SPRING 2011

ACGT® Sequence

THE NEWSLETTER OF THE ALLIANCE FOR CANCER GENE THERAPY

In Memoriam Edward Netter

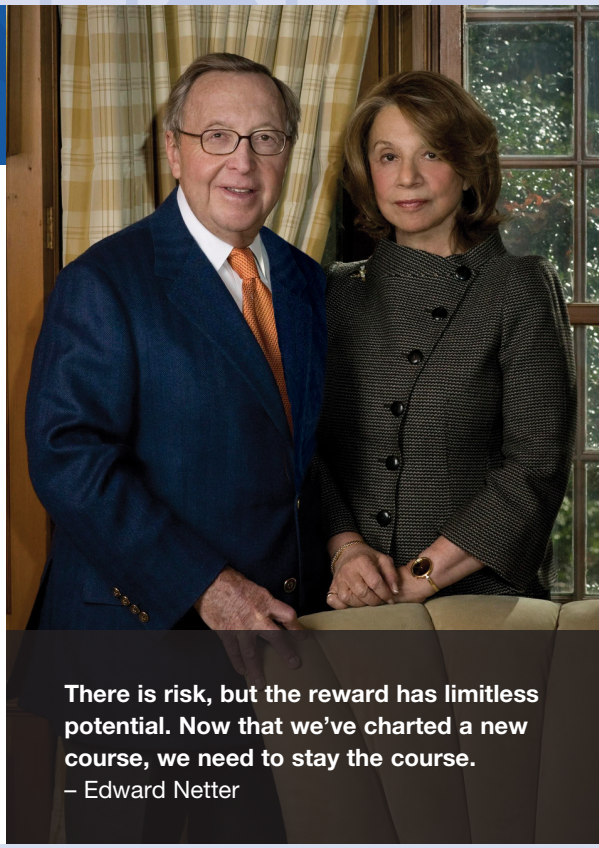
Entrepreneur, Educator, Philanthropist, Friend

Our co-founder and dear friend passed away peacefully on February 16th at his home in Greenwich, CT with his wife of 56 years, Barbara, and his son and daughter and grand-daughters close by. His colleagues and many friends paid tribute to his remarkable life at a memorial service in New York City one week later.

Edward was known for his vision, tenacity, superlative intellect, a desire to make a positive difference in the world, and the willingness to commit his considerable energy and resources to the endeavors he believed in, most notably Alliance for Cancer Gene Therapy, which he and Barbara founded in 2001. He leaves a legacy of leadership, integrity, a commitment to the education of others, and innovative approaches to the discovery of new solutions to the most difficult challenges. He also leaves a legacy of hope and inspiration among those seeking a new paradigm for cancer care.

In remarks made in 2007 in the ACGT annual report, Edward summed up his message and his commitment: *"Like all business enterprises, there are disappointments, and like all scientific methods, there are constant challenges to get it right. There is risk, but the reward has limitless potential. Now that we've charted a new course, we need to stay the course."*

Rest in peace, Edward.



There is risk, but the reward has limitless potential. Now that we've charted a new course, we need to stay the course.
– Edward Netter

Save the date

April 19, 2012

Alliance for Cancer Gene Therapy

Tenth Anniversary Scientific Symposium & Dinner Honoring Edward Netter

THE MISSION OF ACGT
is to support the extraordinary potential offered by cell and gene-based therapies to accelerate effective and safe treatment of all types of cancer.

A message from Barbara Netter

To all of you who have journeyed with us in the last ten years, a special thank you for your support and belief in the vision of ACGT. Edward has ascended to a different sphere, having been taken from us; however, he left us with a vision of a world devoid of harsh treatment and painful suffering. In 2001, after the death of our daughter-in-law Kim Netter, Dr. Savio Woo and Dr. Michael Lotze placed in us the seeds of the possibility of gene therapy and its potential. Ed and I were enormously enthusiastic about putting our energies and resources into this meaningful work. Ed, with his ability to make things happen in an innovative way, took the science and coupled it with the principles of sound business practice.

Ed was a special person, a visionary, an innovative thinker with many passions, and mentored all of us while inspiring us and enlightening us to new ideas. We shall miss him, but perhaps he has lit the way for us. We shall carry on.

We are most proud of our Scientific Advisory Council, of the fact that there are the 17 clinical trials, and the quality of the research we support. We shall continue with even more verve in honor of our leader and co-founder, Ed Netter

As was said in regard to Ed: *"We shall not say goodbye, we shall look for him in others and perhaps if we are lucky we shall meet again."*

Many thanks for your support and working with us to achieve our goals.

Gene Science In The News

Federal Agency Set to Accelerate Research into Alternative Treatments for Cancer

In response to a report by the National Cancer Institute on the rising costs of cancer care, the federal government may establish a new agency to accelerate discovery of alternative treatments. Members of the ACGT Scientific Advisory Council and Board plan to meet with representatives of the initiative to facilitate a public-private dialogue to catalyze progress.

The NCI report suggests that the annual costs of cancer care in the next decade may exceed $200 billion versus $125 billion last year. At the heart of the increase is an aging population, which alone will push the price up to roughly $158 billion by 2020, according to Angele Mariotto, chief of data modeling at NCI's Surveillance Research Program in Maryland. Costs are compounded by advances in technology as well as greater longevity – multiple treatments and lengthy periods of care are costly, especially for breast and prostate cancer patients who have better survival rates.

"It's going to be important in the future to manage the costs of treatments and diagnostic technologies, but it will also be important to further advance the science of cancer prevention and treatment," Mariotto said in a recent interview with Bloomberg.

> **"I am a little frustrated to see how many of the discoveries that do look as though they have therapeutic implications are waiting for the pharmaceutical industry to follow through with them."**
>
> – Dr. Francis Collins, NIH Director, *The New York Times,* January 2011

Two weeks before the report, NCI Director, Harold Varmus expressed concern about the Institute's funding outlook, bracing for flat funding levels at best. In response, the Obama administration has also expressed concern about the slowing pace of new drugs coming out of the pharmaceutical industry and has proposed a federal funding incentive of one billion dollars. The confluence of concerns has resulted in the establishment of a National Center for Advancing Translational Science. The initiative is in the hands of Dr. Francis S. Collins, Director of the National Institutes of Health. Dr. Collins once directed the NIH Human Genome Project and is a proponent of gene sequencing as the foundation for new treatments. Rather than wait out the pharmaceutical companies, he hopes that the new Center will jumpstart the process, with a proposed start date of October 2011, contingent on Congressional approval.

Yale Turns Up the Heat on Genomic Medicine



ACGT Scientific Advisory Council member Lieping Chen, MD, PhD, has been named Director of Cancer Immunology at the Yale Cancer Center in New Haven, Connecticut. Dr. Chen is the world's leading investigator in the identification and characterization of cell surface signaling molecules that modulate immune responses. Center Director Dr. Thomas Lynch, Jr. said that Chen's appointment will ensure that Yale continues as a leader in cancer immunobiology. "His commitment to translating basic discoveries from the lab to develop new strategies to treat cancer using novel biologics in clinical trials will benefit patients at Smilow Cancer Hospital and throughout the world."

Prior to his appointment, Dr. Chen was Professor of Oncology and Dermatology, Director of Research for the Department of Dermatology, and Investigator in the Immunobiology Program at Johns Hopkins University School of Medicine in Baltimore, MD. He received his Medical Degree from Fujian Medical College in China and also completed his internship and residency training in medicine in China. Following completion of his PhD at Drexel University in Philadelphia, Dr. Chen served a postdoctoral fellowship at University of Washington-Seattle. He spent seven years in oncology research and development at the Bristol-Myers Squibb Pharmaceutical Research Institute in Seattle, WA and six years in research and education at the Mayo Clinic in Rochester, MN. Dr. Chen is the author of more than 250 published works.

In Tribute
Edward Netter

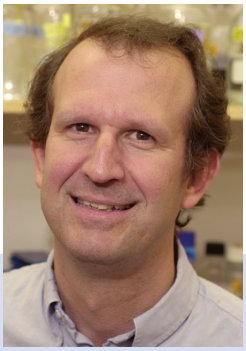
"'There is a wholeness about the person who can give himself away, who can give his time, his money, his strength to others, and not feel diminished.' I admired his wholeness."

– Donald Netter

"Edward was an innovative thinker, whose thoughts were not confined by tradition. We scientists love to think outside-the-box, as otherwise it would have been just some old recycled ideas that would not lead to any real break-through. In talking to Edward however, I often felt like I was the box!"

– Savio Woo, PhD, Chair, ACGT Scientific Advisory Council Mount Sinai School of Medicine

2010 Investigators Announced



Dr. Glenn Dranoff
2010 ACGT Investigator

Focus: Delivery Systems
Therapy: Immunotherapy

Associate Professor of Medicine, Dana Farber Cancer Institute, Brookline, MA

"Funding for manufacture of clinical grade materials for gene therapy trials is extremely limited and difficult to come by. That is what makes this grant from the Alliance especially invaluable, as this support will allow the translation of laboratory ideas into trials."

We welcome Dr. Dranoff as an ACGT Research Fellow and look forward to the results of his translational research, which is based on original lab research also at Dana-Farber Cancer Institute. The focus of this study is the engineering of a cancer cell vaccine that will sensitize the body's natural immune system.

Although vaccines are a promising approach to increase immune responses and potentially improve patient survival, it has been demonstrated in early research that cancer vaccines also appear to have a built-in circuit that limits their potency. An important component of this circuit is a protein called milk fat globule-E8 (MFG-E8). In mouse models, the blockade of this protein function results in a stronger vaccine response and increased tumor destruction. On-going studies of blood samples from humans similarly show that blockade of MFG-E8 can enhance immune responses in model



Dr. Thomas Kipps
2005 & 2010 ACGT Investigator

Focus: Leukemia/Lymphoma
Therapy: Immunotherapy

2011 Swim Across America Grant Designate; Professor of Medicine, Division of Hematology/Oncology Deputy Director of Research, Moores UCSD Cancer Center, University of California, San Diego, CA

"The field has evolved. And there is now renewed interest. There is a tremendous amount of new work that's going on to find the effective targets for gene therapy, and also the delivery vehicles. We're seeing some very encouraging results right now that are being translated into clinical trials."

Dr. Kipps was awarded a 2005 Investigator grant for a Phase I trial to test the safety and efficacy of immune-mediated gene therapy for intractable B Cell Leukemia. We are proud to support a second round of study to further determine the impact of the treatment, before it goes into a full-scale human trial.

Chronic lymphocytic leukemia (CLL), the most common form of the disease in adults in Western societies, is considered incurable. 10-20% of newly diagnosed patients and more than 50% of relapsed patients have limited or no response to treatment, which leads to a poor prognosis for survival. Most of these therapy resistant CLL-patients are frequently associated with dysfunctional p53 due to deletions in the short arm of chromosome 17. Therapeutic options for these patients usually involve high-risk immunosuppressive treatments, which further reduces their lifespan. A new alternative [CD154] has the potential to sensitize leukemia cells to cell death [apoptosis.] Preliminary research findings have been corroborated in vitro and in vivo on patients treated under the phase 1b protocol and the first patients who have completed the proposed treatment course achieved a complete response. This strategy will test the hypotheses in the context of a gene

"Edward Netter, that gentle man, will live on through his sometimes modest and sometimes monumental good deeds."

– Jeffrey Keil, ACGT Board Member
Chair International Real Returns, LLC

"He has made such a contribution in the areas of research and philanthropy over his lifetime. His vision and generosity will not be forgotten and we all mourn his loss."

– Clodagh O'Shea, PhD, Salk Institute for Biological Studies

"We salute him for his wisdom and vision."

– Khalid Shah, PhD,
Harvard Medical School,
Massachusetts General Hospital

systems. The approach involves taking a patient's own tumors and mixing these with engineered cell lines for re-introduction to the immune system. Dr. Dranoff now proposes to build on these results through the manufacture of clinical grade cellular products that will allow testing of this novel vaccination strategy in cancer patients. The Institute has a very active vaccine development program which has previously been tested in roughly 200 patients, but this study is a first, and Dr. Dranoff hopes that this is going to be a significant improvement to the current roster of cancer vaccines. By combining immune stimulation with a specific hormone [GM-CSF] and with the simultaneous blockade of the milk fat globule-E8, the research will further test the hypothesis that anti-tumor immunity and tumor destruction will be increased in patients with many different forms of cancer. Although initially tested as a stand-alone treatment, over a longer time-frame the application may also be used in combination with other forms of cancer treatment for even better results.

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therapy clinical study, with the aim of developing novel chemosensitization alternatives, not only in CLL but potentially in other types of cancer. In previous research, the team observed biologic and clinical activity without dose-limiting toxicity. The goal is to regulate the expression of proteins, genes and microRNA's independently, so as to stimulate greater chemosensitization. Dr. Kipps, who has been working in the field for more than twenty years, is encouraged that a more effective treatment for this disease is within reach.

New Grants Promote Clinical Trials

Investigator Grants are made possible by the ACGT Fund for Advancement, which awards up to $1 million for 3 – 5 year projects in clinical translation. Grant applications undergo rigorous scrutiny by our Scientific Advisory Council which recommends finalists to the Board of Directors for funding. We congratulate all the finalists for their commitment to cell and gene therapies. More detail on these and other ACGT grants can be found at www.acgtfoundation.org.

Gene Science Defined

We know now that all cancer evolves from damaged, missing or mutated genes: a biological misfire. What causes this? Beyond genetics, the effect of our environments and our lifestyles. What makes gene science possible? Every tumor has a blueprint that we will be able to identify and alter, with little or no effect on other parts of the body. The future is now.

Gene therapies employ an approach that inserts a gene into a patient's cells instead of using drugs or surgery. The gene might replace a mutated gene that caused the disease, or inactivate a gene that is functioning improperly, or add a new gene to help the body fight the disease.

- Gene drugs may be delivered directly to the tumor to facilitate cancer cell death.
- Cell and gene vaccines are able to boost the immune system to reject and destroy cancers.
- Targeted cell and gene therapeutics are able to destroy cancer stem cells, which are believed to be the root of many kinds of cancers.
- Gene medications are able to destroy cancer cells by cutting off their blood supply.

Cell therapy is the infusion or transplantation of whole cells into a patient for treatment of an inherited or acquired disease, including cancers.

Angiogenesis is the growth of new capillary blood vessels, an important natural process in the body that promotes healing and reproduction. Anti-angiogenesis is the process of cutting off that blood supply around a tumor, to strangulate the cancer cells.

Apoptosis is programmed cell death; it is the body's normal method of disposing of damaged, unwanted or unneeded cells – cancer cells could be induced to apoptosis through gene therapy.

In vivo gene therapy uses a vector to directly transfer therapeutic genetic material into select cells in the body.

Ex vivo gene therapy uses cells removed from the patient and cultivated, transduced, then injected back into the body to fight disease.

P53 is a multifunctional tumor suppressor protein and one of the most commonly mutated genes in tumors.

Phase I/IB Trials test a new drug or treatment in a small group to assess safety and efficacy.

"Mr. Netter's legacy will continue to live on through ACGT and all of the scientists' and patients' lives he has touched."

– Antonio Chiocca, MD, PhD, Ohio State University Research Foundation

"We have lost a great man and a visionary leader."

– Carl June, MD, University of Pennsylvania Abramson Family Cancer Research Institute

"His legacy, generosity, kindness, and enthusiasm in pursuing what he believed will be remembered forever, and hopefully followed by many."

– Jian Yu, PhD, University of Pittsburgh School of Medicine

ACGT News & Events



5th Annual Swim Across America Greenwich-Stamford Swim set for June 25th

Calling all aquarians! We invite you to swim or boat through the warm waters of Long Island Sound, from Greenwich to Stamford, CT, enjoy the pleasures of the sea, a great sense of satisfaction and the rewards of celebrating success with like-minded volunteers. In the first four Swim Across America events for Alliance for Cancer Gene Therapy, supporters raised a total $850,000 for research – this year, in honor of our foundation's first decade, we are aiming to shatter the $300,000 single event revenue record and ensure funding of an innovative approach to an especially deadly form of cancer.

Swim Across America is also a great opportunity for local and national organizations to show their support for new alternatives for cancer treatment – step up and sign on as sponsor or advertiser, or make a direct donation of goods or services to the event.

Previous funding helped ACGT Research Fellow Dr. Khalid Shah at Harvard Medical School progress in the development of breakthrough therapies for brain cancers. This year, the Swim Across America grant will support Dr. Thomas Kipps of the Moores Cancer Center at the University of California, San Diego, in his quest for effective treatment for leukemia and lymphoma. According to Dr. Kipps, cancer cells of patients with chronic leukemia and lymphoma are stealth-like in their ability to evade detection by the immune system. His trials focus on cross-linking a protein on the leukemia cell to stimulate an immune system response. Immunotherapy is one of the most promising forms of gene therapies and has the potential to treat many types of cancer.

Many thanks to Event Chairs Jacque Lang and Kerry Anderson, and Honorary Co-Chairs Cindy and John Sites, Arlene and Reuben Mark, Olympic swimmer Donna de Varona, John Pinto, Mary Henry and Howard Rubin.

ACGT Awarded "Best in America" Seal

We are proud to announce that we have been approved for the Independent Charities of America [ICA] Seal of Excellence, which is awarded for the highest standards of public accountability, effectiveness and efficiency. Of the more than one million charities operating in the Unites States today, it is estimated that fewer than 50,000 meet or exceed the levels of excellence required for this award. The ICA "Best in America" seal of approval helps contributors identify an organization as one of the top charities in the country. Member agencies undergo a rigorous annual review and must document and demonstrate integrity and effectiveness. These standards include those required by the federal government for inclusion in the Combined Federal Campaign, perhaps the most exclusive fund drive in the world.

ACGT is also the recipient of the prestigious Better Business Bureau Wise Giving Alliance seal of approval, granted only to charities that meet their highest standards regarding governance, impact, public communications and financial management.

SAC Chair Savio Woo Brings Science to the Arts



Photograph by Elaine Ubina, www.fairfieldcountylook.com

Dr. Savio Woo with Mrs. Emily Woo (on left) and Bruce Museum Supporter, Myrna Haft

What might unite gene therapy and contemporary arts? A special event in support of the Bruce Museum in Greenwich recently invited 16 innovators in disparate fields to educate guests on the fine art of their expertise. From fashion and film, to medicine, architecture, finance, food and wine, "Dimensions in Dining" brought the best of the best to eleven intimate dinners hosted by museum sponsors, matching fundraising with enlightenment. Dr. Savio Woo, of Mt. Sinai School of Medicine, a human genetics and gene therapy expert, and Chair of the ACGT Scientific Advisory Council, engaged the crowd in a spell-binding discussion of the progress and promise of molecular medicine.

A kick-off for the 2011 Swim Across America Greenwich-Stamford Swim to benefit ACGT is planned for Tuesday, April 26, 2011, 6-8PM at the Bruce Museum. Reservations are required.

More information about the kick-off, and registration as sponsor or swimmer can be found at www.acgtfoundation.org

100% OF DONATIONS TO ACGT go directly to research. Separate funding is provided to cover all administrative and fundraising expenses.

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ACGT by the Numbers

37 major grants in nine years: 24 Discovery, 13 Translational

$22.35 million dollars awarded; ACGT Research Fellows attracted $58 million in complimentary funding

ACGT Fellows conduct research at 27 of the 150 universities and research institutions in the US, Canada and Puerto Rico engaged in the investigation of cell and gene therapies for cancer

17 human trials approved of which 11 trials started – 113 patients enrolled

122 publications in leading professional journals have acknowledged ACGT

Many important research projects still await funding including 186 semi-finalists