ACGT®

ALLIANCE FOR CANCER GENE THERAPY

National grants for cancer research



The Future is **Now**

Annual Report 2004

ACGT®

ALLIANCE FOR CANCER GENE THERAPY

National grants for cancer research

Mission

ACGT is committed to building alliances between philanthropic individuals and organizations, and medical and academic institutions, to promote gene therapy research to combat cancer.

To this end, ACGT will identify, fund and monitor innovative research that meets a rigorous set of scientific standards and has the potential, in the foreseeable future, to treat cancers of all types.

Through this endeavor, ACGT will educate the public about the potential for cancer gene therapy and facilitate greater collaboration among the scientific community to foster the best possible research and ultimately the best treatment.

Alliance for Cancer Gene Therapy, Inc. [ACGT] is a 501 (c)(3) non-profit public charity founded in 2001 by Barbara and Edward Netter to facilitate funding for high-potential research into gene therapy, in the hopes of realizing an effective alternative to the treatment and management of cancer.

Dear Friends,

Three short years ago, Alliance for Cancer Gene Therapy, Inc. [ACGT] was founded based on the knowledge that genes play a powerful role in the development of cancer, and the belief that insufficient investigation was underway in a field acknowledged to have enormous potential. Furthermore, we believed that significant research outcomes were most likely to occur within the framework of a more effective business model that encourages stringent scientific standards, innovation and professional collaboration. ACGT was established to make a real difference in the way we attack cancer.

These were not random or serendipitous beliefs, rather thoughts that evolved from the realization that an annual expenditure of $14 billion in this country on cancer research, and another $64 billion on cancer care, calls into question the efficacy of those endeavors. These statistics were further compounded by our concern for the cost of cancer relative to employment issues, health insurance and our nation's economy as a whole. Most importantly, we were profoundly aware of the incalculable emotional cost to families, friends and colleagues of the one million people diagnosed with cancer each year and the more than half a million whose lives are lost annually to this insidious disease.

This is our first report to friends and donors and as such highlights our progress since inception in 2001. We are most grateful to our Board of Directors and to our Scientific Advisory Council, composed of seventeen of the nation's preeminent physicians and researchers in the field, for their expertise and their commitment to the mission of ACGT. We are proud of our first ten research grant recipients, for the caliber of their scientific investigations and the quality of the medical institutions and research centers where they work to fulfill the promise of cancer gene therapy. And we are so thankful to those who have assisted our efforts to become the only private organization in the nation to fund cancer gene therapy research exclusively. We believe, because of your support, the vast potential to manage cancer through gene therapy is within our reach.

We have had an auspicious beginning, but there is much to do. We are committed to promoting the best possible research by creating a powerful alliance between philanthropic individuals, research organizations, and business and community groups, in order to achieve our mutual goals. We hope the information in this report will both enlighten and stimulate your interest in this important field, and generate hope for the promise of cancer gene therapy as the future of cancer treatment. Cancer, perhaps more than any other disease, is likely to affect each and every one of us at some time in some way.

We believe firmly that gene therapy is the future, and the future is now.



Edward Netter
President



Savio L. C. Woo, Ph. D.
Chairman, Scientific Advisory Council

About ACGT

ACGT is the only private organization in the nation committed exclusively to the funding of cancer gene therapy research to combat all forms of cancer.





"It is now approximately 30 years since the concept of human gene therapy began to seriously take shape.

We have witnessed the birth and firm establishment of a concept for a completely new paradigm for the control of human disease."

– Theodore Friedmann, M.D., Director of the Human Gene Therapy Program at UCSD, from The Development of Human Gene Therapy, 1998

"The idea is to use genes as medicine to treat disease, to cure disease.

It is not a question of whether cancer gene therapy will work, but when."

– Savio Woo, PhD., Professor and Chairman, Gene and Cell Medicine, Mount Sinai School of Medicine

ACGT is:

- ***Collaborative***

ACGT works closely with existing research and medical organizations to maximize results.

- ***Efficient***

100% of funds raised by ACGT go directly to support medical research. A separate fund has been established for all operating and administrative costs.

- ***Rigorous***

Research proposals must meet highly selective scientific criteria in order to be considered for funding.

- ***Opportunistic***

ACGT issues substantial grants to select high-potential projects in order to optimize research results leading to clinical application.

- ***Selective***

Donors are true partners in the process, with the option to invest in the type of research and/or the type of cancer that is of most interest.

- ***Committed***

ACGT believes that cancer gene therapy has the greatest potential to not only improve the quality of life of cancer patients, but to ultimately realize a cure for cancer.

ACGT Highlights of Activities Since Inception

2001

- Incorporated 501 (c)(3) public charity
- Scientific Advisory Council and Board of Directors established
- Trademark for ACGT logo and name registered

2002

- **www.acgtfoundation.org** launched
- Inaugural Event: Introduction of ACGT to Public
- "Young Investigator Request for Applications" receives 44 proposals from 27 institutions
- First Donor Luncheon hosted by Barbara Netter
- Scientific Advisory Council recommends finalist applications for funding
- **$1.5 million awarded by the Board of Directors to three Young Investigators**

2003

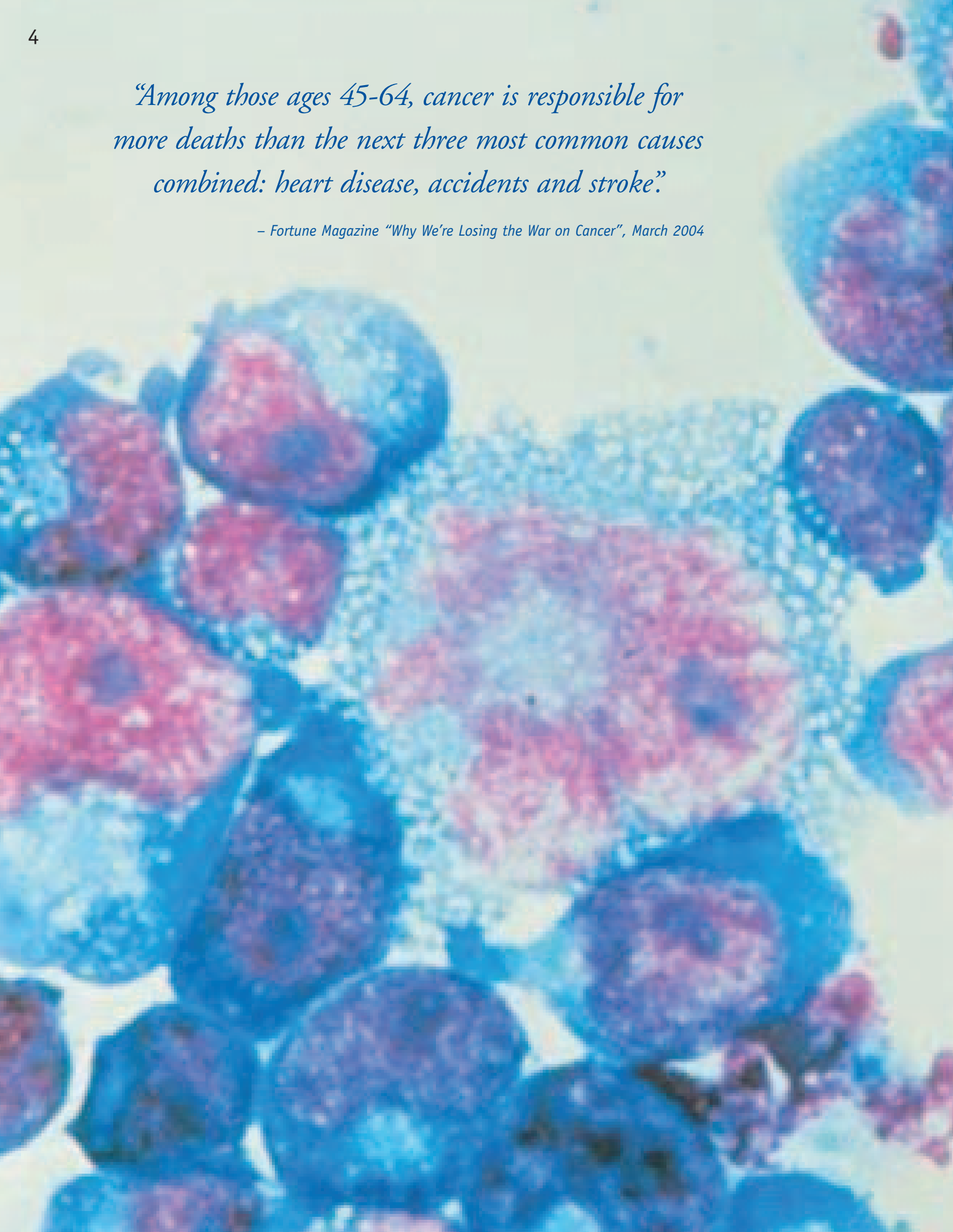
- "Breakfast at 8" Seminar, hosted by Barbara Netter and Anne Scheuer, presented by Dr. Savio Woo for Community and Business Leaders
- *Gene Therapy in the News* issued with current information on gene therapy
- ACGT represented at American Society of Gene Therapy Conference in Washington, DC
- ACGT sponsored Breakfast with Greenwich Bank and Trust Company – presentations by Dr. Savio Woo and Dr. Janice Gabrilove of Mt. Sinai School of Medicine, hosted by Barbara Netter and Anne Scheuer
- "Young Investigator Request for Applications" receives 45 proposals from 36 institutions
- Aspen, Colorado Event sponsored by Nikos and Alison Hecht – presentation by Dr. Savio Woo
- First Gene Therapy for Lymphoma and Leukemia Request for Application announced
- Scientific Advisory Council recommends finalist applications for funding
- **$2.5 million awarded by the Board of Directors to five Young Investigators**

2004

- "Gene Therapy for Lymphoma and Leukemia Request for Applications" receives 21 proposals from 19 institutions
- "Partnering to Advance Health Research Conference: Philanthropy's Role", Washington, D.C. establishes ACGT's cooperative alliance with affinity organizations
- Houston, Texas Event sponsored by Board member Ned Hartline – presentation by Dr. Savio Woo
- San Antonio, Texas Event sponsored by Mimi Zoch – presentation by Dr. Savio Woo
- "An Editor's Roundtable", New York City – ACGT Presentation to members of the Media
- Scientific Advisory Council recommends finalist applications for funding for lymphoma and leukemia gene therapy research
- **$2.0 million awarded by the Board of Directors to two Investigators for Gene Therapy for Lymphoma and Leukemia**
- Johns Hopkins University Field Visit: Drs. Lieping Chen and Drew Pardoll, members of ACGT Scientific Advisory Council, Dr. Todd Reilly and ACGT reviewers
- University of Pennsylvania Field Visit: Carl June, MD and Robert Vonderheide, MD, Ph.D.
- Philanthropy Roundtable Conference, Palm Beach, Florida: ACGT Breakfast Presentation to Participants
- 2004 Young Investigator Request for Applications receives 49 applications from 34 Institutions
- Scientific Advisory Council recommends Young Investigator finalist applications to Board of Directors for funding
- Memorial Sloan-Kettering Presentation and Laboratory Visit by Board Members, Donors and Friends with Michel Sadelain, MD, Ph.D. and team

"Among those ages 45-64, cancer is responsible for more deaths than the next three most common causes combined: heart disease, accidents and stroke."

– Fortune Magazine "Why We're Losing the War on Cancer", March 2004



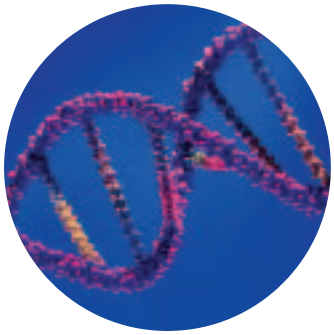
About Gene Therapy

Gene therapy employs therapeutic genes to fight the very disease caused by damaged genes.

Gene research, in the simplest terms, can be likened to car service – replace or repair the defective part and the car will run smoothly again. Cancer is like a run-down car, so that the body can no longer operate at full speed. While strides have been made in the treatment of cancer, these have come slowly and at a great cost. Prevention and early detection, have reduced the incidence of the disease, but not the devastation. The medical community continues to rely on traditional therapies that are often either ineffective or damaging to the patient's health. Normal cells know when to stop growing but cancer cells do not; thus radiation, chemotherapy, and surgery may temporarily slow the spread of cancer, but they do not replace the defective part. Gene Therapy is more than a tune-up, halting the proliferation of cancer cells and returning the body to optimum efficiency.

The concept of gene therapy was born more than thirty years ago; however, the technology to realize that potential is only now available, opening the door to dramatically new possibilities in the treatment of cancers of all kinds.

- The long-term goal of cancer gene therapy is the development of discriminating medicines and drugs that attack only cancer cells, thereby eliminating the adverse effects on the body.
- Gene therapy may someday soon make cancer a manageable disease with nominal side effects to the patients unlike traditional therapies.
- Furthermore, since gene therapy has potential for other diseases such as cystic fibrosis, hemophilia, sickle-cell anemia, muscular dystrophy and Parkinson's, the value of research and discovery has broad applications.



Gene therapy research has the potential to result in totally new forms of treatment, some of which will stand alone, others of which will increase the effectiveness of current treatments.

- Drugs that destroy cancer cells without damage to the patient.
- Medications that boost the immune system to reject cancer cells.
- Injection of new genes to replace cancerous cells or to act as a catalyst for the body to re-regulate its own genetic make-up.
- A vaccine that will cut off the blood supply to isolated cells and in effect strangulate potentially metastatic cancers.
- Inoculations against certain forms of cancer, to ultimately eradicate the disease.

"The road to discovery is long and slow, requiring patience, belief in what can be and the vision to make it happen. As gene therapy pursues the natural course of an emerging science, and technological advances contribute to the ability to produce results, significant gains will surely follow."

– Edward Netter, President of ACGT

About the Grant Award Process

ACGT PROVIDES HIGHLY SELECTIVE GRANTS TO CANCER GENE THERAPY RESEARCHERS IN AMERICAN MEDICAL AND ACADEMIC INSTITUTIONS. AWARDS ENCOURAGE INNOVATIVE RESEARCH OR NURTURE PROJECTS IN PROCESS TO SECURE RESULTS.

The review process is extremely rigorous. All grant applications must evidence both scientific and technical merit, and clearly demonstrate methods of accountability and quality control. Each grant is subject to peer review and then final review by the ACGT Scientific Advisory Council. Only those proposals meeting stringent criteria are recommended to the Board of Directors for funding. Upon completion of the grant process, all proposals receive personalized and qualitative critiques in order to encourage the best science in the field of cancer gene therapy.

Young Investigator Awards

NOTABLE CONTRIBUTIONS TO SCIENTIFIC discovery are frequently made in the earliest stages of research; however, funding at this level is often most difficult to secure. ACGT awards encourage talented young researchers to fulfill their aspirations.

- Up to $500,000 distributed over three years.
- Individuals who are tenure-track assistant professors conducting independent research.

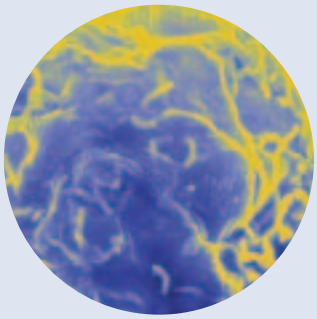
Investigator Awards

GRANTS TO ESTABLISHED RESEARCHERS conducting groundbreaking basic science research and technology development, or whose work is approaching clinical translation leading to the application of new medical treatment. ACGT awards nourish research in progress towards groundbreaking results.

- Up to $1,000,000 distributed over three to five years.
- Associate and full professors for either new or on-going research projects.

INVESTIGATORS FROM THE FOLLOWING INSTITUTIONS HAVE PARTICIPATED IN THE HIGHLY COMPETITIVE SELECTION PROCESS

Albany Medical Center
Albert Einstein School of Medicine
Auburn University
Baylor College of Medicine
Baystate Medical Center
Beth Israel Deaconess Medical Center
Brigham and Women's Hospital, Inc.
Case Western Reserve University
Children's Hospital, Los Angeles
Children's Hospital, Philadelphia
City of Hope National Medical Center
Cold Spring Harbor Laboratory
Columbus Children's Research Institute
Dana-Farber Cancer Institute
David Geffen School of Medicine, University of California, Los Angeles
Duke University School of Medicine
Eastern Virginia Medical School
Georgetown University Medical Center
H. Lee Moffitt Cancer Center
Henry Ford Health System
Indiana University School of Medicine
The Jackson Laboratory
Johns Hopkins University School of Medicine
Kansas University Medical Center Research Institute
Keck School of Medicine at University of Southern California
Louisiana State Health & Sciences Center
Massachusetts General Hospital
Mayo Clinic/Foundation
MD Anderson Cancer Center
Memorial Sloan Kettering Cancer Center
Montefiore Medical Center
Mount Sinai School of Medicine
National Jewish Medical & Research Center
New Jersey Medical School
New York University School of Medicine
Northwestern University Feinberg School of Medicine
Ohio State University College of Medicine
Oregon Health and Science University School of Medicine
Penn State College of Medicine
Pritzker School of Medicine at the University of Chicago
Rockefeller University
Roswell Park Cancer Center
Saint Louis University Medical Center
Salk Institute for Biological Studies



St. Jude Children's Research Hospital
Stanford University School of Medicine
State University of New York Health Science Center
State University of New York, Buffalo School of Medicine
State University of New York, Stony Brook School of Medicine
Thomas Jefferson University, Kimmel Cancer Center
Torrey Pines Institute for Molecular Studies
University of Alabama, Birmingham School of Medicine
University of California, Berkeley School of Medicine
University of California, Davis School of Medicine
University of California, San Diego School of Medicine
University of Central Florida Burnett College of Biomedical Sciences
University of Florida, Gainsville College of Medicine
University of Georgia Biomedical and Health Sciences Institute
University of Illinois Chicago College of Medicine
University of Iowa College of Medicine
University of Kentucky College of Medicine
University of Maryland School of Medicine
University of Massachusetts Medical Center
University of Miami School of Medicine
University of Michigan Medical School
University of Minnesota Medical School
University of Pennsylvania School of Medicine
University of Pittsburgh School of Medicine
University of Rochester Medical Center
University of South Carolina Research Foundation
University of Texas, Austin
University of Utah School of Medicine
University of Washington School of Medicine
University of Wisconsin Medical School
Van Andel Research Institute
Vanderbilt University Medical Center
Wake Forest University School of Medicine
Wayne State University School of Medicine
Yale University School of Medicine

ALLIANCE FOR CANCER GENE THERAPY, INC.
2002-2004 APPLICATION OVERVIEW

2002 YOUNG INVESTIGATOR GRANT
27 Institutions
45 Applicants
18 Finalists

3 Grants awarded

2003 YOUNG INVESTIGATOR GRANT
36 Institutions (Including 23 new)
44 Applicants
21 Finalists

5 Grants awarded

2004 GENE THERAPY FOR LYMPHOMA & LEUKEMIA GRANT
19 Institutions (Including 10 new)
21 Applicants
10 Finalists

2 Grants awarded

2004 YOUNG INVESTIGATOR GRANT
34 Institutions (Including 18 new)
49 Applicants
22 Finalists

Awards to be announced - Spring 2005

Total # of U.S. Medical Institutions, Universities & Research Centers represented by applicants applying for ACGT Grants: **78**

Total # of Finalists: **71**

Total # of Applicants for all ACGT Grant Opportunities 2002-2004: **159**

Total # of Grants awarded 2002 - May 2004: **10***

Totalling
$6 Million

* Does not include 2004 Young Investigator Grants.

About the Investor-Research Alliance

Every Contribution to ACGT is Valued

An investment in ACGT is an investment with both short-term and long-lasting returns. ACGT is intent on making a significant impact on cancer research sooner rather than later. The future of scientific research may well rest on the fusion of sound business principles and philanthropic investment with innovative scientific practice.

Some wish to lead the way. For those whose lives have been profoundly affected by the tragedy of cancer, ACGT makes it possible to make a substantial investment directly in research to protect others from the same devastation. One of the roles of ACGT is to match investor interests with research of greatest interest.

- Investors in ACGT are welcome to designate a specific area of interest, and ACGT will select the research project with the greatest potential return.
- Investors are kept informed on research progress and opportunities.
- As a public charity, individual investor contributions can qualify for an income tax deduction up to 50% of the individual's yearly contribution base, thereby earning maximum tax benefits for investors.

All ACGT administrative costs are secured by a separate fund, so that 100% of investor funding is applied to research.

- Projects are capitalized at unusually high award levels to facilitate meaningful results.
- A rigorous grant review ensures that the most promising projects are rewarded.
- Regular research reports ensure that funds are directed to meet goals and that methods employed meet the standards established in the grant.
- Research findings are shared with the scientific community at professional meetings and/or by publication in scientific journals.
- A unique royalties agreement ensures that earnings from ACGT sponsored research will be reinvested to support future research into cancer gene therapy.

ACGT SEEKS FUNDING FROM INDIVIDUALS, CORPORATIONS AND FOUNDATIONS WHO SHARE OUR COMMITMENT TO THE PROMISE OF CANCER GENE THERAPY.



"We are thrilled to continue our support of ACGT in its entrepreneurial approach of fostering cutting edge, exciting scientific research that will make a real difference in the treatment of cancer."

– Nataly and Toby Ritter, The Ritter Foundation

"Your approach to obtaining substancial input from a distinguished panel of reviewers and advisors that results in feedback to applicant investigators is laudable. It is this rigorous scientific scrutiny plus the level of funding that makes your operation unique and worthwhile."

– Thomas P. Sakmar, M.D., Richard M. & Isabel P. Furland Professor, Former Acting President, The Rockefeller University

Grant Awards 2002-2004

In the first three grant cycles, $6 million has been awarded to ten projects. While there were many worthy investigators seeking funding, approximately one out of ten proposals met ACGT's rigorous research criteria. Awards were granted to eight Young Investigators and two Investigators to support gene therapy research on six forms of cancer.

Breast Cancer Research

- John Hopkins University, Immune-mediated Gene Therapy & Cancer Vaccines
- University of California at Los Angeles, Anti-Angiogenesis

Leukemia

- City of Hope National Medical Center, Immune-mediated Gene Therapy & Cancer Vaccines

Leukemia/Lymphoma

- University of Pennsylvania, Immune-mediated Gene Therapy & Cancer Vaccines
- Memorial Sloan-Kettering Cancer Center, Immune-mediated Gene Therapy & Cancer Vaccines

Neuroblastoma*

- St. Jude's Children's Research Hospital, Anti-Angiogenesis
- University of Pennsylvania, Immune-mediated Gene Therapy & Cancer Vaccines

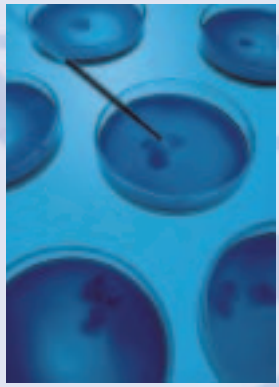
Ovarian Cancer

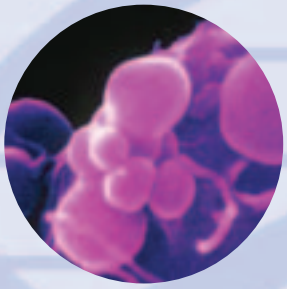
- Ohio State University, Vector Development

Prostate Cancer

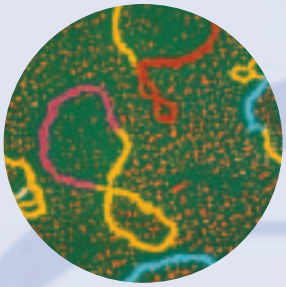
- University of Iowa, Immune-mediated Gene Therapy & Cancer Vaccines
- Louisiana State University, Tumor-Specific Replicating Viruses and Bacteria

**Neuroblastoma is a deadly form of childhood cancer.*









Glossary of Medical Terms

Anti-angiogenesis prevents the growth of new blood vessels. Tumors need their own blood supply to survive and by halting the development of new blood vessels, the tumor's supply of oxygen and nutrients are cut off thus destroying the tumor.

Clinical Translation is the process that transforms research evidence into clinical guidelines and policy. The aim of translation is to provide useful, usable, and relevant packages of summarized evidence to clinicians in a form that suits their time, cost, and care standards. Generically, these evidence-based clinical packages are called clinical practice guidelines.

Gene Therapy is the process of introducing genetic material (DNA or RNA) into a person's cells to fight disease. Gene therapy treats disease by either replacing damaged or abnormal genes with normal ones, or by providing new genes. In cancer, gene therapy targets healthy cells to enhance their ability to fight cancer cells, employs genes to create anti-angiogenesis, destroys cancer cells, or inhibits their growth.

Immune-Mediated Gene Therapy stimulates or restores the ability of the immune system to fight infection and disease. Research strives to harness immune mechanisms against tumor cells, by using the patient's own immune system or the transfer of antibodies or T-cells from an outside source.

Oncogenesis/Apoptosis targets the process in which a damaged cell continues dividing without restrictions, developing into cancer. Apoptosis is one of the primary forms of programmed cell death.

Tumor-Specific Replicating Viruses and Bacteria attack the immune system. Vaccines stimulate the body's immune system to recognize and fight abnormal foreign cells in the body, such as viruses and bacteria. Scientists and doctors are now trying to develop vaccines that can stimulate the immune system to recognize and destroy cancer cells like viruses or bacteria.

Viral vectors produce tumor antigens (proteins found on a tumor cell) and can stimulate an antitumor immune response in the body. Viral vectors may also be used to carry genes that can change cancer cells back to normal cells. Vector development seeks to simulate vectors to combat cancer.

ALLIANCE FOR CANCER GENE THERAPY

Research Grant Recipients

2002 - 2004

Through its **Young Investigator** and **Investigator Awards**, ACGT has funded $6 million in grants to support basic research, technology innovation, pre-clinical validation and clinical translation to expedite development of effective and safe gene therapies for cancer. Initiatives currently underway by ACGT grant recipients address **ovarian cancer, leukemia and lymphoma, childhood cancers such as neuroblastoma, prostate cancer and breast cancer.** The five research areas ACGT supports are tumor-specific replicating viruses and bacteria, anti-angiogenesis, immune-mediated gene therapy, oncogenes/cell cycle control/ apoptosis and tumor targeting/vector development. *(see page 10)*

YOUNG INVESTIGATORS 2002

Jeffrey S. Bartlett, Ph.D.

Assistant Professor, Departments
of Pediatrics, and Molecular Virology,
Immunology
The Ohio State University
Investigator, Center for Gene Therapy,
Columbus Children's Research Institute:
Columbus, Ohio

Development of a targeted AAV vector system for Ovarian Cancer Gene Therapy

OVARIAN CANCER IS ONE of the most common and frequently life-threatening malignancies affecting women in the U.S. today: about 25,000 new cases will be diagnosed with the disease this year and over 15,000 women will die from it. Delivering therapeutic genes efficiently and precisely, so that they reach only the targeted cancer cells, is crucial to success. My group has developed a means of delivering therapeutic genes to a specific population of cells in laboratory experiments. By rearranging the genetic structure of AAV, a common human virus, we have created a class of molecular Trojan horse viruses, known as vectors, from the Latin "to carry." These vectors are aimed at ovarian cancer cells via key sequences in the virus shell that allows it to infect only cells in the body displaying a particular marker that is restricted to cancer cells. We are now testing the Trojan horse system's ability to cure ovarian cancer in laboratory animals. If these studies are successful, this research will help pave the way for clinical trials in women with ovarian cancer and may lead to a new approach to this deadly disease.



Research Grant Recipients

YOUNG INVESTIGATORS 2002



Andrew M. Davidoff, M.D.

Associate Member, St. Jude Faculty
Division Chief, General Pediatric Surgery
Director, Surgical Research
St. Jude Children's Research Hospital:
Memphis, Tennessee

PEDF-mediated anti-angiogenic Gene Therapy for Neuroblastoma

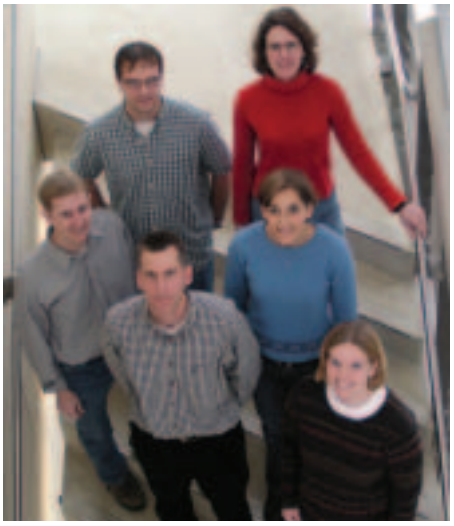
NEUROBLASTOMA IS ONE OF THE most common childhood cancers. Angiogenesis, the formation of new blood vessels, is central to the progression of cancer, and it is known that inhibiting angiogenesis can literally starve a tumor to death. We hypothesize that delivering a particular gene called pigment epithelium derived factor (PEDF) to the liver has the potential to inhibit angiogenesis and restrict the growth of neuroblastoma. PEDF is known to be a highly potent angiogenesis inhibitor and is also capable of inducing neuroblastoma cells to mature, decreasing their malignant potential. My research is focused on using viruses as vectors to carry the gene for PEDF to the liver. The data being developed from these studies are likely also to be applicable to other types of cancer, and even to other diseases in which angiogenesis contributes to the disease process.

Thomas S. Griffith, Ph.D.

Assistant Professor, Urologic
Oncology Research
University of Iowa: Iowa City, Iowa
Induction of Anti-tumor Immunity

Using a TRAIL/Apo-2L Encoding Recombinant Adenovirus: Gene Therapy for Prostate Cancer

PROSTATE CANCER IS THE SECOND leading cause of cancer death among men in the United States. We are studying and testing a new means of inhibiting the formation of prostate tumors, using an agent called TRAIL to induce the death of tumor cells. The TRAIL gene is transferred into a cell with Ad5-TRAIL, a genetically engineered virus known as a viral vector. The vector uses the cell's own machinery to produce the TRAIL protein and induce tumor cell death. Studies with laboratory animals have shown that this form of gene therapy results in the death of tumor cells. My lab is currently studying Ad5-TRAIL's ability to activate the immune system's anti-tumor responses. Tumor cells can deceive the body's immune system into perceiving them as normal cells rather than foreign invaders, but introducing genes into a tumor can counteract this. Determining the effect of Ad5-TRAIL-induced apoptosis (programmed cell death) on the activation of the immune system in patients with localized prostate cancer is the next step in this ongoing research, and is anticipated to begin this year. The goal is to use this type of gene therapy to achieve tumor rejection, and tumor-free survival for the patient.



Research Grant Recipients



Laurence J. N. Cooper, M.D., Ph.D.

Assistant Professor, Department of Pediatric Oncology
City of Hope National Medical Center: Duarte, California

Enhancing the Survival and Anti-Tumor Effector-Functioning of CD-19 Specific T-Cells: Gene Therapy for Leukemia

RELAPSED OR DRUG-RESISTANT **leukemia and/or lymphoma** are very difficult to cure using the traditional work horses of cancer therapy, surgery, radiation and chemotherapy. New classes of therapies need to be developed. In my laboratory we are using the patient's immune system to directly attack the disease. This therapy harnesses the power of T cells, a type of immune cell, and uses gene therapy to redirect the function of the T cell so that it can target a patient's leukemia and/or lymphoma. These are exciting times for immune-based therapy and we expect that the experiments funded by ACGT will provide critical insights into designing new ways of using T-cells to treat patients.

YOUNG INVESTIGATORS 2003

Timothy F. Lane, Ph.D.

Assistant Professor, Departments of Obstetrics, Gynecology, and Biological Chemistry
University of California at Los Angeles: Los Angeles, California

Therapeutic Endothelial Cell Progenitors in Tumor Angiogenesis: Gene Therapy for Breast Cancer

SINCE MOST HUMAN TUMORS must recruit new blood vessels in order to grow and move, anti-angiogenic therapies have been viewed as a potential complement to more traditional cancer treatments. We have identified a genetic element that allows genes to be expressed in a group of bone marrow derived cells that contribute to cancer-associated blood vessels. The cells are called "endothelial cell precursors" (ECPs). ECPs are a special type of stem cell that plays a role in the formation of new blood vessels. We propose to create a simple virus designed to carry genes to ECPs and prevent them from helping tumors to grow. Our research is specifically targeted to **breast cancer**.

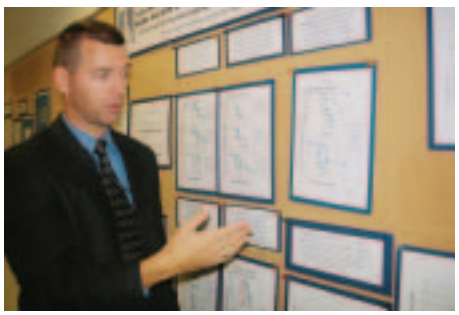


R. Todd Reilly, Ph.D.

Assistant Professor, Department of Oncology
Johns Hopkins University: Baltimore, Maryland

Investigation of Antibody-mediated Cancer Vaccine Endowment: Gene Therapy for Breast Cancer

THIS PROJECT IS FOCUSED on developing a vaccine that harnesses the body's immune system to seek out and eliminate minimal residual disease in women with **breast cancer** and to wipe out any microscopic cancer deposits that may have spread to other parts of the body. Current studies are designed to understand the role of anti-body in facilitating the response to vaccination. The goal is to translate the resulting data into clinical applications as rapidly as possible. As our understanding of the immune response to tumors increases, I believe we will be able to translate that potential into clinical benefit.



Research Grant Recipients

YOUNG INVESTIGATORS 2003

Katherine D. Ryman, Ph.D.

Assistant Professor, Department of Microbiology and Immunology
Louisiana State University Medical Center: Shreveport, Louisiana

Sindbis Virus Vectors in Anti-Cancer Gene Therapy: Gene Therapy for Prostate Cancer

RECENTLY, THE USE OF tumor-killing viruses has gained favor in cancer gene therapy in an approach that has become known as "virotherapy." Virotherapy exploits viruses that are able to target and destroy cancer cells, while sparing the surrounding normal tissue. We are developing a virotherapy approach for the treatment of prostate cancer based on infection with Sindbis virus. The ability of Sindbis virus to travel rapidly throughout the body in the bloodstream will improve access to metastasized cancer cells. We intend first to develop and test these agents in cultured cells. We will then test and optimize the ability of the virus to cure **prostate cancer**.









Robert Vonderheide, M.D., D.Phil.

Assistant Professor, Department of Medicine
University of Pennsylvania: Philadelphia, Pennsylvania

Cancer Vaccination Using RNA Transfected CD40-Activated B-Lymphocytes in Pediatric Patients: Gene Therapy for Neuroblastoma

A PROMISING APPROACH in cancer treatment is to vaccinate patients against molecules expressed by cancer in hopes of starting or awakening an immune response that will kill tumor cells. One leading strategy bases the center of such vaccines on the patient's own immune cells, which are removed from the body and re-engineered outside the body before re-injection. With this grant, we will evaluate a novel gene therapy vaccine specifically designed for children with cancer, for whom very few attempts at cancer vaccination have been undertaken. This work will establish the scientific and manufacturing rationale for translating this gene therapy technology to the clinic, especially for **children with cancer**.

Research Grant Recipients

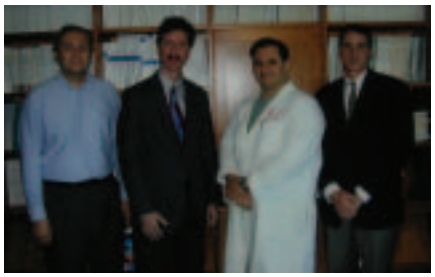
INVESTIGATORS 2004

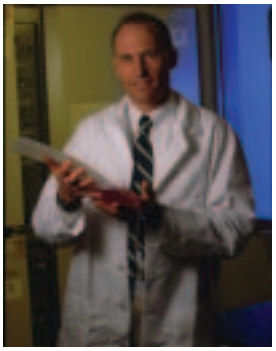
Carl H. June, M.D.

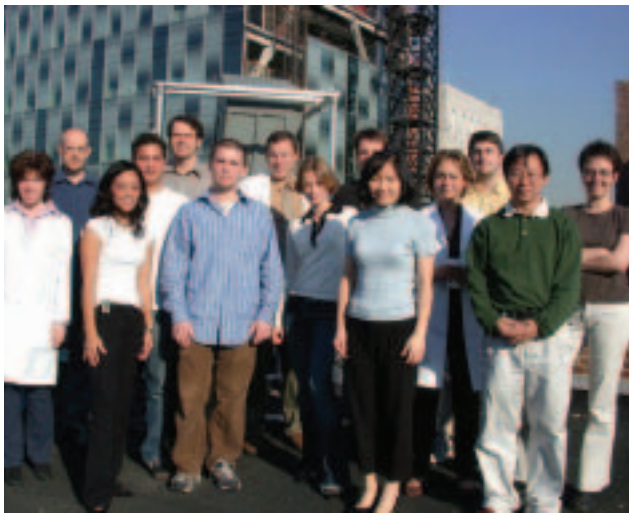
Professor, Department of Pathology and Laboratory Medicine
Director of Translational Research, Abramson Family Cancer Research Institute
University of Pennsylvania: Philadelphia, Pennsylvania

Leukemia Immunotherapy Using Lentiviral Engineered T-Cells: Gene Therapy for Leukemia

FOR YEARS IT HAS BEEN KNOWN that the immune system could be harnessed to kill tumor cells, however, difficulties in routinely applying this as a practical cancer therapy have prevented widespread adoption of the approaches that work well in laboratory mice. However, recent advances in gene transfer therapy promise to make this treatment a reality. This program will test whether the immune system's T cells can be altered genetically so that they become "guided missiles". In this project advanced gene transfer technology will be used to permanently modify the immune system by inserting a tracking system into the T cells so that T cells are engineered to kill tumor cells specifically. This approach will be first tested in adults with leukemia that is resistant to currently available chemotherapy.







Michel Sadelain, M.D., Ph.D.

Member, Department of Medicine and Immunology
Memorial Sloan-Kettering Cancer Center: New York, New York

Targeting Leukemia and Lymphoma with CD19-specific T-cells co-stimulated by CD28 and interleukin-15: Gene Therapy for Leukemia

THIS PROGRAM AIMS TO assess the therapeutic potential of genetically targeted T-cells in the treatment of leukemia and lymphoma. We recently demonstrated that human peripheral blood T-cells can be genetically redirected to recognize the CD19 antigen and eradicate established, systemic human B-cell tumors borne by immune-deficient mice, demonstrating for the first time that genetically modified human T-cells can induce durable remissions in an in-vivo setting. As the final aim of this project, we plan to assess this therapeutic strategy in patients with relapsed B-cell malignancies.


WATERPROOF
SMEAR-PROOF
PEN.

ACGT Scientific Advisory Council

ACGT'S SCIENTIFIC ADVISORY COUNCIL IS COMPOSED of seventeen of the nation's preeminent physicians and researchers in gene therapy. The Council, whose members serve without financial remuneration, established the scientific criteria for review of all grants and developed strict accountability guidelines requiring periodic progress reports. The Council submits recommendations to the Board of Directors, which is responsible for final selection of award recipients.

Savio L.C. Woo, Ph.D., Chairman
Professor and Chairman
Department of Gene and Cell Medicine
Mount Sinai School of Medicine,
New York, NY

Stuart A. Aaronson, M.D.
Jane B. and Jack R. Aron Professor of Neoplastic Diseases
Chairman, Department of Oncological Sciences.
Mount Sinai School of Medicine,
New York, NY

Xandra O. Breakefield, Ph.D.
Professor of Neurology, Harvard Medical School; Geneticist, Center for Molecular Imaging Research
Massachusetts General Hospital
Boston, MA

Lieping Chen, M.D., Ph.D.
Director of Research, Department of Dermatology, Professor of Dermatology, Oncology, Johns Hopkins University School of Medicine, Baltimore, MD

David A. Cheresh, Ph.D.
Professor in the Departments of Immunology and Vascular Biology
The Scripps Research Institute,
La Jolla, CA

Stephen L. Eck, M.D., Ph.D.
Executive Director
Pfizer Global Research and Development,
Ann Arbor, MI

Judah Folkman, M.D.
Director Vascular Biology Program,
Children's Hospital Boston
Andrus Professor of Pediatric Surgery and Professor of Cell Biology
Harvard Medical School, Boston, MA

Joseph C. Glorioso III, Ph.D.
Chairman and Professor of the Department of Molecular Genetics and Biochemistry
University of Pittsburgh School of Medicine, Pittsburgh, PA

Carl H. June, M.D.
Director, Translational Research and Professor, Department of Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia, PA

Wen-Hwa Lee, Ph.D.
Donald Bren Professor of Biomedicine
Department of Biological Chemistry
University of California at Irvine,
Irvine, CA

Michael T. Lotze, M.D.
Director, Clinical and Translational Research at the Molecular Medicine Institute; Professor of Surgery, Molecular Genetics and Biochemistry; Co-director of the Human Gene Therapy Program
University of Pittsburgh Medical Center,
Pittsburgh, PA

Robert Martuza, M.D., F.A.C.S.
Chief of Neurosurgery Service
Massachusetts General Hospital
Higgins Professor of Neurosurgery
Harvard Medical School, Boston, MA

Frank McCormick, Ph.D., F.R.S.
Director, University of California at San Francisco Comprehensive Cancer Center and Cancer Research Institute
David A. Wood Chair of Tumor Biology and Cancer Research, Department of Microbiology and Immunology
San Francisco, CA

A. Dusty Miller, Ph.D.
Member of the Divisions of Human Biology and Basic Sciences, Fred Hutchinson Cancer Research Center, Affiliate Professor of Pathology, University of Washington, Seattle, WA

Drew Pardoll M.D., Ph.D.
Seraph Professor of Oncology, Professor of Medicine, Pathology and Molecular Biology and Genetics
Co-Director, Cancer Immunology and Hematopoieis Program
Sidney Kimmel Cancer Center
Johns Hopkins University School of Medicine, Baltimore, MD

Erkki Ruoslahti, M.D., Ph.D.
Distinguished Professor
The Burnham Institute, La Jolla, CA
Adjunct Professor of Bioengineering, University of California at San Diego
San Diego, CA

Thomas J. Wickham, Ph.D.
Director
Non-Clinical Development
EMD Lexigen, Billerica, MA



Donors

MANY THANKS TO THESE DONORS WHO ARE OUR PARTNERS IN THE ALLIANCE FOR CANCER GENE THERAPY. TOGETHER WE BELIEVE WE WILL SEE NEW BREAKTHROUGHS IN CANCER TREATMENT AND HOPEFULLY, SOMEDAY, A CURE.

Without the vision, commitment and contributions of the following donors, ACGT would not have been able to support the research of our ten outstanding investigators. We are grateful for this and for establishing ACGT as the largest private funder of cancer gene therapy in the nation.

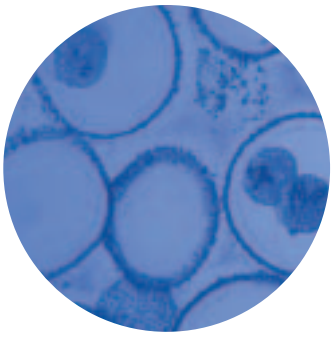
The Adler Foundation, Inc.
Ms. Aracelis Alonso
Ms. Belinda Amsterdam
Mr. & Mrs. Roy Anderes
Mr. Steven C. Annus
In Memory of Ingeborg Annus
ANONYMOUS
Ms. Catherine Arkins
Mr. Raymond Armstrong
Mr. & Mrs. Fareed Ashraf
Aspen Advisors
Mr. & Mrs. Gary Balzofiore
Ms. Margaret M. Benjamin
Mr. George W. Benoit
Ms. Paula Bentivegna
Berkshire Hathaway, Inc
Charitable Program
Mr. & Mrs. Allan Bernard
Mr. & Mrs. J. Michael Bireley
In Memory of Stella Hartline
The Birnbaum Foundation
Mr. Brady Bizal
Mr. Andrew M. Blum
Mr. & Mrs. Myron Blumenfeld
Mr. & Mrs. Harry Bower
Mr. & Mrs. Daniel J. Brereton
Mr. & Mrs. Fred Brooks
Mr. & Mrs. Brett Brown
The Browne Lounge, Ltd.
Ms. Margaret Brylinski
Mr. & Mrs. Paul E. Bunning
Mr. & Mrs. John Calimafde
The Sam and Louis Campe Foundation, Inc.
Ms. Randy Cappiello
Mr. & Mrs. Nicholas T. Cappiello III
Mr. James Carey
In Memory of Diane Middleburg
The David F. Chazen Charitable Trust
Ms. Anita Cheng
Mr. & Mrs. Ronald A. Christopher
Mr. Chan Sau Chun
Mr. & Mrs. Jeffrey Cianci
In Memory of Arthur Netter
Mr. Milton Cooper
Mr. Adolph B. Cramer
Mr. & Mrs. John Cross
Mr. Frank J. Dalicandro
Mr. & Mrs. Diane Darst
Mr. & Mrs. Richard DeMarco
Mr. Robert G. Donnalley
Mr. & Mrs. John Donovan
Mr. Donald K. Drelich
Mr. & Mrs. Jeb Embree
Mr. & Mrs. Alan Englander
Everest Reinsurance Company
Mr. & Mrs. Conner Fay
Mr. & Mrs. Bill Fitzgerald
Fidelity Charitable Gift Fund
Mr. George Fowlkes
Ms. Alison Galante
Mr. & Mrs. Paul Gardner
In Honor of Barbara Netter
Garfield & Hecht, P.C.: Attornies at Law
Ms. Michele D'Angelo Garvey
General Cologne RE: Corporation
Mr. & Mrs. Sean George
Mr. David Getz & Ms. Doreen Jablons
Mr. Thomas A. Gibbons
Mr. & Mrs. Alex Giordano
Golden Family Foundation
Mr. & Mrs. Carl A. Goldman
Gordon Textiles International, LTD.
Mr. & Mrs. Larry R. Graber
Mr. Robert Hahn
Mr. & Mrs. John W. Hanauer
Mr. Brenton W. Harries
Mr. Edward Hartline
Mr. & Mrs. Curt Hebeler
Mr. & Mrs. Nikos Hecht
Mr. & Mrs. William Heiligbrodt
In Memory of Stella Hartline
Mr. & Mrs. Henry Herbert
Ms. Christine Herman
Mr. & Mrs. Mark Holton
In Memory of Arthur Netter
Mr. & Mrs. Tony Houseman
Mr. James M. Hudnall
Mr. & Mrs. Elihu Inselbuch
Ms. Bebi Ishmail
Mr. Gregory Jacobson
Mr. & Mrs. Cyril Jalon
Ms. Joanne E. Janson
Jewish Communal Fund
Ms. Michele L. Jourdain
Mr. & Mrs. Ronald E. Kahanek
In Memory of Stella Hartline
Mr. & Mrs. Douglas E. Karpenko
Mr. Stephen G. Kenny
Mr. Glenrick Kerr
Mr. & Mrs. David Kettig
Kramer, Levin, Naftalis & Frankel LLP
Mr. & Mrs. Brett M. Lalonde
The Lapin Foundation
Law Office of C. Michael Davis
In Memory of Stella Hartline
Mr. Jeffrey Lee
Mr. Robert M. Leopold
Mr. Arthur Levitt, Jr.
Mr. Warren Lichtenstein
Ms. Rachel Lipari
Mr. & Mrs. Robert E. Lord, Jr.
Mr. & Mrs. Alan C. Lucke
In Memory of Stella Hartline
Mr. Kevin S. Lynyak
Mr. & Mrs. Malcolm W. Macleod
Mahindra USA, Inc
In Memory of Stella Hartline
Ms. Christine M. Marx
The Virginia & Leonard Marx Foundation
Mr. William Matteson
Ms. Alexis Maynard
Mr. Thomas McDermott
Merchant's National Properties, Inc.
Mr. & Mrs. Neal M. McGarrity
Mr. & Mrs. Michael J. Meise
Mr. & Mrs. James Mendler
Mr. & Mrs. Michael Morris
Mulago Foundation
Mr. & Mrs. Mark A. Musser
Mr. & Mrs. Joel Myrold
Mr. Arthur Nesbitt
Mr. & Mrs. Edward Netter

We have made every effort to ensure the accuracy of this report. If your name has been omitted or misprinted, please accept our sincere apologies and notify us by e-mail at aneslage@acgtfoundation.org. To talk to someone directly, call Allison Neslage at 203-358-8000 x. 495.

Mr. Donald Netter
In Memory of Kimberly Lawrence Netter
NY Community Trust
Mr. & Mrs. William T. Orth
Ms. Dawn Palmer
Ms. Lizza Parrilla
Mr. Leo F. Perron, Jr.
Mr. & Mrs. Myron Picoult
Ms. Marcelle Pierrot
The Pines Bridge Foundation
Mr. Raymond Pleyer
Mr. Paul R. Pollock
Mr. & Mrs. Morton Porwick
Mr. Jerald L. Pullins
In Memory of Stella Hartline
Mr. & Mrs. Robert M. Ragan
Mr. John S. Recanatini
Mr. & Mrs. Brad Reh
Mr. Martin L. Rein
Mr. Kurt Reinsberg
Mr. Peter C. Rekow
Mr. & Mrs. Robert Repke
The Ritter Foundation
Ms. Martha Rodriguez
The Robert and Dale Rosen Charitable Foundation
Mr. & Mrs. Robert Rosenberg
Mr. Donald Santarsiero
Mr. & Mrs. Christopher J. Schaal
In Memory of Stella Hartline
Mr.& Mrs. Brian R. Schlier
Mr. Jonathan Schneider
Mr. Alois Schoenhuber
Mr. & Mrs. Jeff Scrivener
Mr. & Mrs. Michael B. Sebastian
Ms. Elena Seha
Ms. Miriam J. Senft
Mr. & Mrs. Michael Sexton
SFD Enterprises
In Memory of Stella Hartline
Mr. Richard C. Shanks
In Memory of Stella Hartline
Mr. & Mrs. Robert Shea
Ms. Lilian Sicular
In Honor of Barbara Netter
Mr. & Mrs. Anne & Ronald Simon
Mr. & Mrs. Roger N. Simpson
In Memory of Stella Hartline
Mr. & Mrs. John Sites
Mr. Barnet B. Skelton
In Memory of Stella Hartline
Mr. Thomas C. Slaughter
Dr. J. Marvin Smith III
Mr. & Mrs. Thomas W. Smith
Mr. H. William Smith and Ms. Sarah A. Thomas
Mr. & Mrs. Scott A. Sodokoff
Mr. & Mrs. Richard Solomon
Mr. Gary Stanco
Mr. & Mrs. Roy L. Standfest
Ms. Cynthia Stella
Ms. Joann Straglinos
Mr. & Mrs. Keith Strobel
Mr. & Mrs. Thomas A. Strong
In Memory of Stella Hartline
Summus Limited
Sunset Limited Partnership
Mr. & Mrs. C. Winfield Swarr
Mr. James G. Tatum
In Memory of Arthur Netter
Ms. Peggy Tavares
Ms. Pauline Thomas
Dr. & Mrs. Melish A. Thompson
Ms. Alexandra Thompson
Mr. Andrew Thung
Mr. Roy & Dr. Swan Thung
Mr. & Mrs. Bill Todd
In Memory of Stella Hartline
Dr. Deborah Tolchin
Mr. Peter C. Trent
Mr. Haralambos Tsourides
Turtle Creek Sod Farms, LLC.
In Memory of Stella Hartline
Mr. & Mrs. Frederick C. Umstead
Mr. Adam T. Vengrow
Mr. & Mrs. Russell S. Ward
In Memory of Stella Hartline
The Watson Foundation
Mr. Daniel C. Weber
Wegner Associates
Mr. & Mrs. Robert Weisman
Ms. Toby M. Weiss
Westward Communications, LP
Mrs. Joan Whipple
Mr. Stephen F. Wiggins
Mr. & Mrs. Richard J. Williams
Mr. & Mrs. Cecil Wray
Ms. Marion C. Zoch

"In 2004, 563,700 Americans will die of some form of cancer… nearly the same number as in 1950… Long term survival for advanced cancer has barely budged since the 1970's."

– Fortune Magazine
"Why We're Losing the War on Cancer", March 2004





Financial Report

APRIL 30, 2004 and 2003

CONDENSED STATEMENTS OF ACTIVITIES

	2004	2003
Support and revenue:		
Contributions	$ 2,202,377	$ 1,343,709
Contributions for administrative expenses (special designated)	43,600	66,813
Contributions for program support (special designated)	–	8,600
Contributed services	127,760	59,316
Interest and dividend income	26,490	26,822
Realized and unrealized gains on investments, net	196,424	13,584
TOTAL SUPPORT AND REVENUE	**2,596,651**	**1,518,844**
Expenses:		
Program services:		
Research grants and awards	2,239,948	1,125,734
Program support	–	8,600
Supporting services	171,360	126,129
TOTAL EXPENSES	**2,411,308**	**1,260,463**
Increase in total net assets	185,343	258,381
Total net assets at beginning of year	959,380	700,999
TOTAL NET ASSETS AT END OF YEAR	**$ 1,144,723**	**$ 959,380**

CONDENSED STATEMENTS OF FINANCIAL POSITION

	2004	2003
Assets:		
Cash and cash equivalents	$ 1,235,043	$ 1,515,042
Investments, at fair value	2,316,199	320,672
Contributions receivable	9,724	–
TOTAL ASSETS	**3,560,966**	**1,835,714**
Liabilities and net assets:		
Liabilities:		
Grants payable	2,408,808	875,734
Accounts payable and accrued expenses	7,435	600
TOTAL LIABILITIES	**2,416,243**	**876,334**
TOTAL NET ASSETS	**1,144,723**	**959,380**
TOTAL LIABILITIES AND NET ASSETS	**$ 3,560,966**	**$ 1,835,714**

Alliance for Cancer Gene Therapy, Inc.'s complete financial statements, which are audited by KPMG LLP, are available upon request.

ACGT Board of Directors

Edward Netter, *President*
Chairman, Geneve Corporation
Stamford, CT

John Adler
President, Adler Foundation, Inc.
Greenwich, CT

Diane Wassman Darst, Ph.D
Art Historian and Director,
Learning to Look
Greenwich, CT

Edward E. Hartline, Esq.
Managing Partner,
Brown, McCarroll, LLP
Houston, Texas

John L. Lahey, Ph.D
President, Quinnipiac University
Hamden, CT

Eric A. Rothfeld, Esq.
Chairman, REI Capital, LLC
New York, NY

John C. Sites, Jr.
Principal, Daystar Partners
Rye, NY

Swan Thung, M.D.
Director, Liver Pathology Division
Mount Sinai School of Medicine
New York, NY

Peter C. Trent
Private Investor
New York, NY

Senior Staff

Margaret C. Cianci
Executive Director

Allison A. Neslage
Marketing and Communications

Virginia V. Boldt
Development and Strategic Planning

H. William Smith, Esq.
Legal/Secretary

Christine A. Herman
Finance/Treasurer

Barbara Netter
Chairman, Special Events

Founded by
Barbara and Edward Netter

ACGT Scientific Advisory Council

Savio L.C. Woo, Ph.D., *Chairman*
Mt. Sinai School of Medicine,
New York, NY

Stuart A. Aaronson, M.D.
Mt. Sinai School of Medicine,
New York, NY

Xandra O. Breakefield, Ph.D.
Harvard Medical School
Massachusetts General Hospital
Boston, MA

Lieping Chen, M.D., Ph.D.
Johns Hopkins University School
of Medicine, Baltimore, MD

David A. Cheresh, Ph.D.
The Scripps Research Institute,
La Jolla, CA

Stephen L. Eck, M.D., Ph.D.
Pfizer Global Research
and Development,
Ann Arbor, MI

Judah Folkman, M.D.
Children's Hospital
Harvard Medical School
Boston, MA

Joseph C. Glorioso III, Ph.D.
University of Pittsburgh
Pittsburgh, PA

Carl H. June, M.D.
University of Pennsylvania,
Philadelphia, PA

Wen-Hwa Lee, Ph.D.
University of California at Irvine,
Irvine, CA

Michael T. Lotze, M.D.
University of Pittsburgh Medical Center,
Pittsburgh, PA

Robert Martuza, M.D., F.A.C.S
Massachusetts General Hospital
Harvard Medical School,
Boston, MA

Frank McCormick, Ph.D., F.R.S
University of California
at San Francisco
San Francisco, CA

A. Dusty Miller, Ph.D.
Fred Hutchinson Cancer Center,
University of Washington
Seattle, WA

Drew Pardoll M.D., Ph.D.
Sidney Kimmel Cancer Center
Johns Hopkins University School of
Medicine, Baltimore, MD

Erkki Ruoslahti, M.D., Ph.D.
The Burnham Institute,
La Jolla, CA
University of California
at San Diego
San Diego, CA

Thomas J. Wickham, Ph.D.
EMD Lexigen,
Billerica, MA

It is the linear sequence of the letters A (Adenine), C (Cytosine), G (Guanine), and T (Thymine) from top to bottom along one of the two DNA strands that makes up the genetic code of all genes.



ACGT®

ALLIANCE FOR CANCER GENE THERAPY

National grants for cancer research

Ninety six Cummings Point Road
Stamford, Connecticut 06902
203 358.8000
203 348.3103 FAX
acgtfoundation.org