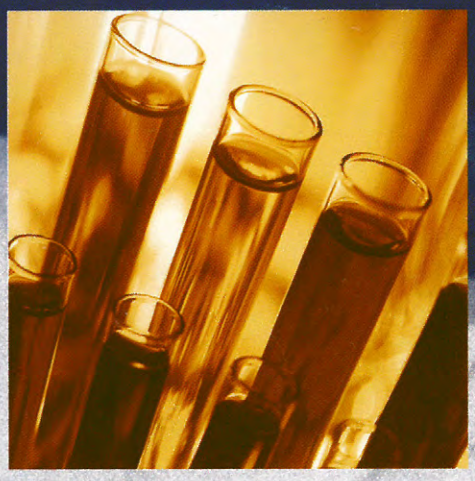
The National Foundation for Cancer Research was founded in 1973 to support cancer research in the laboratory. NFCR research conducted at both the cellular and molecular levels is leading to better prevention, earlier diagnosis, new treatments, and eventually a cure for cancer. By supporting the best ideas of the best minds and by facilitating collaboration among NFCR Project Directors, advances in one field contribute to discoveries in another. This is what NFCR's "Laboratory Without Walls" makes possible.

NATIONAL FOUNDATION FOR CANCER RESEARCH

2000 ANNUAL REPORT



MISSION >>

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President's Message

AT NFCR WE ARE EXCITED about the new era in cancer research. We realize that coping with cancer remains the most difficult problem many Americans will ever face. At NFCR, we draw our inspiration from these individual stories—many of people just stricken with cancer and others of cancer survivors. Their determination inspires us to take risks in expanding our programs. Their patience reminds us that sometimes a long fought battle yields the sweetest victory and greatest rewards.

Because more than 1,500 lives are lost each day, NFCR has intensified its commitment to the fight against cancer. With your ongoing support, you can be certain your dollars are being used to help NFCR scientists bring a cure for cancer from laboratory benches to the bedsides of cancer patients.

In many aspects, this year was much like the last. New cancer-related organizations popped up over night—each one trying to find its purpose, education, diet or prevention. They are all trying to be everything to everyone. Yet as we have done for 27 years, NFCR steadfastly maintained its focused research efforts and adherence to our mission, believing that the cure for cancer lies only in laboratory research.

Since we rely on your support and the support of others like you for every dollar of our research funding, NFCR is grateful for what you helped us achieve this year. Your gifts provided funding to 44 individual research projects in long established university scientific centers. In addition, your support enabled NFCR to launch initiatives and programs to capitalize on the new technology that has changed the way research is conducted and findings are shared.

And we are excited to announce that because of people like you, NFCR was able to expand our laboratory without walls by creating six Discovery Research Centers at institutions like the University of Cambridge and the University of California at Berkeley. Using the power of the Internet to collaborate with leading scientists worldwide, our project directors at these centers are finding answers to the fundamental question of how cancer can be stopped.

For the first time since our inception, NFCR committed long-term funding to seven of the brightest minds in cancer research today. As NFCR Fellows, these researchers now have access to flexible, unrestricted funds for a five-year period, during which time they will be engaged in ongoing, vital cancer research.

As you review NFCR's 2000 Annual Report, keep in mind that your continued dedication to finding a cancer cure has provided the backbone for all of our research programs. Without your support, NFCR would not have been able to make this transition into the new technology-driven climate, nor could it have continued to fund the ongoing research that holds so much promise for the future.

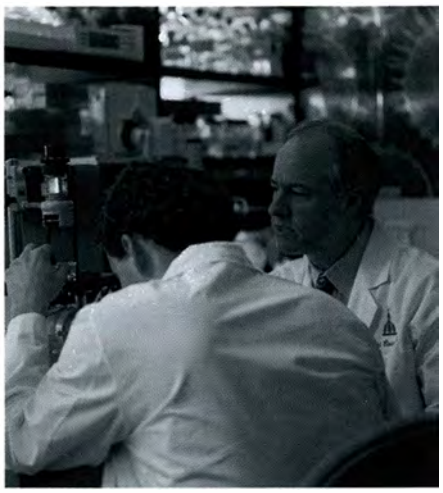
Each time you give to NFCR you not only provide the money we need to fuel our scientists and research labs, but you do something even better. You provide hope . . . hope that NFCR scientists will solve the mystery of cancer . . . hope that cancer survivors will no longer live in fear that one day their illness may return . . . and hope that one day the words, "you have cancer" will be a thing of the past.

If we stay the course and stay together, we will cure cancer.

Sincerely,

Franklin C. Salisbury, Jr., President

>>solving the mysteries of cancer



SINCE 1973 THE NATIONAL FOUNDATION FOR CANCER RESEARCH has spent over $170 million to fund the research of distinguished scientists at more than a hundred universities and research facilities throughout the world.

Many of NFCR's project directors are internationally recognized leaders in their fields and recipients of prestigious awards, including the Nobel Prize, the National Medal of Science, and the Lasker Award. We believe, by supporting the best ideas of the best minds and by facilitating collaboration among the scientists, advances in one field will contribute to discoveries in another.

Instead of focusing on stopgap remedies that only treat the symptoms associated with cancer, NFCR and its project directors seek to understand, prevent and cure cancer through basic science research. NFCR's scientific discoveries have led to new treatments for cancer and other diseases. Selected highlights of major discoveries made possible with NFCR funding follow:

Curing cancer may or may not be at hand, but it is evident that basic science research has put investigators on target for the first time in history. To cure cancer we must understand how and why a normal cell turns into an invasive and destructive cancer cell. Basic science remains the only hope for victory in curing cancer.

>> Bruce Ames, at the University of California at Berkeley, developed a simple, inexpensive and rapid screening test for detecting mutagenic and carcinogenic compounds and identified the cause and effect relationships for oxidative DNA damage. These findings have been translated into public policy recommendations on diet and cancer risk.

>> Cesar Milstein, at MRC Laboratory of Molecular Biology, discovered how to make monoclonal antibodies and developed new methods to produce humanized antibodies suitable for tumor therapy. Several drugs, such as Herceptin for breast cancer and Rituxan for non-hodgkin lymphomas, are derived from this discovery.

>> Curt I. Civin (pictured above), at Johns Hopkins University, discovered the DC34+ protein on the surface of hematopoietic stem cells that identifies those among the differentiated blood cells in bone marrow.

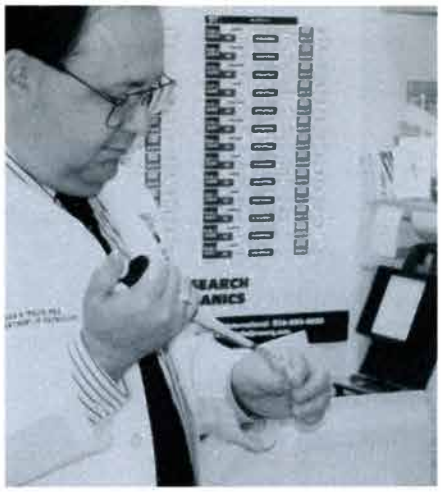
>> Bert Vogelstein and others at Johns Hopkins extensively researched the tumor suppressor gene p53, mutations of which are implicated in over half of all human cancers. It has become the most studied gene in medicine.

>> Stephen Benkovic, at Pennsylvania State University, has researched transformylase enzymes which are targets for new chemotherapeutic agents directed against a variety of solid tumors. There are several compounds based on transformylase in advanced stage clinical trials to treat tumors.

>> Raymond Damadian was provided initial NFCR funding to develop the MRI (magnetic resonance imaging machine), a widely used diagnostic tool.

>> Hector Deluca, at University of Wisconsin-Madison, has developed vitamin D compounds which effectively prevent multiple sclerosis and transplant rejection, both unexpected discoveries from cancer research. These vitamin D compounds have entered clinical trials with human patients for both diseases.

>> Danny Welch (pictured right), at Pennsylvania State University College of Medicine, has found a gene that keeps tumors from spreading, which should make the cancer easier to treat. This discovery brings us a step closer to an entirely new class of drugs and gives hope to breast cancer patients.



>> Kathryn Horwitz, at University of Colorado Health Sciences Center, has discovered progesterone receptors in breast cancer which are markers of hormone dependence and indicators of disease prognosis. Patients with breast cancer now routinely have their tumors assayed for the presence of progesterone receptors to guide decisions about the kind of therapy to pursue.

>> Wayne Marasco, at Dana-Farber Cancer Institute of Harvard Medical School, developed the intrabody technology for the treatment of HIV infection in AIDS and adult T cell leukemia. This technology has been licensed to a biotech company, Chiron, which is conducting clinical gene therapy trials for the treatment of HIV infection.

>> Helmut Sies, at Heinrich Heine University, discovered that lycopene from tomatoes prevents oxidation and has anticancer effects, especially in processed or heated form which allows the lycopene to be easily absorbed by the human body. Clinical trials on lycopene are now underway for the prevention of prostate cancer.

solving the mysteries of cancer>>

SELECTED HONORS, AWARDS AND MEMBERSHIPS OF THE PROJECT DIRECTORS OF THE NATIONAL FOUNDATION FOR CANCER RESEARCH

Bruce N. Ames, Ph.D.

Member, American Academy of Arts and Sciences, 1970

National Academy of Sciences, 1972

Fellow, American Society for Microbiology, 1992

Fellow, American Academy of Toxicological Sciences

Presidential Medal of Science

Jacqueline Barton, Ph.D.

Member, American Academy of Arts and Sciences

Fellow, American Association for the Advancement of Science

Stephen J. Benkovic, Ph.D.

Member, American Academy of Arts and Sciences, 1984

National Academy of Sciences, 1985

Institute of Medicine, National Academy of Sciences, 1994

Yung-Chi Cheng, Ph.D.

Member, Academia Sinica, Republic of China, 1994

Outstanding Investigator Award, National Cancer Institute,1987-97

Member, Connecticut Academy of Science and Engineering, 1998

Curt I. Civin, M.D.

Fellow, Society for Pediatric Research

American Society for Clinical Investigation, 1992

National Inventor of the Year Award, Intellectual Property Owners Association, 1999

Stanley Cohen, M.D.

Fellow, American Academy of Arts and Sciences, 1978

Albert Lasker Basic Medical Research Award, 1980

Institute of Medicine of the National Academy of Sciences, 1988

National Medal of Science, 1988

Fellow, American Academy of Microbiology, 1992

Hector F. DeLuca, Ph.D.

Member, National Task Force of the NIH Strategic Plan, 1992

Member, Food and Nutrition Board of the National Academy of Sciences, 1992

Fellow, American Institute of Nutrition, 1996

Peter B. Dervan, Ph.D.

National Academy of Sciences

Member, Institute of Medicine

Member, The American Academy of Arts and Sciences

Harold F. Dvorak, M.D.

Member, American Association of Immunologists

New York Academy of Science

American Society for Investigative Pathology (Immediate Past President)

Donald M. Engelman, Ph.D.

Member, Connecticut Academy of Arts and Sciences, 1992-present

National Academy of Sciences, 1997

Ivar Giaever, Ph.D.

Nobel Prize in Physics, 1973

Waun Ki Hong, M.D.

Member, Association of American Physicians

American Cancer Society Distinguished Service Award, 1993

AARC President-Elect, 2000

Csaba Horvath, Ph.D.

Member, Connecticut Academy of Arts and Sciences, 1993

Fellow, American Institute of Chemical Engineers, 1994

Kathryn Horwitz, Ph.D.

President, International Society for Endocrinology, 1998-99

Rakesh Jain, Ph.D.

Eugene M. Landis Award, Microcirculation Society, 1996

Outstanding Investigator Grant, National Cancer Institute, 1993-2000

Fellowship, John Simon Guggenheim Memorial Foundation, 1983-84

Kenneth Kinzler, Ph.D.

The John Hopkins University, School of Medicine Sandoz Award in recognition of superior academic achievement and contributions to health care, 1988

The John Hopkins University, School of Medicine, David Israel Macht Award for Excellence in Research, 1988

Sir Aaron Klug, Ph.D.

Fellow Royal Society, London, 1969

Honorary Foreign Member, American Academy of Arts and Sciences, 1969

Nobel Prize For Chemistry, 1982

Foreign Associate, National Academy of Sciences, 1984

Foreign Associate of Academie des Sciences, Paris, 1989

Member of the Order of Merit, 1995

Janos Ladik, Ph.D.

Elected President of the International Society of Theoretical Chemical Physics, 1990, 1993, 1996, 1999

External Member of the Hungarian Academy of Sciences (Physics), 1993

Full Member of the European Academy of Arts, Sciences and Letters, 1993

Cesar Milstein, Ph.D.

Royal Medal, Royal Society, 1982

The Albert Lasker Basic Medical Research Award, 1984

The Nobel Prize in Physiology for Medicine, 1984

Manfred F. Rajewsky, M.D.

Honorary Membership, Japanese Cancer Association, 1987

German Cancer Prize, 1989

Alexander Rich, M.D.

National Medal of Science, Washington, D.C., 1995

Foreign Member, Russian Academy of Sciences, Moscow, Russia, 1994

Honorary Member, Japanese Biochemical Society, Tokyo, Japan, 1986

Foreign Member, French Academy of Sciences, Paris, France, 1984

Member, Pontifcal Academy of Science, The Vatican, 1978

National Academy of Sciences, 1970

Leo Sachs, Ph.D.

Warren Alpert Foundation Prize, Harvard Medical School, Boston, Mass.

Fellow of the Royal Society, London

Alanna Schepartz, Ph.D.

Presidential Award for Undergraduate Research, 1982

National Science Foundation Presidential Young Investigator Award, 1991

A.C.S. Eli Lilly Award in Biological Chemistry, 1997

Harold A. Scheraga, Ph.D.

National Academy of Sciences, 1966

American Academy of Arts and Sciences, 1967

Honorary Member, Hungarian Biophysical Society, 1989

Honorary Member, Society of Polymer Sciences, Japan, 1995

Honorary Member, American Peptide Society, 1996

Fellow of the Biophysical Society, 1999

Paul Schimmel, Ph.D.

Fellow, American Academy of Arts and Sciences, 1987

National Academy of Sciences, 1990

American Philosophical Society, 1999

Helmut Sies, M.D., Ph.D.

Ernst Jung Preis fur Medizin, 1988

Werner Heisenberg Medal, Alexander von Humboldt Foundation, 1999

Michael Sporn, M.D.

American Association for Cancer Research

American Society for Biological Chemistry and Molecular Biology

Bristol-Myers Squibb Award for Distinguished Achievement in Cancer Research, 1998

I. Bernard Weinstein, M.D.

Member, Institute of Medicine, National Academy of Science, 1978

Fellow, Royal Academy of Medicine, 1993

Member, American Association of Physicians, 1994

Fellow, American Academy of Arts and Sciences, 1995

Danny R. Welch, Ph.D.

American Cancer Society

American Association for Cancer Research

American Society for Cell Biology

Metastasis Research Society

>>laboratory without walls

NFCR Research Centers

NFCR's vision for an expanded laboratory without walls creates a virtual network of scientists working collaboratively toward a common goal—a cure for cancer.

ONE OF THE MAJOR OBSTACLES to breakthroughs in cancer research is the bureaucracy that ties the hands of scientists and the way they are allowed to use their funding. For more than 25 years, NFCR has rejected the status quo by providing flexible funding, allowing scientists to explore blue-sky ideas that might otherwise have been delayed or gone unfunded.

As many scientists can attest, flexible funding will allow NFCR's Centers to move quickly to pursue promising leads arising from unexpected observations or new ideas. NFCR has established a fully flexible system whereby each research center may use NFCR funding to explore any new and exciting concept within the center. The director of each discovery research center will provide regular progress reports to NFCR, and we will then share this information with you.

In setting up these discovery centers at premier research institutions worldwide, NFCR is expanding the flexibility of its funding even further. Using the Internet, NFCR enables top scientists from different disciplines around the world to communicate and collaborate key steps in speeding up the discovery process. Breakthroughs will come from sharing knowledge as we fight for our common goal—a cure for cancer.

NFCR CENTER FOR COMPUTATIONAL DRUG DISCOVERY AT THE UNIVERSITY OF OXFORD >>

Computers are big news in the field of drug design, and the NFCR Center for Computational Drug Discovery in Oxford University's chemistry department (Oxford, UK) is well positioned to make collaboration among international research groups easier, faster and more effective.

"This is a wonderful opportunity to utilise the Internet and World Wide Web in order to amass a powerful set of groups who should be able together to make real inroads into the overwhelmingly important problem of anticancer drug design."

—GRAHAM RICHARDS, PH.D., UNIVERSITY OF OXFORD

Under the direction of Professor Graham Richards (pictured on opposite page), an international leader in this field, and with four Nobel laureates and ten Fellows of the Royal Society among its present staff, the department is well placed to be chosen as the hub of the world's first virtual center for designing anticancer drugs by computer. This initiative offers the capability to save three to five years in the design of anticancer drugs, meaning promising medicine will get to cancer patients much more quickly.

This is a wonderful opportunity to use the Internet to bring together top scientists around the world, and to make real inroads into the overwhelmingly important problem of designing anticancer drugs. Researchers will have access to a range of expertise that could not be assembled in one place and will be able to cover a wider span of problems.

NFCR CENTER FOR GENOMICS AND NUTRITION AT THE UNIVERSITY OF CALIFORNIA, BERKELEY >>

Researchers estimate that 20 to 30 percent of all cases of cancer in the United States could be prevented by improving nutrition. The NFCR Center for Genomics and Nutrition at Berkeley, under the direction of Drs. Bruce Ames and Martyn Smith (pictured below), will zero in on those specific factors in diet that contribute to increased cancer risk. They will then identify the biochemical pathways by which nutrients, such as folic acid and vitamins B6 and B12, can protect you from cancer.

Research at the Berkeley center will focus on children. In the United States today, one child dies of cancer every two minutes. Many of these lives could

"This is the largest computational chemistry project ever undertaken. Our project aims to screen as many as 250 million molecules against a range of cancer drug targets and it is expected that approximately 10,000 new drug candidate molecules may be identified."—DR. GRAHAM RICHARDS

How You Can Help Cure Cancer with Your Computer >>

NFCR recently joined together with Intel and United Devices, to harness the processing power of your home computer for cancer research at the NFCR Center for Computational Drug Discovery. At this center, research focuses on the proteins marked as possible targets for cancer therapy.

To participate, computer users download a drug-discovery software application called THINK (To Have Information and Knowledge) and an initial packet of 100 molecules. Once processing of the initial packet of molecules is complete (about a day after installation), THINK sends the data back to the server (based at United Devices) and requests another packet of molecules for processing. This occurs when you establish an Internet connection.

During the first stage of the process, 3.5 billion small molecules will be screened against sixteen protein targets known to play a role in cancer.

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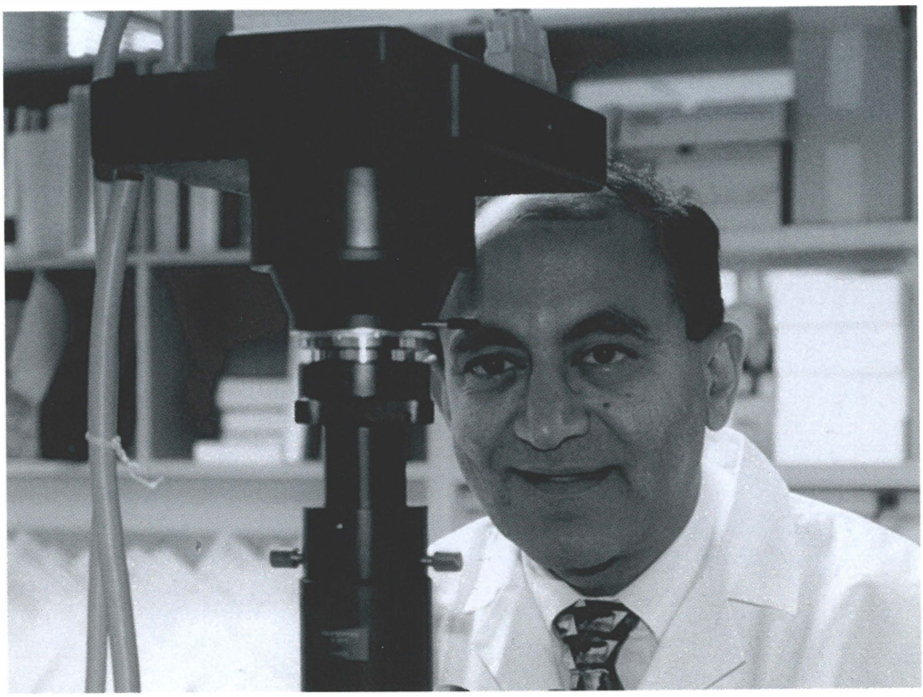
laboratory without walls>>

be saved with proper nutrition. Eighty percent of these children do not eat the recommended five servings of fruits and vegetables per day. These micronutrient deficiencies are a major cause of DNA damage, a leading cause of childhood cancers.

The research being conducted at this NFCR center has already led to significant breakthroughs in the understanding of nutrition-genetic interaction, hailed by leading scientists as a prerequisite for effective action in preventing cancer.

NFCR CENTER FOR MOLECULAR ANALYSIS AND IMAGING AT MASSACHUSETTS GENERAL HOSPITAL >>

In recent years, an extraordinary opportunity for studying cancer has emerged using in vivo molecular analysis and imaging. Under the direction of Drs. Ralph Weissleder and James Basilion, researchers at the NFCR Center for Molecular Analysis and Imaging will perform basic investigation and molecular analysis of cancers to better understand the abnormalities that are unique to cancers. This data will be used to inform the development of novel imaging probes.



Based on this identification of new cancer genes and their function, scientists at the NFCR Center for Molecular Analysis and Imaging will be able to transform these discoveries into gene imaging that would allow doctors to detect cancer at its inception. Genetic analysis could also be used to establish a patient's "molecular" remission and to detect the earliest signs of recurrence.

Until now, the field of imaging science has had to wait for the fortuitous discovery of genes with characteristics suitable for imaging technologies. The research at this NFCR center will now proactively identify non-invasive, cancer-specific markers for use as novel molecular imaging targets, not only for detecting cancer but for monitoring the effectiveness of treatments as well.

NFCR's discovery research centers foster synergistic interaction and collaboration between scientists worldwide.

The three NFCR-funded research centers described here will be joined by three more centers that are being established worldwide. These research centers include:

>> NFCR Center for Protein Chemistry at Yale University, where scientists will focus on analyzing the actions of proteins and nucleic acids to create individualized anticancer therapies;

>> NFCR Center for Molecular Oncology at the Institute of Medicinal Biotechnology in Beijing, China, where finding new anticancer drugs is the mission; and

>> NFCR Center for RNA Cancer Research at Freie Universitat in Berlin, Germany, where scientists are examining the origins of disease at a genomic level, approaching the pathology of disease as a computational problem that might be solved in the laboratory.

All of the NFCR centers are in the process of being interactively linked through the Internet. The concept represents a unique opportunity to utilize the powerful reach of the Internet to amass a stellar set of scientists in complementary disciplines to make real inroads into the overwhelmingly important problems of cancer prevention, diagnosis, and treatment. ■

(pictured left, Rakesh Jain, Ph.D.)

Help Cure Cancer continued >>

The THINK software will analyze data by creating a three-dimensional molecular model and changing its shape (or conformation) to attempt to dock it into a protein site. When a molecule docks successfully and triggers an interaction with the protein, it registers as a "hit" and is ranked according to the strength of interaction with the target. The research hinges on these hits.

With a goal of one million participants, the search time for valuable protein combinations can be reduced by more than 10 years. Combined with the advanced technology being used at the NFCR Center at Oxford, you can participate in a truly revolutionary technology that is changing the face of cancer research. Using the power of the Internet and your home computer, you help to create a virtual supercomputer able to analyze data faster than ever before bringing valuable anticancer drugs to the market sooner.

THINK runs in the background of your system while you are using your computer and leaps to the foreground when the computer is idle, allowing you to watch as the software performs the analyses. The software is available as a free downloadable application at the NFCR Web site **www.NFCR.org.** *It will in no way negatively affect your computer or interfere with its performance.* ■

>>research for a cure

NFCR Fellows

NFCR makes a difference in the war against cancer by supporting basic science cancer research in the laboratory.

The NFCR fellowship program was designed to provide the most promising minds in cancer research with five years of unrestricted, flexible funding, during which time they are free to explore any avenue of research they choose. At the same time, it provides each NFCR fellow with the stable funding that helps produce long-term results.

The seven scientists chosen for the NFCR fellowship program are recognized leaders in their fields, having greatly contributed to our understanding of the structure and function of the building blocks of life.

Armed with this fundamental knowledge, NFCR fellows hope to correct errors in how cells function—and discover how to intervene in the formation and progression of diseases, including cancer. They will investigate the effects of nutrition on our bodies' ability to fight off invasive attacks from viruses and bacteria—and thus show us how to contain and destroy malignancies as they develop. They will delve into the interaction between drugs and disease—and take their findings into clinical trial settings and to get cancer-fighting drugs to market.

Details of research efforts and current findings of the NFCR fellows that follow illustrate that the best hope for a cancer cure does indeed lie in basic laboratory research.

"...the ability to follow-up new leads promptly, even though they deviate from previously contracted or agreed upon experiments, is the way breakthroughs occur that allow science to advance most rapidly. Nowhere is this observation more true than in basic cancer research. And it is here that NFCR has played such an important role over the years."

—HAROLD DVORAK, M.D., BETH ISRAEL DEACONESS MEDICAL CENTER, HARVARD MEDICAL SCHOOL

YUNG-CHI CHENG, PH.D.

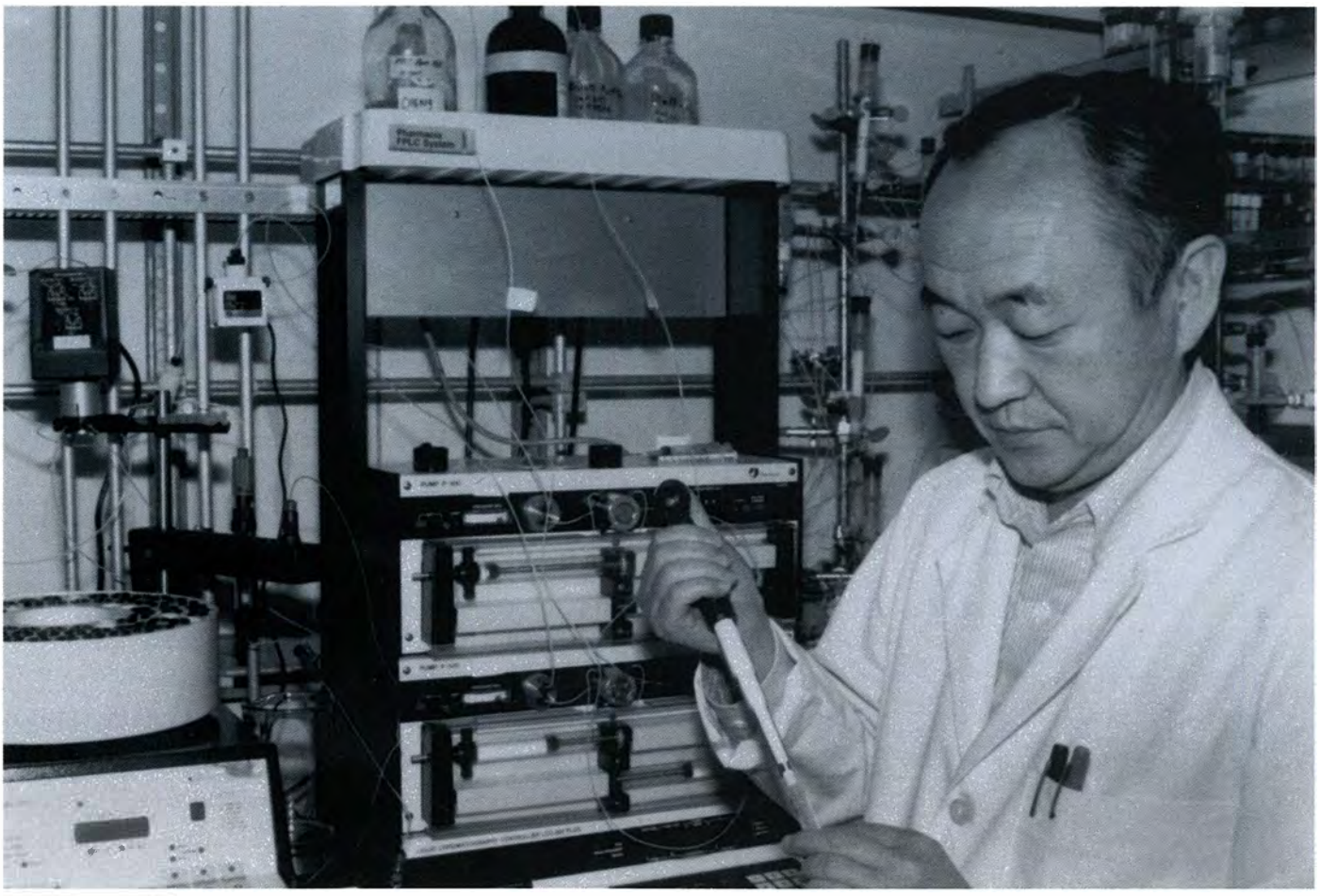
<Developing and Improving Drugs for Better Treatment of Cancer>

In order to discover or better utilize drugs in the treatment of cancer, an understanding of the nature of drug compounds used to treat cancer and viruses associated with cancer is important. NFCR Fellow Yung-Chi Cheng, Ph.D., (pictured on opposite page) and his multi-disciplinary team at Yale University's

School of Medicine are focused on the study of several anticancer drug compounds in order to understand drug action, resistance, and toxicity.

To determine the efficacy of an anticancer drug, Dr. Cheng studies several viruses that have a strong association with cancer, including hepatitis B, Epstein-Barr, herpes zoster, and human immunodeficiency virus (HIV). In his research, he examines the detailed biochemistry and molecular biology of disease, gaining insight into how disease acts in the body and reacts to preventive agents introduced in the body. With NFCR funding, Dr. Cheng discovered six compounds in his laboratory which are in clinical trials. His research also led to the successful development of drugs for hepatitis B, HIV, and cytomegalovirus infection.

Dr. Cheng believes that an effective and selective antiviral compound without toxicity will be useful not only for the treatment of viral infectious diseases, but also for the prevention of viral-associated cancers. Combining an understanding of a drug interaction with disease progression offers hope for a better prognosis for cancer and more individualized treatment—which provides hope for us all.



research for a cure>>

HAROLD DVORAK, M.D.

<Angiogenesis and Tumor Growth>

Harold Dvorak, M.D., (pictured left) was the first scientist to discover a molecule called vascular endothelial growth factor (VEGF) that promotes angiogenesis—the growth of new blood vessels cancerous cells need to spread throughout the body. Since his discovery in 1983, Dr. Dvorak has gained a better understanding of tumor biology and the process by which cancer cells metastasize. His discoveries have led to numerous research efforts nationwide, leading to the discovery of other molecules and proteins that support angiogenesis. Today, there are 20 different anti-angiogenic drugs in various stages of clinical testing.

In addition to this important application, Dr. Dvorak's research could also be used to remedy other angiogenesis-driven illnesses such as rheumatoid arthritis, heart disease and stroke.

With NFCR's unrestricted funding, Dr. Dvorak is looking at new ways to inhibit angiogenesis so that malignancies can no longer grow new blood vessels. He and his associates at Beth Israel Deaconess Medical Center are considering the interaction between the transcription factor Sp1 and a specific type of protein kinase C (PKC) in renal cell carcinoma. Working together, Sp1 and PKC have created a new pathway of cell signaling and regulation of VEGF. Further analysis of this interaction could lead to inhibitors that block the creation of new blood vessels feeding cancerous cells, possibly slowing or destroying the growth of these cells entirely.

WAUN KI HONG, M.D.

<Women and Lung Cancer>

With a five-year funding opportunity, Dr. Waun Ki Hong is focusing his research efforts on a cancer generally perceived as a "man's disease"—lung cancer. Lung cancer is currently the leading cause of cancer death for both women and men. In fact, available data suggests that lung cancer may be a greater health threat to women than men. Lung cancer incidence in women has increased by 451 percent in the last 30 years, with only a 14 percent survival rate.

With these statistics in mind, Dr. Ki Hong will investigate several hypotheses. 1) Because estrogen and its ligand, estradiol, play an important role in lung cancer development, women are genetically more susceptible to tobacco carcinogens; 2) molecular and genetic markers of lung carcinogenesis differ between men and women; 3) treatment outcomes in women with early-stage, non-small cell lung cancer differ from those of men; and 4) overall outcome of chemoprevention efforts differ between men and women.

With this research, Dr. Ki Hong hopes to develop ways to identify those women who are at a higher risk for lung cancer so that they can receive preventive therapy before the disease strikes.

PAUL SCHIMMEL, PH.D.

<Translating and Decoding Genetic Information to Stop Disease>

Just like every living organism, each cell undergoes a life cycle from birth to death. In a cancerous cell, the mechanism by which a cell is turned off, or dies, is lost, allowing the cells to grow in an uncontrolled way. A delicate interaction at the genetic level, involving enzymes, amino acids and transfer RNA (tRNA), controls protein synthesis and cell function. Understanding this interaction may allow scientists to turn off a variety of disease processes, particularly cancer.

With flexible funding from NFCR, Dr. Schimmel is investigating the components in cells that are responsible for protein synthesis and cell signaling. Dr. Schimmel and his team recently discovered that a component of the protein synthesis apparatus in human cells seems to play a role in cellular events related to programmed cell death, inflammation, and potentially, cancer.

Dr. Schimmel's detailed understanding of how RNA directs protein synthesis has shed light on how breakdowns occur in cell behavior. As an NFCR fellow, Dr. Schimmel's research on tumor cells can possibly block the action of specific proteins leading to the spread of cancer, while sparing healthy cells. Dr. Schimmel's groundbreaking work has the potential to extend and improve life for all of us.

HELMUT SIES, M.D., PH.D.

<Nutrition and Disease>

NFCR is funding research by Helmut Sies, M.D., Ph.D., and his group that focuses on peroxynitrite, an oxidant generated by our body to defend against bacteria. If the defense is too efficient, the oxidant will attack and damage healthy cells as well. Peroxynitrite damage to DNA makes cells more susceptible

NFCR's Peer Review Process

As NFCR presses onward at the most fundamental level in the battle against cancer, we ensure the scientists and science we fund are of the highest caliber by using an extensive multi-level peer review process.

The 2000 NFCR Peer Review and Planning Committee was composed of leading scientists from research institutions across the United States including Yale University, the University of Arizona, University of Minnesota, and University of California, San Diego. The peer review process takes into account multiple factors: the significance of the application, the researcher's scientific approach to the project, their long-term objectives, innovation, qualifications, experience and productivity, and the facilities and resources at their disposal.

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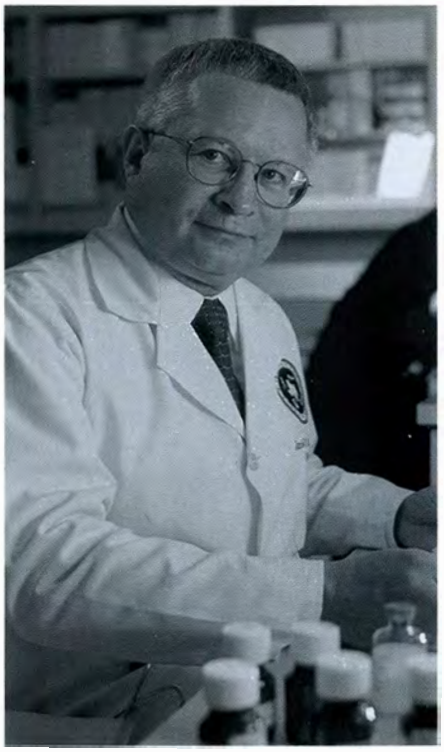
research for a cure>>

to cancer and, when modified by nitration of protein, interferes with normal cell signaling pathways and other important cell functions.

Dr. Sies has found that enzymes containing selenium play a special role in protecting the body from the oxidant peroxynitrite. Based on this finding, he and his group focused on the biological defense properties of selenocysteine and selenomethionine, which in turn led to the question of whether these enzymes could be used nutritionally to prevent cancer.



Dr. Sies found that selenium supplements can indeed prevent peroxynitrite damage to DNA. In fact, Dr. Sies's NFCR-funded research is making possible the development of a new drug for cancer patients, Ebselen—a compound containing selenium that has been shown to alleviate stroke but has not been tested against cancer until now.

DANIEL VON HOFF, M.D.

<Gene Mutation and Better Treatment Options>

As the director of the Arizona Cancer Center, NFCR Fellow Daniel Von Hoff, M.D. (pictured left), is building on findings from the past year to begin clinical trials for treatment of prostate cancer that has become resistant to hormone treatments. This same hormone resistance is found in some breast cancer cell lines. Dr. Von Hoff has determined that an inhibitor called DHAC could restore the sensitivity of prostate cell lines to antiandrogens.

In his research, he takes advantage of a very specific abnormality found in a broad spectrum of human cancer. That abnormality is a mutation in mismatch repair genes. Mutations in mismatch repair genes are very common in a variety of human tumors, particularly those that are resistant to treatment. Dr. Von Hoff's research has led to a way to eliminate the tumor cells which have the genetic abnormality that creates resistance.

Using the DHAC inhibitor, Dr. Von Hoff believes he will be able to induce prostate cancer cell death. Further investigation into DHAC inhibitors may lead to the development of an estrogen receptor antagonist that is effective in treating breast cancer as well.

BERNARD WEINSTEIN, M.D.

<Treating and Preventing Cancer by Attacking the Cell Cycle>

Building on his previous research on cell cycle control proteins, Bernard Weinstein, M.D., has undertaken a study on the relevance of cyclic GMP (a messenger that controls the action of several hormones and neurotransmitters) and PKG (a protein kinase) to cancer. Cell cycle control proteins play key roles in mediating the action of cell to cell growth factors, interaction, communication and behavior. When expressed, uncontrolled cell proliferation can occur. Disturbances in specific protein kinases can play an important role in the carcinogenic process.

There are relatively few studies on the role PKG plays in cell growth control and carcinogenesis. Some research suggests that PKG may be relevant to cancer prevention and therapy because of its role in signaling transduction and gene expression that are relevant to controlling cancer.

Dr. Weinstein will carry out his research using colon, breast and prostate cancer cells, to determine how different types of PKG affect cancer cell proliferation, and apoptosis, or pre-programmed cell death. The findings from Dr. Weinstein's research will indicate whether GMP and PKG provide novel cellular targets for cancer chemoprevention and therapy.

Dr. Weinstein has made outstanding contributions to our understanding of the molecular actions taken by carcinogens during the multiple-step process that culminates in cancer. His research has led to new approaches for identifying the origins of human cancer. He also had made major contributions related to the mechanisms of action found in tumor promoters. Dr. Weinstein's work has wide-ranging implications for developing more effective ways to both prevent and treat cancer. ■

Peer Review Process continued >>

The NFCR science director distributes project applications to two peer review committee members for initial scientific review. After the applications are reviewed by two members of the peer review committee, the full Peer Review and Planning Committee then discuss the applications. Projects are given a priority ranking and assessed in the context of funds available and NFCR's objectives. The Peer Review and Planning Committee, in conjunction with the NFCR president and science director, then make decisions on which projects to fund for the next year.

The success of the peer review process is evident in those scientists selected by NFCR for funding. They reflect our ambition to support the best ideas of the best minds. Their essential research, which includes collaboration with other groundbreaking scientists in related fields, are examples of how NFCR continues to break down multidisciplinary scientific barriers and expand our laboratory without walls for basic science cancer research. ■

>>realizing the mission

New NFCR Project Directors

BASED ON THE BELIEF THAT CANCER cannot be understood by a single approach, NFCR fosters discovery-oriented research in diverse fields like chemistry, biophysics, biochemical and molecular pharmacology, carcinogenesis, molecular/cellular biology and genetics, computational chemistry and protein chemistry. NFCR's long-time support of basic science cancer research is responsible for many important discoveries, breakthroughs in prevention and diagnosis, and new treatment options for all types of cancer.

For the next three years, NFCR has chosen to fund the work of 22 outstanding research scientists engaged in the most promising cancer research. Located at universities, institutions, and hospitals world-wide, these scientists and doctors are engaged in research to further our understanding of the complexities of cancer. Their research ranges from studying the intricate workings of DNA/RNA, cell formation, and protein synthesis, to examining ways that we can reduce our risk of cancer with better nutrition. They are designing advanced diagnostic and imaging tools to catch cancer in its earliest stages, and searching for less toxic compounds to treat cancer patients.

The four new project directors profiled below demonstrate the range of research that NFCR is dedicated to funding. Dr. Susan Horwitz is extending her research into the powerful antitumor drug Taxol in order to combat resistance to the drug's early forms; Dr. Xiaolian Gao is undertaking an effort to map the molecular recognition of DNA/RNA by a powerful antitumor antibiotic using nuclear magnetic resonance (NMR) spectroscopy, a state-of-the-art imaging tool used for biomacromolecular studies; Dr. Phyllis Bowen is exploring the effects of tomato products on prostate cancer—with a goal of developing a promising biomarker/locator for cancer; and Dr. Lawrence J. Marnett, is investigating methods of detecting cancer at its earliest stages and developing chemopreventive drugs to combat the onset of cancer.

"The National Foundation for Cancer Research provides support for innovative and high-risk research that has potential for the sorts of discoveries that push science into new areas. Funding for that type of work is often quite difficult to come by, so we are very appreciative of [NFCR's] support."

—LAWRENCE J. MARNETT, PH.D., VANDERBILT UNIVERSITY

SUSAN HORWITZ, PH.D.

Albert Einstein College of Medicine

With funding from NFCR, Dr. Susan Horwitz is engaged in extended research into the powerful antitumor drug Taxol. In the 1990s, Dr. Horwitz's laboratory was the first to examine the mechanism of action in Taxol that later heralded a dramatic advance in the treatment of ovarian, breast and lung cancer. Her findings on Taxol encouraged the National Cancer Institute to move forward with clinical trials that eventually brought the drug to market.

Dr. Horwitz's challenge is to understand the molecular-level basis for Taxol-like compounds to circumvent Taxol resistance in tumors. Taxol resistance in tumors is a serious hurdle in the battle against cancer because many such tumors develop multidrug resistance—not just to Taxol, but to other antitumor drugs.

Dr. Horwitz is undertaking the challenge of understanding the molecular basis of resistance that will lead to the development of second generation Taxol medications that will overcome certain drawbacks of first generation taxane-based treatments.

DR. XIAOLIAN GAO

University of Houston

Project Director Dr. Xiaolian Gao is undertaking an effort to map the molecular recognition of DNA/RNA by the powerful antitumor antibiotic known as neocarzinostatin chromophore (NCSC). Dr. Gao is combining microarray technology—which allows hundreds of simultaneous experiments—with traditional methods to determine the drug targets for which NCSC is best suited. Her efforts in this NFCR-funded project will be the first time automated light-directed, on-chip DNA synthesis has been performed in a traditional laboratory.

An associate professor of chemistry who has received numerous awards for research excellence, Dr. Gao seeks to shed light on the basic principles of molecular design for new antitumor drugs that have chemical and biological properties for gene targeting and regulating—which now play essential roles in our fight against cancer.

realizing the mission>>

PHYLLIS BOWEN, PH.D.

University of Illinois-Chicago

Project Director Phyllis Bowen, Ph.D., is exploring the effects of tomato products on prostate cancer—with a goal of halving the rates of the cancer in American men. Lycopene—the red pigment found in tomato products—is thought to be the most likely bioactive ingredient since it is a powerful anti-oxidant.

Recent studies suggest that lycopene can help reduce prostate cancer rates, which increase with age. In the United States for example, 85 percent of American men over the age of 80 have prostate cancer.

Dr. Bowen's NFCR-funded research includes a promising plan to develop a biomarker for cancer—a comparative marker to high blood pressure and heart disease. She will explore the cellular mechanisms of cancer during a human clinical trial involving 150 men recently diagnosed with prostate cancer, or at higher risk for prostate cancer. All of the men are already involved in a larger clinical trial. Dr. Bowen's investigation will evaluate the effectiveness of tomato sauce and lycopene in preventing prostate tissue damage in these men.

LAWRENCE J. MARNETT, PH.D.

Vanderbilt University

NFCR project director Lawrence J. Marnett, Ph.D., is investigating methods of preventing cancer with chemotherapy drugs before the cancer begins. The centerpiece of Dr. Marnett's efforts is cyclooxygenase-2 (COX-2), which plays a role in several cancers. COX-2 is responsible for turning a fatty acid into compounds known as prostaglandins, which are like hormones and control many different functions within a cell, including some that are necessary for cancer development.

Based upon recent discoveries in his laboratory, Dr. Marnett believes there may be new means for testing the presence of COX-2 in individuals. Such testing would be invaluable in assessing the stage a cancer has reached and the extent to which therapy is helping.

Dr. Marnett's efforts promise to define a unique role for COX-2 that will explain how cancer develops—and provide means of prevention. His efforts have the potential to aid the development of a new generation of pharmaceuticals that prevent and treat cancer by identifying new molecular targets involved in a cancer's progression.

PROJECT DIRECTORS OF THE NATIONAL FOUNDATION FOR CANCER RESEARCH

IT IS AN EXCITING TIME IN CANCER RESEARCH, with findings by NFCR-funded research scientists leading the way to a cancer cure. As you review the full list of project directors funded by NFCR, you will see that NFCR has dedicated funds to the fields of research that offer the hope for the most promising breakthroughs in a cure for cancer.

Many of the project directors funded last year continued their innovative research, expanding on recent developments both in their laboratories and research centers nationwide, bringing their discoveries to clinical trial settings. Others expanded on the breadth of knowledge garnered from past NFCR-funded research to enhance our understanding of the prevention, treatment and diagnosis of cancer.

Bruce N. Ames, Ph.D.
University of California, Berkeley
Berkeley, California
"Vitamins B12 and Folic Acid in Cancer Prevention"

Jacqueline Barton, Ph.D.
California Institute of Technology
Pasadena, California
"Recognition of DNA Sites with Metal Complexes"

Robert C. Bast, Jr., M.D.
University of Texas
M.D. Anderson Cancer Center
Houston, Texas
"Identification of Novel Tumor Suppressor Genes in Epithelial Ovarian Cancer"

Stephen J. Benkovic, Ph.D.
Pennsylvania State University
University Park, Pennsylvania
"Enzymes in Nucleotide Biosynthesis and DNA Replication"

Phyllis Bowen, Ph.D.
University of Illinois, Chicago
Chicago, Illinois
see page 18

Esther H. Chang, Ph.D.
Georgetown University
Washington, DC
"Modulation of the Radiation Resistant Phenotypes of Tumor Cells by Sequence Specific Oligonucleotides"

Yung-Chi Cheng, Ph.D.
Yale University
New Haven, Connecticut
see page 10

Curt I. Civin, M.D.
Johns Hopkins University
Baltimore, Maryland
"Transduction of Human Hematopoietic Stem Cells"

Stanley Cohen, M.D.
Stanford University School Of Medicine
Palo Alto, California
"Genes that Suppress the Growth and Metastasis of Cancer cells"

continued >>

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Hector F. DeLuca, Ph.D.
University of Wisconsin-Madison
Madison, Wisconsin
"Vitamin D Analogs as Anti-Leukemia Agents/Biochemical Basis of Chemical Carcinogenesis"

Peter B. Dervan, Ph.D.
California Institute of Technology
Pasadena, California
"Studies in DNA Recognition"

Harold Dvorak, Ph.D.
Beth Israel Deaconess Medical Center
Boston, Massachusetts
see page 12

Donald M. Engelman, Ph.D.
Yale University
New Haven, Connecticut
"Receptor Interactions within Membrane Bilayers"

Xiaolian Gao, Ph.D.
University of Houston, Houston, Texas
see page 17

Ivar Giaever, Ph.D.
Rensselaer Polytechnic Institute
Troy, New York
"Cell Substrate Interactions"

Waun Ki Hong, M.D.
M.D. Anderson Cancer Center
Houston, Texas
see page 12

Csaba Horvath, Ph.D.
Yale University
New Haven, Connecticut
"High-Resolution Separation of Glycoconjugates"

Kathryn Horwitz, Ph.D.
University of Colorado
Denver, Colorado
"The Molecular Biology of Progesterone Action in Breast Cancer"

Susan Horwitz, Ph.D.
Albert Einstein College of Medicine
New York, New York
see page 17

Keith U. Ingold, Ph.D.
Steacie Institute for Molecular Sciences
Ottawa, Canada
"Antioxidants in Normal and in Tumor Tissues"

Rakesh Jain, Ph.D.
Massachusetts General Hospital
Boston, Massachusetts
"Tumor Pathophysiology"

Kenneth Kinzler, Ph.D.
Johns Hopkins Univ. School of Medicine
Baltimore, Maryland
"Novel Approaches to Identifying Cancer Chemotherapeutics"

Sir Aaron Klug, Ph.D.
MRC Laboratory of Molecular Biology
Cambridge, England
"Zinc Finger"

Janos Ladik, Ph.D.
Universitat Erlangen-Nurnberg
Erlangen, Germany
"Quantum Theory of Proteins and DNA and Their Interactions; Chemical Carcinogens and Radiations Activating Oncogenes and Inactivating Antioncogens"

Wayne A. Marasco, M.D., Ph.D.
Dana-Farber Cancer Institute
Boston, Massachusetts
"Mechanism of Transformation of Human Lymphocytes by the HTLV-1 Virus"

Lawrence J. Marnett, Ph.D.
Vanderbilt University
Nashville, Tennessee
see page 18

Thomas C. Merigan, M.D.
Stanford University School of Medicine
Palo Alto, California
"Drug Resistance in Infection with HIV: A Cancer Promoting Virus"

Cesar Milstein, Ph.D.
MRC Laboratory of Molecular Biology
Cambridge, England
"Site-Directed Modification of Genes of the Immune System"

Ronald Pethig, D.Sc.
University of Wales
Bangor, Gwynedd, Wales
"Electrokinetic Properties and Manipulation of Cells"

Ilya Prigogine, D.E.S.
Instituts Internationaux de Physique et de Chimie Solvay
Brussels, Belgium

University of Texas, Austin
Austin, Texas
"Modelisation of Cellular Proliferation and Supercellular Morphological Instabilities"

Terence H. Rabbitts, Ph.D.
MRC Laboratory of Molecular Biology
Cambridge, United Kingdom
"Role of Chromosomal Translocations in Development of Human Cancer"

Manfred F. Rajewsky, M.D.
University of Essen
Essen, Germany
"Chemically-Induced Tumorigenic Conversion in the Developing Rat Nervous System: DNA Modifications and Repair, and Cell Lineage-Specific Gene Alterations"

Alexander Rich, M.D.
Massachusetts Institute of Technology
Cambridge, Massachusetts
"Nucleic Acid Structure and Carcinogenesis"

W. Graham Richards, D.Sc.
Oxford University
Oxford, England
"Design of Anticancer Drugs"

Robert D. Rosenberg, M.D., Ph.D.
Beth Israel Deaconess Medical Center
Boston, Massachusetts
"Role of Heparin Markers in the Regulation of Cell Growth"

Leo Sachs, Ph.D.
Weizmann Institute of Science
Rehovot, Israel
"The Reversibility of Malignant Cell Transformation"

Ramaswamy Sarma, Ph.D.
State University of New York at Albany
Albany, New York
"Structure and Dynamics DNA-Drug Complexes"

Alanna Schepartz, Ph.D.
Yale University
New Haven, Connecticut
"Non-Natural Metalloregulated, AP-1 Site-Specific DNA Binding Peptides"

Harold A. Scheraga, Ph.D.
Cornell University, Ithaca, New York
"Molecular Recognition"

Paul Schimmel, Ph.D.
Massachusetts Institute of Technology
Cambridge, Massachusetts
see page 13

Pravinkumar Sehgal, M.D., Ph.D.
New York Medical College
Valhalla, New York
"Interleukin-6 in Cancer"

Helmut Sies, M.D., Ph.D.
Heinrich-Heine-Universitat
Dusseldorf, Germany
see page 13

Jeffrey L. Sklar, M.D., Ph.D.
Brigham and Women's Hospital
Boston, Massachusetts
"Molecular Genetic Analysis of Tumor Spread in Malignant Gliomas of the Brain"

Martyn Smith, Ph.D.
University of California, Berkeley
Berkeley, California
"Genes Involved in Leukemia"

Michael Sporn, M.D.
Dartmouth Medical School
Hanover, New Hampshire
"Triterpenoids and Cancer Prevention"

Daniel D. Von Hoff, M.D.
Arizona Cancer Center
Tucson, Arizona
see page 14

I. Bernard Weinstein, M.D.
Columbia University
New York, New York
see page 15

Danny R. Welch, Ph.D.
Pennsylvania State University
College of Medicine
Hershey, Pennsylvania
"Regulation of Metastasis in Human Cancer"

>>progress through partnership

NFCR—Gene Medicine: Breaking Down Cancer

10TH ANNIVERSARY OF THE FIRST GENE THERAPY CLINICAL TRIALS / A LOOK BACK AT THE CLINICAL TRIAL

On September 14, 2000, doctors and scientists, the media, and pioneering patients and their families gathered to celebrate the 10th anniversary of the first gene therapy clinical trials. The trials, which began in 1990, treated the rare disease severe combined immune deficiency (SCIDS), the disease that afflicted David Vetter, the "Boy in the Bubble" immortalized in a 1980s movie starring John Travolta.

Carol Anne Deameret (David Vetter's mother) and two young girls, Ashanthi DeSilva and Cynthia Cutshall, the first gene therapy patients, attended the conference with their families and the scientists who saved their lives. Kenneth Culver, M.D., French Anderson, M.D., and Michael Blaese, M.D., the researchers who led these gene therapy clinical trials, told the story of their research and the challenges they overcame during the trials, and what the successful outcome will mean for the future of gene medicine and cancer research.

"Tumors within single patients differ and we don't know why certain patients respond to treatment and others with what we thought were the same tumors, don't. It's one thing to treat a disease where a single gene is involved. Cancer involves many genes and people are different."

—DR. KENNETH CULVER, NOVARTIS

NFCR sponsored the day-long conference, GENE MEDICINE: BREAKING DOWN CANCER, because of its role in the continuing fight to cure cancer. SCIDS, the disease treated by the original gene therapy trials, is significant to the understanding of cancer because the disorder has only one genetic pathway. Scientists chose to tackle this rare disease first, thinking if they could discover how to repair one genetic pathway, others might build on this breakthrough and begin to repair the dozens of genetic pathways involved in cancer.

The conference was a celebration of life and a look back at the events surrounding this breakthrough clinical trial. Drs. Anderson, Blaese and Culver (pictured opposite page with Ashanti DeSilva and Cynthia Cutshall), along with NFCR-funded Project Directors Bruce Ames, Ph.D., Martyn Smith, Ph.D.,

(pictured below) Harold Dvorak, Ph.D., and Danny Welch, Ph.D., participated in a panel discussion about the events surrounding the clinical trials and the future of gene medicine in the fight against cancer and other genetic diseases.

Drs. Anderson and Blaese began by recounting the doubt and insecurities they felt as they began gene therapy on the young girls. Bad press, controversial sentiments and fear of the unknown aside, the treatment was ultimately successful. Ashanthi and Cynthia expressed their thanks to the doctors for their experimental treatments. Joining the girls were Kevin Klug, who received gene therapy for a deadly form of brain cancer, and five-year-old Taylor Daley, the first person to receive an in utero bone marrow transplant to cure SCIDS.

A LOOK FORWARD—GENE MEDICINE: BREAKING DOWN CANCER

The future of gene medicine and cancer research was an equally important theme at the conference. Drs. Anderson, Blaese and Culver joined NFCR project directors Drs. Ames, Smith and Welch, to discuss the future of medical research.

A primary topic was progression in the field of bioinformatics. Bioinformatics is the use of computers in solving medical problems, primarily the creation of extensive electronic databases on genomes, protein sequences, etc., and secondarily, techniques such as the three-dimensional modeling of biomolecules and biologic systems.

The consensus among the scientists present was that the advent of more comprehensive and accurate bioinformatics would allow doctors to more effectively and efficiently treat their patients. "It's going to individualize medicine," says Dr. Smith, NFCR project director and professor of toxicology at the University of California-Berkeley.

Computers are expected to be more prevalent within doctor's offices, allowing data to be tracked and analyzed to better diagnose and treat patients. One issue raised was the efficacy of computers in analyzing data that is beneath the surface, the human element that only a doctor may surmise.

"Human beings are human beings," says Dr. French Anderson. "One of the things that's important about doctors is to be able to see into the patient and realize things that aren't what the black and white says or what the computer may say."

progress through partnership>>

The consensus was that computer diagnostics will complement, but not replace, the physician. "Medicine is always going to be individualized," says Danny Welch, NFCR project director and cell biologist at Pennsylvania State University College of Medicine. "The effect of gene analysis will be to help give the physician more information so that the diagnosis is more accurate."

Even with dramatic progress and breakthroughs in the field of cancer research, the road to a cure is still long, and breaking down cancer is an arduous process. NFCR's mission is to speed up the process by funding innovative research without the red tape and restrictions common in other sources of funding. NFCR allows scientists to follow the hunches that lead to groundbreaking discoveries.

"I think virtually every cancer starts as a single cell," Dr. Welch adds. "The smallest cancers that we can routinely catch are a billion cells. We all look differently, we behave differently, but our genomes are virtually the same. Where the genome exists in a different environment, it behaves differently. DNA does not exist in a vacuum."

Dr. Culver continues: "Tumors within single patients differ and we don't know why certain patients respond to treatment and others with what we thought were the same tumors, don't. It's one thing to treat a disease where a single gene is involved. Cancer involves many genes and people are different."

This illustrates the significance of the gene therapy and the cure for SCIDS that was celebrated. "This is an example of the fact that studying rare disorders may have an impact across the board on the population," Dr. Blaese says. "It's the nature of a rare disease to teach you the critical piece of information you need to generalize the information."

"I think virtually every cancer starts as a single cell. The smallest cancers that we can routinely catch are a billion cells. We all look differently, we behave differently, but our genomes are virtually the same. Where the genome exists in a different environment, it behaves differently. DNA does not exist in a vacuum."

—DANNY WELCH, PH.D., PENNSYLVANIA STATE UNIVERSITY COLLEGE OF MEDICINE

NFCR & THE AMERICAN ASSOCIATION FOR CANCER RESEARCH

Daniel Haber, M.D., Ph.D., Awarded the AACR-NFCR Tamara and Franklin Salisbury, Sr., Professorship >>

The National Foundation for Cancer Research (NFCR) and the American Association for Cancer Research (AACR) announced that Daniel Haber, M.D., Ph.D., is the recipient of the AACR-NFCR Professorship in Basic Cancer Research. The two-year, $100,000 award, granted in honor of NFCR founders Franklin and Tamara Salisbury, was presented to Dr. Haber to support his basic science research in the genetics of cancer.

Dr. Haber, at the Massachusetts General Hospital Cancer Center and Harvard Medical School, conducts research in the genetics of cancer with particular emphasis on studying genetic predisposition and characterizing tumor suppressor genes involved in Wilm's tumor, a pediatric kidney cancer, and its relationship to increased risk of breast cancer.

"Dr. Haber's research of the ataxia telangiectasia (AT) genetic disease is an important study of the link between children's genetic diseases and the risk of a mother's early development of breast cancer," says NFCR Science Director Sujuan Ba, Ph.D.

The professorship is granted to individuals who show promise for substantive contributions to basic cancer research and to foster productivity and allow the individual to devote more time to research.

"We are pleased that the American Association for Cancer Research chose to award this first Tamara and Franklin Salisbury, Sr., Professorship to Dr. Haber. It is exactly this type of research that the NFCR supports in our efforts to discover the genetic mutations that cause cancer. Dr. Haber's research brings us one step closer to this understanding."

—SUJUAN BA, PH.D., NFCR SCIENCE DIRECTOR

Fang Liu, Ph.D., Awarded AACR-NFCR 1999-2000 Career Development Award>>

The American Association for Cancer Research (AACR) has named Fang Liu, Ph.D., at Rutgers University as the AACR-NFCR 1999-2000 Career Development Award winner. Dr. Liu, an assistant professor in the department of chemical biology of the Laboratory for Cancer Research of the Center for Advanced Biotechnology and Medicine, was selected for her work in the role of TGF-beta-inducible gene regulation in tumorigenesis.

The Career Development Award is given annually by NFCR in conjunction with the AACR. The award is designed to recognize junior faculty members in their first or second year of a full-time, tenure-track appointment as assistant professor. The winner must be conducting cancer research at an academic institution.

>>funding for a cure

Linking Past and Present to Imagine a World Without Cancer

NFCR was founded in 1973 when Franklin and Tamara Salisbury learned Nobel Laureate Albert Szent-Gyorgyi was unable to find funding for his latest cancer research project.

The world-renowned scientist was rejected by potential funding sources because unlike his contemporaries who tended to tread on familiar scientific ground Szent-Gyorgyi could not predict the results of his research. So, inspired by Szent-Gyorgyi's dilemma, the Salisburys sent the scientist a modest check of $25, and asked him to join them in establishing NFCR.

"The wonderful thing about NFCR support is its continuity and flexibility. I can count on it to . . . start an interesting new project that another granting agency may consider 'risky.' It is an important safety net for my laboratory, for which I am very grateful."

—KATHRYN HORWITZ, PH.D., UNIVERSITY OF COLORADO HEALTH SCIENCES CENTER

While much has changed since NFCR's founding, one thing has remained constant: the benevolence of the many private individuals who generously support our efforts. So to our donors and supporters who imagine a world where no man, woman or child must face the terrible threat of cancer, we say thank you.

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While gifts of all sizes are gratefully received and carefully expended, NFCR is deeply grateful to the donors listed on the following pages who have made gifts of $250 or more to NFCR in fiscal year 2000. Donors who contribute at this level are enrolled in NFCR's Chairman's Circle.

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Ms. Mary E. Ewing

The Gluckman Foundation
Thomas Gluckman

The Kandell Fund

The Graham Family
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Peter & Diane B. Hoyt Family Foundation

The Itri Family Foundation
Ms. Sue Itri

The Bellini Foundation

Paul & Annetta Himmelfarb Foundation

The Litwin Foundation, Inc.
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Wiegand Family Foundation

W. Ford Schumann Foundation
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Ros-Herb Foundation
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Mr. & Mrs. Morton John Barnard

William R. Windsor Charitable Foundation

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Morgenthau Foundation
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William & Anita Newman Foundation

Chaplains Office
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Fred Pasternak Foundation
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The Riggio Foundation
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Deering Family Trust
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The Freuhauf Foundation

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Mrs. Theresa F Gross

Fraternal Order of Eagles #3773

Tillie & Wm. Blumstein Foundation

Emitom Watson Foundation

Fresco Painting & Decorating, Inc.

Samiyatex

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Aurora Foods, Inc.

Robert & Mary Litterman Foundation
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The Doi Family*

*Honor/Memorial gifts

funding for a cure>>

You can make a difference in the war against cancer by continuing to fund the vital, cutting-edge research that offers our best hope for a cure for cancer.

MEMORIAL/HONOR GIFTS

All of us know someone special whom we admired, respected and loved. We invite you to celebrate that special person's life with a donation made in his or her honor to the National Foundation for Cancer Research. Or perhaps you would like to send a memorial contribution instead of sending flowers at the death of a loved one. This is truly a gift so others might live, for it goes to support lifesaving cancer research. A handsome card is sent to the honoree, or in the case of a memorial gift, an "In Memory of" card with the name of the donor is sent to the family. We are deeply grateful for all gifts of this kind and sincerely regret that space limitations do not allow us to include a complete list of all such honorees.

If you would like more information about how to contribute through NFCR's Honor/Memorial program, please call us at 1-800-321-CURE (2873) and ask to speak with the Honor/Memorial Coordinator.

PLANNED GIVING

Planned giving is an increasingly popular way for donors to make charitable gifts, meet their current income needs and take advantage of tax incentives. The benefits of your generosity will be deferred into the future, but your planned gift will have a significant impact on cancer research. By providing us with the financial stability we need to plan for the long term, together we can ensure our project directors will always have the support they need. For more information, contact NFCR at 1-800-321-CURE (2873).

"The philosophy of NFCR has been to find research which is delving into the root problem [of cancer] . . . This is the most important issue related to funding by NFCR [and] it can explain why so many of the investigators supported by NFCR are recognized as the world's leaders in cancer research."

—DANNY WELCH, PH.D., PENN. STATE UNIV. COLLEGE OF MEDICINE

LEGACY FOR A CURE

Many individuals have demonstrated their support of our mission by notifying us of their plan to contribute to the foundation through their estate plan. If you have remembered NFCR in your estate, please call us at 1-800-321-CURE and ask to speak with our Planned Giving Coordinator.

BEQUESTS

A donor may include a bequest to NFCR in a will. A bequest may be for a specific amount, a percentage of the donor's estate, or even a residual portion. Bequests help offset estate taxes and allow a donor to make a significant gift that might not have been possible during his or her lifetime.

CHARITABLE REMAINDER TRUST

Through a remainder gift, a donor may contribute assets, such as securities or real estate, to NFCR while retaining the income from those assets for themselves or a beneficiary. A remainder gift allows the donor to take a charitable deduction for a portion of the value of the gift on his or her income tax.

CHARITABLE GIFT ANNUITY

With a gift annuity, you can make a contribution of cash, securities or other assets to NFCR. In return, NFCR agrees to make fixed payments to you and/or a beneficiary for life. A portion of your gift is tax-deductible depending on factors such as age and the amount of your contribution. In addition, a portion of the payments you receive from NFCR may provide tax benefits. For more information, call us at 1-800-321-CURE (2873).

Sample Will Language

A will is the cornerstone of your plan for the future. With a provision in your will for NFCR, you can make a significant investment in a healthy future for your loved ones.

Here is sample language you might use to remember NFCR in your will:

"I give, devise and bequeath to the National Foundation for Cancer Research, a charitable organization incorporated in the state of Maryland with its principal office at 4600 East West Highway, Bethesda, Maryland $_____ (or ___% of the residue of my estate) to be used for NFCR's basic science cancer research program."

Although the process is simple, you should seek the advice of your attorney to ensure your will or codicil is drafted effectively.

2000 Financials

In view of the critical link between our donors, the research initiatives of our project directors, and NFCR's mission to cure cancer, it is important to provide our supporters with detailed information regarding our management of their contributions. The following pages contain NFCR's statements of financial position and activities for your consideration.

NATIONAL FOUNDATION FOR CANCER RESEARCH, INC.
STATEMENTS OF FINANCIAL POSITION
SEPTEMBER 30, 2000 AND 1999

Assets	2000	1999
Cash and cash equivalents	$ 135,173	$ 263,211
Accounts receivable	369,122	282,474
Contributions receivable	364,783	1,220,936
Prepaid expenses and other assets	467,567	243,006
Furniture and equipment, net 145,878	146,036	
Investments	6,580,988	5,677,251
Amounts held in trust by others	1,741,078	1,662,736
	$ 9,804,589	$ 9,495,650
Liabilities and Net Assets		
Liabilities:		
Accounts payable and other liabilities	$ 1,997,133	$ 2,364,916
Accrued salaries and vacation	100,129	62,985
Deferred revenue	27,446	44,416
	2,124,708	2,472,317
Net assets:		
Unrestricted:		
Designated for research	4,411,141	4,550,838
Undesignated	1,507,662	799,759
	5,918,803	5,350,597
Temporarily restricted	309,469	312,564
Permanently restricted	1,451,609	1,360,172
Total net assets	7,679,881	7,023,333
	$ 9,804,589	$ 9,495,650

"...the ability to follow up new leads promptly, even though they deviate from previously contracted or agreed upon experiments, is the way breakthroughs occur that allow science to advance most rapidly. Nowhere is this observation more true than in basic cancer research. And it is here that NFCR has played such an important role over the years."

—HAROLD DVORAK, M.D., BETH ISRAEL DEACONESS MEDICAL CENTER, HARVARD MEDICAL SCHOOL

To receive a copy of NFCR's Financial Statements and Schedule for September 30, 2000 and 1999 (with Independent Auditors' Report) by the auditing firm of KPMG, LLP, please call us at 1-800-321-CURE or go to our website, www.NFCR.org.

NATIONAL FOUNDATION FOR CANCER RESEARCH, INC.

Statements of Activities

Years ended September 30, 2000 and 1999

	2000	1999
Changes in unrestricted net assets:		
Support and revenue:		
Public support	$ 12,477,946	$ 9,975,658
Bequests	1,233,146	1,732,992
University support	1,938,473	1,740,857
Mailing list rentals	741,424	522,846
Net investment income	938,980	964,129
Other revenue	56,790	27,786
Total support and revenue	17,386,759	14,964,268
Net assets released from restrictions	0	1,996
Total revenue	17,386,759	14,966,264
Expenses:		
Program services:		
Research	6,706,445	5,966,236
Public education and information	5,888,928	4,296,722
Total program services	12,595,373	10,262,958
Supporting services:		
Fundraising	3,605,222	3,776,076
Management and general	617,958	638,296
Total supporting services	4,223,180	4,414,372
Total expenses	16,818,553	14,677,330
Change in unrestricted net assets	568,206	288,934
Changes in temporarily restricted net assets:		
Changes in value of charitable remainder trusts	<3,095>	<8,409>
Net assets released from restrictions	0	<1,996>
Change in temporarily restricted net assets	<3,095>	<10,405>
Changes in permanently restricted net assets:		
Increase in beneficial interest in perpetual trusts	81,437	108,134
Contributions	10,000	0
Change in permanently restricted net assets	91,437	108,134
Change in net assets	656,548	386,663
Net assets, beginning of year	7,023,333	6,636,670
Net assets, end of year	$ 7,679,881	$ 7,023,333

NFCR—and you

PUBLIC EDUCATION

NFCR is dedicated to funding the brightest minds in science whose basic laboratory research offers the most hope for a cancer cure. At the same time, we are dedicated to providing you with the most up-to-date information available about cancer prevention, detection and treatment.

Because of your contributions in the past year, we were able to continue funding cutting-edge research, as well as update our public education offerings. These publications are available to you at no charge whether or not you make a contribution to NFCR at this time. Helpful hints in these publications are found throughout this annual report. Publications include:

On Your Health. Insightful guides provide common-sense ways you can reduce your risk of cancer. The six publications in the *On Your Health* series include: Choose Crucifers: The Vital Veggies, The Facts about Fat, Walk Your Way to Wellness, Seek Shade—Not Sun, Finding Fiber, and Weigh Less—Live Longer.

NFCR's Cancer Chart. A detailed list of 22 of the most common cancers, this chart contains information about each cancer's signs and symptoms, diagnostic aids, treatment options, risk factors and suggested prevention methods.

NFCR's Cancer FAQs. Your frequently asked questions are answered in depth. Topics include cancers of the breast, lung, prostate, colon, ovarian, liver, kidney, bladder, uterine, testicular and skin. This series also includes guides that answer your questions about treatment options such as radiation and chemotherapy.

Research for a Cure newsletter. A quarterly publication that reports on the latest findings at NFCR—with accounts from NFCR-funded project directors, fellows, and research centers. The newsletter also addresses how to prevent and detect cancer in its earliest stages, and how to participate in NFCR-funded programs.

Self-exam guides for breast and testicular cancer. Convenient door hangers that show you how to perform self-examinations at home, with illustrations to help you perform the exams correctly.

To request complimentary copies of any of the materials described here, please call us at **1-800-321-CURE** (2873) or write to us at the **National Foundation for Cancer Research, 4600 East West Highway, Suite 525, Bethesda, MD 20814.** If you have access to a personal computer, you may request copies of these publications by email at: info@nfcr.org, or order publications online at www.nfcr.org.

Bulk orders are accepted.

NFCR's flexible funding allows its project directors to explore new and unexpected basic science discoveries in these areas of cancer research at prestigious universities and institutions worldwide:

AIDS
Stanford University School of Medicine
Stanford, California

BRAIN
University of Essen
Essen, Germany

Brigham and Women's Hospital
Boston, Massachusetts

Georgetown University
Washington, D.C.

Stanford University School Of Medicine
Stanford, California

University of Colorado
Denver, Colorado

Pennsylvania State University
College of Medicine
Hershey, Pennsylvania

COLO-RECTAL
Johns Hopkins University
School of Medicine
Baltimore, Maryland

HEAD & NECK
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Washington, D.C.

M.D. Anderson Cancer Center
Houston, Texas

LUNG
M.D. Anderson Cancer Center
Houston, Texas

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Baltimore, Maryland

University of Wisconsin-Madison
Madison, Wisconsin

Dana-Farber Cancer Institute
Boston, Massachusetts

MRC Laboratory of Molecular Biology
Cambridge, England

University of California, Berkeley
Berkeley, California

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Stanford, California

Pennsylvania State University
College of Medicine
Hershey, Pennsylvania

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Georgetown University
Washington, D.C.

PROSTATE
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OVARIAN
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Anderson Cancer Center,
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>>research for a cure
>>laboratory without walls

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