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JAN 14 1991

Worcester Foundation for  
Experimental Biology, Inc.  
ATTN: Richard Eastman  
Business Manager  
222 Maple Avenue  
Shrewsbury, MA 01545

Dear Mr. Eastman:

This is in response to your September 19, 1990, letter concerning the applicability of the exemption provisions of §170.11(a)(4), 10 CFR 170, to License 20-01225-01. Based on the information you provided, specifically that the Foundation is a non-profit organization chartered by the Commonwealth of Massachusetts to carry out education programs for training and education of students and to grant degrees, and since License 20-01225-01 no longer authorizes human use as pointed out in your July 15, 1988, letter, the fee exemption in §170.11(a)(4), 10 CFR 170, is applicable to License 20-01225-01. We have determined that the exemption also applies to License 20-01225-10. The reclassification of these licenses is effective with the July 2, 1990, revision to 10 CFR 170.

/s/

Glenda C. Jackson, Chief  
Materials License Fee Section  
License Fee & Debt Collection Branch  
Division of Accounting and Finance  
Office of the Controller

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Glenda C. Jackson, Chief  
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License Fee & Debt Collection Branch  
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# WORCESTER FOUNDATION FOR EXPERIMENTAL BIOLOGY

222 Maple Avenue, Shrewsbury, Massachusetts 01545 Telephone: 508-842-8921 FAX: 508-842-7762

An Independent Research Institute in the Medical and Life Sciences

September 19, 1990

Ms. Glenda Jackson  
License Fee Management Branch  
Division of Accounting & Finance  
Office of Administration & Resources  
Management  
U.S. Nuclear Regulatory Commission  
Washington, DC 20555

Dear Ms. Jackson:

I am responding to your request for a complete explanation of the Foundation's educational activities.

Although no one at this institution would deny that the Foundation is a basic research organization that offers educational opportunities as an adjunct activity, the Foundation has been very proud of its academic offerings ever since its inception by two college professors at Clark University in 1944. I can enumerate the present educational aspects of the Foundation as follows:

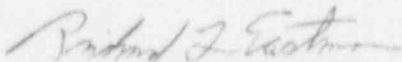
- 1) The Foundation's Charter, copy enclosed, speaks of the authority "to carry on educational programs for the training and education of students." Additionally the Charter empowers the Foundation to grant the earned Doctor of Science degree (Sc.D.), as well as honorary degrees.
- 2) The Foundation participates in a consortium Ph.D. program for exceptional students with backgrounds in the natural sciences. At any one time the Foundation has a dozen or so graduate students on its campus.
- 3) During the summer months the Foundation sponsors a Summer Training Program for undergraduate college students. This program typically involves 15 or so students who spend 10 weeks in an intensive research training atmosphere.

- 4) Postdoctoral training is recognized as an essential component of the fledgling scientist's education. The Foundation is proud of its long history of providing research training experiences for newly minted Ph.D's. A portion of current postdoctoral training activity at the Foundation is supported by a training grant from the National Institute of Child Health and Human Development, evidence that the National Institutes of Health holds the Foundation's ability to provide meaningful postdoctoral training in high regard.

A complete description of the Joint Ph.D. Program, the Summer Training Program and Postdoctoral Training Programs can be found in the enclosed Annual Report for 1989 on pages 24 and 25.

If I can provide additional information in this regard, please let me know.

Sincerely,



Richard L. Eastman  
Business Manager

RLE:mc



CHAPTER  
THE COMMONWEALTH OF MASSACHUSETTS

Be it known that whereas Harlow Shapley, Dwight E. Priest, R. G. Hoskins, Chandler Bullock, W. J. Crozier, Samuel C. Gwynne, William Malamud, Myles Morgan, Levi A. Olan, Carl E. Wahlstrom and Joseph Talano

have associated themselves with the intention of forming a corporation under the name of Worcester Foundation For Experimental Biology, Inc.,

for the purpose of the following:--To carry on investigation in the biological sciences, including the medical sciences, and to receive, hold, and administer funds for the purpose of endowing, assisting, and publishing the results of such investigations. Also to hold, receive, maintain and administer fund or funds for scientific and educational services, and the corporation may expend or apply the fund or funds, or income therefrom, either directly or through other corporations, associations or individuals, for the promotion and promulgation of science and scientific data. Recognizing that this work must involve studies not only in those fields in which knowledge is fairly well systematized but also in others, the nature of which is less well defined both as to character, expression and classification of the phenomena involved, it is the purpose of this corporation to exercise the greatest liberality in the designation of the fields of study to be investigated and in the selection of those who will direct the chosen lines of research. This corporation shall have full power to follow the purposes above set forth, although this research may lead to fields unmentioned therein and unknown at the present time; and nothing herein contained shall be considered as in any way limiting the rights of the corporation to pursue its objects as aforesaid. And, in addition to the above, to carry on educational programs for the training and education of students in the biological sciences and related sciences with power to grant degrees of Doctor of Science. Students to be selected as candidates for such degrees shall already have received the degree of Doctor of Medicine, Doctor of Philosophy, or a similar doctorate degree, and also shall have completed with distinction the academic portions of those training programs at this institution which do not lead to degrees, or in lieu of having completed such training programs at this institution shall, by having carried out independent research at this institution, have demonstrated to the satisfaction of the representatives of the Trustees that they are individuals of superior academic ability and have great scientific potential. Candidates for the Doctor of Science degree shall enter a program of courses designed to enhance their ability to recognize and appreciate important problems in biology and medicine and to devise solutions to them, and to a program of courses consisting of lectures, laboratories and demonstrations to familiarize such candidates with the important tools and instruments used in modern biological research. Each candidate for the Doctor of Science degree will be required to demonstrate his ability to contribute to scientific advancement by the completion of a dissertation containing the results of independent research studies, this dissertation to be judged by a suitable committee of faculty or distinguished scientists representing the Trustees; and to award such appropriate honorary degrees as are usually conferred by colleges in this Commonwealth excluding medicine to individuals who, by their scientific activity, or by other means, have had a beneficial influence on the advancement of knowledge. And, in addition to the above, to establish, equip, maintain, operate and conduct a clinic or clinics, either independently or in conjunction with hospitals, sanitarium and other institutions, for the treatment, care and relief of the diseased, sick, infirm and injured, and for the study of the cause, nature, prevention, treatment and cure of various diseases, and for the dissemination of knowledge relating thereto, and the erection, equipment and maintenance of buildings, laboratories and other facilities necessary or incidental --eto; to employ superintendents, doctors, interns, nurses, medical officers, laboratory technicians, and such other employees as may be necessary for the proper conduct of the clinic and the institution, and to do any and all things necessary or proper in carrying out the purposes and objects hereof within the general scope and purpose of this Foundation. Any income derived therefrom shall be used for the general welfare purposes of the Foundation. In carrying out the purpose of this corporation, it may acquire, hold and manage all kinds of property, whether real or personal, as will enable it to carry on. In connection with the above purpose to carry on any other activity permitted by chapter 180 of the General Laws;

and have complied with the provisions of the Statutes of this Commonwealth in such case made and provided, as appears from the Articles of Organization of said corporation duly approved by the Commissioner of Corporations and Taxation and recorded in this office:

Now, therefore, I, Frederick W. Cook, Secretary of the Commonwealth of Massachusetts, Do hereby Certify that said Harlow Shapley, Dwight E. Priest, R. G. Hoskins, Chandler Bullock, W. J. Crozier, Samuel C. Gwynne, William Malamud, Myles Morgan, Levi A. Olan, Carl E. Wahlstrom and Joseph Talano,

their associates and successors, are legally organized and established as, and are hereby made, an existing corporation as of February 11, 1944 under the name of

Worcester Foundation For Experimental Biology, Inc.,

with the powers, rights and privileges, and subject to the limitations, duties and restrictions, which by law appertain thereto.

Witness my official signature hereunto subscribed,  
and the Great Seal of the Commonwealth of Massachu-  
setts hereunto affixed, this fourteenth day of  
March in the year of our Lord one thousand  
nine hundred and forty-four

Secretary of the Commonwealth

WORCESTER  
FOUNDATION  
FOR  
EXPERIMENTAL  
BIOLOGY  
ANNUAL  
REPORT  
1989





The Worcester Foundation for Experimental Biology is one of the largest and internationally best known of a small number—fewer than fifty—of freestanding, nonprofit biomedical research institutes in the United States. Founded in 1944 by the late Drs. Gregory Goodwin Pincus, a renowned reproductive physiologist, and Hudson Hoagland, a distinguished neurophysiologist, the Worcester Foundation's pioneering role in the development of the oral contraceptive launched its world-wide reputation, and contributed mightily to the ability of women to control their fertility.

Today, the Worcester Foundation continues its pursuit of solutions to the diseases that cut short the 80 to 90-year lifespan humans are genetically endowed to otherwise enjoy. Its mission is basic research, aimed at understanding normal biology. The players in this drama are scientists who, beyond all else, are fueled by their curiosity. Occasionally, when the heavens smile, there are discoveries. Today, this story is being played out against vigorous opposition—in the form of the most under-funded federal budget for basic research in decades. To continue, the support of friends in the community and of private foundations is more important than ever.



Worcester Foundation for Experimental Biology  
Shrewsbury, Massachusetts 01545

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## Report of the President and Scientific Director

*Every art and every inquiry, and similarly every action and choice, is thought to aim at some good. But a certain difference is found among ends; some are activities, others are products apart from the activities that produce them. Where there are ends apart from the actions, it is the nature of the products to be better than the activities.*

Aristotle  
Nicomachean Ethics, Book I

When Barbara Walters interviewed Richard Nixon several years after he had left office, she chose to end with a characteristically wide-open, penetrating query: "Mr. President, of all your achievements in the White House, in which do you personally take the greatest pride?" I thought it likely that the former President would have said "Opening the door to China." His answer was both surprising and (to me) pleasing: "When we decided, in 1971, to declare war on cancer, through the National Cancer Act. That has subsequently proven to be the most innovative and successful thing we did, and the one in which I take the greatest pride."

It is just conceivable that Mr. Nixon's reply was not only honest, but correct. Notwithstanding this conjecture, I am more certain of the fact that the National Cancer Act was what brought me to the Worcester Foundation in 1971, due to the award to Mahlon Hoagland of a Cancer Center "core grant" from the National Cancer Institute. I well remember Mahlon impressing upon us new faculty members that our research and collegial interactions should produce "a whole greater than the sum of its parts." This viewpoint, which is hardly original as the reader will note from the quotation cited above, became not only the philosophical springboard for our nascent Cancer Center, but was quickly adopted as a unifying metaphor for the "new" Worcester Foundation for Experimental Biology that emerged in the early 1970s. Recognizing that individual excellence is always the most critical factor, I have endeavored to continue the tradition of a non-departmental, highly interactive campus, fostering an enhanced quality of its final product - just as our fellow traveler envisioned some 1350 years ago.

### Scientific Highlights

Last year our Male Fertility Program, employing molecular biology to seek new means of accentuating or blocking sperm production or function, received renewed and increased support from The Andrew W. Mellon Foundation. This adds to the National Institutes of Health (NIH) grant support held by each of the Male Fertility Program scientists, and has also provided the means for us to recruit a new scientist to this program, Dr. Harvey Florman from the University of Wisconsin. This research program represents a new era in the human reproductive biology tradition of the Worcester Foundation, one launched by the pathfinding discoveries of Gregory Pincus and M. C. Chang, who pioneered "the Pill" and *in vitro* fertilization.



We were also gratified this past year to receive a five-year renewal of our National Cancer Institute "core grant," for \$3.6 million over the next five years. This is the largest amount and longest term of funding our Cancer Center has ever received. The Cancer Center's studies of cell growth, gene expression, and particularly cell movements, have brought increasing distinction to the Worcester Foundation over the past few years.

This past February, the Worcester Foundation received a U.S. patent for its discovery of a new class of drugs active against the AIDS virus. The patent is based on research by Drs. Paul Zamecnik and John Goodchild and their colleagues, who have developed "antisense DNA" as a general approach to blocking virus replication. Each drug is tailor-made to interact specifically with the genetic machinery of a particular virus, in a unique lock-and-key fashion. Besides stopping replication of the AIDS virus, this new class of drugs has shown promise against influenza and other human viruses. We are now in the process of licensing this exciting new technology to corporate partners toward the development of an array of new anti-viral drugs.

In our neurobiology program, we were pleased with the award to Dr. Foteos Macrides of a seven-year National Institutes of Health Jacob K. Javits Neuroscience Investigator Award. Recognizing exceptional scientific achievement in neuroscience, this is the second Javits grant awarded recently to a Foundation scientist - one being held already by Dr. Robert O'Connell.

Our reproductive-endocrine biology program has this past year uncovered new clues to the mechanisms of sperm movement, a key feature of fertilization and anti-fertilization. Our scientists have also made new advances in the field of *in vitro* fertilization, employing the techniques of cell and molecular biology to continue the pioneering discoveries made by M. C. Chang and others years ago at the Foundation.

We were also gratified this past year to see our W. M. Keck Foundation Protein Chemistry Facility reach fully-operational status, providing core services to our scientists in their studies of various proteins. We are grateful to Drs. John Hildebrandt and Daniel Kilpatrick for their significant efforts in helping to establish the facility, especially John, who organized a successful National Science Foundation grant application to complement the initial enabling funding provided by the W. M. Keck Foundation.

*Drs. John Goodchild (left) and Paul Zamecnik at press conference announcing the AIDS patent.*



### **In Trust**

The Worcester Foundation has been extremely fortunate in having an enlightened and increasingly motivated Board of Trustees. This past year, four trustees rotated off our board: Bruce Bennett, Joseph Butare, Warner Fletcher and Robert Wetzel. Bruce Bennett served ably on the Executive Committee and was the board's secretary, and Joe Butare was a dedicated and effective chairman of the Nominating Committee. Warner Fletcher was one of our most committed and involved trustees, and served with distinction both on the Executive Committee and as chairman of the Development Committee. Bob Wetzel was also a very effective trustee and made important contributions to the executive, development and investment committees. I am profoundly grateful to these individuals, for their able and amicable service to me and the Foundation.

Particular thanks go to my friend Warner Fletcher, who kindly agreed to serve as chairman of the Development Committee for an additional year - a capacity in which he has, not surprisingly, continued to display impressive leadership of our fund raising programs.

We welcomed several new members to the board this past year. Christopher Bramley, Harold Cotton, James Harrington and Donald Melville bring to the board extensive experience in business, institutional leadership and fund raising. Judah Folkman adds the perspective of a distinguished scientist-physician, and in Nicholas Gage the board gains not only an admired Worcester leader, but an internationally-acclaimed author and journalist.

At its October 1988 meeting, the Board of Trustees conferred on Robert Cushman its Hudson Hoagland Award for distinguished service to the Foundation. Bob served as a trustee of the Worcester Foundation for 18 years (1969-87), and was chairman of the board for four of them. Most notably, Bob led the trustees' initiative to establish and fund a new cancer research program at the Foundation in the early 1970s. To the extent that the success of that effort, under his leadership, created the circumstances through which I was lucky enough to join this institution, I shall always have a special place in my heart for Bob Cushman.

### **In Memoriam**

We were deeply saddened by three deaths this summer. One was a shock, coming long before its due; the others came more naturally - yet are still profound losses.

On July 4, Robert Wetzel died suddenly at the age of 52. Bob was one of our most dynamic and effective trustees, providing sage advice on investments, promotion of the Foundation and fund raising. He had a playful, upbeat personality, and every time I saw Bob approaching for a committee meeting, I knew it would be a warm encounter. I still expect to see Bob walk in as trustees gather, and have to remind myself that he is really gone. A loyal and active supporter of many Worcester institutions, in Bob Wetzel's passing our community has suffered a great loss indeed.

Only five days after Bob Wetzel's death, Worcester lost another of its most caring and supportive leaders, Francis A. Harrington. Fran, father of Foun-

dation Trustee Jim Harrington, was a patron of many Worcester institutions, including the Worcester Foundation for Experimental Biology. He made contributions to our community that were both generous and enabling. His life of selfless community service remains as a legacy and an inspiration to us all.

August saw the passing of Paris Fletcher, another of Worcester's leaders and father of Warner Fletcher. A personal friend of our institution's co-founder, Hudson Hoagland, Paris was most generous and helpful to the Worcester Foundation from very early on. I had only known Paris in the last several years of his life, but found his gracious manner and subtle wit delightful. He will be deeply missed by those who knew and loved him.

Our sympathies go to the families of these three fine gentlemen, who pass on having made a significant difference in the world in which they lived.

#### Awards/Public Events

Gregory Pincus was one of the Worcester Foundation's co-founders and his work led to the oral contraceptive. His estate left a bequest to provide an annual prize to an awardee who has made exceptionally important discoveries in the field of endocrinology, broadly defined. In October 1988, the Worcester Foundation was pleased to confer the Pincus Award on Dr. Stanley Cohen of Vanderbilt University, in recognition of his prescient studies on epidermal growth factor.

Owing to the leadership of two able and dedicated friends of the Worcester Foundation, Mary Melville and Dr. Pengwynne Blevins, our second Women's Health Conference was a great success. Keynote speaker Gail Sheehy addressed motivational aspects of well-being to the interest of a full house, and the other seminars and workshops addressed an array of important topics. Our appreciation to Mary and Penny for their inspired orchestration of this successful event.

The Auxiliary of the Foundation has long been one of our most loyal and inspired support groups. Their annual Horse Show has become one of the major equestrian events in the Northeast, and succeeded once again this year in raising funds for the Foundation. The Auxiliary is one of my favorite groups at the Foundation, and I am profoundly grateful for their work and support.

*Nobel laureate Dr. Stanley Cohen was awarded the Pincus Medal by Dr. Pincus.*







*Gail Sheehy (at left) addressed the Women's Health Conference. In the audience (above) were conference co-chairs Dr. Pengwynne Blevins and Mary Melville.*

The Physicians Research Roundtable, founded by Chairman of the Board Dr. Robert M. Quinlan, and now ably led by Dr. Thomas J. Vander Salm, held a packed meeting last April. The speaker was Dr. Judah Folkman, Andrus Professor of Pediatric Surgery at the Harvard Medical School. Dr. Folkman spoke on his studies of tumor angiogenesis - the process by which new blood vessels develop around a cancerous tumor to sustain it. As indicated above, Dr. Folkman has subsequently joined the Foundation's Board of Trustees.

Our annual meeting of the Hudson Hoagland Society featured Nicholas Gage as speaker. He gave a moving account of his personal odyssey to seek out those who killed his mother during the civil war that erupted in his native Greece during World War II. His 1983 award-winning book, *Eleni*, in which he recounted his journey, was subsequently made into a major motion picture of the same name. Following his talk, I had the pleasure of discussing the Foundation with Mr. Gage, and found him to be very interested in us. We were all deeply pleased when this admired citizen of Worcester and the world joined our Board of Trustees.

#### **The Business of Professing That Science Is Not Business - Yet Recognizing the Partnership**

This past year the Worcester Foundation has increased contact with the world of for-profit biotechnology. We have been issued a patent, and have several others pending, which is all to the good. The Worcester Foundation believes that it has an obligation to expedite the development of its basic research discoveries and inventions into products that ameliorate or advance the human condition. Yet we are not, nor shall we become, a biotechnology company, nor do we intend to veer from our strictly nonprofit, academic research mission.

We have devoted a substantial effort this past year toward the design of corporate alliances to develop needed drugs or other products, but which also properly ensure capital reinvestments in the Worcester Foundation's basic research enterprise. An underlying principle is that no agreement with a for-profit venture shall interfere with the Worcester Foundation's central mission of curiosity-driven basic research. I am convinced that the very different goals of a nonprofit, basic research institute like the Worcester Foundation and the objectives of the biotechnology industry are not mutually exclusive. The year ahead will provide our first taste of how successful we have been in designing corporate partnerships, and it promises to be a most interesting period in the Worcester Foundation's evolution.

#### **Funding: Good News From Private Sources, Not Such Good News From the Federal Sector**

Our current capital fund raising effort, CAMPAIGN DISCOVER, has made excellent progress this past year: under Warner Fletcher's able leadership. Now halfway through the three-year campaign, we have raised just over \$3 million of the \$5.5 million goal. Several other indicators speak very favorably to the success of our fund raising efforts in the private sector. Our Annual Research Fund, up every year since 1985, again set a new record last year. Our leadership donor group, the Hudson Hoagland Society, enjoyed exciting growth this past year, with 18 new members. Membership now totals 115. Gifts from the business community were also up this past year, and a newly-organized Corporate Gift Committee is helping us further expand this important axis of support. And, finally, we have several major new grants from private foundations.

However, this progress in private sector fund raising is being played out against an ominous backdrop. As has been anticipated in my previous annual reports, federal grant support (NIH, NSF) is declining. Worcester Foundation scientists are holding their own: 36 of our 37 scientists have NIH or NSF grant support (the one who doesn't is a recently-appointed scientist who has just applied for grants). But the NIH and NSF are extremely under-funded by Congress. Thus, even though Worcester Foundation scientists are very successful in obtaining grants, they are generally awarded only 50-75% of the funds needed.

Never in my career have I sensed such concern in the American biomedical research community. I know of Nobel laureates (and Nobel laureates-to-be) who have lost their NIH grant support, to say nothing of a problem I really fear more - the daunting disincentives to our top young people who are pondering a career in academic research. *This is a national crisis* - one that has dominated conversation at several major scientific meetings (even at the expense of discussing science).

#### **Meeting the Challenge**

To address this looming problem, we need to move decisively on three fronts. First, the Congress must be brought to an understanding of the short-term and long-term consequences of under-funding of basic research in both the biological and physical sciences. Second, the private sector can and must

do more. Third, research institutions must look into ways to enhance their own financial positions.

The Congress is largely unaware that the highly-touted human genome project was made possible due to "arcane" discoveries of scientists studying DNA cutting by bacteria, and by genetic engineering advances conceived by investigators interested in the embryology of a soil worm. What brought this work to its present state of sophistication was not its relevance to medicine or the human condition, but was the brilliance of the investigators. Similarly, the recent discovery of the genetic mutation that leads (about 70% of the time) to cystic fibrosis can trace its origins to the same, aforementioned "esoteric" studies. Congress needs to learn not how to listen to this message, but how to hear it.

The private sector has been an enormously catalytic and enabling source of support for biomedical research in this country during the past 50 years.<sup>1</sup> Of particular importance are gifts that generate income for support of research. Yet the major private foundations of today have generally adopted very restrictive funding policies regarding endowment gifts. Research institutes like the Worcester Foundation need and, I argue, deserve a broader view on endowment gifts by private foundations - especially in the context of declining federal support.

The third element in the equation is how nonprofit institutions like the Worcester Foundation for Experimental Biology can "look inward" and expand their financial position. We are assiduously studying this issue, with particular reference to the proper deployment of our extensive landholdings. These deliberations reflect the Worcester Foundation's intention to be more in control of its own destiny in the years ahead.

With best wishes,



Thoru Pederson  
President and Scientific Director  
Fall 1989

<sup>1</sup> Weaver, W., "U. S. Philanthropic Foundations," Harper and Row, 1967. Jonas, G., "The Circuit Riders: Rockefeller Money and the Rise of Modern Science," W. W. Norton, 1989.







## Research in Progress

**C**urrent programs at the Worcester Foundation, described over the next few pages, encompass three major areas of biomedical research: cell biology and cancer, reproductive biology, and neurobiology. Separately highlighted, yet integral to the three major programs, are the Cancer Center and the Male Fertility Program.

Over the past year several important discoveries were made by Foundation scientists which have provided new information about fundamental processes in the human body. It is from such advances in basic research that clinical applications eventually spring.

Among the research highlights this past year were the following:

- *discovery of a new "motor" responsible for moving components around inside the cell;*
- *development of novel gene-targeted drugs effective against AIDS and other viral diseases;*
- *identification of a "docking site" for a protein that connects nerve and muscle cells;*
- *elucidation of how alcohol impairs electrical signal transmission along nerve cells;*
- *determination of the molecular structure of an animal protein aphrodisiac;*
- *development of a new gene detection method with promise for faster DNA diagnostics of viruses and genetic diseases.*

## Cell Biology and Cancer

Earl F. Baril, Ph.D.  
*Principal Scientist*

William R. Crain Jr., Ph.D.  
*Senior Scientist*

Grant Fairbanks, Ph.D.  
*Senior Scientist*

John Goodchild, Ph.D.  
*Staff Scientist*

Elizabeth J. Luna, Ph.D.  
*Senior Scientist*

Thoru Pederson, Ph.D.  
*Principal Scientist*

Joel D. Richter, Ph.D.  
*Senior Scientist*

Alonzo H. Ross, Ph.D.  
*Senior Scientist*

Greenfield Sluder, Ph.D.  
*Senior Scientist*

Richard B. Vallee, Ph.D.  
*Principal Scientist*

Samuel C. Wadsworth, Ph.D.  
*Senior Scientist*

Yu-li Wang, Ph.D.  
*Senior Scientist*

George B. Witman, Ph.D.  
*Senior Scientist*

Paul C. Zamecnik, M.D.  
*Principal Scientist*

Carol A. Ziomek, Ph.D.  
*Staff Scientist*

In this research group, Worcester Foundation scientists address how distinct sets of genetic instructions are activated in different cells and tissues, and how such sets of genes fire off precise directions for converting a fertilized egg into a creature as amazingly complex as a human. The ability of synthetic "anti-genes" to block the undesired activity of disease-causing genes is also being investigated. Foundation scientists are also seeking to understand how cells reproduce themselves, from the biochemistry of gene (DNA) replication to the doubling of the cell reproduction machinery itself. Much of what a cell can do is because it is not dependent solely on the physical process of diffusion (*i.e.*, the phenomenon that alerts one to an orange being peeled only a few seconds

after its skin is broken across the room). Instead, the cell contains active motors and tracks for precisely and very rapidly moving various parts of the cell to their physiologically appropriate destinations. This dynamic process of intracellular motility and traffic is being dissected by Foundation scientists as a key aspect of cellular physiology.

A related aspect of biological motility, how cells move from one place to another, is also being investigated. This process is a fundamental feature of metastatic cancers, and is the cellular property (crawling away from its initial location) that gives the disease its name (cancer = crab). Another major focus is how the girder-like structural framework inside cells facilitates the relay of signals to and from the cell exterior, across the cell membrane.

These inquiries into the basic features of cellular organization and function are being pursued because they are profoundly puzzling in their own right. Yet these studies are also relevant to understanding and treating disease. For example, the design of novel "anti-genes" by Paul Zamecnik and John Goodchild offers promise of blocking certain viral diseases. They have established that these new agents can inhibit the replication of the AIDS virus, and promising results are being obtained for other viral diseases (*e.g.*, influenza).





Work on intracellular motility and on nerve growth factors may provide clues to certain degenerative brain disorders, such as Alzheimer's, as well as congenital neurological diseases.

Alterations in the association of the outer membrane with the underlying interior structure of the cell are pertinent to the normalities and abnormalities of cells and to the profound changes in cell shape and crawling that occur in malignant tumors.

Investigations of the motile machinery of sperm cells offers hope for new male contraceptive agents. And studies of *in vitro* fertilization are likely to advance the success of this important technique for overcoming certain forms of sterility.

## Endocrine and Reproductive Biology

- D. John Aberhart, Ph.D.  
*Senior Scientist*
- Eliahu Caspi, Ph.D.  
*Principal Scientist*
- Min-Chueh Chang, Ph.D., Sc.D.  
*Principal Scientist Emeritus*
- Lawrence J. Dangott, Ph.D.  
*Staff Scientist*
- Harvey Florman, Ph.D.  
*Staff Scientist*
- John D. Hildebrandt, Ph.D.  
*Staff Scientist*
- Edward L. Klaiber, M.D.  
*Senior Scientist*
- David Kupier, Ph.D.  
*Senior Scientist*
- John A. McCracken, Ph.D.  
*Senior Scientist*
- Clare M. O'Connor, Ph.D.  
*Senior Scientist*
- David E. Wolf, Ph.D.  
*Senior Scientist*

A major objective of this research program is to understand how cells in the body signal one another, eliciting precise physiological changes, and in particular how these signalling events influence reproductive activities, including the formation of eggs and sperm, fertilization and embryonic development.

The chemical pathways by which cells manufacture various hormones are being investigated, with emphasis on identifying key steps that may control the levels of hormones produced. The physiological mechanisms by which a group of hormones called prostaglandins influence reproductive processes are also being studied. Foundation scientists are interested in how hormones interact with cells and signal new physiological events, through reception and signal relay systems integrated into the outer cell membrane.

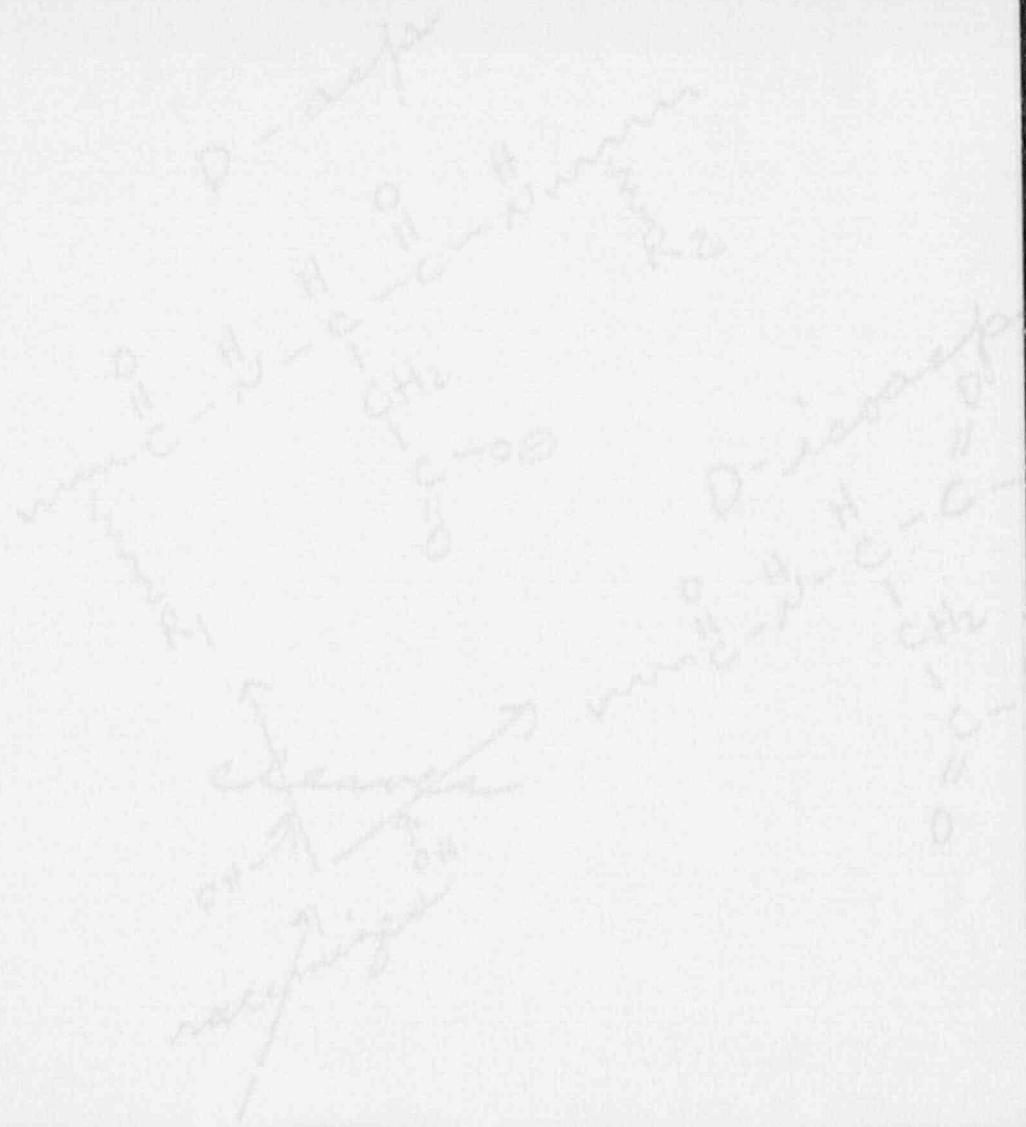
The special enzyme systems of the liver and other organs that help detoxify various toxic chemicals to which humans are exposed in the environment are being investigated. Foundation scientists are also interested in the biochemical longevity of various components of the cell and seek to learn how proteins are earmarked for replacement.

Continuing a long and distinguished tradition of research contributions in reproductive biology, as exemplified in the pioneering, epochal career of M.C. Chang, Foundation scientists are exploring the process by which sperm meets egg, using today's powerful tools of molecular biology and biophysics. The mutual affinity of sperm and egg has been discovered to reside in "lock and key"-type proteins that fit precisely into one another. Foundation scientists have been able to visualize such proteins by ultrasensitive "tagging" methods — involving laser light beam detection — and have also been able to investigate these fertilization-triggering proteins by powerful new gene cloning techniques.





These research programs are propelled by the participating scientists' restless intellectual energy and sense of exploring the unknown. Yet, these studies have direct bearing on human needs. The Foundation's work on sperm-egg interactions is extremely pertinent to problems of infertility. Other studies offer the promise of new hormone-like drugs for the control of a wide array of disorders.



## Neurobiology

Hagan Bayley, Ph.D.  
*Senior Scientist*

Justin R. Fallon, Ph.D.  
*Staff Scientist*

F. Rob Jackson, Ph.D.  
*Staff Scientist*

Michele H. Jacob, Ph.D.  
*Staff Scientist*

Daniel L. Kilpatrick, Ph.D.  
*Senior Scientist*

José R. Lemos, Ph.D.  
*Staff Scientist*

Foteos Macrides, Ph.D.  
*Principal Scientist*

James W. McKearney, Ph.D.  
*Senior Scientist*

Peter J. Morgane, Ph.D.  
*Senior Scientist*

Robert J. O'Connell, Ph.D.  
*Senior Scientist*

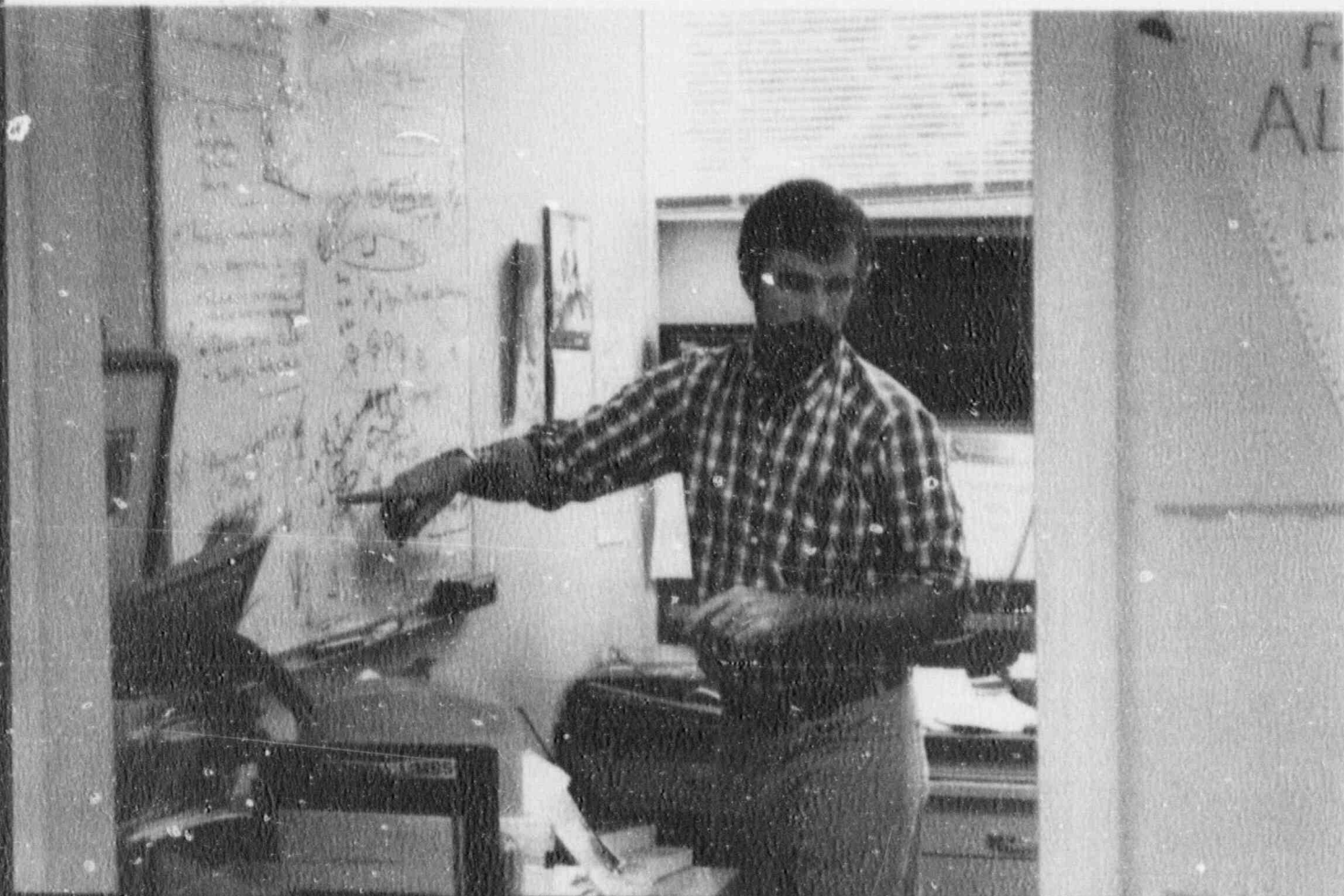
Steven N. Treistman, Ph.D.  
*Senior Scientist*

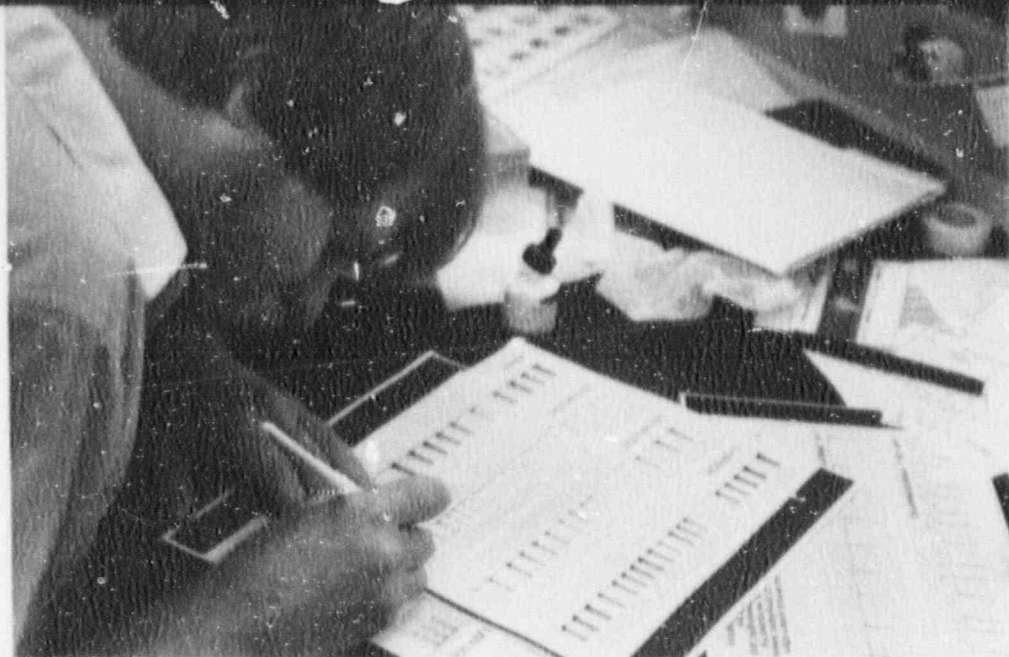
The reception and processing of information from the environment, its storage in the brain and conversion to action are the fundamental functions of nerve cells which are being addressed by scientists in the Neurobiology Group.

Consider the storage function—memory. In biochemical terms (cell proteins, DNA and hormone-like substances), what really happens inside the brain when one has a thought? And if the thought should happen to be a recollection of one's bar mitzvah, or of Grandpa playing the banjo, where [what] was that thought five minutes before? After all, some of the things one thinks of only cross the mind once every ten years or so—or even less frequently. Where [what] are the memories in the meantime?

This profoundly intriguing aspect of the brain is being investigated by members of the Neurobiology Group. Studies are also underway directed at learning how the specific connections among nerve cells are accurately made during embryonic development and post-natal growth. Just as specific "lock and key" proteins facilitate sperm-egg interaction during fertilization, Foundation scientists have identified other proteins that define the particular sites where nerve cells will inter-connect.

Another focus of research deals with the emerging and intriguing question of why certain hormone-like substances, formerly thought to be present only in the brain, are being found in other tissues as well. Enkephalins ("in the head"), for example, have now been discovered by Foundation scientists in several reproductive tissues, speaking to new physiological roles yet to be deciphered.





As an electrical signal moves from one nerve cell across to another, it does not move as electricity (as when a "hot" wire is touched to another). Instead, the electric signal is transformed to a chemical substance, and it is this substance that literally moves to the neighboring nerve, where it then stimulates a new electrical impulse. Foundation scientists are investigating this intriguing electrical-to-chemical signal transduction process in several different types of nerve cells and nerve-muscle connections.

Chemical signals not only traverse between cells, they also pass between organisms themselves. Such odors, or pheromones, are key aspects of communication in animals—and humans too—and are of particular importance in reproductive behavior. It is no accident that the perfumes "subjectively" judged to be most pleasurable by humans often are ones containing extracts of animal scent glands. Neurobiology Group scientists are studying the chemical nature of pheromone-like substances, and are also defining the sensory receptors that transmit these signals.

The Worcester Foundation is proud to have on its faculty two recipients of the prestigious Jacob K. Lavits Neuroscience Investigator Award: Foteos Maerides and Robert O'Connell.

These special seven-year research awards from the National Institutes of Health recognize their respective distinguished contributions to the field of olfactory neurobiology.

Nerve cells and the brain are so fascinating one hardly needs an excuse to study them. But the Worcester Foundation's research in neurobiology has important medical ramifications beyond the basic exploration aspect. As is becoming increasingly apparent, memory dysfunction is not restricted to the acute senile dementias, but exists in an array of degenerative neurological diseases, many of which are poorly understood. The work on the molecular biological correlates of memory is opening new ground on this front. Studies on nerve cell connections address not only how this happens in the first place during embryonic development, but also bear on the fortunate fact that nerve cell connections can often be made again following injury.

The chemical pheromones and intercellular signals that impact on the nervous system do so for physiologically productive purposes. But other, less desirable, chemicals also reach the nervous system in the form of abused substances. Investigations are underway to learn how opioid (morphine-related) drugs influence neuronal function and behavior, which addresses a looming societal need. Also of vast human importance are the Foundation's studies on the nerve "anesthetizing" properties of the most widely abused substance of all—alcohol.



## The Cancer Center

Earl F. Baril, Ph.D.  
*Principal Scientist*

William R. Crain Jr., Ph.D.  
*Senior Scientist*

Grant Fairbanks, Ph.D.  
*Senior Scientist*

John Goodchild, Ph.D.  
*Staff Scientist*

John D. Hildebrandt, Ph.D.  
*Staff Scientist*

Elizabeth J. Luna, Ph.D.  
*Senior Scientist*

Clare M. O'Connor, Ph.D.  
*Senior Scientist*

Thoru Pederson, Ph.D.\*  
*Principal Scientist*

Joel D. Richter, Ph.D.  
*Senior Scientist*

Alonzo H. Ross, Ph.D.  
*Senior Scientist*

Greenfield Sluder, Ph.D.  
*Senior Scientist*

Richard B. Vallee, Ph.D.\*\*  
*Principal Scientist*

Samuel C. Wadsworth, Ph.D.  
*Senior Scientist*

Yu-li Wang, Ph.D.  
*Senior Scientist*

George B. Witman, Ph.D.  
*Senior Scientist*

David E. Wolf, Ph.D.  
*Senior Scientist*

Paul C. Zamecnik, M.D.\*\*  
*Principal Scientist*

Carol A. Ziomek, Ph.D.  
*Staff Scientist*

\*Directs

\*\*Co-Director

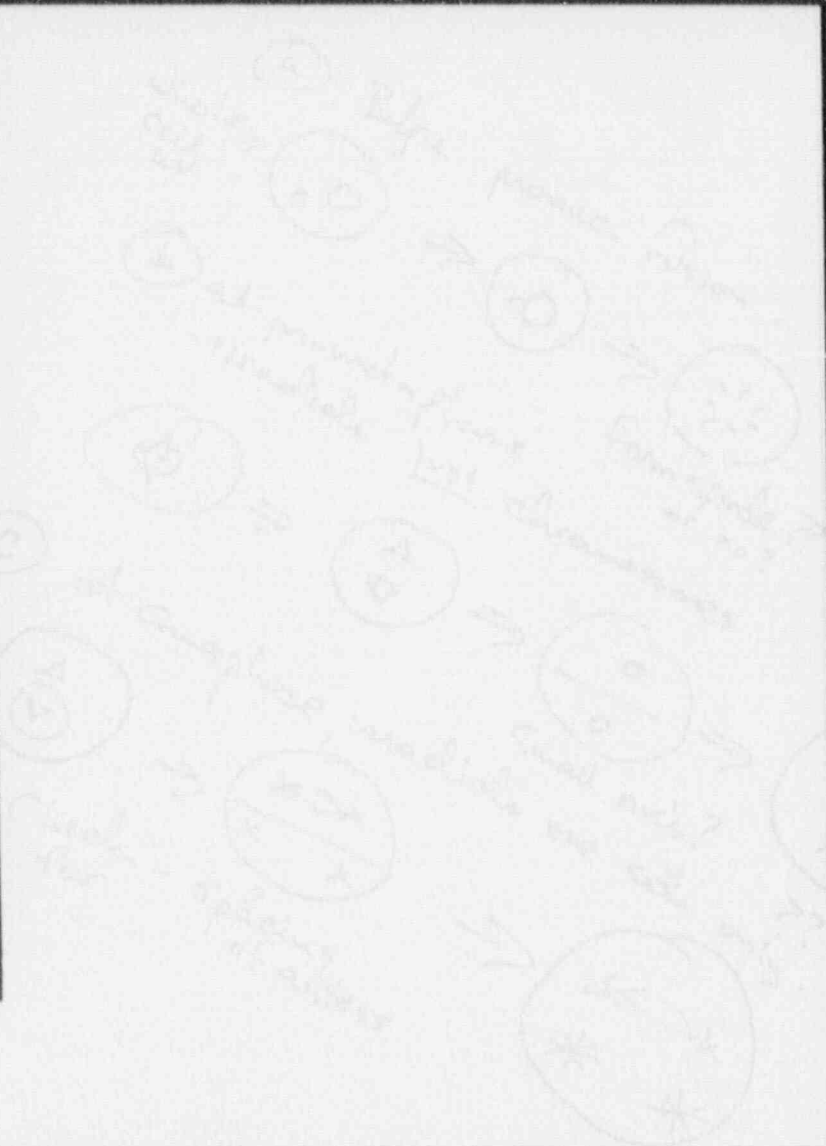
Since 1971, the Worcester Foundation has been designated as a specialized cancer research center by the National Cancer Institute, one of 16 such basic research-oriented cancer centers in the United States, and one of three in Massachusetts.

Collaborative research programs, joint conferences and seminars, and shared core research facilities—including a state-of-the-art electron microscopy unit and a central facility for gene (DNA) synthesis are distinctive features of the Cancer Center. Most importantly, the center is designed to—and does—foster interactions among its members, leading to a more effective scientific program than if its component units were working in isolation.

Research in the Cancer Center focuses on how normal cell growth and metabolism are regulated. The Worcester Foundation's perspective is that cancer can best be understood as the aberrant regulation of normal cellular events, and that these normal processes are still insufficiently understood. The aim of the Cancer Center is to contribute to the cancer problem at the fundamental level of elucidating general principles of cell biology, so that more clinically-oriented researchers can benefit, in their important endeavors, from a sound framework of underlying biological information.

The Cancer Center is supported by a major core grant from the National Cancer Institute, by National Institutes of Health research grants to the member scientists, and funds from private foundations and individual donors.





## The Male Fertility Program

Lawrence J. Dangott, Ph.D.  
Staff Scientist

Grant Fairbanks, Ph.D.  
Senior Scientist

Harvey Florman, Ph.D.  
Staff Scientist

Daniel L. Kilpatrick, Ph.D.  
Senior Scientist

John A. McCracken, Ph.D.  
Senior Scientist

Clare M. O'Connor, Ph.D.  
Senior Scientist

George B. Witman, Ph.D.\*  
Senior Scientist

David E. Wolf, Ph.D.  
Senior Scientist

Carol A. Ziomek, Ph.D.  
Staff Scientist

\*Program Director

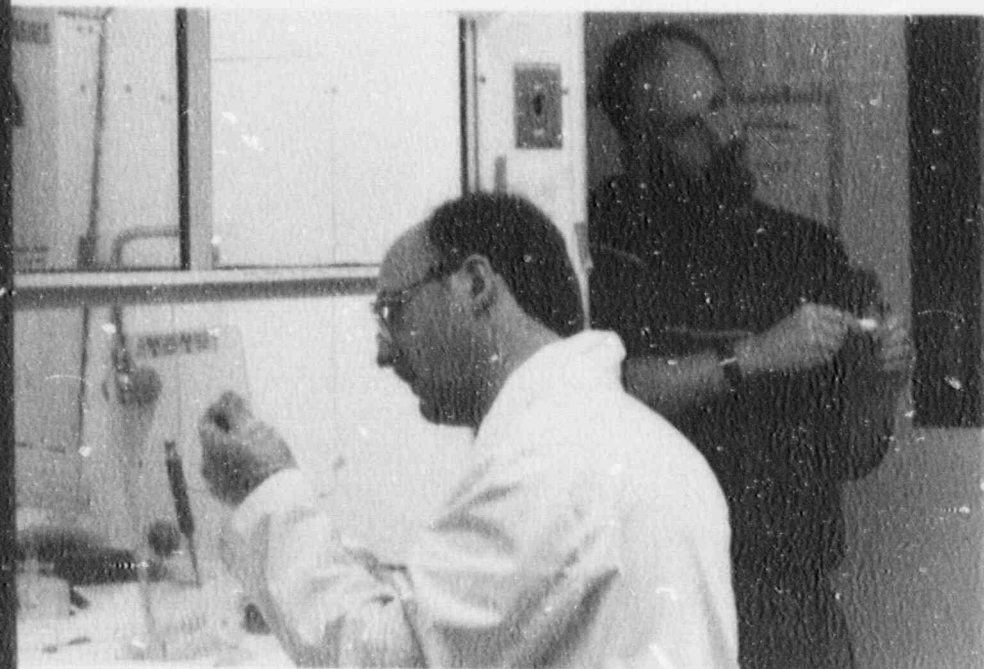
The Worcester Foundation's long-held interest in endocrine-reproductive biology, and its historic role in the discovery and development of the oral contraceptive, provide a strong context for current research activities in the area of *male* fertility and reproduction.

While individual scientists at various times in the past had worked on male reproductive biology at the Foundation, it was not until the early 1980s that an attractive "critical mass" situation was reached. In 1982, the Male Fertility Program was formally organized, sparked by a major grant from the Andrew W. Mellon Foundation, and complemented by other grants from the Edward John Noble Foundation, the Jessie Smith Noyes Foundation and the Educational

Foundation of America. These funds have made it possible for the Worcester Foundation to assemble its scientific talent and efforts into an integrated research program on male fertility.

The emphasis of this research program has been on the maturation of immature, non-moving sperm cells in the testis into actively swimming sperm, capable of fertilizing an egg. Particular emphasis has been placed on learning about possible points along the sperm maturation pathway where biochemical intervention for contraceptive purposes might be most effectively directed. Central to this focus is the issue of specificity. The sperm cell's machinery for movement is virtually unique among all cells of the body. Therefore, it is unlikely that agents designed to block sperm cell motility would have side effects on other cells and tissues. In contrast, the current female oral contraceptives, which are steroid hormone analogs, are known to affect many cells and tissues in addition to the ovaries.

Members of the Male Fertility Program meet weekly to communicate research progress and exchange ideas, and make use of shared common research facilities. Among the latter is a central facility for the controlled col-



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+ ATP

SYNTHETICAL

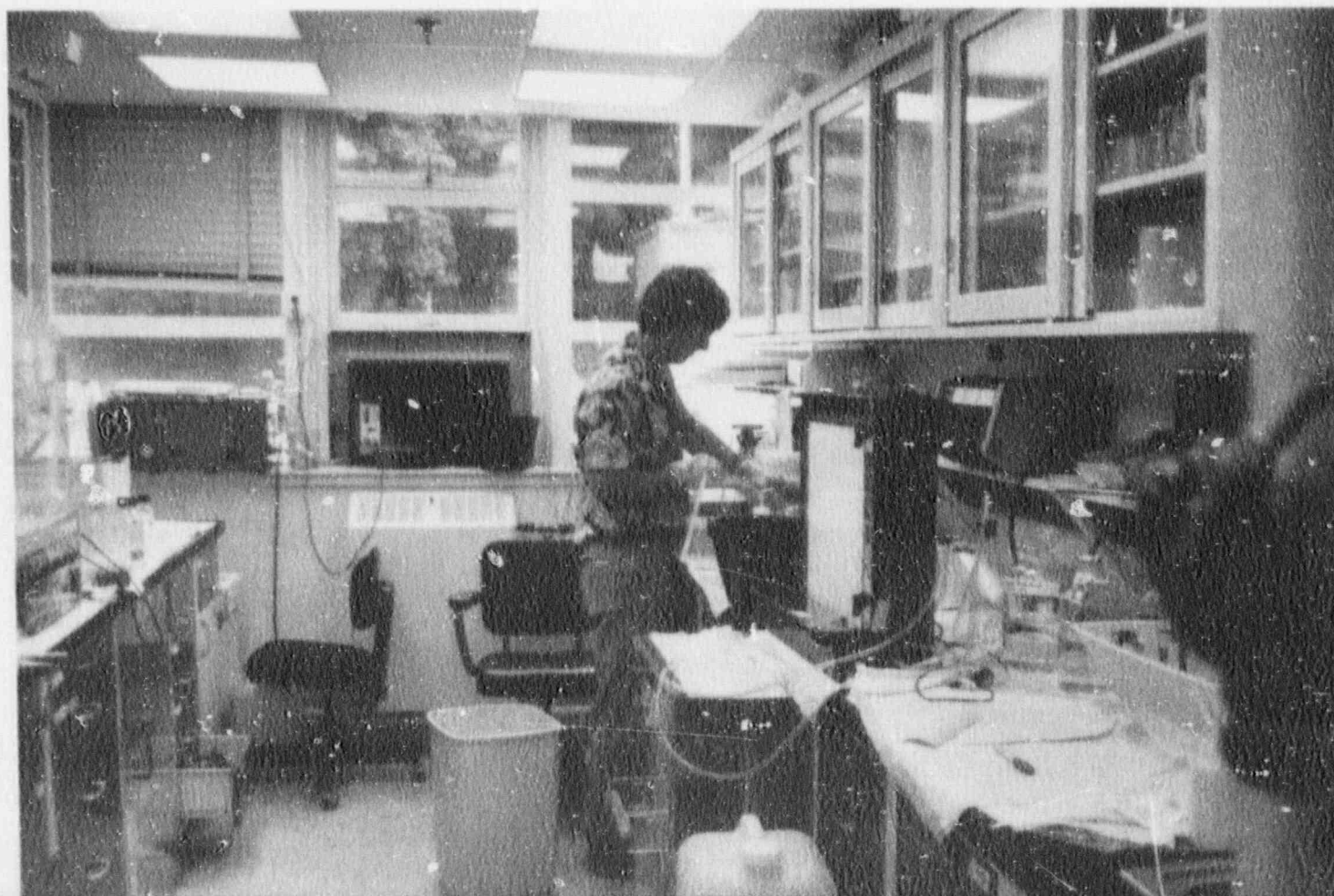
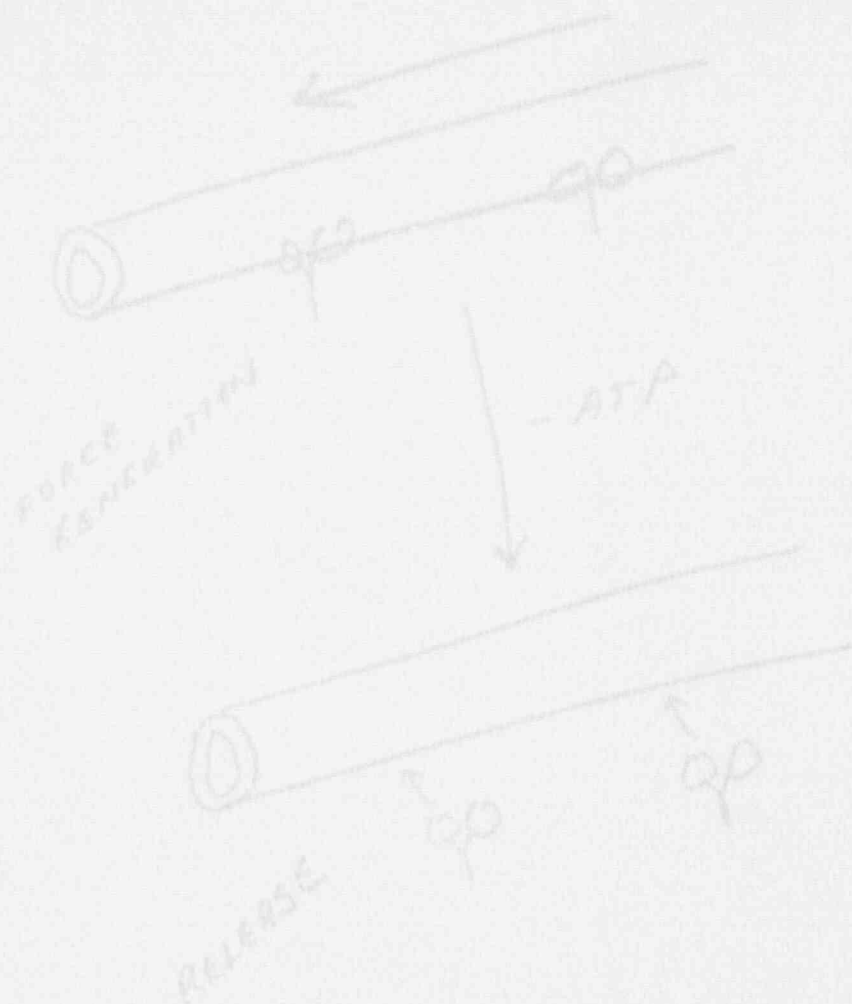
CA<sup>2+</sup> CAMP →

ACSM



iection of ram testicular sperm and fluid, which is a key resource for several program members. The Worcester Foundation's ram sperm facility has been called one of "the best anywhere in the world."

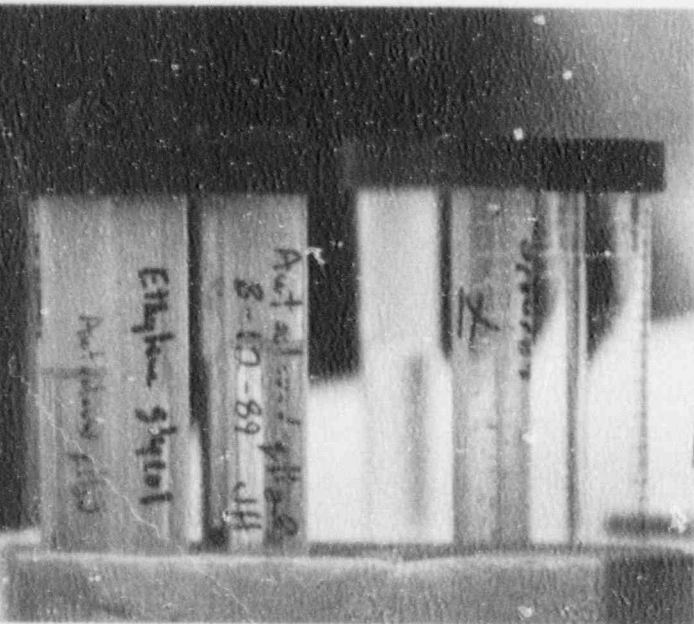
The new Protein Chemistry Core Facility is another major research support component of the Male Fertility Program. Launched by funds from the W. M. Keck Foundation of Los Angeles, this new facility has accelerated and diversified the study of the unique proteins that figure into the process of sperm maturation.



## Visiting Lecturers

(April 1, 1988 - March 31, 1989)

- Dr. Howard Berg  
*Harvard University  
The Rowland Institute for Science*
- Dr. Kerry Bloom  
*University of North Carolina*
- Dr. Rolf Bodmer  
*Howard Hughes Medical Institute*
- Dr. Kathy Buckley  
*Harvard Medical School*
- Dr. Steve Burden  
*Massachusetts Institute of Technology*
- Dr. Ellen Carpenter  
*Bryn Mawr College*
- Dr. Stanley Cohen  
*Vanderbilt University*
- Dr. Margaret Comer  
*Clark University*
- Dr. Louis De Gennaro  
*University of Massachusetts Medical Center*
- Dr. Paul R. Dobner  
*University of Massachusetts Medical Center*
- Dr. Douglas Fambrough  
*The Johns Hopkins University*
- Dr. Harvey Florman  
*University of Wisconsin*
- Dr. Stanley C. Froehner  
*Dartmouth Medical School*
- Dr. Albert Galaburda  
*Harvard Medical School and  
Beth Israel Hospital*
- Dr. Craig Garner  
*University of Hamburg, West Germany*
- Dr. Corey Goodman  
*University of California*
- Dr. Patricia Granahan  
*Hamilton, Brocks, Smith and Reynolds*
- Dr. Joel F. Habener  
*Massachusetts General Hospital*
- Dr. Richard O. Hynes  
*Howard Hughes Medical Institute  
Massachusetts Institute of Technology*
- Dr. Richard Ivell  
*Institute for Hormone Research, West  
Germany*
- Dr. Steve Jones  
*Medical Research Council, England*
- Dr. John S. Kauer  
*Tufts New England Medical Center*
- Dr. Michael Koval  
*Carnegie Institution of Washington*
- Dr. Csaba Levanth  
*Yale University School of Medicine*
- Dr. John D. Leszyk  
*University of Maryland School of Medicine*
- Dr. Robert W. McCarley  
*Harvard Medical School*
- Dr. A. G. McLerran  
*University of Liverpool, England*
- Dr. Ira S. Meilman  
*Yale University School of Medicine*
- Dr. Michael Melner  
*Oregon Regional Primate Research Center*
- Dr. Jose Luis Millan  
*La Jolla Cancer Research Foundation*
- Dr. Claire Moore  
*Tufts Medical School*
- Dr. Stephen Munroc  
*Mazquette University*
- Dr. Michael O'Rand  
*University of North Carolina*
- Dr. Richard Padgett  
*Harvard University*
- Dr. Martin Raff, FRS  
*University College, London*
- Dr. Prem Reddy  
*Wistar Institute for Anatomy and Biology*
- Dr. Patricia Saling  
*Duke University*
- Dr. Jonathan Scholey  
*National Jewish Hospital and Research Center*
- Dr. Obaid Siddiqi  
*Tata Institute of Fundamental Research, India*
- Dr. Oswald Steward  
*University of Virginia School of Medicine*
- Dr. Tom Stosell  
*Massachusetts General Hospital*
- Dr. Patricia Strickler  
*Waters Chromatography*
- Dr. Terrance Tao  
*Boston Biomedical Research Institute*
- Dr. Kevin Van Doren  
*Synergen Inc.*
- Dr. Bassam T. Wakim  
*Integrated Genetics*
- Dr. Kenneth Williams  
*Yale University School of Medicine*



## Scientific Support Personnel

(April 1, 1988 - March 31, 1989)

### Foundation Scholar

Sudhir Agrawal, Ph.D.

### Visiting Scientists

Wei Chen

Marie-Noëlle Raymond, Ph.D.

Jie Chen

### Senior Research Associates

John G. Aghaalian, Ph.D.

Timothy J. Bartness, Ph.D.

William H. Berger, Ph.D.

Andrew Clancy, Ph.D.

Christine A. Collins, Ph.D.

David M. Coppola, Ph.D.

Alan Grant, Ph.D.

Stephen M. King, Ph.D.

Vipin Kohli, Ph.D.

Gary R. Kunkel, Ph.D.

Thomas A. Schoenfeld, Ph.D.

James B. Smith, Ph.D.

### Research Associates

R. Patrick Akers, Ph.D.

Christine M. Benswenger, Ph.D.

Sven A. Benzhafsen, Ph.D.

Paola Borroni, Ph.D.

Dennis Burns, Ph.D.

Richard Cardullo, Ph.D.

Clare L. Chatot, Ph.D.

Stephen B. Cheley, Ph.D.

Maio Su Chen, Ph.D.

Catherine P. Chia, Ph.D.

Richard Desrosiers, Ph.D.

H.R.W. Dharmaratne, Ph.D.

Jane Dingus, Ph.D.

Daniel Gamett, Ph.D.

Jean-Luc Gatti, Ph.D.

Michelle F. Gaudette, Ph.D.

Richard J. Gregory, Ph.D.

James Hammarbuck, Ph.D.

Robert I. Hickey, Ph.D.

Erika Holzbaur-Howland, Ph.D.

Taichang Jang, Ph.D.

Daval Kew, Ph.D.

James L. Kilgore, Ph.D.

Ann M. Kleinschmidt, Ph.D.

Russell Kohnen, Ph.D.

Nancy Kravit, Ph.D.

Shankar J. Kulkarni, Ph.D.

Cynthia A. Ladino, Ph.D.

Justin C. Larisa, Ph.D.

Sophie Le Brun, Ph.D.

Erich Lieth, Ph.D.

Linde H. Mekas, Ph.D.

Melissa Melan, Ph.D.

Anthony G. Moss, Ph.D.

Karl E. Muffy, Ph.D.

Robert Otter, Ph.D.

Jeffrey R. Patton, Ph.D.

Priti J. Raval, Ph.D.

David S. Rezsner, Ph.D.

Elizabeth Rozman, Ph.D.

Amal K. Roy, Ph.D.

Aneesa Shariff, Ph.D.

Pradeep K. Sharma, Ph.D.

Howard Shpetner, Ph.D.

Ruth Simon, Ph.D.

James M. Slavicek, Ph.D.

Pamela Taggart, Ph.D.

Lin Yan Tang, Ph.D.

Jamal Temsamani, Ph.D.

Peter Thorn, Ph.D.

Sandra G. Velleman, Ph.D.

Gita Venkatakrishnan, Ph.D.

Walter S. Vincent III, Ph.D.

Prabhakar Vissavajhala, Ph.D.

Frances E. Weaver, Ph.D.

Steven A. Zinn, Ph.D.

### Senior Research Assistants

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Sandra Mayrand, B.A.

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Andrew H. Wilson, M.S.

Mary V. Zamecnik, A.B.

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Robert G. Audet, B.S.

Ioannis M. Berrios, B.S.

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Balaka Chattopadhyay, M.S.

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Nancy C. Dettemeyer, B.A.

Geraldine R. Farley, M.S.

Carlos Flores, B.S.

Sylvie Catti, M.S.

Celia E. Gelfman, B.A.

Bonnie J. Germain

Joan F. Golrick, B.A.

Steven A. Hecht, B.A.

James L. Johnson, B.S.

Mary Ellen Johnson, B.A.

Cynthia A. Kane, B.S.

Linda D. Kilroy, B.A.

Stanley Kot, B.S.

Jennifer Legg, B.S.

Jennifer Lewis, B.S.

Leslie K. Loe, B.S.

John Madalena, B.S.

Christine A. McKinnon, B.A.

Frederick J. Miller, B.S.

Laurel Newby, M.S.

Louise C. Ohrn, B.A.

Bryce Paschal, B.A.

Matthew B. Potter, B.A.

Mary Murlind, B.S.

Molly J. Rhoadhouse, B.S.

Mitchell C. Sanders, B.A.

Sheryl A. Savage, B.A.

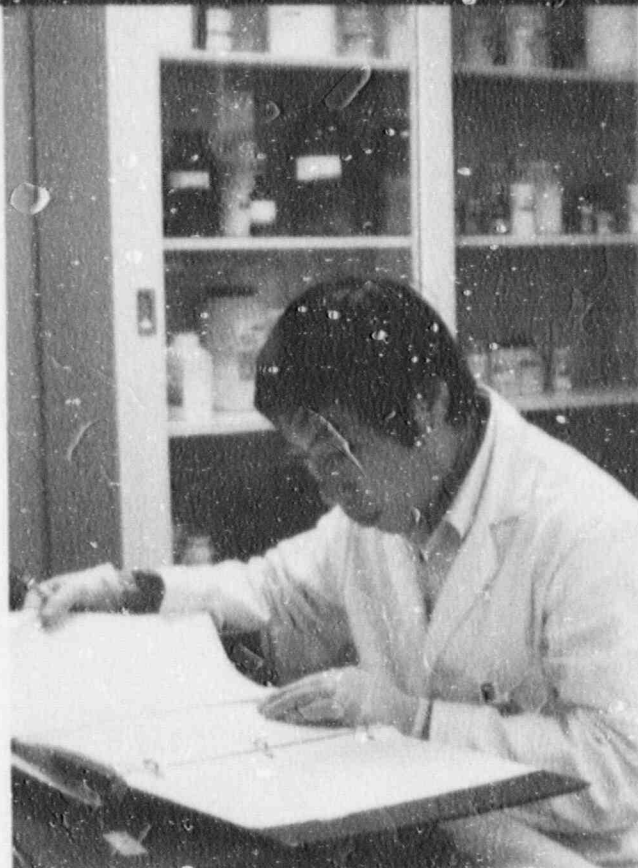
Carl Schell, B.S.

William Silva, B.S.

Ernest J. Spencer

Elizabeth M. Sutton, B.S.

Barbara J. Walker, B.S.



### Laboratory Assistants

Kristine Bocian

Marion Martineau

Rose M. McDonald

Alfred F. Nigro

Ethel J. Zucker

*Summer Help*

Elizabeth McCabe

Sharon Sweetzer

Patrick Nestor

Suzana Quinn

### Animal Care

George A. Aldrich

Anthony A. Danzilio

Victor D. DeStratis

Michael A. Rocheleau

*Summer Help*

Dawn Rocheleau

### Technical Services

Richard Barthelme

David I. Bernklow

Richard T. Cassidy

Peter L. Dudley

Albert G. Gallo

John T. Lydon, B.S.

Clifford F. McDonald

Daphne Yang, M.S.

*Glassware Washers*

Lucrezia Gagen

Lillian Holzapfel

*Summer Help*

Amy Allworth

### Library

Matthew Mayrand

Rebecca Mayrand

Ann H. Moss, M.S.

Joshua Vallee

### Secretarial Services

Rebecca Bell

Kristen DiRuzza

Anne Edgerton

Jacqueline C. Foss

Sandra E. Johnson

Mina Rano

Carol Savage

Gerakline L. Stone

Helen Welch

### Buildings and Grounds

*Plant Maintenance*

Ernest W. Anderson

Gary Bearegard

Ferenc Bentekovics

Wesley J. Burton

Anthony J. Cammuso

Joseph A. Deloitville

Robert E. Deloitville

Michael Dello Stritto

Michael M. Ferranti

Michael Gagliastre

Carroll Gasperski

Henry G. Mitchell

Richard L. Rose

*Watchmen*

Franklyn F. Blanding

John P. Shotts

Robert Smith III

William F. Webster

Joseph J. Williams

*Summer Help*

Anthony Zydlewski



## Educational Programs

**A**lthough the Worcester Foundation is internationally known as an institution devoted to basic biomedical research, its educational programs are an important activity widely recognized in the academic community. Just as research is indispensable to science education in the university, learning is a continuing process in the daily activity of the Foundation's laboratories.

### Postdoctoral Training Program

Since its founding 45 years ago, the Worcester Foundation has trained more than 1000 men and women from over 60 countries holding medical degrees or doctorates in the sciences. Training has focused on reproductive physiology, steroid chemistry, cancer research and neurobehavioral biology. These programs are based on the dual concepts that: 1) there is no training substitute for complete immersion in a specific research endeavor under the guidance of a thoroughly experienced preceptor for a period of at least two years; and 2) a flexible, non-departmental, fully communicating environment is fundamental to maximum productivity in basic research.

### The Cell Biology of Development Training Program

Supported by a training grant from the National Institute of Child Health and Human Development, this program is devoted to training postdoctoral fellows in the field of embryonic development. The director of the training program is Dr. William Crain. The fellows training in the program this past year were:

Susan M. DiBartolomeis, Ph.D.  
Anne L. Hiit, Ph.D.  
Paul E. Nisson, Ph.D.

### Doctoral Program

Since 1975, Clark University, the University of Massachusetts Medical School, Worcester Polytechnic Institute and the Worcester Foundation have jointly sponsored a Ph.D. program in the biomedical sciences. This program is designed for the exceptional, self-motivated student who already has a substantial background in the natural sciences. Students undertake practical, full-time laboratory research without the requirements of extensive course work, though participation in formal classroom studies occasionally supplements actual research work.

The following graduate students were engaged in laboratory research either as part of the Foundation's established training or as part of a scientist's adjunct research team during the 1988-89 academic year:

Ann Allworth, B.A. (Ph.D. 1989)  
Longguang Cao, M.S.  
Joyce Eldering, B.S.  
Marlene J. Juedes, M.S. (Ph.D. 1989)  
Congjun Li, M.S.  
Chitra Mani, M.S.  
Ann McGrew, B.S.  
Sandra McNeil, B.S.  
Robert M. Mungovan, B.S.  
Christopher Palatucci, M.A.  
Sidney Pitt, M.S.  
Jin Wang, M.S.

### Summer Training Program

For several decades, the Worcester Foundation has participated in the training of able college students in basic biomedical research during the summer months. Designed to attract outstanding students majoring in the sciences, the objective of the ten-week program is to introduce interested and capable students to scientific research. Many summer training students have gone on to medical school or graduate study related to their summer work.

On entering the program, each student selects a preceptor for the summer and undertakes a modest research project. A written report on the data collected is then presented at a seminar at the conclusion of the program.

The 1989 Summer Training Program was supported through the generosity of the Educational Foundation of America, the Cornerstone Foundation and Perpetual Trust for Charitable Giving, the George I. Alden Trust of Worcester, Mr. and Mrs. Anthony A. Borgatti of Shrewsbury, and Deluxe Check Printers.





**Summer Training Program Students - 1959**

Yongyi Han

*University of California, Berkeley*

Swati Joshi

*University of Massachusetts at Amherst*

Kelly Ann McLaughlin

*Wheaton College*

Jeffrey Meyerhardt

*Haverford College*

Lisa Misterka

*Massachusetts Institute of Technology*

Ken Mueller

*Haverford College*

Tim Lee Payne

*Wheaton College*

K. John E. Pruett

*Colgate University*

Sharon Savage

*Worcester Polytechnic Institute*

Jeffrey A. Yoder

*Worcester Polytechnic Institute*

Joseph Zydlewski

*Bates College*

**Teaching at Other Institutions**

Many Foundation scientists hold affiliate faculty appointments at the University of Massachusetts Medical School. They are: Drs. Earl Baril, William Crain, Justin Fallon, John McCracken, Thoru Pederson, Joel Richter, Alonzo Ross, Greenfield Sluder, Steven Treisman, Richard Vallee, Samuel Wadsworth, George Witman, and David Wolf.

Other Foundation faculty holding affiliate appointments are: Drs. M. C. Chang, James McKearney and Peter Morgane, Boston University; Drs. David Kupfer, Robert O'Connell and Peter Morgane, Clark University; and Dr. Morgane, Trinity College and Worcester Polytechnic Institute.

Several of the Foundation's faculty have taught summer courses at the Marine Biological Laboratory (MBL) at Woods Hole. This past year, Drs. Greenfield Sluder and Richard Vallee taught in the MBL's Physiology Course.



## The Foundation Auxiliary

The Auxiliary has a long and proud tradition of serving as an adjunct fundraising arm of the Worcester Foundation. Organized in 1947 by women from some of Worcester's leading philanthropic families who were interested in furthering the research efforts of the Foundation, the Auxiliary has grown to now number over 300 members. Its many fund-raising projects — cultural events, antique auctions, dinner theater parties, fashion shows, and their renowned annual Class A Horse Show — have expanded community support and understanding of the Worcester Foundation. In its 42-year history, the Auxiliary has raised close to \$350,000 in support of the Foundation's scientific research programs and other special projects.



Thor and Judy Pederson (above) shopping at the Auxiliary's Antiques Show. At left, Auxiliary members Inez Montgomery (left) and Betty Knight looking over the antique home furnishings.



### Executive Board 1989-90

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*President-Elect*

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Scene from the 1989 Horse Show



## Physicians Research Roundtable

The Physicians Research Roundtable was formed in 1985 to bring physicians interested in biomedical research together with scientists at the Worcester Foundation in a formal exchange of knowledge and ideas. Its scientific seminars offer members the opportunity to share information about basic science and clinical applications and to learn about the latest developments in Worcester Foundation research programs.

The Roundtable met twice during 1988-89. In the fall, Dr. Massimo S. Fiandaca of the University of Massachusetts Medical Center addressed the group on the subject of brain transplants in patients suffering from Parkinson's Disease.

In the spring, Worcester Foundation trustee Dr. M. Judah Folkman, a nationally recognized tumor expert, spoke on the clinical implications of angiogenesis, which is the process by which blood vessels grow and ramify throughout a tumor. Folkman has identified a "tumor angiogenesis factor" that promotes this process. His research is now directed at creating agents that block angiogenesis, and so deny the tumor an adequate blood supply.

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## The Hudson Hoagland Society

**N**amed in honor of the institution's co-founder, the Hudson Hoagland Society was organized in 1985 to recognize major contributors to the Worcester Foundation's Annual Research Fund. The Society brings together those who share a commitment to biomedical research and the Worcester Foundation, as Hudson Hoagland did, to play a leadership role in private giving. Their significant contributions are helping scientists to fight cancer, AIDS, Alzheimer's disease, and Lou Gehrig's and other degenerative nerve diseases... and to shed new light on substance abuse and male and female reproduction.

Membership in the Society is open to individuals who make gifts of \$1,000 or more to the Annual Research Fund. Membership has more than doubled in the four year since the Society's founding, with current membership standing at 115.

Each spring, the Society gathers for a black-tie dinner at which it hears from an engaging speaker who embodies the spirit of exploration — *that same spirit which drives basic research.*

Author and journalist Nicholas Gage was the featured speaker at this year's annual meeting in May. The former *New York Times* investigative reporter gave a moving account of his personal odyssey to seek out those who killed his mother during the civil war that engulfed his native Greece during World War II. He first told that story in his 1983 award-winning book, *Eleni*.

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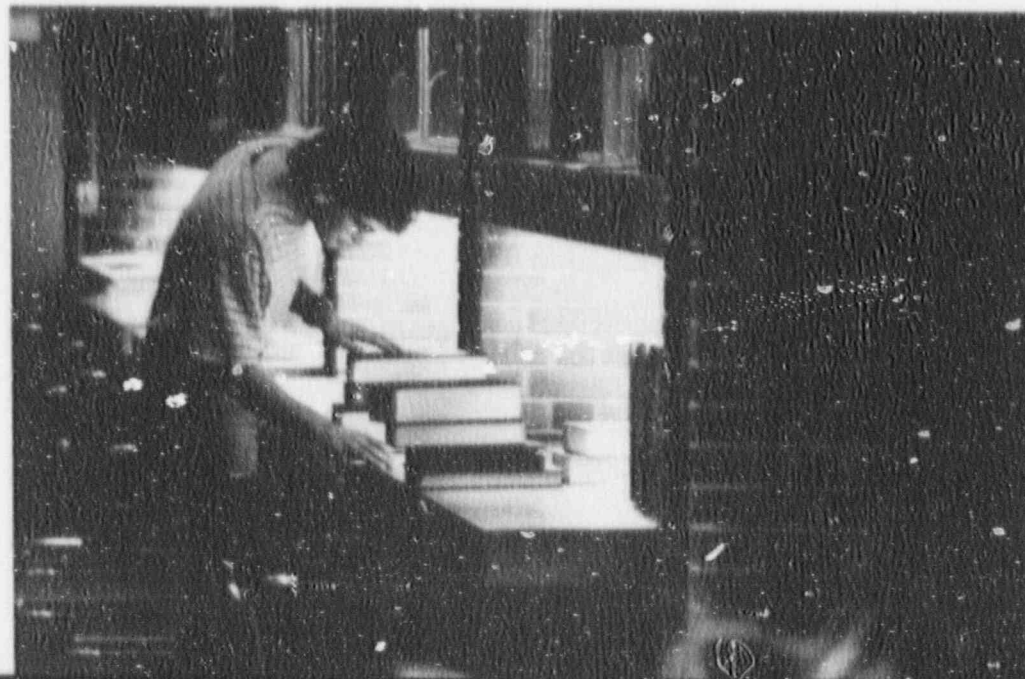
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## Financial Data

### Comparative Statements of Support, Earned Revenue and Expenditures

#### Current Funds

Years Ended March 31, 1989 and 1988

| <u>Public Support and Earned Revenue</u>                 | <u>1989</u>       | <u>1988</u>       |
|--|-------------------|-------------------|
| Research Awards to Faculty                               | \$10,525,551      | \$ 9,873,157      |
| Private Gifts and Grants<br>for Research                 | 715,077           | 432,465           |
| Institutional Research Support                           | 722,130           | 385,047           |
| Total Science Support &<br>Earned Revenue                | 11,962,758        | 10,690,669        |
| Plant Funds Expended                                     | 347,821           | 859,419           |
| Unrestricted Gifts, Investment &<br>Miscellaneous Income | 927,641           | 704,984           |
| Total Public Support &<br>Earned Revenue                 | <u>13,238,220</u> | <u>12,255,072</u> |
| <u>Expenditures</u>                                      |                   |                   |
| Payroll and Related Costs                                | 6,659,063         | 6,000,748         |
| Equipment and Building<br>Improvements                   | 1,521,624         | 1,921,546         |
| Utilities & Building<br>Maintenance Costs                | 1,517,039         | 1,136,006         |
| Costs of Operations                                      | 2,985,825         | 2,694,806         |
| Professional Services                                    | 407,887           | 366,888           |
| Total Expenditures                                       | <u>13,091,438</u> | <u>12,119,994</u> |
| Excess of Support & Revenue<br>Over Expenditures         | <u>\$ 146,782</u> | <u>\$ 135,078</u> |



**Comparative Balance Sheet**

March 31, 1989 and 1988

| <u>Assets</u>                                  | <u>1989</u>         | <u>1988</u>         |
|--|---------------------|---------------------|
| Cash and Cash Investments                      | \$ 1,752,670        | \$ 2,379,298        |
| Managed Investments (at cost)                  | 5,013,852           | 4,097,644           |
| Research Awards Receivable                     | 5,853,437           | 4,957,163           |
| Pledges Receivable                             | 821,223             | 1,909,579           |
| Accounts Receivable                            | 71,831              | 76,213              |
| Inventory of Laboratory Supplies               | 28,544              | 26,426              |
| Prepaid Expenses                               | 154,261             | 90,132              |
| Property, Plant & Equipment<br>(net value)     | 7,713,890           | 7,228,132           |
| <b>Total Assets</b>                            | <b>\$21,409,708</b> | <b>\$20,764,587</b> |
| <br>   |                     |                     |
| <u>Liabilities and Fund Balances</u>           | <u>1989</u>         | <u>1988</u>         |
| Note Payable - Current                         | \$ 400,000          | \$ 450,000          |
| Accounts Payable                               | 569,193             | 479,398             |
| Accrued Expenses & Other<br>Liabilities        | 83,350              | 148,514             |
| Deferred Revenue                               | 821,223             | 1,909,579           |
| Fund Balances                                  | 19,535,942          | 17,777,096          |
| <b>Total Liabilities and<br/>Fund Balances</b> | <b>\$21,409,708</b> | <b>\$20,764,587</b> |



Research grant and contract awards for fiscal 1989 totaled \$12,398,725, nearly 90% of which was provided by federal granting agencies. The table below reflects a summary of research awards by research area and source of funds for the fiscal year ended March 31, 1989.

| <u>Research Area</u>                         | <u>Number<br/>of Awards</u> | <u>Federal<br/>Government</u> | <u>Other<br/>Faculty-<br/>Initiated</u> | <u>Institutional<br/>Gifts and<br/>Grants</u> | <u>Total</u>        |
|--|-----------------------------|-------------------------------|---|---|---------------------|
| Cell and<br>Molecular<br>Biology             | 34                          | \$ 6,025,747                  | \$188,117                               | \$ 128,354                                    | \$ 6,342,218        |
| Endocrine and<br>Reproductive<br>Biology     | 16                          | 1,764,730                     | 26,776                                  | 730,600                                       | 2,522,106           |
| Neurobiology<br>and<br>Behavioral<br>Studies | 18                          | 2,706,913                     | 58,000                                  |   | 2,764,913           |
| General<br>Research<br>Support               | 7                           | 473,671                       |   | 295,817                                       | 769,488             |
| <b>Totals</b>                                | <b>75</b>                   | <b>\$10,971,061</b>           | <b>\$272,893</b>                        | <b>\$1,154,771</b>                            | <b>\$12,398,725</b> |



The research grants and contracts listed in the preceding table were provided directly or indirectly by the following grantors:

|   | Number<br>of Awards | Amount       |
|---|---------------------|--------------|
| <b>Federal Government</b>   |                     |              |
| National Institutes of Health<br>Alcohol, Drug Abuse, and Mental<br>Health Administration | 50                  | \$ 9,833,949 |
| National Science Foundation   | 3                   | 699,599      |
|   | 5                   | 437,513      |
| Total Federal Government  | 58                  | 10,971,061   |
| <b>Other Faculty-Initiated</b>  |                     |              |
| The American Cancer Society Inc.  | 2                   | 105,906      |
| The McKnight Foundation   | 1                   | 35,000       |
| Muscular Dystrophy Association  | 3                   | 84,376       |
| The National Neurofibromatosis<br>Foundation Inc.   | 1                   | 20,835       |
| The Whitaker Foundation   | 1                   | 26,776       |
| Total Other Faculty-Initiated   | 8                   | 272,893      |
| <b>Institutional Gifts and Grants</b>   |                     |              |
| The George I. Alden Trust   | 1                   | 45,000       |
| Mr. and Mrs. Anthony A.<br>Borgatti Jr.   | 1                   | 5,000        |
| Educational Foundation of<br>America  | 1                   | 7,500        |
| George F. and Sybil H. Fuller<br>Foundation   | 1                   | 50,000       |
| G. Harold and Leila Y. Mathers<br>Charitable Foundation                                   | 1                   | 121,120      |
| The Andrew W. Mellon Foundation   | 1                   | 750,000      |
| Edward John Noble Foundation  | 1                   | 45,000       |
| Gustavus and Louise Pfeiffer<br>Research Foundation                                       | 1                   | 23,000       |
| Fannie E. Rippel Foundation   | 1                   | 84,117       |
| Miscellaneous   |                     | 24,034       |
| Total Institutional<br>Gifts and Grants   | 9                   | 1,154,771    |
| Total Awards  | 75                  | \$12,398,725 |

The financial statements of the Worcester Foundation for Experimental Biology Inc., for fiscal years ended March 31, 1989 and 1988 were examined by KPMG Peat Marwick Main & Co., Certified Public Accountants. Their complete audit report and financial statements are available upon request to:

Mr. A. Bradford Bull  
Vice President for Administration and Finance  
Worcester Foundation for Experimental Biology Inc.  
222 Maple Avenue  
Shrewsbury, Massachusetts 01545



## Gifts to the Foundation

This is the record of individuals, families, corporations, foundations and friends who provided financial resources during the fiscal year ending March 31, 1989 to assist the Worcester Foundation and its scientists in their search for new knowledge about major disease.

CAMPAIGN DISCOVER, a three-year campaign for \$5.5 million to support scientific research, laboratory improvements, new equipment, and endowment, reached a new total of \$3 million.

The Annual Research Fund also reached \$233,699 with the help of increased contributions from the business community and a growing Hudson Hoagland Society. The Annual Research Fund provides critically needed unrestricted funds for the Foundation's research programs and promising new lines of research not yet funded by grants from foundations and federal agencies. These are the venture capital funds which make a real difference in the quality of the research enterprise.

Private gift support is an increasingly important factor in maintaining the scientific excellence which has earned the Worcester Foundation an international reputation as a center for biomedical research. Foundation scientists, the board of trustees and the administration join in expressing their deep appreciation to all who have helped by their investment in the future good health of mankind.

In this publication, donors are listed in four major categories:

### Major Grants for Special Projects and Programs

Both local and national foundations provide extraordinary grants which enable the Worcester Foundation to undertake major projects and programs which span several years.

### Capital Campaign Gifts

Capital gift contributors to CAMPAIGN DISCOVER are listed according to their pledges and gifts in the following categories:

|                  |                       |
|------------------|-----------------------|
| Great Benefactor | \$100,000 or more     |
| Benefactor       | \$ 50,000 to \$99,999 |
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| Sustaining       | \$ 1,000 to \$ 2,499  |

### The Annual Research Fund

Donors to the Annual Research Fund are listed based upon gifts received during the fiscal year, April 1, 1988 - March 31, 1989.

### Memorial/Special Occasion Gifts

Each year the Foundation receives many gifts from individuals and families who choose support of biomedical research as an appropriate way to honor friends on special occasions such as anniversaries, graduations, etc., or to express their condolences at the time of death. All such gifts are used to support further research into the cause and cures for cancer and other major illnesses. Attractive notification of each gift of \$25 or more is mailed immediately to the individual or family designated. For further information concerning special occasion or memorial gifts, write the Foundation or call 508/842-8921, Ext. 296.

### Bequests and Endowment

Bequests have played an important role in building the Foundation's endowment, which now totals \$5 million and generates critically needed income to counterbalance the less flexible funding from the National Institutes of Health and National Science Foundation. Last year the Worcester Foundation received \$926,000 from the estates of six generous benefactors.

### Planned Giving

Through a newly established Pooled Income Fund, the Worcester Foundation is now able to assist donors who would like to help the Foundation, but need the income for their lifetime.

For information about the tax advantages of the Pooled Income Fund, please call Charles L. Taggart, vice president for development, at 508/842-8921.

*Although the greatest possible care has been taken in the preparation of this record the Foundation recognizes the possibility of omissions or inaccuracies. If any are noted, please accept our apology and advise us of any correction to be made.*



## Major Grants for Special Projects and Programs

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**E**ach year foundations provide grants to support projects and programs integral to the Worcester Foundation's mission. The Worcester Foundation gratefully acknowledges the following grants:

- |  |                  |
|--|------------------|
| <b>The Andrew W. Mellon Foundation</b><br><i>New York, New York</i>  | <b>\$750,000</b> |
| Research support over three years for the Male Fertility Program, to encourage young investigators and underwrite other costs in reproductive biology.     |                  |
| <b>W. M. Keck Foundation</b><br><i>Los Angeles, California</i>   | <b>\$425,000</b> |
| A three-year grant to create and start up a protein chemistry core facility, fundamental to the study of molecular biology of cell structure and function. |                  |
| <b>The Stoddard Charitable Trust</b><br><i>Worcester, Massachusetts</i>  | <b>\$400,000</b> |
| A three-year grant enabling the Worcester Foundation to undertake a major physical plant renovation project.   |                  |
| <b>G. Harold and Leila Y. Mathers Charitable Foundation</b><br><i>White Plains, New York</i>   | <b>\$242,240</b> |
| A two-year grant to support the AIDS research program being led by Drs. Paul C. Zamecnik and John Goodchild.   |                  |
| <b>George F. and Sybil H. Fuller Foundation</b><br><i>Worcester, Massachusetts</i>   | <b>\$150,000</b> |
| A three-year grant in support of a central computer system for scientific research and administration.   |                  |
| <b>George I. Alden Trust</b><br><i>Worcester, Massachusetts</i>  | <b>\$135,000</b> |
| A three-year grant in support of postdoctoral education and the Summer Student Training Program.   |                  |
| <b>Edward John Noble Foundation</b><br><i>New York, New York</i>   | <b>\$120,000</b> |
| A three-year grant for support of research on male fertility, toward population control.   |                  |
| <b>Fannie E. Rippel Foundation</b><br><i>Madison, New Jersey</i>   | <b>\$84,117</b>  |
| A grant to provide a peptide synthesizer for the protein chemistry core facility.  |                  |
| <b>Gustavus and Louise Pfeiffer Research Foundation</b><br><i>Redlands, California</i>   | <b>\$75,000</b>  |
| A three-year grant in support of neurobiology research, with emphasis on development and aging.  |                  |
| <b>Wyman-Gordon Foundation</b><br><i>Worcester, Massachusetts</i>  | <b>\$50,000</b>  |
| A five-year grant to the endowment.  |                  |



## Capital Gifts

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(April 1, 1988 - March 31, 1991)

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#### A number of gifts in this year's roster were designated to the following funds:

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The Clarence E. Heiler Endowment  
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The Judith M. Isaacson Memorial  
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#### The following bequests were received during the fiscal period 1988-89:

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## 1988-89 Annual Research Fund

### The Research Team

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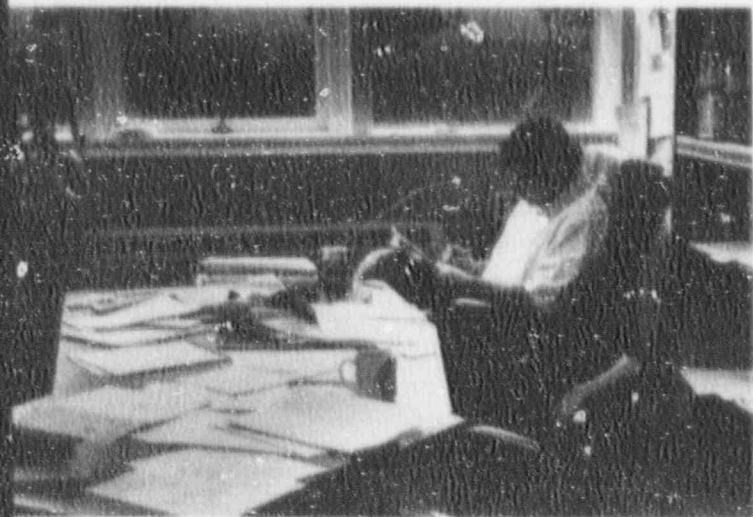
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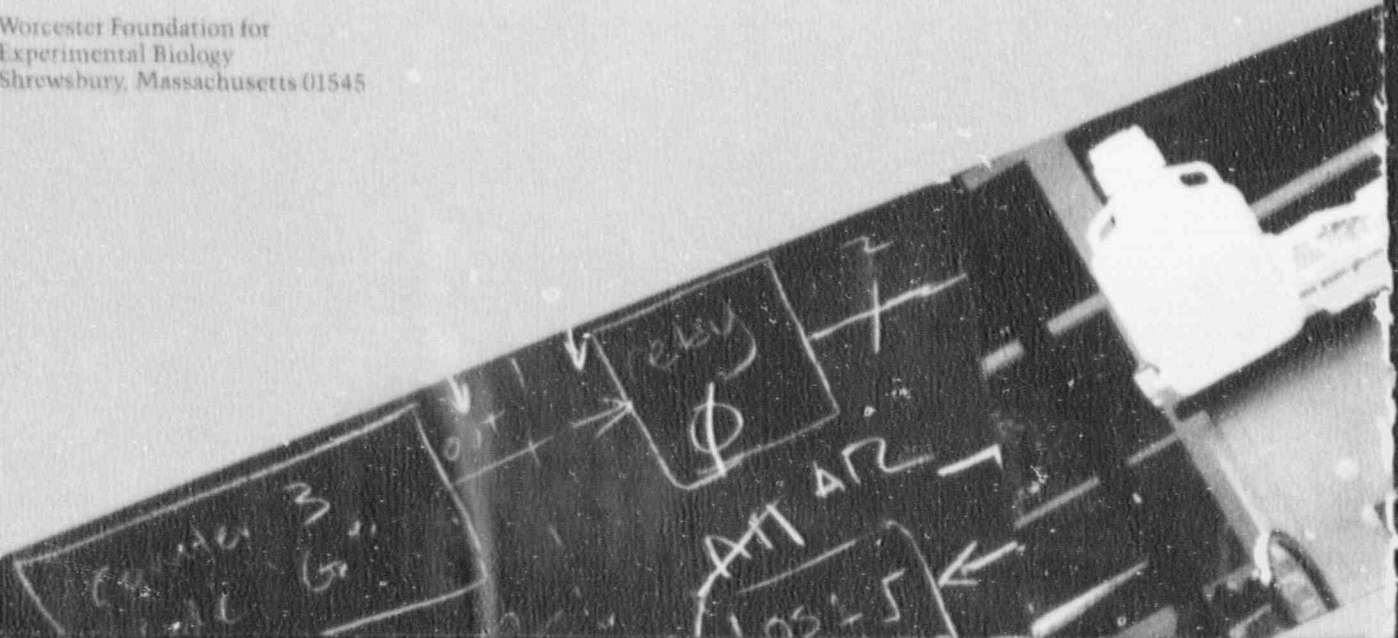
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Worcester Foundation for  
Experimental Biology  
Shrewsbury, Massachusetts 01545





DATE 9/14/80

TELEPHONE OR VERBAL CONVERSATION RECORD

TIME  A.M.  
 P.M.

INCOMING CALL

OUTGOING CALL

VISIT

PERSON CALLING

H Jackson

OFFICE/ADDRESS

OC/RFDCB

PHONE NUMBER

EXTENSION

PERSON CALLED

Richard Eastman

OFFICE/ADDRESS

Worcester Foundation

PHONE NUMBER

EXTENSION

508-842-8921

CONVERSATION

SUBJECT

His 7/15/88 ltr for exemption of license

SUMMARY

20-01225-01

Mr. Eastman will send me a letter  
confirming the following:

- they provide post-doctoral training
- have been granted authority by MA  
to grant Doctorate of Science Degrees
- their State Charter states they are  
a scientific research and educational  
institution.

They do not have formal curriculum, faculty  
or classrooms, and not educational for  
Federal tax purposes.

REFERRED TO:

ACTION REQUESTED

ACTION TAKEN

ADVISE ME OF  
ACTION TAKEN.

INITIALS

DATE

INITIALS

DATE



# WORCESTER FOUNDATION FOR EXPERIMENTAL BIOLOGY

222 Maple Avenue  
Sturwobury, Massachusetts 01545  
Telephone (617) 842-8921

July 15, 1988

Ms. Glenda Jackson  
License Fee Management Branch  
Division of Accounting and Finance  
Office of Administration and  
Resources Management  
United States Nuclear Regulatory Commission  
Washington, DC 20555

Re: Control Number 108942

Dear Ms. Jackson:

By this letter the Worcester Foundation for Experimental Biology requests review of its status under Part 170 of Title 10 Code of Federal regulations. Because human use was allowed under license 20-01225-01 we have paid fees listed under 170.31 since Part 170 was published as a final rule. Since we are discontinuing human use of regulated material, it appears that, as a nonprofit institution engaged in biomedical research, teaching and training, we fall under the exemption issued in 170.11(a)(4).

Please review our status and if appropriate, refund the most recent renewal fee. Checks should be made payable to the Worcester Foundation for Experimental Biology. If you have any questions, please contact me at 508-842-8921.

Sincerely yours,

Richard Eastman  
Business Manager

RE/r

*This letter is  
part of the discussion  
on licensing (170.11(a)(4))  
(checked off 7/1/90).*