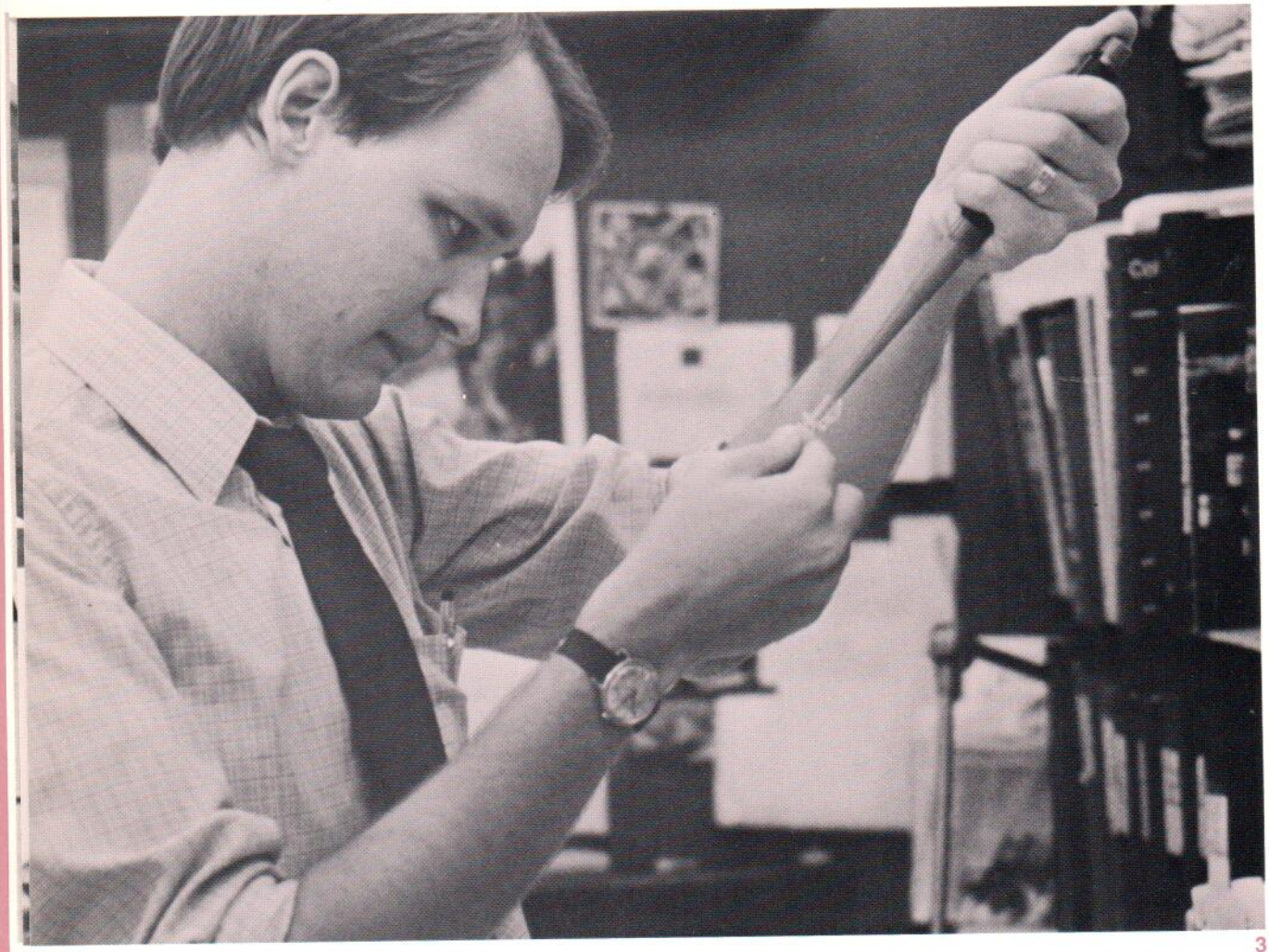
One of our research programs relates to the body's protective mechanisms that counteract the cancer-producing effect of ultraviolet radiation on skin. Different races and individuals have different levels of protection, but our understanding of the protective mechanisms appears to be still incomplete.

Another research program that relates to the cancer problem involves the study of the active components of tissue extracts capable of controlling the proliferation of blood vessels. Vessel outgrowth is necessary for the development of solid tumors, and its control might prevent the growth of large cancers. Control of the growth of blood vessels in the eye, e.g. in the retinal disease associated with diabetes, might also be an effective way to combat what is now a major cause of blindness in the USA.

Finally, in a joint program with the Department of Metabolic Regulation, a method for the preparation of hybrids from two different monoclonal antibodies has been devised. Such hybrids can with enormous selectivity bind together two large molecules, and appropriate mixtures of hybrids could form precisely organized complexes of many molecules. Hybrid antibodies have many potential applications in diagnostics, analysis, chemotherapy and chemical synthesis.

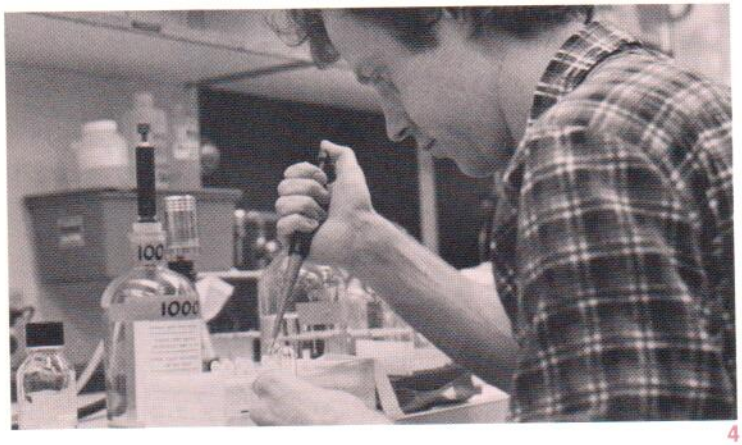
1

2



3

1. Phang Tai discusses research results with Evelyn Schweig and Ling Ling Chen.
2. Nilima Sarkar and Henry Paulus are isolating DNA by high voltage electrophoresis.
3. Robert Bondaryk studies the regulation of gene expression.
4. Wolfgang Pschorr a visiting scientist from Germany, studies nucleic acid synthesis.



4

Metabolic Regulation

At every moment in a cell's life, thousands of chemical reactions are occurring at rates which are precisely controlled by an equivalent number of enzymes. This staggeringly complex process is what we call metabolism. Its complexity is even more overwhelming when we consider that the enzymes, whose catalysis controls metabolism, must themselves be regulated. That regulation is twofold, affecting the efficiency of enzymes as catalysts, which changes from minute to minute in response to the cell's need, and the synthesis of enzymes, which represents an adaptation to the long-term requirements of the organism. Additional complexity derives from the fact that, although the program defining enzyme synthesis, structure, and regulation is encoded in the genes, the maintenance and replication of these genes in turn depends on enzymes. One can easily appreciate how even minor disturbances in any of these control processes can have disastrous consequences to the organism, leading to disease and death. Their elucidation will thus not only provide fundamental insights into the functioning of an organism but also an understanding of what might cause malfunctions or disease.

The scientists in the Department of Metabolic Regulation have chosen a number of different control mechanisms as the subject of their investigations. One research project deals with the mechanisms which assure that chromosomes are replicated in an orderly manner. These mechanisms help to avoid chromosome damage or loss and the production of supernumerary copies, both major causes of birth defects. A related program deals with the question of how the cell produces the building blocks for chromosome replication at just the right time and in proper amounts. A failure of these mechanisms is seen in a number of congenital diseases, such as the combined immunodeficiency syndromes.

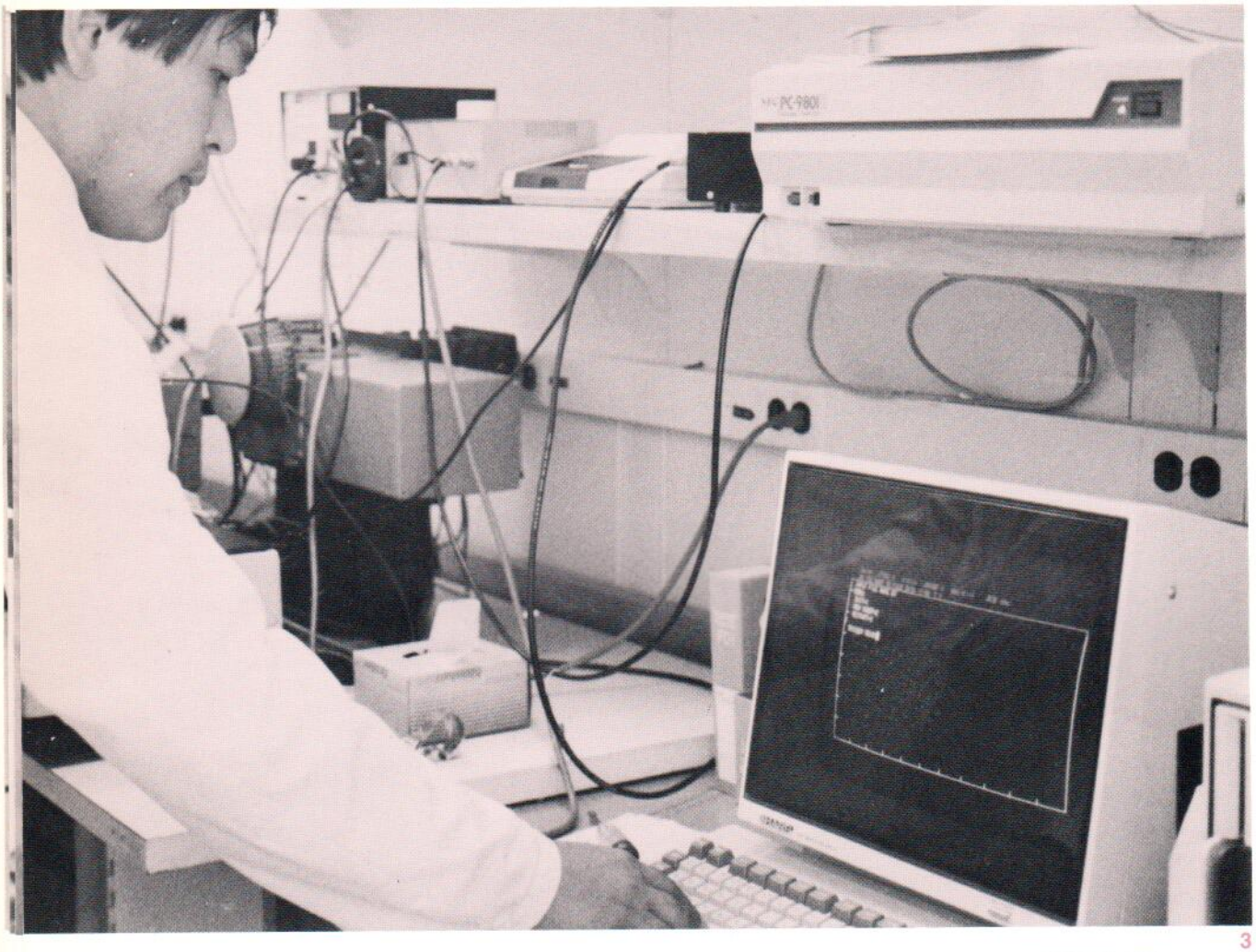
Another level of control, investigated by several research programs, is the regulation of gene activity. One project examines the way in which gene activity changes when leukemia cells are induced to change to normal blood cells, in the hope that the information obtained will reveal the regulatory defect responsible for malignancy.

A third level of control being studied deals with the assembly of enzymes from their components and the regulatory signals that determine where in the cell an enzyme will operate and whether or not an enzyme is to be secreted by the cell. The latter process, protein secretion by cells, is of special interest, since it is involved both in the production of harmful toxins by bacteria and the secretion of hormones by our endocrine glands.

A final type of control mechanism under investigation is the response of enzyme activity to the availability of nutrients and the needs of the cell and organism, which provides the basis for balanced and efficient growth and maintenance of the body.

1

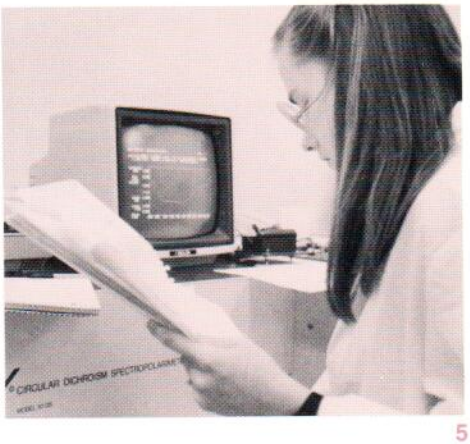
2



3

1. Noriaki Ikemoto and Bozena Antoniu analyze data.
2. John Gergely preparing grant application.
3. Magotoshi Morii performs computer modelling of calcium flow in muscle.
4. Satyapriya Sarkar and Katsuhide Mabuchi study protein synthesis in cardiac muscle.
5. Nancy Nelson performs computerized optical study on tropomyosin.

4



5

Muscle Research

The research program of the Department addresses fundamental questions of muscle function and structure. Although most of the projects deal with normal muscle, their relevance for clinical problems is obvious. Many baffling diseases of skeletal muscles (e.g. muscular dystrophy), the cardiovascular system (heart disease, hypertension), and of internal organs that contain certain so-called smooth muscle (intestines, bladder, uterus) require additional knowledge.

Several investigators of the Department are studying the structure of those protein constituents of muscle that make up the contractile apparatus itself. According to generally accepted views, the contraction of muscle is based on the sliding past each other of two sets of protein filaments. Many details of this mechanism—which is energized by a phosphate compound resulting from cell metabolism, ATP—require clarification by chemical and physical techniques.

Another set of problems centers on how muscle contraction and relaxation are regulated. In all three types of muscle (skeletal, cardiac and smooth) calcium ions play a crucial role, either by their combining with a specialized protein built into one set of the filaments—this is the case in skeletal and cardiac muscle—or by promoting the combination of phosphate with a component of the other set of filaments. Since transport of calcium across cellular membranes is involved, an investigation of the structure and function of such membranes is a logical extension of these studies.

Finally, questions of development and aging relating to the muscular system are being investigated, as well as processes by which changes in muscle activity affect the properties of muscle tissue. Many intriguing questions center on the specialization of muscle in terms of contraction velocity. Certain muscles contract faster and liberate energy from ATP without the need to oxidize foodstuffs at the same time. Slower muscles, usually involved in maintaining posture, rely heavily on oxidative processes. Individuals who have many fast-type muscle cells (fibers) make good sprinters while successful marathoners have a greater number of slow fibers. Through studies of the effect of changed activity pattern in the muscle type, information is being obtained on the mechanism by which fast fibers are transformed to slow ones and vice versa. These studies are of interest not only from the point of view of muscle, but they also illuminate gene expression: how is it that in a given cell only a certain set of genes is active? And how are genes turned on and off in response to a variety of stimuli, both in the narrower muscle context and in the broader framework of the whole organism?

Whenever appropriate, leads to problems of clinical relevance are followed. This is currently the case in connection with the role of calcium in muscle tissue in its relation to malignant hyperthermia. Similarly, knowledge about the structural details of proteins of the contractile apparatus is put to use in characterizing changed forms of muscle proteins found in diseased hearts. Information of this type may be helpful both in understanding the disease process and developing diagnostic procedures.

THANK YOU!

BBRI is deeply grateful to all its good friends, old and new, who helped us reach our $150,000 gift goal. The Institute's research program is absolutely dependent upon private financial contributions from that select group who appreciate the importance of basic medical research.

FOUNDATIONS

Anonymous
Adelaide Breed Bayrd Foundation
Connor Foundation, Inc.
Marie G. Dennett Foundation
Eaton Foundation
The Fuller Foundation, Inc.
G.E. Employees' Good Neighbor Fund, River Works Plant
Haffenreffer Benevolent Corporation
Henderson Foundation
Walter R. and Helen P. Hennessey Charitable Foundation
The Mitchell B. Kaufman Charitable Foundation
Lawrence Foundation
Pappas Family Foundation
Amelia Peabody Foundation
G. Gorham Peters Testamentary Trust
The Harold Whitworth Pierce Charitable Trust
Fred M. Roddy Foundation
The Shipley Foundation, Inc.
Sholley Foundation, Inc.
Phineas W. Sprague Memorial Foundation
Stop & Shop Foundation
The Tamarack Foundation

BUSINESSES

Caribbean Yacht Charters
McCullen Partners, Inc.
New England Biolabs, Inc.
Sensor Diagnostics, Inc.

BENEFACTORS

Anonymous
Anonymous
Endre A. Balazs, M.D.
Horace W. Cole
Mr. and Mrs. Lewis S. Dabney
Mrs. Charles M. Ewing
Jacquelyn MacL. Findlay
Mrs. George P. Fogg, Jr.
Mrs. James B. Greason, Jr.
Ernest Henderson, III (See Henderson Foundation)
Mohandas M. Kini, M.D., Ph.D.
Mrs. Ellery W. Rogers
Mrs. John W. (Ruth H.) Scott
John A. Shane
Peter B. Sholley (See Sholley Foundation, Inc.)
Mrs. H. Hollingsworth Smith
Gilbert L. Steward, Jr.
Mr. and Mrs. William B. Tyler
Mrs. Henry (Olga M.) Wheeler, Jr.
Mr. and Mrs. Dudley H. Willis

SPONSORS

Dr. Elkan R. Blout
Richard B. Cole
Mr. and Mrs. David C. Crockett
Wesley M. Dixon, Jr.
Mrs. J. H. Means
Charles E. Merrill
Stanley Paterson
Anne B. Stone
Charles P. White

SUSTAINERS

Mr. and Mrs. Arthur L. Coburn, Jr.
Mike Coleman
Mr. and Mrs. William Congleton
Claes H. Dohlman, M.D.
Granton H. Dowse, Jr.
Mr. and Mrs. John B. French
John and Nora Gergely
David A. Gibbs
William C. Greene
Henry Paulus
Mr. and Mrs. Vincent F. Raso
Alford P. Rudnick
D. Rao and Mary Jane Sanadi
Jack Trefry
Monte J. Wallace
Howland S. Warren

President John French and Corporation member John Buchanan chat with BBRI's first president, Carol Means.

ASSOCIATES

J. L. Armstrong
Gerard and Ruth Emyanitoff Badler
Lillian M. Clancy
Edward D. Cole
Mrs. Usher P. Coolidge
Mrs. Bigelow Crocker
Peter and Bjorg Davison
Mr. and Mrs. William Elfers
Mrs. Reginald B. Elwell
Alan Campbell Fagan
W. Sidney Felton
Ronald Garmey
Henry Gesmer
H. Shippen Goodhue
James S. Hughes
Denholm M. Jacobs
Mr. and Mrs. Caleb Loring, Jr.
Laurens MacLure
Mrs. Nathaniel C. Nash
Mrs. John T. G. Nichols
William R. Page
Mr. and Mrs. Daniel A. Phillips
Jerome Preston, Sr.
Dale and Tamson Schuparra
Mr. and Mrs. Robert W. Selle
Dr. and Mrs. Irwin W. Sizer
Mr. and Mrs. Sidney A. Slobodkin
Mr. and Mrs. Richard D. Stone
Norman R. Veenstra
Eustis Walcott, Jr.
Webb B. White
Barbara E. Wright

FRIENDS

Mr. and Mrs. Joseph Bachrach
Robert H. Binstock
Mr. and Mrs. F. Gorham Brigham, Jr.
Mrs. John C. Campbell
Dr. W. B. Castle
Haskell Cohn, Esq.
John M. Cole
Mrs. Charles M. Cutler
Christopher Grant
Prescott L. Kettell
Ralph Lowell, Jr.
Mrs. Robert J. Maine
Harry Margulius
Jeffrey Morby
Mr. and Mrs. H. Gilman Nichols, Jr.
Alex Nussbaum
Mr. and Mrs. Hans Ohlin
Theodora Perry
Mrs. George R. Poor
Mr. and Mrs. Charles M. Pyle, Jr.
Mrs. Merion M. Ritter
Margaret G. Shane (Mrs. H. E.)
Mary Ann Spadafora
Mr. and Mrs. Charles A. Steward
Mrs. Harborne W. Stuart
Mr. and Mrs. Harry Syrigos
Gertrude L. Turner
Mrs. Constance V. R. White

A gift in honor of BBRI Trustee David C. Crockett, featured in last fall's "Messenger", was received *from Haskell Cohn,* Esq., along with a note saying the "gift is a token of my appreciation for all I have learned from my association with David Crockett. He is a person of great wisdom and compassion."... BBRI echoes Mr. Cohn's sentiments.

Trustee of BBRI and President of BBC, John Shane (left) with Trustee David Gibbs and member of the Corporation Mike Coleman. John Gergely in background.

Trustees Denholm Jacobs (left), Peter Sholley (center) and Corporation member Endre Balazs.

PRO BONO PUBLICO

A priceless asset of BBRI is the outstanding group of distinguished professional, academic, and community leaders who have chosen to serve as BBRI's officers, Trustees, members of the Corporation, and Visiting Committee. These friends give generously and tirelessly of themselves pro bono publico—for the public good. Their wisdom, support, and dedication underlie the Institute's strength and vitality.

OFFICERS AND TRUSTEES

William B. Tyler
Chairman

John B. French
President

Chilton S. Cabot
Vice President

Mrs. Charles M. Ewing*
Vice President

Eustis Walcott, Jr.
Vice President

Ernest Henderson, III
Treasurer

Ronald Garmey
Secretary-Clerk

John Gergely, M.D., Ph.D.
Executive Director

Henry Paulus, Ph.D.
Deputy Executive Director

Elkan R. Blout, Ph.D.
David C. Crockett
David A. Gibbs, Sc.D.
Denholm M. Jacobs
Stanley C. Paterson
John A. Shane
Peter B. Sholley
Gilbert L. Steward, Jr.
Mrs. Galen L. Stone
John T. Trefry

Enjoying Open House are (left) Horace Cole, Corporation member, with Peter Davison, Director of Fine Structure Department, and Eleanor and his fellow Corporator, John Buchanan.

CORPORATION MEMBERS

Raymond D. Adams, M.D.
Endre A. Balazs, M.D.
Herbert Bremner
John M. Buchanan, Ph.D.
Horace W. Cole
Mike M. Coleman
Donald G. Comb, Ph.D.
William H. Congleton
Mrs. Nelson J. Darling, Jr.
Peter F. Davison, Ph.D.
Wesley M. Dixon, Jr.
Claes H. Dohlman, M.D.
Roberta Duvarney
Ruth G. Emyanitoff, Ph.D.
Alan Campbell Fagan
W. Sidney Felton
Mrs. George P. Fogg, Jr.
Jerome Gross, M.D.
Edgar Haber, M.D.
James S. Hughes
Roger W. Jeanloz, Ph.D.
Edward C. Johnson, 3rd
Manfred V. Karnovsky, Ph.D.
Mohandas M. Kini, M.D., Ph.D.
Joseph B. Martin, M.D., Ph.D.
Cornelius J. McCarthy
Mrs. J. Howard Means
Charles E. Merrill
Jeffrey L. Morby
James J. Myers
Mrs. Nathaniel C. Nash, Jr.
Mrs. John T. G. Nichols
Alexander Nussbaum, Ph.D.
William R. Page
Daniel A. Phillips
Mrs. Richard D. Phippen
Mrs. George Poor
Kenneth Rainin
Laurie W. Raymond, M.D.
D. Rao Sanadi, Ph.D.
Robert W. Selle
Irwin W. Sizer, Ph.D.
Mrs. H. Hollingsworth Smith
Mrs. Harborne W. Stuart
Lloyd D. Taylor, Ph.D.
Norman R. Veenstra
Charles P. Waite
Monte J. Wallace
Barbara E. Wright, Ph.D.

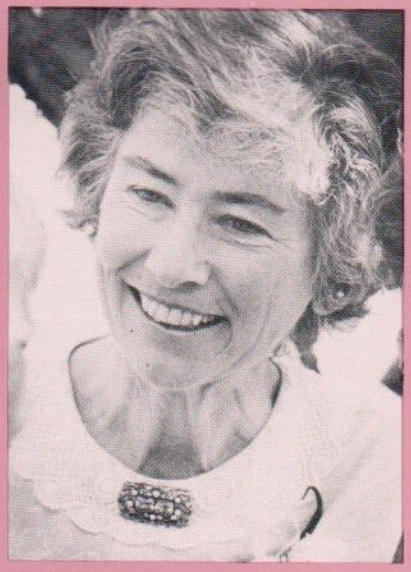
Chairman William Tyler (right) with Corporation members Alan Campbell Fagan, Anne Smith, and Gladys Poor.

VISITING COMMITTEE

Robert A. Alberty, Ph.D.
George F. Cahill, Jr., M.D.
William P. Jencks, M.D.

IN MEMORIAM

**Esther Ewing died October 16, 1984. Her deep conviction that medical solutions come from basic medical research led to her twelve-year association with BBRI as Corporation Member, Trustee, Vice President, and Co-Chairman of the Development Committee. Esther's thoughtful approach to Institute affairs and her sunny personality will be greatly missed, but her influence on BBRI continues.*



Corporation members Carol Means and Endre Balazs.

The Institute's steady flow of contributions to basic biomedical knowledge derives from the talents and insights of a superb team. Each member of the organization gives his best. And that best has earned world-wide respect for the productivity and high quality of BBRI's research.

DEPARTMENTAL DIRECTORS

Peter F. Davison, Ph.D.
Fine Structure Research

John Gergely, M.D., Ph.D.
Muscle Research

Henry Paulus, Ph.D.
Metabolic Regulation

D. Rao Sanadi, Ph.D.
Cell Physiology

SENIOR STAFF SCIENTISTS

Eiji Fujimori, D.Sc.
Jen-shiang Hong, Ph.D.
Noriaki Ikemoto, Ph.D.
Bernard J. Jacobson, Ph.D.
Sherwin S. Lehrer, Ph.D.
Nilima Sarkar, Ph.D.
Satyapriya Sarkar, Ph.D.
John C. Seidel, Ph.D.
Frank A. Sreter, M.D., D.V.M., Ph.D.
Phang C. Tai, Ph.D.
Hartmut Wohlrab, Ph.D.

STAFF SCIENTISTS

Maureen Brennan, Ph.D.
Robert J. Fisher, Ph.D.
Philip J. Graceffa, Ph.D.
Cecilia Hidalgo, Ph.D.
James B. Hughes, Ph.D.
Saroj Joshi, Ph.D.
Paul C. Leavis, Ph.D.
Renne C. Lu, Ph.D.
Malcolm G. Pluskal, Ph.D.
Michael J. Pringle, Ph.D.
Mario S. Rosemblatt, Ph.D.
Mario Kumar Roy, Ph.D.
Terrence L. Scott, Ph.D.
Walter F. Stafford, III, Ph.D.
Terence C. Tao, Ph.D.
Vladimir Z. Volloch, Ph.D.
Chih-Lueh Albert Wang, Ph.D.

RESEARCH ASSOCIATES

Tatyana Dorfman, Ph.D.
Zenon Grabarek, Ph.D.
Suresh Kaplay, Ph.D.
Rebecca B. Kucera, M.S.
Katsuhide Mabuchi, Ph.D.
Barbara Ann Manuck, Ph.D.
Sumitra Nag, Ph.D.

STAFF FELLOWS

Dipak Chakrabarty, Ph.D.
John Peder Erickson, M.D.
Chilliah Jayabaskaran, Ph.D.
Donald E. Jones, M.D.
B. C. Lakshmi Kantham, Ph.D.
Pratima Karnik, Ph.D.
Hanno V. J. Kolbe, Ph.D.
Magotoshi Morii, Ph.D.
Tsutomu Nono, Ph.D.
Lajos Papp, M.D.
Barbara Pliszka, Ph.D.
B. K. Ahmed Rasheed, Ph.D.
Ulla Rasmussen, Cand. Scient.
Maria Sasvari-Szekely, Ph.D.
Bruce Schweitzer, Ph.D.
Thomas Tharayil, Ph.D.
Li-Wen Wang, Ph.D.

RESEARCH FELLOWS

Shashiprabha Dasgupta, Ph.D.
Mark Eller, Ph.D.
Ana Maria Garcia, Ph.D.
Do Han Kim, Ph.D.
Gale Strasburg, Ph.D.
Hiroshi Suzuki, Ph.D.

RESEARCH ASSISTANTS

Bozena Antoniu, B.S.
Robert Bondaryk, A.B.
Cheryl L. Brown, B.S.
Adelaida D. Carlos, B.S.
Stefania Danko, M.S.
Rafi Dekermendjian, M.S.
Dianne Goldrick, B.A.
Elizabeth Gowell, B.S.
Karen Ann Hunt, B.S.
Yoshiharu Ishii, M.S.
Deborah LaPenta
Laszlo Meszaros, M.S.
Ralph Nelson, B.S.
Valeria Nemeth, C.T.
Valerie G. Overton, B.A.
Joan B. Petkun, B.S.
Sharon Lee Pickering, B.A.
Sophia Rits-Volloch, M.S.
Arpana Roy, M.S.
Cathy Scheiner, B.A.
Evelyn S. Schweig, B.A.
Richard Siber, B.A.
Archana Srivastava, B.A.
Magdalena A. Taber, M.A.
Jean Elizabeth Thaxter, B.S.
Elizabeth A. K. Thompson, B.A.
Pamela Jean Tupper, B.A.
Anna G. Wong, B.A.
Eileen Wong, B.A.

VISITING SCIENTISTS

Gaspar Banfalvi, Ph.D.
Aharon Farberov, Ph.D.
Yuoguo Huang, Ph.D.
Wolfgang Pschorn, Ph.D.
John F. Ryan, M.D.
Guan-chiao Yu, Ph.D.

ADMINISTRATION

Vincent F. Raso, C.P.A.
Assistant Executive Director/ Controller

Patricia Brouillette
Administrative Assistant

Helene Clinton
Financial Assistant / Bookkeeper

Virginia Cahill
Assistant Bookkeeper

DEVELOPMENT

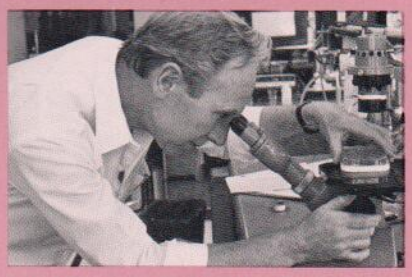
Jacquelyn MacL. Findlay
Director of Development

DEPARTMENTAL ADMINISTRATION

Carol G. Burke
Mary Caulfield
Arlene Clark
Katherine M. Dempsey
Dorothy Syrigos

HOUSEKEEPING

Maria Bozzella
Shirley Eiland
Phuong Ngoc Huynh
Lucille Konjoian



John Gergely, Satyapriya Sarkar, Shashiprabha Dasgupta, Ana Maria Garcia, John Seidel (seated), Natalie Jacobson and Chet Curtis (MDA State Co-Chairpersons), Sherwin Lehrer, and Paul Leavis at Muscular Dystrophy Association presentation of Research Awards.

Peter Davison examines the growth of monoclonal antibody-producing cells.

BOSTON BIOMEDICAL RESEARCH INSTITUTE
BALANCE SHEETS
AUGUST 31, 1984 AND 1983

	1984	1983
ASSETS		
CURRENT ASSETS:		
Cash	$ 566,939	$ 101,095
Grants receivable	4,054,098	2,963,803
Pledges receivable	26,000	25,000
Overhead and fringe benefit adjustment receivable	—	235,922
Prepayments, deposits and other receivables (note 7)	130,298	52,936
Investments, at market value (cost 1984—$1,344,663 1983—$1,135,897) (note 5)	1,433,116	1,235,449
Total current assets	6,210,451	4,614,205
FIXED ASSETS: (notes 1 and 2)		
Leasehold improvements	1,935,632	1,935,632
Research equipment	3,103,710	3,025,833
Furniture and fixtures	47,129	47,129
Total	5,086,471	5,008,594
Less accumulated depreciation and amortization	3,030,130	2,648,275
	2,056,341	2,360,319
	$8,266,792	$6,974,524
LIABILITIES AND FUND BALANCES		
CURRENT LIABILITIES:		
Accounts payable and accrued expenses	$ 40,703	$ 40,000
Overhead & fringe benefit adjustment payable	287,002	—
Deferred grant income (note 4)	3,908,190	3,034,589
Deferred fund (building) (notes 4 and 6)	115,702	115,702
Total current liabilities	4,351,597	3,190,291
FUND BALANCES: (note 1)		
Operating	315,555	107,556
Plant and equipment (note 6)	1,224,969	1,022,338
Permanent research	318,330	294,020
Fixed assets (notes 1 and 2)	2,056,341	2,360,319
Total fund balances	3,915,195	3,784,233
	$8,266,792	$6,974,524

See accompanying notes to financial statements.

BOSTON BIOMEDICAL RESEARCH INSTITUTE
STATEMENTS OF REVENUES, EXPENSES AND CHANGES IN FUND BALANCES
FOR THE YEARS ENDED AUGUST 31, 1984 AND 1983

	1984	1983
REVENUES:		
Grants	$4,371,936	$4,139,929
Equipment replacement	108,127	125,221
Contributions and pledges	150,292	107,293
Property and equipment purchased (notes 1 and 2)	77,877	139,945
Investment income	139,904	178,040
Total	4,848,136	4,690,428
EXPENSES: (by department)		
Muscle Research	2,110,150	2,341,382
Cell Physiology	1,127,505	909,504
Fine Structure	427,003	369,149
Metabolic Regulation	581,048	403,623
General Research	47,207	140,039
Fund Raising	31,975	30,951
Purchase of fixed assets (note 1)	10,431	9,800
Depreciation and amortization (note 2)	381,855	385,842
Total	4,717,174	4,590,290
NET ADDITION (DEDUCTION) TO FUND	130,962	100,138
TRANSFER OF INVESTMENT INCOME FROM BUILDING FUND: (notes 4 and 6)	—	113,241
FUND BALANCES, BEGINNING OF YEAR (note 1)	3,784,233	3,570,854
FUND BALANCES, END OF YEAR (note 1)	$3,915,195	$3,784,233

See accompanying notes to financial statements.

NOTES TO FINANCIAL STATEMENTS AUGUST 31, 1984 AND 1983

Note 1: Significant Accounting Policies:

Fund Accounting:

The accounts are maintained on the accrual basis and in accordance with the principles of fund accounting. Funds that have similar characteristics have been combined into the following fund groups:

- Unrestricted funds include two groups representing the portion of expendable funds available for support of operations: a) The operating fund includes unrestricted contributions and investment income less the cost of grants not reimbursed in full by granting agencies, and further reduced by transfers to other funds; b) Other unrestricted funds represent reserves transferred from the operating fund, and a building program fund derived from unrestricted contributions.
- Restricted funds represent resources restricted for research grants or building additions. These funds are deemed to be earned and reported as revenues when the Institute has incurred expenditures in compliance with the specific restrictions. Amounts received but not yet earned are reported as restricted deferred amounts (See Note 4).
- Fixed assets fund represents the undepreciated cost of leasehold improvements, equipment and furniture and fixtures.

Other Matters:

All income, gains, and losses arising from the sale, collection, or valuation at market of investments are allocated to the fund owning the assets.

A portion of the overhead chargeable to research grants is deemed to be reimbursement for equipment and is shown as an addition to the Equipment Replacement Fund. This amounted to $108,127 in 1984 and $125,221 in 1983. In addition, $10,431 of equipment was charged to the operating fund in the year ended August 31, 1984, $7,579 in 1983 and added to the plant fund.

Note 2: Plant Assets and Depreciation:

The Institute, under an agreement dated June 16, 1970, shares with Retina Foundation the use of research facilities for fifty years at 20 Staniford Street, Boston, and of a research farm in Townsend, Massachusetts.

The leasehold improvement asset category represents the cost of the Institute's long-term leasehold in the building and improvements, and is being amortized over the 50-year lease term. The furniture and equipment categories represent, at cost, acquisitions from operating funds and restricted research grant awards. Depreciation is primarily on the straight-line basis over the estimated ten year useful life of the assets. All depreciation and amortization is charged to the plant fund.

Note 3: Government Grants:

All grant costs to the U.S. government and most private grants are subject to audit by the granting agency.

Note 4: Changes in Deferred Restricted Amounts:

	1984			1983
	Building Fund	Grants & Contracts	Total	Total
Balance, beginning of year	$115,702	$3,034,589	$3,150,291	$3,543,321
Additions:				
New grants awarded		5,142,152	5,142,152	3,832,608
Contributions and pledges		1,000	1,000	
Investment income	9,660	23,362	33,022	52,669
	125,362	8,201,103	8,326,465	7,428,598
Deductions:				
Funds expended for designated purposes		4,292,913	4,292,913	4,140,900
Transfer of investment income from Building Fund: (Note 6)				
Current year	9,660		9,660	24,166
Prior year				113,241
Balance, end of year	$115,702	$3,908,190	$4,023,892	$3,150,291

Note 5: Investments:

Investments consist of corporate and government bonds and listed stocks. Also included is an $800 investment made in 1982 in Boston Biotechnology Corporation. This company was formed to utilize and commercialize certain technical processes originated at Boston Biomedical Research Institute and elsewhere.

The investment holding represents the entire outstanding stock of Boston Biotechnology Corporation and is shown at cost since Boston Biotechnology was inactive through the Institute's year end.

Note 6: Transfer of Investment Income from Building Fund:

During 1983 the Board of Trustees of the Institute voted to transfer the Unrestricted Building Fund balance at August 31, 1982 of $49,057 and Restricted Building Fund investment income from prior years of $113,241 to the Plant and Equipment Fund. Investment income allocated to the Building Fund during 1984 of $9,660 was also transferred to the Plant and Equipment Fund.

Note 7: Advances to Subsidiary:

The Institute has advanced $57,595 to Boston Biotechnology Corporation. This amount is included in the category Prepayments, deposits and other receivables.

October 4, 1984

Board of Trustees
Boston Biomedical Research Institute
Boston, Massachusetts

I have examined the balance sheet of Boston Biomedical Research Institute as of August 31, 1984 and the related statement of revenues, expenses and changes in fund balances for the year then ended. My examination was made in accordance with generally accepted auditing standards and accordingly included such tests of the accounting records and such other auditing procedures as I considered necessary in the circumstances. The financial statements of Boston Biomedical Research Institute for the year ended August 31, 1983 were examined by Singer & Lusardi, CPA's, whose report dated October 5, 1983 expressed an unqualified opinion on those financial statements.

In my opinion, the aforementioned financial statements present fairly the financial position of Boston Biomedical Research Institute as of August 31, 1984, and the results of its operations and changes in fund balances for the year then ended, in conformity with generally accepted accounting principles applied on a consistent basis.

John Vecchi / Certified Public Accountant
400 Hillside Avenue/Needham, Massachusetts 02194
(617) 449-5545

Boston Biomedical Research Institute is an independent, non-profit organization with a staff of M.D. and Ph.D. investigators who carry out a broad program of basic and applied research in biology and medicine, and provide highly specialized training for future physicians and scientists. For over a decade the Institute has maintained its position among the leaders in the world-wide effort to prevent and cure disease. Areas currently under investigation range from the study of birth defects to the biology of aging. The findings of Institute scientists are used by others in clinical projects including those aimed at helping people suffering from cancer, heart disease, muscular diseases, nerve degeneration and premature aging. The Institute's research programs will ultimately bring lasting benefits to the future well-being of mankind.

BOSTON BIOMEDICAL RESEARCH INSTITUTE
20 Staniford Street
Boston, Massachusetts 02114
Tel. (617) 742-2010