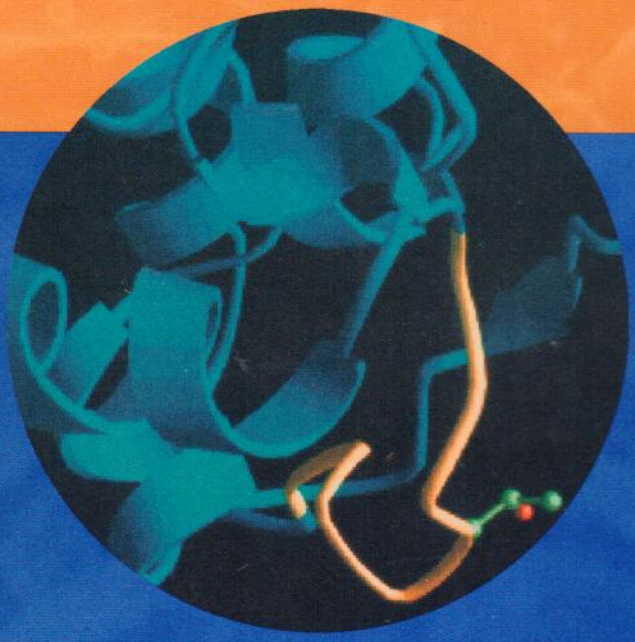
Boston Biomedical Research Institute



ANNUAL REPORT 1998

Carol Lord Means

Carol Lord Means died on April 30, 1998. Mrs. Means was the Founding President of the Boston Biomedical Research Institute, a Trustee and most recently an Overseer in her thirty-year affiliation with the Institute. BBRI was fortunate indeed to have her strong and talented leadership at the time of its founding in the late 1960's. Mrs. Means remained an active supporter of BBRI well into her 80's and until that time was a regular attendee at Board Meetings and other Institute events. Her vision for BBRI and her enthsiastic support of biomedical research will always be remembered by those who had the privilege to know Carol Means.

Carol Lord Means with Former BBRI Director, Peter F. Davison, Ph.D.

FRONT COVER

Model of the structure of the kinase core of protein kinase C zeta. The model was obtained by threading the amino acid sequence of the kinase domain of the protein using a ProteinPredict program at the European Molecular Biology Laboratory. The model obtained shows the classical kinase domain structure and highlighted in yellow is the 'activation loop' which interfaces the two lobes of the kinase core. In red at the center is the threonine residue (T410) which is phosphorylated by the PDK-1 protein kinase. Model courtesy of Drs' Toker, Harrison & Bohm, BBRI.

MESSAGE FROM THE PRESIDENT

One consideration in formulating our five-year Strategic Plan was the notion of critical mass. To achieve our goal of maintaining BBRI's leadership position in our biomedical research field required expansion of the scope of our muscle research and adding complementary research areas. Dr. Kathleen Morgan, BBRI's Director will summarize the excellent progress in this regard.

To further strengthen the research programs, significant additions to the scientific staff are required. Our ongoing recruitment program has been extremely successful in attracting dedicated, promising young scientists. However, new scientists and new equipment lead to pressures on our laboratory facilities, which we share with our landlord, Schepens Eye Research Institute (SERI).

The Schepens Eye Research Institute has also undertaken expansion that has necessitated leasing space in the surrounding neighborhood. During the latter part of fiscal year 1998 BBRI and SERI have explored various options for satisfying our mutual need for space. We anticipate in Fiscal Year 1999 adopting a facilities plan consistent with BBRI's vision of its future programs.

Hand-in-hand with assembling a critical mass of faculty and research programs is the need to expand the circle of BBRI friends whose generous gifts provide the seed money for these efforts. While our successes to date significantly increased our grant base, grants do not cover the costs of supporting new scientists, equipping laboratories or providing bridge support for experienced scientists.

1998 was a very successful year for BBRI and I thank all our loyal donors for their support. 1999 promises to be another tremendous and challenging year – one which should be invigorating for us all. It will provide a superb opportunity to introduce the exciting world of biomedical science to a new group of friends. What could be more rewarding than being a part of an organization, which has, and will continue to have, a beneficial impact on the health of this generation and that of our children and grandchildren!

"1998 was a very successful year for BBRI and I thank all our loyal donors for their support. 1999 promises to be another tremendous and challenging year – one which should be invigorating for us all."

David A. Gibbs, Sc.D.

MESSAGE FROM THE DIRECTOR

This has been an exceptionally active and satisfying year at the Institute. We are three years into the five-year Strategic Plan for the Institute that was put together at my arrival at the Institute and it is a delight to see how much of that plan the faculty and friends of the BBRI have accomplished. In this short time we have: significantly increased our grant base, added eight new members to our faculty, had a record breaking fundraising campaign to purchase state of the art crystallography equipment, increased the number of collaborations with researchers in area hospitals, and, most importantly, we have "pushed back the frontiers of our knowledge" in areas relevant to heart disease, stroke, Alzheimer's and cancer! You will find some of those stories in this Annual Report.

As our supporters know, the fundamental science at the Institute has always been strong in the field of muscle research. As part of the Strategic Plan, we have significantly expanded the scope of our muscle research and have strengthened our research in two new, but intentionally overlapping areas, signaling (or cell communication) and regulation of cell growth. Indeed the continued success of our research programs and our plans to expand them has lead us into negotiations with our landlord and neighbor, the Schepens Eye Research Institute. Both institutes require more research space and we are looking closely at what will be most beneficial and appropriate to the future plans of BBRI.

The scientists featured in this Annual Report work at the intersection of BBRI's three main research areas. Dr. Coluccio is an expert in the field of non-muscle motility – a term that may seem to be a bit of an oxymoron at first glance – but in reality, it is a hot new field of muscle research. Work in this field has resulted in the discovery that the same sort of "molecular motors" that allow our arms and legs to move also control processes as diverse as the metastasis of cancer cells and the directional growth of neurons in a baby's brain.

Dr. Toker works primarily in the field of signaling, but as you will read, in the process of trying to figure out how the cell signals are communicated – and move from one molecule to a neighboring molecule – his research has taken him into the areas of cell motility and cancer research.

Dr Leavis, who has made many significant contributions in the field of muscle proteins with his past publications, has now applied his expertise in protein chemistry to the development of a novel screening technique to discover new factors that regulate cell growth. As you will read, these newly discovered substances have tremendous potential to be developed as new therapeutics for the treatment of cancer.

To those of you who have been loyal supporters of the BBRI, I hope you will continue to share in the excitement and fascination that accompanies the ongoing development of these scientific stories – and, I thank you! To those of you who are new to the BBRI and would like to hear more, I welcome you and invite you to join me for a tour of our facilities!

Kathleen G. Morgan

Kathleen G. Morgan, Ph.D.

Introduction

We are all familiar with the story about the three blind men who tried to describe an elephant. Depending on what part of the elephant each of the blind men happened to touch – its tail, its leg, or its trunk – a quite different creature was perceived. As scientists, we are in much the same position as the three blind men, because we try to "see" biological processes that cannot be perceived by the eye. We therefore use one or another experimental approach to examine a process, for example the growth of a human cell, and describe it in terms of what we have learned from our experiment. Needless to say, scientists using different experimental approaches may end up with very different perspectives. Only when we put our results in the context of other findings do we get the whole picture and important conceptual breakthroughs can result. This is why interdisciplinary and highly interactive research institutes such as the BBRI, where scientists approach research problems in many different ways and then compare their diverse observations, have a much better chance of answering fundamental biological questions than do narrowly focused research groups. It would have been easy for BBRI just to keep building on the strength for which it has achieved world-wide renown, that is, investigating the structure of muscle proteins – but instead, BBRI has elected to broaden its horizon and study muscle in a much wider biomedical context by not only focusing on the molecular basis of motility but also on mechanisms of cell communication and the control of cell growth.

This principle is well illustrated by the accounts of the three research

projects that are the subject of this Annual Report. Each of these projects – molecular motors, lipid signaling, control of embryonic growth – looks at animal cells from a quite different point of view, yet all provide insights into factors that underlie cancer. This is because cancer is caused by the loss of growth control and becomes deadly when rapidly proliferating cancer cells become motile and invade other tissues and organs. One can hardly underestimate the medical impact of research on the growth and invasiveness of cancer cells. Cancer is one of the primary causes of death in the United States, second only to cardiovascular disease.

Estimates from the American Cancer Society and the National Cancer Institute indicate that every day 1500 people die as a direct result of cancer, with over 2 million new cases expected this year alone and an annual cost of more than $100 billion in terms of direct medical costs and lost productivity.

Connections

What do embryonic growth inhibitors, signaling kinases, and molecular motors have in common? Superficially, they appear as quite independent research projects, each with some relevance to the understanding of cancer. But if we think about it more carefully, we realize that the embryonic growth inhibitors identified by Dr. Leavis must have cellular targets, which are among the signaling pathways studied by Dr. Toker. Once one identifies a target for a drug, one can use rational drug design to synthesize even more potent inhibitors with fewer side effects. In turn, Dr. Toker's signaling pathways modify proteins such as the integrins that interact with the cytoskeleton, along which Dr. Coluccio's molecular motors move to help cancer cells invade tissues. Drugs that modulate these interactions may be a new class of anti-cancer agents. It is the ability to make connections such as these which makes the type of interdisciplinary research that is done at BBRI extremely rewarding.

MYOSIN I – AN UNUSUAL MOLECULAR MOTOR

Lynne M. Coluccio, Ph.D.

B.S. SUNY Albany, Biology, 1978

M.S. Rensselaer Polytechnic Institute, Biology, 1980

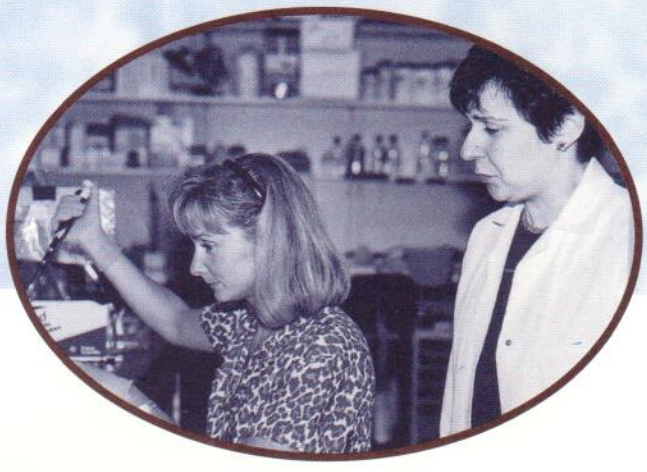
Ph.D. Rensselaer Polytechnic Institute, Biology, 1982

Cells have different shapes depending on their functions. For example, brain cells called neurons extend long processes called axons along which signals are carried from one part of the body to another. Intestinal cells have multiple short projections that assist in the absorption of foods and nutrients. In these cases and others, an underlying network of tracks, called the cytoskeleton, comprised primarily of actin filaments, allows for the formation and maintenance of these specialized extensions.

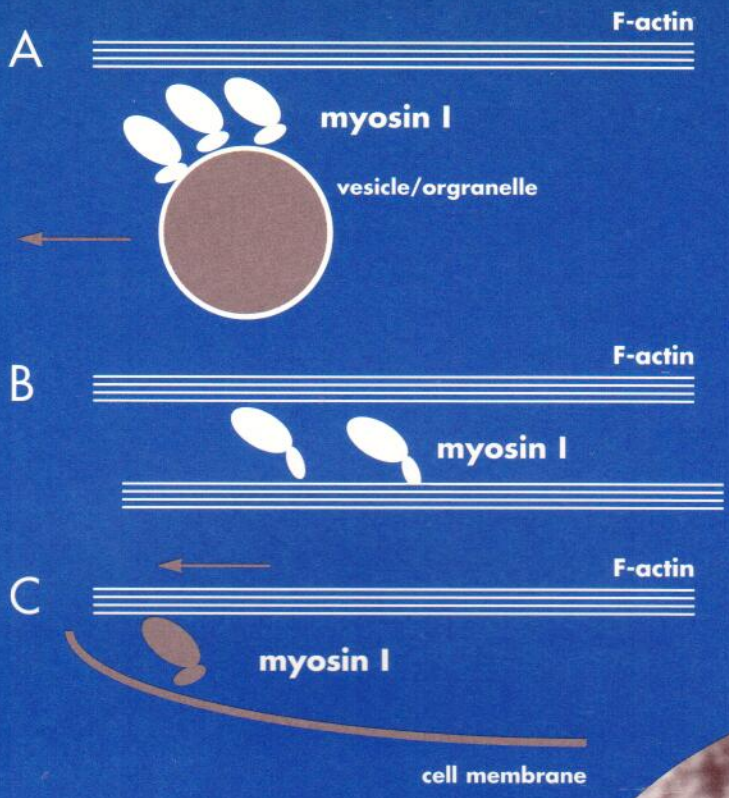
Associated with the actin filaments are a class of small molecular motors called myosin I. Myosin I is thought to transport cargo along the actin filaments by using the energy derived from hydrolyzing ATP and also helps in rearranging the actin filaments when a cell changes its shape in order to migrate. Its properties and presence at the leading edge of migrating cells suggest the involvement of myosin I in cell movement.

BBRI Principal Scientist Dr. Lynne Coluccio has been a pioneer in the study of myosin I in liver. Her studies have led to the purification of three different forms of myosin I from rat liver and now focus on the precise roles of these molecules. Recent studies in her laboratory have shown that there is considerable overlap in the distribution of these myosins in rat liver cells. One possible interpretation is that the different types of myosin I have overlapping functions; alternatively, the various kinds of myosin I in any particular location may perform different jobs. In two very rewarding collaborations, Dr. Coluccio is studying the mechanism by which myosin I interacts with actin filaments. She and Dr. Justin Molloy at the University of York, England, have found that myosin I moves along the actin tracks by taking double steps. This has not been observed before (skeletal muscle myosin takes single steps along actin) and has provided an exciting new look at how myosin-actin interactions occur.

Another study, which is being done in collaboration with Dr. Michael Geeves, Group Leader at the Max Planck Institute for Molecular

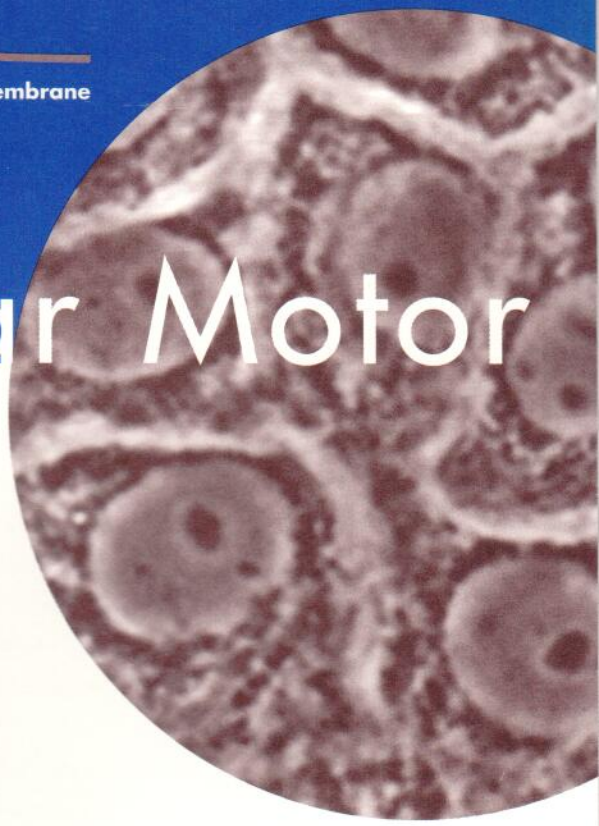


Dr. Coluccio and Dr. Perreault-Mical preparing myosin I samples.



Proposed roles for myosin I include vesicle transport (A), filament cross-linking (B), and morphological changes at the cell surface (C).

Molecular Motor



Physiology in Dortmund, Germany and Adjunct Scientist at BBRI, deals with the mechanism by which myosin I interacts with actin filaments. It has revealed that the dissociation of actin-myosin I complexes, which occurs in the presence of ATP, is much slower than that observed with other kinds of myosin, including the myosin responsible for muscle contraction. These studies indicate that myosin I is best suited for maintenance of cytoskeletal tension, which is essential for processes such as cell migration.

Given the potential role of myosin I in cell migration, Dr. Coluccio's research is of relevance to the understanding of cancer metastasis, which involves the migration of cancer cells to form remote tumors, and has attracted the support of the American Cancer Society and the National Institutes of Health. Another health-related aspect of myosin I is suggested by the large amount of this substance in the brain. Given the potential role of myosin I in normal embryonic development, Dr. Coluccio has recently been awarded a grant from the March of Dimes Birth Defects Foundation to pursue her studies on myosin I.

LIPID SIGNALING

Alex Toker, Ph.D.

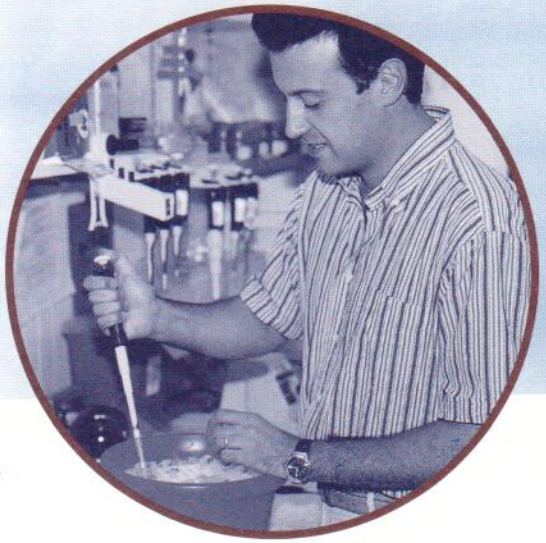
B.Sc. King's College, London, England, Biology, 1987

Ph.D. National Institute for Medical Research, England, Biochemistry, 1990

One of the earliest stages of cancer is carcinoma in situ, an abnormal proliferation of epithelial cells. This non-invasive cancer is typically confined to the tissue in which it formed and has not yet invaded the rest of the organ or other parts of the body. A cancer becomes metastatic when this mass of cells acquires the ability to become motile and invasive. Non-invasive cancers are almost always curable. In contrast, invasive carcinomas, or metastasis, are the most intractable forms of cancer and account for most of the mortality rates attributed to cancer.

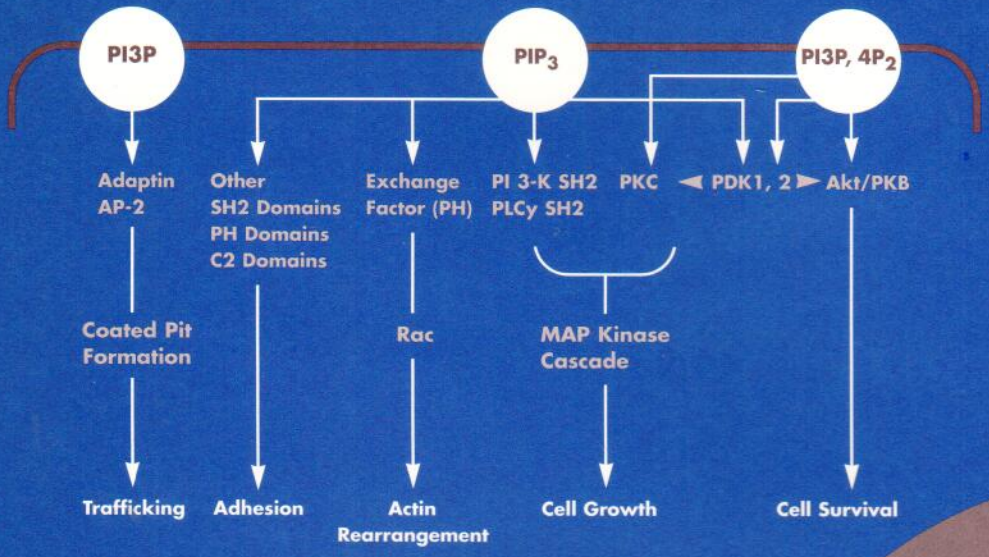
The research in the laboratory of Staff Scientist Dr. Alex Toker focuses on both the proliferative and the invasive aspects of carcinoma. Proliferation of cells depends on their ability to respond to external signals such as hormones and growth factors, which are transmitted to the nucleus of the cell where they activate the cellular machinery for DNA synthesis and cell division. This process, known as signal transduction, is often deregulated in cancer cells. A large number of proteins have been identified which participate in this signaling process. Of particular importance are enzymes known as kinases, which transfer phosphate from ATP to other proteins or to phosphoinositides, one group of lipids that make up cellular membranes. Dr. Toker has made important contributions to the understanding of the role of phosphoinositide 3-kinase (PI 3-K) in mediating signals from the outside of the cell to the interior. This enzyme is a lipid kinase and produces novel phosphoinositides, or lipids, which are elevated in all tumor cells studied to date. In addition, Dr. Toker's laboratory is working on a family of protein kinases known as protein kinases C and B (PKC and PKB). A better understanding of the cell biology and biochemistry of these protein kinases will provide insights into how their deregulation leads to carcinoma progression.

In addition to studying the role of these enzymes in the proliferation of cells, Dr. Toker is addressing their role in carcinoma invasion, an important event in the formation of metastatic tumors. One of the



Dr. Toker preparing a kinase reaction assay

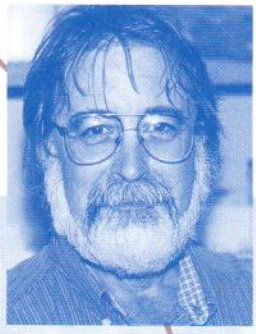
PROTEINS KNOWN TO BIND PHOSPHOINOSITIDES IN VITRO: POSSIBLE ROLES IN CELLULAR RESPONSES. The diversity of proteins which bind to thses lipids may provide an explanation for how PI-3-kinse family members regulate so many diverse physiological functions.



Protein kinases

hallmarks of metastatic cells is their ability to become motile and move through the matrix of proteins to which they are normally attached. Dr. Toker has established collaboration with Dr. Arthur Mercurio at the Beth Israel Deaconess Medical Center, whose laboratory has been studying the pathobiological characteristics of invasive breast and colon carcinoma cells. Their collaborative studies, which were recently published in the prestigious journal *Cell*, make a very strong case for the role of PI 3-K in mediating carcinoma invasion in these two model systems. The ability of PI 3-K to stimulate invasion depends on the activation of integrins, a family of cell surface receptor proteins which bind to the extracelular matrix and play a role in cell contact and motility. These studies are also focusing on other signaling proteins such as PKC to evaluate their role in invasiveness. One exciting prospect for the outcome of these studies is the development of drug inhibitors that can specifically block either integrins or PI 3-K and thus could eliminate carcinoma invasion and tumor metastasis.

EMBRYONIC GROWTH



Paul C. Leavis, Ph.D.

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

Research Associate in Neurology, Harvard Medical School

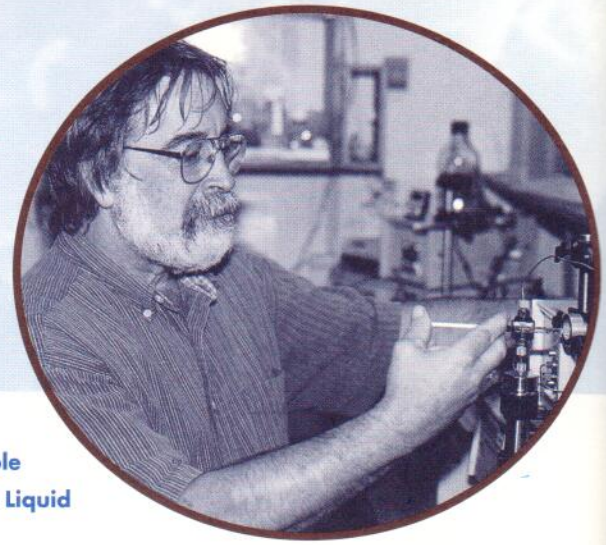
B.S. University of Notre Dame, Biology, 1966

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

At early stages of embryonic development, cells destined to form the various organs of the body begin as undifferentiated, primitive precursor cells. These precursor cells proliferate extremely rapidly, dividing dozens of times, and ultimately differentiate into some 250 different identifiable adult cell types such as muscle, nerve, or liver cells. Adult cells typically grow very slowly or may cease proliferating altogether. The rapid growth of the primitive precursor cells as well as their differentiation and growth arrest are thought to be carefully regulated by chemical growth factors secreted by the embryo.

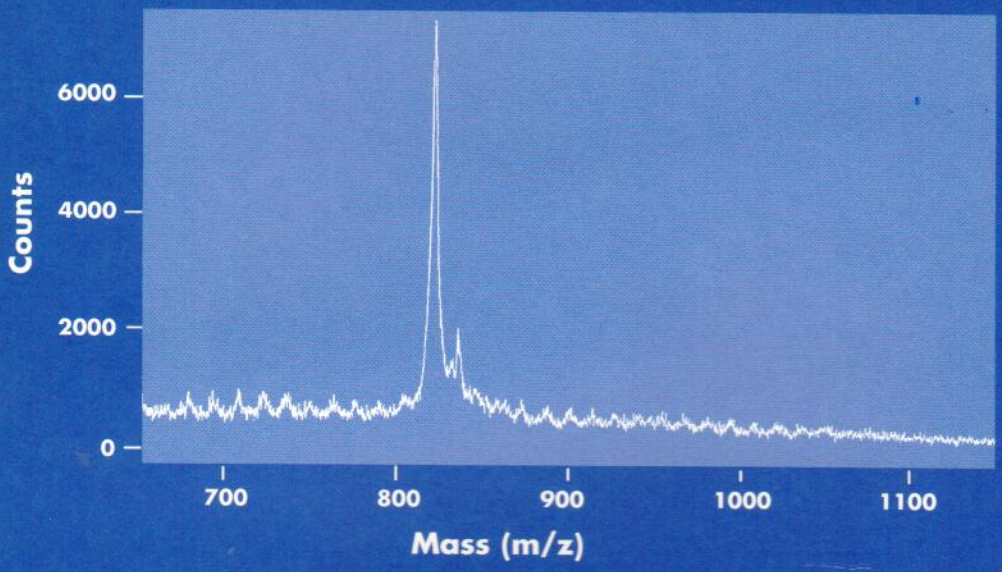
Cancer cells share some of the characteristics of undifferentiated embryonic cells. Although they may initially arise from differentiated adult cells, they regress to a more primitive form reminiscent of embryonic cells that tend to multiply at breakneck speed. But whereas the growth of embryonic cells is ultimately arrested by the factors secreted by the embryo, these factors are not produced by the adult organism and tumors therefore can grow out of control until they overwhelm the body.

Intrigued by the parallels between the growth of embryonic and cancer cells, Senior Scientist Dr. Paul Leavis wondered whether chemicals secreted by embryos to control their own growth might not also be able to control cancer cell proliferation. In collaboration with Dr. Eytan Barnea of enVision Biomedical Consulting in Cherry Hill, New Jersey, and with the support of a grant from the Defense Advanced Research Projects Agency (DARPA), Dr. Leavis recently initiated a research program to isolate possible tumor growth inhibitors from gestational pig tissue. He succeeded in isolating several factors from brain and liver that can inhibit the growth of various types of human cancer cells including breast, kidney, ovarian and cervical cancers as well as lymphomas. These factors also inhibited the growth of various non-human cancers but had no effect on non-cancerous cells. In order to screen many different fractions, Dr. Leavis developed a method for measuring their inhibitory effect on cancer cells grown in laboratory culture dishes.

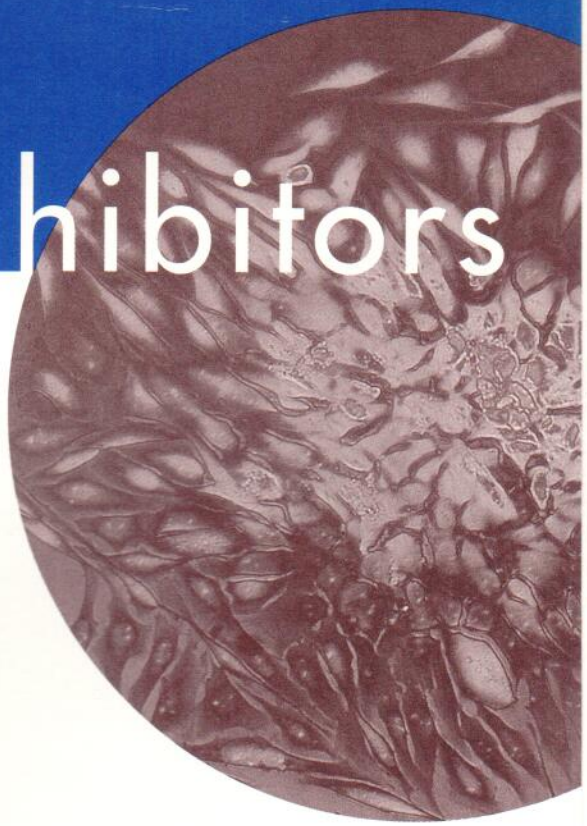


Dr. Leavis injecting a sample into the High Performance Liquid Chromatography System.

Mass spectrometric analysis of a tumor growth inhibitor from embryonic pig tissue. Mass spectrometry can be used to analyze as little as one picogram (one-trillionth of an ounce) of material and gives the exact molecular mass of the sample, in this case 819.035 Daltons, from which important structural information can be deduced. BBRI's state-of-the art mass spectrometer which was used in this experiment was purchased last year with the help of grants awarded by the National Institutes of Health and the National Science Foundation.



Growth Inhibitors



His results showed that the growth factors could inhibit growth of cancer cells at extremely low concentrations. Owing to their high potency, the factors are present in embryonic tissue in extremely minute amounts.

A major challenge at this early stage of the project is to purify one or more of the active factors in amounts sufficient to determine its chemical structure and thereby allow it to be synthesized for further testing. Dr. Young-Jin Choi, a postdoctoral fellow, is developing techniques for the rapid purification of the active factors from gestational tissue and to stockpile the material for further analysis. Based on structural analysis of one factor using BBRI's new state-of-the art mass spectrometer, the factor has now been synthesized chemically and is being tested for its anti-cancer activity. The possibility of identifying anti-cancer agents from embryonic tissue provides an exciting new approach, which offers unique benefits for cancer treatment. The very high potency of these agents and the fact that they originate from mammals raises the hope that they may act aggressively to inhibit cancer cells while being relatively non-toxic to normal cells.

DEVELOPMENT REPORT

Thanks to the tremendous support of our generous and loyal donors, the 1998 fiscal year was a very successful one for fundraising! We reached the 1998 Annual Fund target of $350,000 with two days to spare and ended the year with $355,000 raised from 178 gifts. This is a record amount for the Annual Fund and means that more Annual Fund support than ever was provided to launch new scientific careers and programs at BBRI, purchase state of the art scientific equipment, and give bridge support to experienced scientists awaiting funding from other sources.

I would like to thank the Development Committee for their hard work and expertise during the year – they not only worked tirelessly to ensure that we reached the Annual Fund target but also helped two Special Task Force's discover new ways of attracting funds from foundations and corporations. My thanks also to the trustees and corporators who shared their knowledge and insight as Task Force members.

We are constantly working to increase the number of friends and donors at BBRI. It is most encouraging to see 178 gifts to the Annual Fund this year, which is thirty-five more than 1997 and seventy-four more than 1996. I continue to believe that the finest way to introduce this wonderful, yet somewhat complex Institute to friends is by inviting them to join us at the Evening of Discovery or to bring them in for a tour of the facility. The excellent new *Case for Public Support* document produced by Harry Johnson and the Public Relations Committee should be a real help to us all as we talk to our friends about BBRI and the impact it has on the health of this generation and generations to come. There are always new things to discover when you visit BBRI – let's share this with as many people as we can in the year ahead!

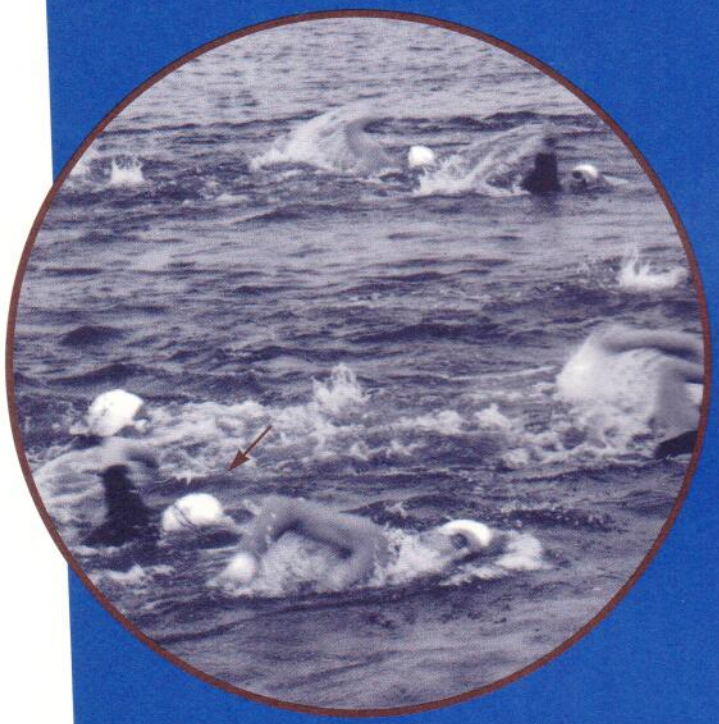
My sincerest appreciation to everyone that made a gift to BBRI this year – with your continued commitment and generosity, I am confident we can achieve our fundraising goals in the future.

Allie Blodgett
Development Committee Chair

"There are always new things to discover when you visit BBRI – let's share this with as many people as we can in the year ahead!"

Donors

Swimming for Science – Lauren Graham a Research Assistant in Dr. Toker's laboratory successfully completed a 34-mile triathlon raising over $2,000 for BBRI! Thank you Lauren!



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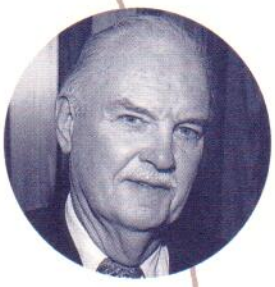
Ronna G. Woodward

* *deceased*

TREASURER'S REPORT



The fiscal year ended June 30, 1998 produced solid results, due in great part to the ongoing excellence of our scientific programs and the insight and fiduciary management of our Investment Committee. The investment portfolio had an overall return of 19% which generated over $1,773,000 in new funds. Grants from the National Institutes of Health (NIH) continue to be our financial anchor with grant revenue in excess of $4,500,000. This represents 88% of total grant revenue up from 83% in the previous fiscal year. Five new grants were received this fiscal year, including the renewal of the prestigious Program Project Grant for $7,696,000 over the next five years. BBRI is one of only a handful of research institutes in New England that currently has a Program Project Grant for a muscle research program. It is also most encouraging to see new grants from organizations such as the March of Dimes and the Hereditary Disease Foundation. Of special note is the fact that our $500,000 investment in crystallography equipment has already resulted in the recruitment of three new faculty members and multiple grants totaling over $1.4 million.

"Five new grants were received this fiscal year, including the renewal of the prestigious Program Project Grant for $7,696,000 over the next five years."

Indeed, we expect far greater returns in the coming years' as projects started in the last year begin to bear fruit. The Development Committee, coming off its most successful equipment campaign during fiscal year 1997, has produced the largest Annual Fund results in Institute history, over $355,000. Allie Blodgett deserves particular credit as her inspirational, creative leadership continues to thrive.

As we embark on the third year of the strategic plan, we should pause to reflect on the investment in the future made by the Institute through the addition of new researchers. To date, each new researcher on board for more than 12 months has secured significant funding from the NIH. Indeed five of the eight new scientists recruited since 1995 have been awarded major research grants totaling $6 million. In addition, BBRI's experienced scientists continue to compete successfully for peer reviewed grants from the NIH and other sources.

As mentioned earlier in this Annual Report, discussions with our landlord, Schepens Eye Research Institute, about the shortage of research space both organizations face began towards the end of this fiscal year. The Investment Committee, the Budget and Finance Committee and a Special Facilities Finance Committee are closely examining the financial implications and opportunities of any prospective move.

Respectfully submitted,
Ernest Henderson, III

BOSTON BIOMEDICAL RESEARCH INSTITUTE
STATEMENTS OF FINANCIAL POSITION

June 30, 1998 and 1997

	1998	1997
Assets		
Cash	$ 312,762	$ 718,342
Grants receivable	3,280,609	2,916,957
Unconditional promises to give:		
Unrestricted		250
Restricted	29,448	89,941
Investments	8,886,190	8,238,723
Prepayments, deposits and other receivables	137,683	136,707
Property and equipment	1,943,712	1,617,075
Deferred compensation investments	2,242,596	1,554,891
Total assets	16,833,000	15,272,886
Liabilities and net assets:		
Accounts payable and accrued expenses	$ 261,751	$ 156,613
Deferred income	3,396,889	3,018,464
Deferred compensation payable	2,242,596	1,554,891
Total liabilities	5,901,236	4,729,968
Net assets:		
Unrestricted	10,109,607	9,287,600
Temporarily restricted	353,716	859,175
Permanently restricted	468,441	396,143
Total net assets	10,931,764	10,542,918
Total liabilities and net assets	$ 16,833,000	$ 15,272,886

Copies of our complete, audited financial statements are available upon request from the Chief Financial Officer, Boston Biomedical Research Institute.

BOSTON BIOMEDICAL RESEARCH INSTITUTE
STATEMENTS OF ACTIVITIES

For the Ended Year June 30, 1998 and the Ten Months Ended June 30,1997

Changes in unrestricted net assets:	1998	1997
Revenues:		
Grants and contracts	$ 5,164,438	$ 4,400,559
Contributions	340,546	280,888
Investment income	1,635,513	1,859,970
Other income including licensing fees	21,663	241,667
Total unrestricted revenues	7,162,160	6,783,084
Net assets released from restrictions	583,747	67,453
Total unrestricted support	7,745,907	6,850,537
Expenses:		
Salaries and benefits	4,298,300	3,487,294
General support and services	1,375,233	878,256
Occupancy costs	890,404	572,483
Depreciation	315,619	169,458
Fund raising	44,344	55,110
Total expenses	6,923,900	5,162,601
Increase in unrestricted net assets	822,007	1,687,936
Changes in temporarily restricted net assets:		
Contributions	14,531	514,724
Investment income	63,757	119,200
Net assets released from restrictions	(583,747)	(67,453)
Increase (decrease) in temporarily restricted net assets	(505,459)	566,471
Changes in permanently restricted net assets:		
Investment income	72,298	74,731
Increase in permanently restricted net assets	72,298	74,731
Increase in net assets	388,846	2,329,138
Net assets at beginning of year	10,542,918	8,213,780
Net assets at end of year	$ 10,931,764	$ 10,542,918

GRANTS AND FELLOWSHIPS

Research Grants

National Institutes of Health

Drs. Adam & Badwey	MAPK in the contractile phenotype of smooth muscle	3/96 - 2/01	$1,128,000
Dr. Badwey	Enzymes modulating second messengers in neutrophils	4/93 - 3/98	639,000
Dr. Badwey	A novel signaling pathway in neutrophils	5/96 - 4/00	787,000
Dr. Coluccio	Myosin-I mediated processes in liver cells	8/97 - 7/01	1,407,000*
Dr. Gergely (MERIT)	Biochemistry of muscle contraction	7/89 - 10/97	2,733,000
Dr. Graceffa	Smooth muscle and non-muscle caldesmon	5/93 - 4/99	748,000
Dr. Ikemoto	Structure and function of sarcoplasmic reticulum	9/96 - 8/01	2,416,000
Dr. Lehrer	Tropomyosin and myosin interaction in muscle	12/95 - 11/00	2,044,000
Dr. Lehrer	Cooperative effects in smooth muscle regulation	5/97 - 3/98	171,000
Dr. Lu	Voyager TM Elite biospectrometry research station	4/97 - 4/98	162,000
Dr. Morgan	Regulation of contraction and growth of blood vessels	7/96 - 6/99	713,000
Dr. Morgan	Contraction of vascular smooth muscle cells	4/97 - 3/01	768,000
Dr. Paulus	Control of diaminopimelate and lysine biosynthesis	4/93 - 3/98	1,202,000
Dr. Paulus	Mechanism of protein splicing in Mycobacterium	4/97 - 3/01	1,403,000
Dr. Sarkar	Function of polyadenylate sequences in bacterial RNA	12/93 - 11/98	1,211,000
Dr. Sherman	Molecular chaperones and protein phosphorylation	5/96 - 4/00	1,081,000
Dr. Tao (MERIT)	Proximity relationship among muscle proteins	5/96 - 3/01	2,201,000
Dr. Volloch	Globin mRNA hyperproduction in response to anemia	11/96 - 2/98	89,000
Dr. Wang (Pro. Proj.)	Molecular mechanism of smooth muscle regulation	9/92 - 8/97	6,790,000
Dr. Wang (Pro. Proj.)	Molecular mechanism of smooth muscle regulation	12/97 - 11/02	7,696,000*
Dr. Wohlrab	Proton-coupled inorganic phosphate transport	4/92 - 3/98	1,231,000
Dr. Wohlrab	Phosphate path within homodemeric mitochondrial PTP	5/98 - 4/02	1,412,000*

National Science Foundation

Dr. Stafford	XL-A Analytical ultracentrifuge for the analysis of protein-protein interactions	3/96- 2/98	158,000
Dr. Lu	MALDI-TOF Mass spectrometer	4/97- 3/99	113,000

Alzheimer's Association

Dr. Volloch	Molecular mechanism of B-amyloid overproduction in Alzheimer's disease	4/97- 3/98	50,000

American Cancer Society

Dr. Coluccio	Myosin-I in liver	4/96- 12/98	187,000

Defense Advanced Research Projects Agency

Dr. Leavis	Embryonal factors as antiinfective agents	2/97- 1/00	844,000

Hereditary Disease Foundation

Dr. Stafford	Biophysical analysis of Huntington expanded repeats	9/97- 8/98	53,000*

March of Dimes

Dr. Coluccio	Mechanochemical properties of mammalian myosin I's	6/98- 5/99	59,000*

The Medical Foundation-Harcourt General Charitable Foundation, Inc.

Dr. Sherman	Molecular chaperones and degradation of oxidatively damaged protein	7/96- 6/98	100,000

Muscular Dystrophy Association

Dr. Ikemoto	Excitation-contraction coupling in malignant hyperthermia	7/94- 12/97	130,000

Sponsored Research

Dr. Stafford	Analytical ultracentrifugation	5/97- 7/98	60,000

Fellowships

Dr. D'Angelo	National Institutes of Health	3/96- 2/99	71,500

* *New grants in fiscal 1998*

BOSTON BIOMEDICAL RESEARCH INSTITUTE STAFF

Director

Kathleen G. Morgan, Ph.D.

Deputy Director

Henry Paulus, Ph.D.

Senior Scientists

John A. Badwey, Ph.D.
Peter S. Coleman, Ph.D.
John Gergely, M.D., Ph.D., D.Sc.M.(hon.)
Philip J. Graceffa, Ph.D.
Noriaki Ikemoto, Ph.D.
Saroj Joshi, Ph.D.
Paul Leavis, Ph.D.
Sherwin S. Lehrer, Ph.D.
Renne C. Lu, Ph.D.
Kathleen G. Morgan, Ph.D.
Henry Paulus, Ph.D.
Victor A. Raso, Ph.D.
Nilima Sarkar, Ph.D.
Walter F. Stafford, III, Ph.D.
Terence Tao, Ph.D.
Chih-Lueh Albert Wang, Ph.D.
Hartmut Wohlrab, Ph.D.

Principal Scientists

Leonard Adam, Ph.D.
Lynne M. Coluccio, Ph.D.
Zenon Grabarek, Ph.D.
Vladimir Z. Volloch, Ph.D.

Staff Scientists

Andrew Bohm, Ph.D.
Roberto Dominguez, Ph.D.
Celia J. Harrison, Ph.D.
Michael Sherman, Ph.D.
Alex Toker, Ph.D.

Senior Research Associates

Roque El-Hayek, M.D.
Yin Luo, Ph.D.
Katsuhide Mabuchi, Ph.D.
Katherine Sheldon, Ph.D.

Research Associates

Shu-Qin Jiang, Ph.D.
Jing-Lun Wu, Ph.D.

Fellows

Xiaolei Ao, Ph.D.
Corrado Bacchiocchi, Ph.D.
Gong-Jie Cao, Ph. D.
Young Jin Choi, Ph.D.
Gerard D'Angelo, Ph.D.
Chantal Dessy, Ph.D.
Vladimir Gabai, Ph.D.
Nina Golitsina, Ph.D.
Emmanuel Guelin, Ph.D.
Michael Jacobsen, Ph.D.
Jolanta Kordowska, Ph.D.
Knut Langsetmo, Ph.D.
Regent Laporte, Ph.D.
Young-Ho Lee, Ph.D.
Barbara Leinweber, Ph.D.
Jian Ping Lian, Ph.D.
Constance Menice, Ph.D.
Anatoli Meriin, Ph.D.
Cynthia Perreault-Micale, Ph.D.
Yukio Saiki, Ph.D.
Kaori Shingledecker, B.A.
Gisele Tavares, Ph.D.
Motohisa Tofukuji, Ph.D.
Carlos Witte-Hoffmann, Ph.D.
Guanming Wu, Ph.D.
Qian Zhan, Ph.D.

Emeritus Scientists

Peter F. Davison, Ph.D.
Jen-shiang Hong, Ph.D.
D. Rao Sanadi, Ph.D.
Frank Sreter, M.D., D.V.M., Ph.D.

Adjunct Scientist

Michael Geeves, Ph. D.

BBRI Scholars

Judith Gallant, Ph.D.
Julia Yaglom, Ph.D.

Research Assistants

Mitch Balish, Ph.D.
Minhua Chai, B.S.
Adelaida D. Carlos, B.S.
Molly Dixon, M.S.
Paula F. Geary, B.A.
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Elizabeth Gowell, B.S.
Lauren Graham, B.A.
Hongqui Guo, B.S.
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Jessica Jaime, B.S.
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Christine Kearney, B.S.
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Yanhua Li, M.B.
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Samantha Matson, B.S.
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Marie-Claire Overgaag, B.S.
Gina M. Pagani, B.S.
Sophia Rits-Volloch, M.S.
Anna G. Wong, B.A.

Visiting Scientists

John Codington, Ph.D.
Satyapriya Sarkar, Ph.D.
In-Kyeom Kim, M.D., Ph.D.
Naruto Matsuda, M. D., Ph. D.
Michael Taggart, Ph.D.

Students

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Taylor Ripley
Anna Shefrin
Alexander Shushan
Carrie Sougnez, B.S.

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Human Resources Manager
Virginia Cahill
Helene Clinton
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Michael Procopio
Asst. Dir. of Computer Services

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Jesse Ward Putnam
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