

**Warren Alpert Foundation Prize
Press Releases
1997 – 2006**

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**CANCER RESEARCH PIONEER JUDAH FOLKMAN, MD, WINS
WARREN ALPERT FOUNDATION PRIZE
FOR DISCOVERING THAT TUMORS ARE DEPENDENT ON BLOOD VESSEL DEVELOPMENT
(ANGIOGENESIS) AND FOR CHAMPIONING
ANTI-ANGIOGENIC THERAPIES**

BOSTON – The Warren Alpert Foundation has awarded the 18th annual foundation prize to Judah Folkman, MD, the Julia Dyckman Andrus professor of surgery at Harvard Medical School and Children's Hospital Boston, for discovering that tumors require the formation of new blood vessels, a process known as angiogenesis, and for championing the concept of anti-angiogenic therapies for cancer and other diseases. The foundation will award Dr. Folkman a \$150,000 prize.

"Judah Folkman absolutely pioneered this field," says Bruce Zetter, PhD, Chief Scientific Officer at Children's Hospital Boston, and one of the nominators of Folkman for the award. "His angiogenesis concepts were ahead of their time, but through outstanding creativity and dogged persistence, he ultimately proved his theories. The Alpert Prize was created to support investigators whose innovative work has led to new therapies. Dr. Folkman's work is just such a tale, and is one that will benefit many patients with a variety of diseases," says Zetter, who is also the Charles Nowiszewski professor of cancer biology at Harvard Medical School.

"I am extremely grateful for receiving the Alpert prize," says Folkman. "The resources will allow graduate students and post-doctoral fellows in my lab to pioneer novel research concepts themselves. Such support is tremendously beneficial to the research community and ultimately the development of new therapies."

For nearly 40 years, Folkman, director of Children's Hospital's Vascular Biology Program, has pursued his groundbreaking hypothesis that new blood vessel development is central to various disease processes. Folkman and his research colleagues showed that cancer and other diseases are supported by excessive or insufficient blood vessel growth.

Due in large measure to Folkman's innovative research, more and more researchers throughout the world are studying the complex biology creating and halting the formation of the body's blood vessels. Knowledge from angiogenesis research has allowed clinical investigators to better understand how some already active drugs function, and by using novel dosage strategies, attack disease more effectively.

Folkman and other investigators have also isolated molecules that specifically regulate angiogenesis, some of which are now FDA approved or in the drug-testing pipeline. Unlike traditional cancer therapies, including chemotherapy and radiation, anti-angiogenic approaches appear to have few side effects, and drug resistance has not been observed.

New blood vessel inhibitors and stimulators are being studied to treat many diseases including macular degeneration, a condition that afflicts more than 11 million Americans and countless others throughout the world. Angiogenesis inhibitors have helped restore the sight of 40% of the 1.5 million Americans made blind from macular degeneration. In addition to various forms of cancer, this work holds promise

for patients with arthritis, endometriosis, hemangiomas and other non-cancer diseases, and coronary heart disease.

Therapies and treatment strategies based on angiogenesis research now benefits many thousands of patients.

The Warren Alpert Foundation

<http://warrenalpert.org/home/>

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To choose subsequent recipients of the prize, Alpert asked Dr. Daniel Tosteson, then dean of Harvard Medical School, to convene a panel of experts to select and honor renowned scientists from around the world whose research has had a direct impact on the treatment of disease.

Each year the Foundation receives 30 to 50 nominations for the Alpert Prize from scientific leaders worldwide. Prize recipients are selected by the foundation's scientific advisory board, made up of internationally recognized biomedical scientists and now chaired by Joseph B. Martin, MD, PhD, dean of Harvard Medical School.

Alpert, a first-generation American, started his business in 1950 with, as he tells it, "\$1,000 and a used car." Today, Warren Equities and its subsidiaries—which market petroleum, food and spirits, and engage in transportation and real estate improvements—generate approximately \$1 billion in annual revenue and have more than 2,200 employees in 11 states.

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HARVARD MEDICAL SCHOOL

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Harvard Medical School has more than 7,000 full-time faculty working in eight academic departments based at the School's Boston quadrangle or in one of 47 academic departments at 18 Harvard teaching hospitals and research institutes. Those Harvard hospitals and research institutions include Beth Israel Deaconess Medical Center, Brigham and Women's Hospital, Cambridge Health Alliance, the CBR Institute for Biomedical Research, Children's Hospital Boston, Dana-Farber Cancer Institute, Forsyth Institute, Harvard Pilgrim Health Care, Joslin Diabetes Center, Judge Baker Children's Center, Massachusetts Eye and Ear Infirmary, Massachusetts General Hospital, Massachusetts Mental Health Center, McLean Hospital, Mount Auburn Hospital, Schepens Eye Research Institute, Spaulding Rehabilitation Hospital, and VA Boston Healthcare System.

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2005

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CANCER RESEARCHER SUSAN BAND HORWITZ, PHD WINS WARREN ALPERT FOUNDATION PRIZE FOR WORK DEVELOPING TAXOL

BOSTON-Susan Band Horwitz, Ph.D., the Falkenstein Professor of Cancer Research and Co-Chair of the Department of Molecular Pharmacology at the Albert Einstein College of Medicine, will today be awarded the 17th annual Warren Alpert Foundation Prize. The foundation recognizes Dr. Horwitz, a molecular pharmacologist, for her seminal contributions to the understanding of how the antitumor agent Taxol inhibits the growth of cancer cells. Her research helped pave the way for studies leading to approval of the plant compound for the treatment of ovarian, breast and lung cancers.

"One thing that Mr. Alpert stipulated when he developed this prize was that it should go to someone who had already made major contributions to helping patients. The impact of Susan's work has been quite extraordinary in the cancer field," said Professor Dominick Purpura, MD, Dean of Albert Einstein College of Medicine, who nominated Dr. Horwitz for the prize. In fact, earlier this year, shortly after Dr. Horwitz was selected as winner of the prize, she was acknowledged by her peers for her contributions to cancer research when she was elected to the National Academy of Sciences.

In the US, Taxol was first approved by the Food and Drug Administration (FDA) for the treatment of refractory ovarian cancer in 1992. Approval for metastatic breast cancer followed in 1994, and more recently for non-small cell lung cancer in 1999. "Taxol has become one of the most valuable cytotoxic chemotherapeutic agents we have in clinical oncology. It has proven effective in ovarian, breast, lung, and head and neck cancer and it has contributed immensely to the quality of life of cancer patients," said Larry Shulman, associate professor of medicine at the Dana-Farber Cancer Institute, Boston. The drug has been used in well over a million patients worldwide.

In 1977, Dr. Horwitz was approached by the National Cancer Institute to study the biological activity of Taxol. In 1966, the compound had been isolated from the bark of the Pacific Yew tree (*Taxus brevifolia*) as part of a concerted effort to find natural products that might cure cancer. At that time it was shown that Taxol was cytotoxic to cells growing in tissue culture, but over the next ten years there was almost nothing further gleaned about its biological action. However, within a few months of receiving her first samples of the compound, Dr. Horwitz with her then graduate student, Peter Schiff, found that Taxol, which had a unique chemical structure, inhibited cell division, which is deregulated in cancer, thereby promoting uncontrolled cell growth. In subsequent studies she showed that Taxol interferes with mitosis, the process whereby the chromosomes in the nucleus of a cell are duplicated and then segregated equally into two daughter cells.

"Susan's discovery that Taxol bound to and stabilized microtubules, thereby blocking cells in mitosis meant, in fact, that Taxol was a prototype for a new class of chemotherapeutic drugs. Susan recognized this immediately, and it was also quickly sensed by the NCI and others, who then moved Taxol into clinical trials and then pervasive clinical use," said Purpura.

The discovery of Taxol's unique structure and mode of action gave oncologists a new weapon in the fight against cancer. Dr. Horwitz found that unlike many of the cancer drugs that were approved or under development at the time, such as cisplatin and nucleotide analogs that interact with DNA, the mechanism of action of Taxol was not mediated by a direct interaction with DNA. Instead, she found that Taxol interferes with the normal functions of microtubules.

Microtubules are dynamic polymers, hollow cylindrical tubes that are constantly being remodeled by the addition or removal of tubulin subunits. During mitosis, microtubules act like long tethers to pull duplicate

chromosomes to opposite poles of the cell so that they can be incorporated into two new nuclei as the cell divides. To complete the process, the microtubules must be shortened as the chromosomes draw near their final destination. Dr. Horwitz reported that Taxol stabilizes microtubules, preventing them from shrinking and therefore blocks the segregation of the chromosomes. It is now known that Taxol perturbs cellular growth at various stages including mitosis, which leads to cellular stress resulting in eventual death. In fact the drug has become a valuable tool in basic cancer research to help delineate the function of microtubules.

Work from Dr. Horwitz's laboratory revealed that Taxol binds specifically to beta-tubulin in the microtubule and causes microtubule bundle formation within the cell. But there are many different types of tubulin in the human body that are expressed in tissue-specific patterns. Today, Dr. Horwitz, who was a past-President of the American Association for Cancer Research (AACR) (2002-2003), continues her work with Taxol, investigating whether the presence of different forms of tubulin might explain why some cancer cells are more responsive to the drug than others. She studies other natural products, from bacteria and marine animals, which have totally different chemical structures from that of Taxol but which bind to microtubules and are functionally similar to Taxol. Such new drugs may offer useful alternatives for Taxol in cases where the drug is poorly tolerated, or ineffective.

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Harvard Pilgrim Health Care, Joslin Diabetes Center, Judge Baker Children's Center, Massachusetts Eye and Ear Infirmary, Massachusetts General Hospital, Massachusetts Mental Health Center, McLean Hospital, Mount Auburn Hospital, Schepens Eye Research Institute, Spaulding Rehabilitation Hospital, VA Boston Healthcare System.

2004

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Creators of Groundbreaking Anti-Viral Therapy Win Sixteenth Annual Warren Alpert Foundation Prize

Discoveries Led Directly to Successful Treatment of Hepatitis C Infection

BOSTON--June 8, 2004--Three scientists whose pioneering research made interferon therapy for hepatitis C and other viral diseases a reality were named today as winners of the sixteenth annual Warren Alpert Foundation Scientific Prize.

The Foundation recognizes Sidney Pestka, MD, Professor and Chairman of Molecular Genetics, Microbiology and Immunology at the Robert Wood Johnson Medical School of the University of Medicine and Dentistry of New Jersey and Chairman and Chief Scientific Officer of PBL Biomedical Laboratories, for his seminal accomplishments in purifying, characterizing and cloning human interferon-alpha, or Hu-IFN-a, a virus-fighting substance produced by white blood cells.

David V. Goeddel, PhD, founder and Chief Executive Officer of Tularik, Inc., and Charles Weissmann, MD, PhD, of the Institute of Neurology, University College London and Director of the Department of Infectology, Scripps Florida Research Institute, share the prize for crucial work in which they cloned Hu-IFN-a in the bacterium *E. coli* and demonstrated that biologically active interferon could be produced in large enough quantities to make it a practical treatment for disease.

The Foundation will divide among the winners a \$150,000 award.

Interferon-alpha is the key component of the only known treatment regimen for hepatitis C, a viral disease of the liver spread by exposure to the blood of those already infected. Approximately 170 million persons suffer from chronic hepatitis C infection worldwide, and two to three million new cases are diagnosed each year. If untreated, chronic hepatitis C can lead to cirrhosis, and infection raises the risk of liver cancer 100-fold. But using a combined regimen of pegylated interferon-alpha and ribavirin, doctors now cure about 50 to 80 percent (depending on the viral strain) of chronically infected hepatitis patients, heading off permanent liver damage and cancer.

Interferon-alpha is used to treat several other viral diseases, including hepatitis B and human papillomavirus, or HPV, the most common sexually transmitted disease in the United States and the cause of most cervical cancer. Interferon is also used in the treatment of cancer. It has been shown to be effective in various forms of leukemia and in Kaposi's sarcoma, a cancer associated with HIV infection.

Scientists had noticed during the 1930s that viruses tend to strike one at a time. It is quite rare, for example, for a child to have measles and chickenpox simultaneously. Researchers explained this phenomenon by way of a theory of "viral interference," which proposed that cells exposed to a virus release some agent that protects the body from infection by other viruses.

In 1957, scientists in London discovered a highly potent protein that played just such a protective role after viral infection, and they accordingly named it interferon.

The discovery of interferon, a natural cell product that acts against a wide range of viruses by protecting cells from infection and stimulating the immune system, was greeted with great excitement, and its clinical future seemed bright. However, cells produce interferon in miniscule amounts, and two decades' worth of attempts to purify and characterize the protein met with repeated failure.

Pestka first found he could greatly increase the interferon yield in his experiments by using white blood cells from leukemia patients, and then, after developing a new technique—reverse-phase high-performance liquid chromatography, now used in biological laboratories throughout the world—he successfully purified ten unique interferon-alpha proteins in 1978.

In 1980, Weissmann, then at the University of Zurich, cloned Hu-IFN- α complementary DNA (cDNA) in *E. coli*, and found that the bacteria synthesized interferon-alpha with a demonstrable anti-viral effect in human cells. Weissmann also showed that the different proteins purified by Pestka were encoded by a large family of related interferon-alpha genes. Just a few months later, Goeddel, then at Genentech, published results from experiments he had conducted with Pestka in which Hu-IFN- α genes were sequenced to guide the construction of synthetic Hu-IFN- α cDNA. When this precisely bioengineered cDNA was cloned in *E. coli*, the bacteria produced as much human interferon-alpha per liter as could be made from the white blood cells of 100 donors. Moreover, the protein created in these experiments was potent enough to protect monkeys from otherwise deadly viral infections.

The translation of this combined research from the laboratory to the clinic was remarkably rapid. Recombinant interferon-alpha was first injected into a human patient in 1981, and the drug received FDA approval for the treatment of leukemia just five years later. Today, millions of patients throughout the world have received interferon-alpha for many conditions that were previously untreatable, and other potential uses for interferon continue to be explored in clinical trials and in basic research.

The Warren Alpert Foundation

In awarding the sixteenth annual scientific prize to researchers who have made an impact on hepatitis therapy, the Warren Alpert Foundation has come full circle. Chelsea, Massachusetts native Warren Alpert first established the prize in 1987 after reading that Kenneth Murray of the University of Edinburgh had developed a successful vaccine for hepatitis B. Alpert decided immediately that he would like to reward such far-reaching breakthroughs, so he called Murray to tell him he had won a prize, and then set about creating the Foundation. To choose subsequent recipients of the prize, Alpert asked Dr. Daniel Tosteson, then dean of Harvard Medical School, to convene a panel of experts to select and honor renowned scientists from around the world whose research has had a direct impact on the treatment of disease.

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2003

<http://www.hms.harvard.edu/news/releases/0503alpert.html>

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Wendy Spivak, Alpert Foundation, 617-227-0012, ext. 225 (wspivak@thecastlegrp.com)

Alfred Sommer, Dean, Johns Hopkins Bloomberg School of Public Health Wins Fifteenth Annual Warren Alpert Foundation Prize

Sommer's Research Led To Vitamin A Supplements Saving Millions of Lives and Preventing Blindness In Developing World

BOSTON--May 27, 2003--Alfred Sommer, MD, MHS, Dean, Johns Hopkins Bloomberg School of Public Health, was honored with the fifteenth annual Warren Alpert Foundation Scientific Prize for his pioneering work that showed that four cent vitamin A capsules can prevent the deaths of millions of lives and blindness in the developing world. The ceremony to bestow the \$150,000 prize was held at Boston's Four Seasons Hotel.

Alfred Sommer

15th Annual Warren Alpert Foundation Prize Winner In the early 1980s, Dr. Sommer, an ophthalmologist and epidemiologist by training, was searching for ways to prevent xerophthalmia, or childhood blindness, in Indonesian children. While treating children with capsules of vitamin A -- vitamin A deficiency was a known cause of the disease -- Sommer recognized a startling trend: children in the trial who received Vitamin A -- in addition to retaining their vision -- were dying at much lower rates than children who were receiving a placebo.

Sommer went on to replicate this work in Nepal and Africa, proving the trend in different countries and showing that even mild vitamin A deficiency dramatically increases childhood mortality rates, primarily because this deficiency reduces resistance to infectious diseases such as measles and diarrhea.

Moving from science to practice, Sommer next showed that the debilitating consequences of vitamin A deficiency could be effectively, quickly, and cheaply treated with oral high-dose vitamin A supplementation. In 1995, a United Nations Children's Fund report estimated that 1 million to 3 million lives could be saved annually if young children in the Third World took a vitamin A pill two or three times a year. The annual cost per child: 4 to 6 cents.

As a result, the World Development Report (World Bank) declared vitamin A supplementation one of the most cost-effective of all health interventions. The latest research by Dr. Sommer and his colleagues has shown that supplementing women of childbearing age with vitamin A or beta-carotene can reduce maternal mortality by an average of 45 percent. These dramatic results are now being tested in a new, large, randomized, controlled, field trial in Bangladesh, where the potential benefits of simultaneous supplementation with other micronutrients (zinc, folate, iron, B-complex) are being determined.

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Previous Alpert Prize Recipients

2001

Eugene Braunwald, MD, Partners Healthcare System and Harvard Medical School, and **Barry S. Collier, MD**, Rockefeller University, for their pioneering work in cardiovascular research which has dramatically reduced the mortality rate for heart attacks.

2000

David Baltimore, PhD, California Institute of Technology; **Brian J. Druker, MD**, Oregon Health Sciences University; **Nicholas B. Lydon, PhD**, Amgen; **Alex Matter, MD**, Novartis Pharama AG; and **Owen N. Witte, MD**, University of California, Los Angeles, for their research that contributed to the development of a drug that effectively treats chronic megelogenous leukemia and other forms of cancer.

1999

Michael Brown and **Joseph Goldstein**, University of Texas Southwestern Medical School; and **Akira Endo**, Tokyo Noko University, for their research in the development of statins which lower the level of cholesterol in the heart.

1998

K. Frank Austen, Harvard Medical School, for elucidating the pathway forming the leukotrienes and their role in bronchial asthma.

1997

Robert C. Gallo, University of Maryland School of Medicine, and **Luc Montagnier**, Queens College, New York, for their discovery of human immune deficiency virus (HIV).

1996

Leo Sachs, Weizmann Institute of Science, and **Donald Metcalf**, University of Melbourne, for their discoveries of molecules that regulate the growth and differentiation of bone marrow cells in health and disease.

1995

John A. Clements, University of California, San Francisco, for the development of the lung susfactant used for treating pulmonary hyaline membrane disease.

1994

J.R. Warren, Royal Perth Hospital, and **Barry J. Marshall**, University of Virginia, for identifying *Helicobacter pylori* as the organism that causes gastric and duodenal ulcers.

1993

Stuart H. Orkin, Harvard Medical School, for developing a complete description of thalassemia at the molecular level.

1992

Roscoe O. Brady, National Institutes of Health, for discovering the enzymatic basis of Gaucher's disease leading to its effective treatment.

1991

David W. Cushman and **Miguel A. Ondetti**, Bristol Myers-Squibb, for designing a powerful new approach to the treatment of high blood pressure and congestive heart failure.

1989

Yuet Wai Kan, University of California, San Francisco, for pioneering the use of DNA in the diagnosis of congenital anemias.

1988

Louis Kunkel, Harvard Medical School, for defining the genetic basis of muscular dystrophy.

1987

Kenneth Murray, University of Edinburgh, for elaborating the genetics of Hepatitis B as the basis for its vaccine.

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2002

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Jessica Edreich, Alpert Foundation, 617-227-0012 ext. 229

Pioneers in Cardiovascular Research Win Fourteenth Annual Warren Alpert Foundation Prize

Philanthropist bestows \$100,000 award May 8

BOSTON – May 7, 2002 - Two scientists whose cardiovascular research has been credited with saving many thousands of lives will be honored tomorrow with the fourteenth annual Warren Alpert Foundation Scientific Prize at a ceremony at Boston's Ritz Carlton Hotel.

Eugene Braunwald, MD, chief academic officer of Partners Healthcare System and the Hersey Distinguished Professor of the Theory and Practice of Physic at Harvard Medical School, and Barry S. Collier, MD, the David Rockefeller Professor of Medicine at the Rockefeller University, are being recognized for their work that has dramatically improved survival and quality of life for those suffering myocardial infarction.

Dr. Braunwald made the seminal discovery that a heart attack is a progressive event and that much of the heart muscle placed in jeopardy by the event can be rescued. This fundamental discovery changed the entire paradigm for the treatment of patients with acute myocardial infarction. Dr. Braunwald went on to conceive or play integral roles in numerous trials of methods to reduce heart muscle damage after myocardial infarction. According to The Institute of Scientific Research, Dr. Braunwald is the most prominently cited biomedical researcher in the world over the last four decades.

In his distinguished career, Dr. Braunwald has had a meaningful and sustained positive impact on the translation of science into the practice of medicine. "The dramatic declines over the past several decades in the mortality and morbidity due to acute myocardial infarction can, in many ways, be attributed to Dr. Braunwald's discoveries," said Dennis Kasper, MD, executive dean for academic programs at Harvard Medical School.

Barry Collier, MD developed one of the most widely used and effective therapeutic agents in modern cardiology. Following his pioneering work in the study of normal platelet function, he isolated a monoclonal antibody that was a highly potent and a more selective inhibitor of platelet aggregation – a

cause of infarction – than aspirin. That antibody, abciximab, commonly referred to as Reopro, is now used extensively in angioplasty procedures making them safer for reducing infarct size during heart attack, and reducing the incidence of infarction consequent to the procedure when done to prevent heart attacks.

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Previous winners include Sir Kenneth Murray, professor of molecular biology at the University of Edinburgh; David Baltimore, PhD, president and professor of biology at the California Institute of Technology; Leo Sachs, Otto Meyerhoff Professor of biology at the Weizman Institute of Science, Israel; Robert Gallo, professor of medicine, microbiology and immunology, University of Maryland School of Medicine; and Luc Montagnier, professor and director of the Center for Molecular and Cellular biology, Queen's College, University of New York.

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2001

AWARD CEREMONY OPEN TO JOURNALISTS

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DAY OF EVENT CALL: 617-872-2075

Wendy Spivak, Alpert Foundation, 617-227-0012, ext. 225 (wspivak@thecastlegrp.com)

Five Creators of Revolutionary Cancer Therapy STI571 Win Thirteenth Annual Alpert Foundation Scientific Prize

Drug's Precise Action Against Faulty Cancer Cells Eyed as Early Victory for Human Genome Studies

BOSTON—May 1, 2001—Five scientists whose research ultimately led to the development of STI571, a new cancer therapy that in clinical trials has shown remarkable effectiveness against chronic myelogenous leukemia (CML), will today be awarded the thirteenth annual Warren Alpert Foundation Scientific Prize at a ceremony at Boston's Four Seasons Hotel.

Created by understanding the fundamental mechanisms by which CML occurs, STI571 was cited by Dr. Francis Collins, Director of the National Human Genome Research Institute, as an early example of the kind of rational drug design that will stem from human genome studies. At a recent lecture at Harvard Medical School he stated that the STI571 clinical trials have shown "pretty dramatic results and ones which we hope will be repeated in other disorders as we get this kind of molecular understanding of what's gone awry in disease."

Phase I clinical trials of STI571 have produced encouraging results for patients with CML, a form of cancer characterized by rising white blood cell counts. Currently approved treatments are all very aggressive and difficult for patients to tolerate. A person with CML, which affects an estimated 5,000 Americans each year, typically dies within five years. With STI571, however, clinical investigators report that so far, 51 of 53 patients who received the highest dose in one study have gone into remission with few and modest side effects.

The Alpert Foundation recognizes David Baltimore, Ph.D., president and professor of biology at the California Institute of Technology, and Owen N. Witte, M.D., Howard Hughes Medical Institute investigator and professor of microbiology, immunology and molecular genetics at the University of California, Los Angeles and Jonsson Cancer Center, for the basic science investigations that characterized the genetic pathway to CML. For their preclinical work that led to the creation of STI571, the Alpert Foundation awards Alex Matter, M.D., head of oncology research, Novartis Pharma AG, and Nicholas B.

Lydon, Ph.D., formerly of Novartis and now vice president for small molecule drug discovery at Amgen, Inc. Brian J. Druker, M.D., professor of medicine at Oregon Health Sciences University, is recognized for both his preclinical work and clinical trial investigations. The Foundation will divide among the winners a \$150,000 award.

CML is caused by a genetic anomaly triggered by the rearrangement of chromosomes nine and 22, forming what is called the Philadelphia chromosome. A molecular consequence of this anomalous chromosome is the Bcr-Abl gene, whose product is a member of the tyrosine kinase family of proteins, which play a central role in a variety of cellular processes. Bcr-Abl's cancer-causing properties were identified and characterized by Drs. Baltimore and Witte.

The presence of Bcr-Abl in 95 percent of CML patients made this molecule a particularly attractive target for design of a selective kinase inhibitor. Dr. Matter, an early champion of kinase inhibitor research at Novartis, recruited Dr. Lydon to take on the effort of identifying Bcr-Abl inhibitors. Dr. Lydon, while working on this effort, began collaborating with Dr. Druker, whom he met years earlier when Druker was an oncology fellow studying kinases in the 1980s at the Dana Farber Cancer Institute, a Harvard Medical School teaching affiliate. They ultimately identified STI571, and in 1998, after curing mice, the drug was taken into clinical trials, and today Dr. Druker continues to take a lead role in the development of STI571 for CML. The drug works by blocking Bcr-Abl's ability to transfer phosphate groups to acceptor proteins, a key process in signaling the continued growth of the tumor cells.

Recently, STI571 has also shown effectiveness against gastrointestinal stromal tumors (GISTs), which occur in an estimated 2,000 Americans each year. GISTs originate in the stomach or small intestine in cells that form the organs' connective tissue. Patients with malignant GISTs that cannot be removed by surgery generally die within a year or two of diagnosis. Researchers found that STI571 blocked another tyrosine kinase, KIT, the flawed protein found in GISTs, and one patient has shown significant shrinkage in tumor size.

The foundation's Scientific Advisory Committee comprises physicians and scientists from Harvard Medical School and Massachusetts Institute of Technology and is chaired by Harvard Medical School dean Joseph B. Martin, M.D., Ph.D. Each year the Committee recognizes creative research that has dramatically affected the human condition.

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THE WARREN ALPERT FOUNDATION SCIENTIFIC PRIZE
Awarded by the Warren Alpert Foundation in Association with
Harvard Medical School

Every year, the prestigious Warren Alpert Foundation Prize honors scientists and researchers who have made significant discoveries in the prevention, treatment, or curing of disease. Prize recipients are selected by the foundation's Scientific Advisory Committee, comprising internationally renowned biomedical scientists and chaired by the dean of Harvard Medical School.

Selected from a group of the world's foremost scientific and medical professionals, prize recipients are presented with a cash award from the foundation. The previous prize recipients are:

- 1999** Michael Brown and Joseph Goldstein, *University of Texas Southwestern Medical School*; and Akira Endo, *Tokyo Noko University*
- 1998** K. Frank Austen, *Harvard Medical School*
- 1997** Robert C. Gallo, *University of Maryland School of Medicine*, and Luc Montagnier, *Queens College, New York*
- 1996** Leo Sachs, *Weizmann Institute of Science*, and Donald Metcalf, *University of Melbourne*
- 1995** John A. Clements, *University of California, San Francisco*
- 1994** J.R. Warren, *Royal Perth Hospital*, and Barry J. Marshall, *University of Virginia*
- 1993** Stuart H. Orkin, *Harvard Medical School*
- 1992** Roscoe O. Brady, *National Institutes of Health*
- 1991** David W. Cushman and Miguel A. Ondetti, *Bristol Myers-Squibb*
- 1989** Yuet Wai Kan, *University of California, San Francisco*
- 1988** Louis Kunkel, *Harvard Medical School*

1987 Kenneth Murray, *University of Edinburgh*

The Warren Alpert Foundation does not solicit funds. It is a private, philanthropic effort funded solely by Mr. Warren Alpert, Chairman of Warren Equities, Inc.

2000

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Twelfth Annual Alpert Foundation Prize Honors Research Which Led To Development of the First Statin to Lower Cholesterol

Philanthropist Bestows \$100,000 Award May 19 for Post-Nobel Work

BOSTON—May 19, 2000—Showing creative scientists don't rest on their laurels, Nobel Prize winners Michael S. Brown and Joseph L. Goldstein of the University of Texas Southwestern Medical School will share the Twelfth Annual Warren Alpert Foundation Prize with Akira Endo of Biopharm Research Laboratories, Inc. for work they did after their Nobel-earning discovery of the cholesterol receptor.

The Foundation's Scientific Advisory Committee—comprised of experts from Harvard and Massachusetts Institute of Technology—chose Drs. Brown, Goldstein, and Endo because their work on cholesterol metabolism, which led to the development of the first statin drug to lower high cholesterol levels, has had a profound effect on the prevention of cardiovascular disease. Each year, the Committee recognizes creative research that has dramatically impacted the human condition.

The trio will receive the \$100,000 award at a luncheon ceremony in their honor on Friday, May 19 at the Four Seasons, New York, from Warren Alpert, philanthropist, businessman, and sole benefactor of the Warren Alpert Foundation. All three researchers will speak at a symposium at Mount Sinai Hospital earlier that day, which will also feature introductory remarks by Alpert Prize Scientific Advisory Committee Chair Dr. Joseph B. Martin, dean of Harvard Medical School.

Brown and Goldstein won the Nobel and other prizes for their work at the fundamental biological level characterizing the receptor for the cholesterol-carrying particles called low density lipoproteins (LDL). They are receiving the Alpert prize for subsequent work and its clinical impact on patients. After discovering the LDL receptor they went on to track every step of its regulation that can lead to the rise and fall of LDL in the blood. Building on their work, Endo reasoned that a chemical inhibitor of the enzyme HMG CoA reductase might be useful in inhibiting cholesterol synthesis. He then isolated such a compound from fungus and it became the first statin drug, lovastatin.

The Warren Alpert Foundation

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1999

No release available

1998

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**Tenth Annual Alpert Foundation Prize Honors
HIV Discoverers Gallo and Montagnier**
Boston Native Bestows \$100,000 Award at April 30 Ceremony

BOSTON—April 30, 1998—Dr. Robert Gallo, of the University of Maryland at Baltimore, and Dr. Luc Montagnier, of Queens College, Flushing, N.Y., and Pasteur Institute, Paris, who discovered and isolated HIV, the virus that causes AIDS, are the winners of the Tenth Annual Warren Alpert Foundation Prize.

The pair will receive the \$100,000 award at a reception in their honor on Thursday, April 30 at 11:00 a.m. at the Four Seasons Hotel, Boston. The luncheon will feature introductory remarks by former United States Senator Bill Bradley, as well as comments by Alpert Prize Scientific Advisory Committee Chair Dr. Joseph B. Martin, dean of Harvard Medical School, and Warren Alpert, philanthropist, businessman, and sole benefactor of the Warren Alpert Foundation.

The Foundation's Scientific Advisory Committee—comprised of experts from Harvard and Massachusetts Institute of Technology—chose Gallo and Montagnier because of the widespread and rapid impact of their research findings. Each year, the Committee recognizes creative research that has dramatically impacted the human condition.

The Impact of the Research — Knowing the cause of AIDS had almost immediate worldwide implications on the health and well-being of both those infected with the virus and those not infected. The rapid development of a test to determine whether an individual was infected allowed blood banks to screen donors and almost completely eliminate a major source of infections. It also allowed those at high risk for infection to be tested, calming many who had lived for years with anxiety, and enabling those infected to monitor their health more aggressively.

Detailed knowledge of HIV resulted from the ability to grow it in the lab, a complex task perfected by this year's Alpert Prize winners. This knowledge has led to the creation of multiple drug therapies that now allow many who are infected to live for years with few symptoms. By understanding the virus, scientists have been able to find drugs that act on different parts of its life cycle and prevent it from replicating.

This multi-front attack has proven essential because the virus can quickly mutate and evade any one strategy.

Gallo and Montagnier — Gallo, internationally recognized for his achievements in retrovirology, is director of the University of Maryland at Baltimore's Institute of Human Virology as well as head of the Tumor Biology Program within its Cancer Center. Gallo's research has focused on the biology of blood cells and their disorders linked to viruses, especially AIDS and leukemia. In 1984, he and his colleagues grew HIV and developed a test that could detect the presence of HIV in blood. Gallo has received nearly 100 honors and has authored, or co-authored, more than 1,000 publications. From 1965-95 he held several positions at the National Cancer Institute, including chief of the Laboratory of Tumor Cell Biology from 1972-95.

Montagnier is director of the Bernard and Gloria Salick Center for Molecular and Cellular Biology at Queens College, president of the World Foundation for AIDS Research and Prevention, Paris, and professor at the Pasteur Institute. Montagnier and his Pasteur Institute colleagues discovered HIV-1 in 1983 and HIV-2 in 1985. His most recent research efforts have focused on identifying infectious cofactors of HIV. Montagnier, who earned a medical degree from Paris University and a Diplome d'Etudes Superieures Sciences Naturelles from Pontiers, France, has received more than 20 major awards, including the Commandeur de la Legion d'Honneur. He has authored, or co-authored, more than 350 publications, including the 1994 book *Of Viruses and Men*, to be published in English later this year. Since 1972, he has held several positions at the Pasteur Institute, including head of both the Viral Oncology Unit and the Department of AIDS and Retroviruses.

Warren Alpert Foundation Prize — Chelsea, Massachusetts native Warren Alpert, chairman of Warren Equities, established the Alpert Prize in 1987 after reading an article about University of Edinburgh's Kenneth Murray, who developed a vaccine for hepatitis B. Alpert decided he would like to reward such far-reaching breakthroughs, called Murray to tell him he had won a prize, then set about creating the Foundation. To choose subsequent recipients, he asked Dr. Daniel Tosteson, then dean of Harvard Medical School, to convene a panel of experts to select and honor renowned scientists from around the world.

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1997

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Alpert Prize Honors Scientists Who Pioneered Cancer-Treatment Breakthrough

The \$100,000 Prize Given for Discovery of Molecules That Regulate Blood-Cell Growth,
Which Has Revolutionized Cancer Therapy

BOSTON—On April 17, the Warren Alpert Foundation will present its ninth annual prize to Professors Leo Sachs and Donald Metcalf for their breakthrough discovery of protein molecules that regulate the growth of bone-marrow cells. Their research has led to the worldwide use of a protein, called granulocyte colony-stimulating factor, as a major support drug in cancer treatment.

The drug counteracts the destruction of bone-marrow cells from chemotherapy, reducing patients' risk of infection and increasing the chances they can tolerate a "curative" dose of chemotherapy. Other life-threatening blood disorders also respond to the medication.

Sachs, of the Weizmann Institute of Science in Rehovot, Israel, and Metcalf, of the Walter and Eliza Hall Institute of Medical Research at the University of Melbourne in Australia, will share the \$100,000 award. The ceremony will take place at Harvard Medical School, which administers the prize.

[Editors: The awards will be bestowed at 1:00 p.m. in the Waterhouse room in Building A of the Medical School. If you want to send photographers or reporters, call the above number.]

The Alpert prize was established in 1987 by Warren Alpert, chairman of Warren Equities. A native of Chelsea, Mass., Alpert started his own business in 1950 with little money and no customer base. Today, Warren Equities and the Warren Companies market petroleum, food and spirits with \$900 million in annual volume, and engage in transportation and real estate investments. *Forbes Magazine* lists Warren Companies as one of America's 400 largest privately held companies.

The eminent recipients illustrate the Alpert Foundation's tradition of recognizing scientists who have made basic discoveries and then cultivated their findings from clinical research to practical applications with a dramatic impact on patients. Winners are selected by a scientific advisory committee chaired by Medical School Dean Daniel Tosteson and composed of leading experts from Harvard, MIT, the National Institutes of Health, and the National Academy of Sciences.

The pioneering studies that Sachs has conducted provide insight into the molecular basis of normal and abnormal cell development in blood-forming tissues. His findings illuminate the molecular controls that regulate blood-cell viability, growth, and maturation into distinct types of cells. In 1963, Sachs discovered the first cell-culture system able to clone blood cells. Using the new method, he identified the first proteins that regulate growth in these cloned cells. He discovered that the proteins, later named colony-stimulating factors, promote viability, growth, and differentiation into blood-cell lines such as macrophages and granulocytes. The proteins thereby boost the immune system.

Sachs also has shown that normal regulatory proteins can stimulate some leukemic cells to differentiate into noncancerous cells. The finding signals an approach to curing leukemia by reversing malignancy through stimulating differentiation.

Parallel to these investigations, Metcalf's research has led to the current understanding of individual molecules that regulate the development of blood cells. His purification of these factors enabled their production through recombinant DNA technology. In the mid-1960s, while conducting research on leukemia, Metcalf noticed that cells from bone marrow and other organs and body fluids proliferate and form colonies. He reported this finding in 1966, the same year Sachs reported the growth and colony formation of a certain type of cell in bone marrow.

By 1984, Metcalf and his colleagues had purified four specific factors that stimulate the formation of cell colonies. Three years later, it became possible for the first time to produce colony-stimulating factors by recombinant DNA technology. Large quantities soon became available for animal and clinical testing.

These fundamental studies by Metcalf provided a completely new understanding of the growth regulation of bone marrow stem cells, which are blood-cell progenitors. His research also paved the way for a new patient-care field in which bone-marrow growth can be therapeutically regulated.

The Alpert Prize was inspired by an article Warren Alpert read in 1987 on Kenneth Murray of the University of Edinburgh, who developed a vaccine for hepatitis B. He called Murray, told him he had won a prize, and then set about creating the foundation. To choose subsequent recipients, he asked Dean Tosteson to convene a panel of leading scientists. Each year since, this group has sought to recognize creative research that has had a dramatic impact on the human condition.