FACES OF CANCER GENE THERAPY

ANNUAL REPORT 2004 - 2005

ALLIANCE FOR CANCER GENE THERAPY
National grants for cancer research
The faces of cancer gene therapy are pioneers in molecular medicine, scientific research, and philanthropic investment – all working together to forge a new future towards innovative treatment and the ultimate eradication of cancer.

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.
An Alliance to Save Lives

ACGT IS THE ONLY PUBLIC CHARITY in the nation dedicated exclusively to investing in research into cancer gene therapies. This is a crucial time. Private funding is essential to bridge the wide and growing gap between limited research expenditures by government and industry, and greater requests for project funding. Of a $4.5 billion budget, the National Institutes of Health (NIH) spends $90 million on cancer gene therapy. Research spending by pharmaceutical and biotechnology companies is largely devoted to drug treatments with demonstrated market potential. Thus, investment in discovery is critically needed.

ACGT investors play a vital role in fostering discovery and moving molecular medicine more rapidly from laboratory to clinical translation, trials and ultimately application. And, in a unique partnership, investors have the opportunity to target their funds to research of the greatest interest – investors select from one of two funds and from a number of important research projects. In this way, ACGT is the catalyst between those who wish to make a commitment to better cancer treatment, and the promise of cancer gene therapies.

• The Fund for Discovery
  $500,000 to YOUNG INVESTIGATORS (tenure track professors) seeking new methods to treat cancer.

Notable contributions to scientific discovery are frequently made in the earliest stages of research; however, funding at this level is most often difficult to secure. ACGT grants encourage talented young researchers to fulfill their aspirations and maintain their commitment to research.

• The Fund for Advancement
  Up to $1,000,000 to SENIOR INVESTIGATORS conducting projects entering clinical translation.

Grants to established projects nourish research further and stimulate more rapid progressions to clinical translation, human trials and medical application.

“Gene research for cancer cures accounts for less than 2.2% of the NIH budget of $4.5 billion spent annually on cancer research. The more private investment in cancer gene therapy research the greater the chance to treat cancer beyond surgery, chemotherapy and/or radiation – the standard treatments of the last thirty plus years.

– JOHN C. SITES, JR., PRINCIPAL, DAYSTAR PARTNERS
MADAME MARIE CURIE’S RELENTLESS search for once hypothetical radioactive substances, under the most horrid conditions, is legendary. Today, radiation is deployed daily in the battle against cancer and we think nothing of its significance in the grander scientific scheme.

“It’s about innovation,” says Edward Netter, co-founder with his wife Barbara, of ACGT. “Science isn’t only about proving hypotheses; science is about discovery. And it is only through discovery that breakthroughs in medicine will be revealed.”

Now in its fifth year, ACGT, the nation’s only public charity dedicated exclusively to funding cancer gene therapy research, has sponsored seventeen research projects that promote discovery as well as progress. “Gene therapy makes sense to me,” says Mr. Netter. “We know cancer is in the genes and we have the knowledge and the technology to alter the diseased genes, or replace them, as the way to at least manage if not eliminate cancer.”

The Netters, and many supporters, have put their heart and soul and significant financial resources behind their faith in molecular medicine. “Who among us has not been touched by cancer? We know the devastation. We know the loss. We cannot continue on the same road when there are potentially extraordinary possibilities,” says Mrs. Netter.

“Have there been failures? Of course,” says Mr. Netter. “But no more than other medical science. Polio vaccine, transplantation, chemotherapy, all medical breakthroughs, have experienced failure along the way. Only through research and yes, failures, will we learn, and ultimately discover the path to success.”

Mr. Netter’s interest in medicine was sparked by his cousin, renowned medical illustrator Dr. Frank Netter, but his predisposition toward business prevailed at the University of Pennsylvania. He evaluates medical research the same way as any enterprise – a solution orientation, collaboration and efficiency. “We seek out the best scientists, make certain they have resources for the best possible research, and then track and monitor their progress. It’s about discovery, of course, but also about building an alliance committed to moving the science forward.”

“Discovery is a major factor in scientific research,” says Dr. Savio Woo, Chairman of ACGT’s Scientific Advisory Council, “but we embark on gene therapy research with a great arsenal of knowledge about the formation of cancers. In the simplest terms, the normal process of cell division is highly regulated in the body – cells pass through a sophisticated quality control sequence. However, if there is damage to the
DNA, the process comes to a halt. Healthy genes, and their proteins, make certain that the integrity of cell division is preserved, and when this does not happen, tumors will result. Gene therapies foster cell activity in a way that deconstructs cancers, with little or no adverse affect on other parts of the body.”

Scientific discovery cannot be equated with either error or with serendipity. It is most often the result of years of serious study, but only if those with curiosity and tenacity have the resources they need to facilitate that moment of invention. This is of particular importance today because reduced funding has forced young scientists to abandon research, exactly at the time when innovation and collaboration are crucial.

2005 has shown promise for the science of gene therapy. The first ACGT Research Fellows presented a range of positive results at this past November Board Meeting. China approved a gene therapy drug based on research conducted in the United States. And, most important, the number of participants in clinical trials grows every day, and the results have been impressive – lives are being saved by cancer gene therapies.

“There are young investigators throughout the country who are well-trained and working in wonderful laboratories, eager to bring forward new theories and ideas. The more we can support early research, the more it will advance the field, and faster,” says Dr. Woo.

“We believe that medical science can do better,” says Mrs. Netter. “Discovery is not only possible, it is imperative.”

EDWARD NETTER, Co-founder, is President of the ACGT Board of Directors and Chairman of Geneve Corporation.

BARBARA NETTER, MS, Co-Founder, is a member of the ACGT Board of Directors, and a Psychotherapist.

SAVIO WOO, PhD, Chairman of the ACGT Scientific Advisory Council, is Professor and Chairman of the Department of Gene and Cell Medicine, Mount Sinai School of Medicine.
There are about 1.6 million Americans stricken with cancer each year; half of them will die of their cancer, which says there is a substantial need for new therapies. Of all the therapies we have, perhaps the one that has the greatest promise is gene therapy because, in effect, we simply smooth the exit for cancer cells and show them the door.

– MICHAEL T. LOTZE, MD, DIRECTOR, CLINICAL AND TRANSLATIONAL RESEARCH AT THE MOLECULAR MEDICINE INSTITUTE, UNIVERSITY OF PITTSBURGH MEDICAL CENTER

“By 2010, 15 million Americans will have cancer in one form or another and in one stage or another. While 5-year survival rates have improved overall, many of those who survive continue their battle with cancer.

Surgery is an option in only one out of twenty cancers.
Radiation depends on location.
Chemotherapy attacks the entire body to treat the cancer, and the treatment may be as debilitating as the disease.

We know now that all cancer is the result of a biological misfire that takes place in the genes. Normal cells know when to stop growing and when it is time to die, but cancer cells do not – the result is a tumor. Every tumor has a blueprint that molecular medicine seeks to identify so that it can be altered or destroyed, without damage to the healthy cells of the body.

Cancer gene therapy is actually several possible therapies:

• Genes that are delivered directly to the tumor and facilitate cancer cell death.

• Medications that boost the immune system to recognize and reject cancers (Immunotherapy).

• Injection of healthy genes that act as a catalyst for the body to re-regulate itself.

• Chemical inhibitors that strangulate cancer cells by cutting off their blood supply (Anti-angiogenesis).

• An inoculation that will ultimately prevent cancer.

The challenge ahead is to refine the agents that will be used to attack the cancer, and perfect delivery systems so that only the cancer gene is impacted by the treatment. Gene therapy will first be utilized as an adjunct to current treatments, and, once perfected, as the treatment of choice, until the disease is controlled or eradicated.
“It’s because of gene therapy that I’m alive.”

– EILEEN FRANGIOSA

Over 3,000 patients worldwide have participated in gene therapy trials, of which two-thirds were for cancer, and over 600 clinical protocols are currently awaiting NIH/FDA approval and funding.

Saving Lives

Eileen Frangiosa: Six Years Later

EILEEN FRANGIOSA MIGHT HAVE stepped out of a billboard for Pennsylvania farm country – freckles line her nose on a fresh face lit by a bright smile. She greets visitors with hot hoagies and homemade apple pie. She seems younger than her 49 years and hardly the mother of four strapping grown sons and one grand-daughter. You would also never imagine that in 1998 she was diagnosed with glioma, a deadly form of brain cancer.

“It’s because of gene therapy that I’m alive,” she said recently. She participated in a gene therapy trial at the University of Pennsylvania in August 1999. “No one thought I had much of a chance. They started with regular treatments – first I had radiosurgery, then chemotherapy. I had an allergic reaction to the drugs. Then came the radiation. Within six months the tumor was back.”

A science teacher at her neighborhood school helped to research options. “He got me interested in gene therapy. I went into it thinking this isn’t a cure, it’s a fix, like insulin, for a while, but the more I learned about it, the more it made sense to me. It was amazing – gene therapy has given me six years of healthy living, more than I ever expected.”

Eileen participated in a trial utilizing an adenovirus vector injected directly into the tumor, to produce a protein to destroy cancer cells. A week later the tumor was removed. “That was it. No side effects, none, and I felt great. Three months later, when the swelling was down, I saw the images of the injection site; looked kind of like lollipops, but no cancer. The only side effect was from the steroids for the residual swelling. Now I am checked every six months, that’s all. I would choose gene therapy again, it’s truly amazing.”

Lung cancer patients treated with a gene therapy drug at the University of Texas M. D. Anderson Cancer Center in 1997 are alive and well. In 20 clinical studies using the drug on eight different types of cancer, there were minimal side effects.

Researchers at Columbia University Medical Center are incorporating gene therapy into a virus that has eradicated prostate cancer cells in the lab and in animals, leaving normal cells unscathed.
At the November 2005 ACGT Board Meeting, the first three grant recipients presented the findings of their research—all investigating different approaches and all making important discoveries on their path to the fulfillment of the promise of gene therapy.

PROSTATE CANCER IS THE SECOND leading cause of cancer in males over age fifty, and accounts for 30,000 cancer deaths annually. This cancer is particularly amenable to gene therapies as there is currently no cure, the tumor is accessible, and there are a variety of DNA-specific proteins involved. Dr. Griffith, in pre-clinical studies, demonstrated the safety of large systemic doses of TRAIL, a TNF (tumor necrosis factor) related agent that has generated great excitement because of its unique ability to induce apoptosis (cell death) in a wide range of tumor cells, but not in normal cells or tissues. However, the drawback has been that large amounts of TRAIL were required to inhibit tumor formation, since most of the protein was cleared from circulation shortly after injection.

“The development of an alternative means of delivery may increase the relative activity of TRAIL such that larger, more established tumors might be eradicated as efficiently as the smaller. Previous data from my laboratory described the transfer of a recombinant replication-deficient adenoviral vector encoding the human TRAIL gene (Ad5) into human tumor cells in vitro, that led to the rapid production and expression of the TRAIL protein resulting in apoptotic death of tumor cells. Based on this, ACGT funding made it possible to further examine the potential to utilize this gene therapy for prostate cancers. The research has yielded a profound effect! We have produced a clinical-grade vector that facilitates cancer cell suicide. We have also been able to learn how to combine this treatment with other compounds to enhance the effect. And we have received FDA approval to move forward to human clinical trials.”

Dr. Griffith has published findings twice during the three-year research project, and has generated additional funding from NCI, the Department of Defense Prostate Cancer Research Program, and the University of Iowa Holden Comprehensive Translational Project Development and Clinical Trials grant program.
DURING THE PAST DECADE, much attention has been given to the identification of agents that may be useful for the treatment of cancer by inhibiting the formation of new blood vessels – a process known as anti-angiogenesis – which can literally starve a tumor to death. Dr. Davidoff’s research focused on neuroblastoma, which accounts for ten percent of childhood cancers and is the most common malignancy in kids less than a year old. Previous research indicated that there are shared blood vessels common to this cancer, and that neuroblastoma is an easily distinguishable and stable target, unlike other tumor cells that rapidly mutate. In addition, earlier research indicated that a particular gene called pigment epithelium derived factor (PEDF) delivered to the liver has the potential to inhibit angiogenesis and restrict the growth of neuroblastoma.

“Based on this encouraging early data, we expanded our studies to evaluate the interactions of various inhibitors of blood vessel formation both among this class of anti-cancer agents and among the various drugs already used. During this three-year period, we made the exciting observation that AAV (adeno-associated virus) mediated delivery of PEDF combined with Interferon and used with conventional chemotherapy is extremely effective, with an almost total repression of tumors. In fact, we shifted our focus from PEDF to Interferon, which had been previously disappointing because of toxicity – the research suggests that gene therapy utilizing Interferon in a sustained low dose produces anti-angiogenesis.”

Dr. Davidoff’s research indicates broad applicability and efficacy in a variety of solid tumor models, including neuroblastoma, melanoma, renal cell carcinoma, brain and retina tumors. Multiple publications were made possible by the funding, and the next step is further research into Interferon-beta biology.

15,000 WOMEN WILL DIE this year of ovarian cancer, an especially lethal disease because it is difficult to detect. In previous research, Dr. Bartlett’s team was able to rearrange the structure of AAV, a common human virus used as a vector to deliver gene therapies aimed at ovarian cancer cells by changing the sequence of the protein that comprises the virus shell. This allows the vector to infect only cells that display a particular tumor-associated marker. Vector targeted gene therapies have the potential to distinguish tumor cells from normal cells; however, in the past, the available vectors delivered genes to both normal and cancer cells. The goal of this research was to improve the effectiveness and selectivity of gene delivery to tumors by targeting unique markers on tumor cells. “Like a child’s game where the round peg must match the round hole.”

The results were both impressive and promising: 70% of mice were cured of tumors when treated with these modified vectors. “We’ve been able to leverage this research into almost two dozen new flavors of the virus in our attempts to kill cancers. And now we can get genes into all forms of ovarian tumors, and have developed a far more efficient way to engineer the molecular composition of the cells.”

The issues ahead for Dr. Bartlett are dose and duration, and an examination of the best combination of therapies to move into the clinic. “Others in the lab were also helped by this funding – not only to publish and develop research projects, but in optimism that we can do this.”
THE GRANT AWARD PROCESS is rigorous – all grant applications must evidence scientific and technical merit. Each grant is subject to peer review and final review by the ACGT Scientific Advisory Council. Only those proposals meeting stringent criteria are recommended for funding to the ACGT Board of Directors.
2004 YOUNG INVESTIGATORS

MUKEK K. JAIN, MD
Assistant Professor at Harvard Medical School and Director of the Cardiovascular Transcriptional Biology Program at Brigham and Women’s Hospital.

Treatment for cancer known as anti-angiogenesis.

SUZIE PUN, PhD
Assistant Professor at the University of Washington.

Treatment of tumors using a targeted non-viral mode of delivery.

DR. PUN’S AWARD IS IN HONOR of Patricia Zoch Tate who succumbed to pancreatic cancer in 2005. The study will research treatment of tumors using a targeted non-viral mode of delivery. “Tumors exist as dense masses in the body. The physical structure of these solid tumors presents a formidable challenge to drug delivery vehicles that need to penetrate and reach all cancer cells in order to be optimally effective. The goal of this research is to develop synthetic nanoparticles that efficiently penetrate solid tumors. I am convinced that the efficacy of gene therapy can be substantially improved by designing delivery systems that overcome physical barriers.”

CHIEN-FU HUNG, PhD
Assistant Professor at Johns Hopkins University.

Treatment for ovarian cancer utilizing immunotherapy.

JIAN YU, PhD
Assistant Professor at University of Pittsburgh’s School of Medicine.

Treatment for lung cancer.

“LUNG CANCER REMAINS one of the greatest public health threats, despite advancement in the understanding of molecular genetics. We have been accumulating preliminary data and developing reagents for this project for the past two years, and we are encouraged by the early results of using PUMA, a protein, as a novel target to selectively encourage apoptosis, cell death, in lung cancer cells. With this funding, we will be able to expand the research into animal model trials, and it is our hope that these efforts will allow us to examine the feasibility of moving PUMA gene therapy towards clinical trials.”

OVARIAN CANCER ACCOUNTS for approximately 25% of gynecological cancers in women, but over 50% of deaths. Current treatments rarely result in long-term cure. “This study will focus on an approach taken by gene therapy known as immunotherapy. Cancer cells are not recognized by the body’s immune system because they are not foreign, rather mutations of existing cells. The intent of immunotherapy is to induce the individual’s immune system to recognize cancer cells as if they are foreign, and thus a threat, so that these cells are destroyed.”
"THE CANCER CELLS OF PATIENTS with CLL are stealth-like in their ability to evade immune detection. Cross-linking a protein, CD40, on the leukemia-cell can change the tumor into cells that stimulate the immune system. In previous research, we observed biologic and clinical activity without dose-limiting toxicity. We propose to generate sufficient quantities for the research to administer direct injection into enlarged lymph nodes of patients with NHL/CLL. This can be achieved using a modified cold virus to insert a gene that transforms the ligand. With this grant, we can perform a dose-escalation study testing the safety of injecting the virus directly into the lymph nodes of leukemia patients and monitor the clinical and biologic responses to therapy."

"PRE-CLINICAL MODELS HAVE demonstrated unequivocal progress in generating increasingly potent vaccine strategies that creatively exploit new pathways governing immune regulation. A major limitation to an approved vaccine has been that most have been studied as single agents in heavily pre-treated patients harboring advanced tumor burdens. Although the safety profile has been found to be remarkably favorable, there is growing consensus that for cancer vaccines to have a clinically meaningful impact, the paradigm must change. Our group seeks to move cancer vaccines into clinical settings that meet several criteria: 1) currently available therapies can reduce the bulk of the cancer without suppressing the host immune system; 2) such therapies themselves create a favorable setting for active immunization; 3) sensitive markers of disease burden exist to give a rapid readout of disease response; and 4) immune responses can be quantified to enable the correlation of vaccine effects with changes in tumor burden. In this proposal, the immuno-gene therapy of MDS represents an opportunity that these criteria, maximizing the probability that a clinically meaningful impact may be observed."

"TUMOR-SPECIFIC T CELL TOLERANCE is one of the major barriers in cancer immunotherapy. Provision of toll-like receptors (TLR) signals significantly enhances the efficacy of tumor vaccines in treating pre-establish murine lymphoma, suggesting an essential role of TLR signals in cancer immunotherapy. The goal of the study is to determine the relationship between TLR signals, regulatory T cells, and tumor specific immunity in vivo, and explore the rational vaccine strategies in the context of murine tumor models as well as human Hodgkin’s lymphoma."
In the first four grant cycles, ACGT awarded $10.7 million to support 17 core research projects into technology innovation and clinical validation and translation for cancer gene therapies. Up to $500,000 was awarded to each of 12 tenure track professors conducting independent innovative research. Up to $1,000,000 was awarded to each of 5 established researchers conducting groundbreaking research entering clinical translation. Projects are three to five years in duration.

ACGT Research Fellows 2002 – 2005

2005 Research Fellows

THOMAS J. KIPPS, MD, PhD
University of California, San Diego
Lymphoma/Leukemia
Immune-Mediated Gene Therapy

HYAM I. LEVITSKY, MD
Johns Hopkins University
Lymphoma/Leukemia
Immune-Mediated Gene Therapy

YIPING YANG, MD, PhD
Duke University
Lymphoma/Leukemia
Immunotherapy

2004 Research Fellows

CHIEN-FU HUNG, PhD
Johns Hopkins University
Ovarian Cancer
Immunotherapy

MUKESH JAIN, MD
Brigham & Women’s Hospital
Tumor Treatment
Anti-Angiogenesis

CARL H. JUNE, MD
University of Pennsylvania
Lymphoma/Leukemia
Immune-Mediated Gene Therapy

SUZIE PUN, PhD
University of Washington
Tumor Treatment
Targeted Non-Viral Delivery
RECIPIENT OF THE PATRICIA ZOCH TATE GENE THERAPY AWARD

MICHEL SADELAIN, MD, PhD
Memorial Sloan Kettering Cancer Center
Lymphoma/Leukemia
Immune-Mediated Gene Therapy

JIAN YU, PhD
University of Pittsburgh
Lung Cancer
Oncogenesis

2003 Research Fellows

LAURENCE COOPER, MD, PhD
The University of Texas
MD Anderson Cancer Center
Leukemia
Immune-Mediated Gene Therapy

TIMOTHY LANE, PhD
University of California, Los Angeles
Breast Cancer
Anti-Angiogenesis
RECIPIENT OF THE KIMBERLY LAWRENCE NETTER GENE THERAPY BREAST CANCER AWARD

RICHARD REILLY, PhD
Johns Hopkins University
Breast Cancer
Immune-Mediated Gene Therapy

KATHERINE RYMAN, PhD
Louisiana State University
Prostate Cancer
Tumor Specific Replicating Viruses

ROBERT VONDERHEIDE, MD, PhD
University of Pennsylvania
Neuroblastoma
Immune-Mediated Gene Therapy

2002 Research Fellows

JEFFREY S. BARTLETT, PhD
Children’s Research Institute
Ovarian Cancer
Vector Development

ANDREW M. DAVIDOFF, MD
St. Jude Children’s Research Hospital
Neuroblastoma Anti-Angiogenesis

THOMAS S. GRIFFITH, PhD
University of Iowa
Prostate Cancer
Immune-Mediated Gene Therapy

ACGT Funded Research To-Date: $10.7 million

17 PROJECTS:
Immunotherapy – 10
Anti-angiogenesis – 4
Delivery Systems – 3

AREAS OF RESEARCH:
Breast Cancer, Lung Cancer, Ovarian Cancer, Prostate Cancer, Lymphoma/Leukemia, Neuroblastoma, Non-specific Tumors.
ACGT IS THE ONLY FOUNDATION in America dedicated exclusively to investment in cancer gene therapy research, and operates in a unique fashion to serve both the science and the investor.

A Scientific Advisory Council, composed of 17 prestigious physicians and researchers in the field, establish criteria for research and thoroughly review grant proposals to recommend to the Board of Directors only the most promising projects for funding.

Funding in support of innovation and translation facilitates research for both discovery and application.

Projects of up to five years in duration help Research Fellows to focus more time on research rather than fundraising.

Projects are capitalized at unusually high award levels to facilitate meaningful results.

Regular research reports ensure that funds are directed towards specific goals, and that methods meet the standards established in the grant.

Research findings are shared with the scientific community at professional meetings and by publication in scientific journals to encourage collaboration.

A unique royalties arrangement ensures that any financial return from ACGT sponsored research will be reinvested by ACGT to support future research into cancer gene therapy.

Investors may designate a specific area of interest for funding – ACGT will identify the most promising research for investment.

Investors may choose to fund early research through the Fund for Discovery, or research focused on clinical translation through the Fund for Advancement.

Investors are kept informed on progress and may attend presentations of findings.

ACGT is a public charity so contributions qualify for income tax benefits.

100% of funds raised go directly to research, as separate funding has been established to cover all administrative and fundraising costs.

ACGT seeks funding from individuals, corporations and foundations who share our commitment to discovery and to the promise of cancer gene therapy.

"There are young investigators throughout the country who are well trained and working in wonderful laboratories, eager to bring forward new theories and ideas. The more we can support early research, the more it will advance the field, and faster."

– DR. SAVIO WOO, PROFESSOR AND CHAIRMAN OF THE DEPARTMENT OF GENE AND CELL MEDICINE, MOUNT SINAI SCHOOL OF MEDICINE
AT THIS TIME, ACGT HAS RECEIVED APPLICATIONS FROM 96 OF THE COUNTRY’S MOST PRESTIGIOUS UNIVERSITIES, RESEARCH INSTITUTIONS AND HOSPITALS THAT CONDUCT RESEARCH INTO CANCER GENE THERAPIES:

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, Boston
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
Duke University School of Medicine
Eastern Virginia Medical School
Fred Hutchinson Cancer Research Center
Georgetown University Medical Center
H. Lee Moffitt Cancer Center
Henry Ford Health System
Indiana University School of Medicine
Jackson Laboratory
Johns Hopkins University School of Medicine
Kansas University Medical Center Research Institute
Keck School of Medicine at University of Southern California
La Jolla Institute for Allergy & Immunology
Louisiana State Health & Sciences Center
Lovelace Respiratory Research Institute
Marshall University Research Corporation
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
Pennsylvania State University
Pritzker School of Medicine at the University of Chicago
Rockefeller University
Roger Williams Hospital
Roswell Park Cancer Center
Rutgers, The State University of New Jersey
Saint Louis University Medical Center
Salk Institute for Biological Studies
Southern Methodist University
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
The University of North Carolina at Chapel Hill
Thomas Jefferson University, Kimmel Cancer Center
Torrey Pines Institute for Molecular Studies
Tulane University
UMDNJ - Robert Wood Johnson Medical School
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 Chicago
University of Florida, Gainesville 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 Minnesota - Twin Cities
University of Missouri - Columbia
University of North Carolina at Chapel Hill
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 Southern California
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

“Imagination is more important than knowledge. For knowledge is limited to all we now know and understand, while imagination embraces the entire world, and all there ever will be to know and understand.”

- Albert Einstein
• Scientific Advisory Council member **Dr. Michael Lotze**, University of Pittsburgh, presents a fascinating program on advancements in molecular medicine, genetic mapping, and the potential for gene therapies.

• **Dr. Michel Sadelain**, Memorial Sloan Kettering Cancer Center, an ACGT Research Fellow, presents a program on the recognition of tumor antigens and T-cell malfunction in cancer patients.

• **Dr. Carl June**, University of Pennsylvania, an ACGT Research Fellow, speaks to friends of ACGT on progress in gene therapy for leukemia and lymphoma.

• ACGT staff attends the American Society of Gene Therapy (ASGT) 8th annual conference in St. Louis. ASGT is the largest medical professional organization in the world representing researchers and scientists dedicated to discovering new gene therapies.

• ACGT Director of Development and Strategic Planning, **Virginia Boldt**, joins ASGT Committee for Public Education to promote greater awareness of gene therapies.

• **Dr. Stephen Eck**, Vice President Molecular Medicine, Pfizer Global Research and Development, and member of the ACGT Scientific Advisory Council, explains the science behind gene therapy and the opportunities for cancer treatment.

• Harvard Business School team joins forces with ACGT to help develop long-term investment and planning strategies.
● Three new board members installed:

Daniel Cummings, Managing Director, Carlyle Group, Washington DC.

Barbara Netter, MS, Psychotherapist, Co-Founder of ACGT.

Jeffrey Keil, Chairman, International Real Returns LLC.

● Scientific Advisory Council adds five new members:

Xandra O. Breakefield, PhD, Professor of Neurology at Harvard Medical School and Geneticist of the Neurology and Radiology Services at Massachusetts General Hospital.

Stephen L. Eck, MD, PhD, Vice-President, Molecular Medicine, Pfizer Global Research and Development.

Joseph C. Glorioso, III, PhD, Chairman of the Department of Molecular Genetics and Biochemistry at University of Pittsburgh’s School of Medicine.

Carl June, MD, Director of Translational Research, Abramson Cancer Center at University of Pennsylvania.

A. “Dusty” Miller, PhD, Professor of Pathology at University of Washington.

● 2002 Research Fellows present their findings at ACGT’s November 2005 Board meeting.

● ACGT Executive Director, Margaret C. Cianci, discussed findings from the first round of research awards at the November 2005 Board meeting.

● Board of Directors approves four Young Investigator Awards for gene therapy research on anti-angiogenesis, lung cancer, ovarian cancer and non-viral delivery systems.

John Sites, John Adler and Ned Hartline at the November 2005 Board meeting.

Barbara and Edward Netter, with Research Fellows Jeffrey Bartlett, Andrew Davidoff, and Thomas Griffith.

● Board of Directors approves three Senior Investigator Awards into gene therapy research on immune-mediated therapies for lymphoma and leukemia.
ACGT is in the right place at the right time. The tools available to today’s great creative and motivated scientists are unprecedented. ACGT provides the other ingredients, substantial financial resources, in a fraction of the time required by the great public institutions, research universities or even pharmaceutical companies. With cancer, time is of the essence. ACGT is focused and fast.

– JEFFREY C. KEIL, CHAIRMAN, INTERNATIONAL REAL RETURNS LLC

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 SOMEDAY A CURE.

Donors Who Believe that Medical Science Can Do Better

The Adler Foundation, Inc.
Mr. & Mrs. George Akshar
Ms. Aracelis Alonso
Mr. & Mrs. Antonio Alvarez II
In Memory of Gail Paonessa
Ms. Belinda Amsterdam
Mr. & Mrs. Roy Anderes
Mr. Steven C. Annus
In Memory of Ingeborg Annus
Ms. Catherine Arkins
Mr. & Mrs. John Arkins
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Mr. & Mrs. Ira Birnbaum
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Mr. Andrew M. Blum
Mr. & Mrs. Myron Blumenfeld
Dr. & Mrs. Joseph Boldt
Mr. & Mrs. Harry Bower
Mr. & Mrs. Daniel J. Brereton
Mr. & Mrs. Fred Brooks
Mr. & Mrs. Brett Brown
Ms. Margaret Brylinski
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### CONDENSED STATEMENTS OF ACTIVITIES

<table>
<thead>
<tr>
<th></th>
<th>2005</th>
<th>2004</th>
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</thead>
<tbody>
<tr>
<td><strong>Support and revenue:</strong></td>
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<tr>
<td>Contributions</td>
<td>$3,334,719</td>
<td>$2,202,377</td>
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<tr>
<td>Contributions for admin.</td>
<td>47,000</td>
<td>43,600</td>
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<tr>
<td>expenses (specially</td>
<td>145,864</td>
<td>127,760</td>
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<tr>
<td>designated)</td>
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<tr>
<td>Interest and dividend</td>
<td>47,006</td>
<td>26,490</td>
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<td>income</td>
<td>196,142</td>
<td>196,424</td>
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<td>**TOTAL SUPPORT AND</td>
<td>3,770,731</td>
<td>2,596,651</td>
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<tr>
<td>REVENUE</td>
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<td></td>
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<tr>
<td><strong>Expenses:</strong></td>
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<td></td>
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<tr>
<td>Program services:</td>
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<tr>
<td>Research grants and</td>
<td>3,425,510</td>
<td>2,272,515</td>
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<tr>
<td>awards</td>
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<td>Supporting services</td>
<td>148,439</td>
<td>138,793</td>
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<td><strong>TOTAL EXPENSES</strong></td>
<td>3,573,949</td>
<td>2,411,308</td>
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<td>Increase in total net</td>
<td>196,782</td>
<td>185,343</td>
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<tr>
<td>assets at beginning of</td>
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<td>year</td>
<td>1,144,723</td>
<td>959,380</td>
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<td>**TOTAL NET ASSETS AT</td>
<td>$1,341,505</td>
<td>$1,144,723</td>
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<td>END OF YEAR</td>
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### CONDENSED STATEMENTS OF FINANCIAL POSITION

<table>
<thead>
<tr>
<th></th>
<th>2005</th>
<th>2004</th>
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</thead>
<tbody>
<tr>
<td><strong>Assets:</strong></td>
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<tr>
<td>Cash and cash equivalents</td>
<td>$1,196,688</td>
<td>$1,235,043</td>
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<td>Investments, at fair</td>
<td>2,515,608</td>
<td>2,316,199</td>
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<td>value</td>
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<td>Contributions receivable</td>
<td>1,507,304</td>
<td>9,724</td>
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<td><strong>TOTAL ASSETS</strong></td>
<td>5,219,600</td>
<td>3,560,966</td>
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<tr>
<td>**Liabilities and net</td>
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<tr>
<td>assets:**</td>
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<tr>
<td><strong>Liabilities:</strong></td>
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<td>Grants payable</td>
<td>3,877,495</td>
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<td>Accounts payable and</td>
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<td>7,435</td>
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<td>accrued expenses</td>
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<td><strong>TOTAL LIABILITIES</strong></td>
<td>3,878,095</td>
<td>2,416,243</td>
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<td><strong>TOTAL NET ASSETS</strong></td>
<td>1,341,505</td>
<td>1,144,723</td>
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<tr>
<td>**LIABILITIES AND NET</td>
<td>$5,219,600</td>
<td>$3,560,966</td>
</tr>
<tr>
<td>ASSETS**</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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