

REPORT

Fall 2004

Renowned Scientific Advisory Committee Praises Foundation

Dr. I. Bernard Weinstein, one of the four members of SWCRF's Scientific Advisory Committee (SAC), an external, independent group of prominent peer reviewers stated, "In this time of strife, it is refreshing to see science bringing together people from so many nations to do something good." The comment was made at the annual SAC meeting, held at the New York Academy of Sciences on June 21, and attended by Board members, friends, SWCRF-funded investigators and leadership from the Mount Sinai School of Medicine.

The evening began with Dr. Samuel Waxman, Scientific Director, citing the triple-fold growth of the Foundation over the past several years. Such growth has increased both research support and the number of funded investigators from six to more than 30.

He went on to walk attendees through a visual display of the Foundation's "Institute Without Walls" and described a new research program spearheaded by SWCRF. The Liver and Pancreatic Program is a multi-institutional collaboration investigating the correlation between Hepatitis C and liver cancer. Dr. Joseph Llovet, Visiting Professor at Mount Sinai from the University of Barcelona in Spain, serves as principal investigator. This project is being funded in part by the Beverly Yaffe Memorial Fund and the Mark Family Fund.

Dr. Waxman, in recognizing the generosity of SWCRF's donors, made a special presentation to Joan Safir, for 20 years of outstanding leadership and philanthropy as a past Chairman and President.

He then introduced the SAC members: Dr. Frank Rauscher, Professor and Chairman of the Molecular Genetics Program and Deputy Director of the Wistar Institute Cancer Center; Dr. Franco Muggia, Director of



Members of the SWCRF Scientific Advisory Committee: From left: Dr. Frank Rauscher, Dr. Bernard I. Weinstein, Dr. Samuel Waxman, Dr. I. David Goldman and Dr. Franco Muggia.

the Division of Medical Oncology at the Kaplan Comprehensive Cancer Center, New York University; Dr. I. David Goldman, Director of the Albert Einstein College of Medicine Cancer Research Center; and Dr. Weinstein, Frode Jensen Professor of Medicine at Columbia University.

After a day-long review of presentations and

(continued on page 7)

Inside

- 2 From Our Chairman
- 2 Scientific Director's Message
- 3 Meet Our Investigators
- 5 Fundraising Events
- 6 News Briefs



Michael Nierenberg



Samuel Waxman, M.D.



SAMUEL WAXMAN
CANCER RESEARCH
FOUNDATION

From the Chairman

Dear Friends,

Thanks to so many of you - colleagues, friend, and generous supporters - I'm pleased to report that this year has been one of dynamic collaborations and explosive growth.

Over the past several years, we have tripled our revenue and the number of funded researchers throughout the US and abroad has grown accordingly. Likewise, we have launched several cancer research programs: the international, multidisciplinary program in liver cancer, tumor dormancy and gene transcription. These programs contain basic, translational and clinical research arms. Clinical trials in leukemia, lymphoma, melanoma, multiple myeloma, and breast, liver, colon, lung, and pancreatic cancer are in progress as part of the three programs.

As you know, the research supported by the SWCRF is unique in that it is concept driven and based on the principle that cancer is reversible. Likewise, it requires its funded researchers to collaborate within its "Institute Without Walls".

The reality is that there are more than 100 different cancers. It is our fervent hope that within the next year, we will expand our programs further. As we lead into our major Fall/Winter fundraiser, we look to you to help us collaborate for a cure.

Scientific Director's Message

I am all too frequently asked, "Why do breakthroughs in the laboratory take so long?" — an appropriate question when we see so many friends and family members succumb to cancer because of inadequate treatment. I would like to respond based on my experience developing novel cancer therapies.

Research begins in the laboratory utilizing sophisticated systems and technology to address gene function. Once a dysfunction is discovered, a biochemical evaluation is undertaken to design a chemical compound to correct or bypass it. And once a compound is designed, it must then be converted to a drug and go through various developmental phases before clinical trials. Each arduous step requires many breakthroughs in basic, translational and clinical research, as well as persistence, patience and multidisciplinary collaboration. To illustrate, let us track two of the more recent novel cancer therapies.

For over 50 years, we have known through basic science that vitamin A is required for normal differentiation and that its deficiency is associated with changes that predispose to cancer. For the past 30 years, a growing database has uncovered specific defects in vitamin A's function that cause certain forms of cancer. And in the past 20 years, drugable targets for vitamin A derivatives that can be utilized to treat cancer have been identified. Clinical studies in the past 15 years have demonstrated that vitamin A derivatives can effectively treat acute leukemia, neuroblastoma, skin lymphomas

(continued on page 6)

OFFICERS OF THE BOARD

CHAIRMAN
Michael Nierenberg

PRESIDENT
Tamar A. Spilo, Ph.D

VICE-PRESIDENTS
Gary Jacob
J. Jay Mautner
Dena K. Weiner

SECRETARY
Laurie L. Schaffran

TREASURER
Gary Gladstein

BOARD OF DIRECTORS

Lawrence Altman
Philip T. Brudner
Peter Claman
Dasha Epstein
Robert E. Fischer
Arminio Fraga
Judi Gladstein
Eric Goldstein
Clifford Greenberg
Linda Herman
Mary Kantor
Costas Kondylis
Leslie Elliot Krause
Abner Levine
Mildred Levine
Shumer S. Lonoff*
Thomas Marano
Richard Mazer
Alan P. Safir†
Alfred J. Seaman†
Edward Sheldon
Tony M. Shogren
Spencer Waxman
David T. Workman*†

HONORARY BOARD

Maureen Cogan
Martin L. Coyne
Susan W. Rose
Selma Ruben*
Joan A. Safir†
Edwin C. Scheurer
Michael A. Wiener
Zena Wiener

SCIENTIFIC DIRECTOR
Samuel Waxman, M.D.

ASSOCIATE SCIENTIFIC DIRECTOR
Jonathan Licht, M.D.

SCIENTIFIC ADVISORY COMMITTEE

Franco M. Muggia, M.D.
Frank J. Rauscher III, Ph.D.
Max S. Wicha, M.D.
Stuart Yuspa, M.D.

EXECUTIVE DIRECTOR
Ann H. Jackowitz

†Chairman Emeriti
*deceased



Julio Aguirre-Ghiso, M.D., Ph.D.



Beverly Emerson, Ph.D.



Neil Rosen, M.D., Ph.D.



David Tuveson, M.D., Ph.D.

“Institute Without Walls” Welcomes Four New Grantees

From among 37 excellent applications from institutions worldwide, the Samuel Waxman Cancer Research Foundation (SWCRF) has selected four to receive research grants. The awards launch the third phase of the Foundation’s three-year, \$3.25 million research initiative. A 15-investigator panel conducted an intensive peer-review of each application, a process modeled on that used by the National Institutes of Health. To ensure that each application reflected the Foundation’s goals, the Board of Directors’ Scientific Task Force Committee held a second review.

The grants, which commenced on July 1, 2004 cover a three-year period. After two years, scientists must demonstrate collaboration with other SWCRF investigators and receive a positive review from the Foundation’s external Scientific Advisory Committee to receive an additional year of funding.

Joining the SWCRF “Institute Without Walls” are Julio Aguirre, Ghiso, M.D., Ph.D., of the State University of New York (SUNY) at Albany; Beverly Emerson, Ph.D., of The Salk Institute; Neal Rosen, M.D., Ph.D., of Memorial Sloan-Kettering Cancer Center; and David Tuveson, M.D., Ph.D., of the University of Pennsylvania.

Julio Aguirre-Ghiso, M.D., Ph.D., Assistant Professor of Biomedical Sciences, SUNY-Albany Gen*NY*Sis Center for Excellence in Cancer Genomics

In patients with residual disease after treatment, cancer cells that may be dormant can begin to proliferate again in time. With his Waxman Foundation grant, Dr. Aguirre-Ghiso will use an animal model to determine which genes contribute to the induction of dormant cancer cells.

“More than half of cancer patients will die from metastatic disease that develops months, years, or even decades after an initial tumor is removed,” he says. “The aim of our research is to discover the molecular genetic programs that govern a disseminated cancer cell’s decision to proliferate or stay dormant so we can force cancer cells to stay dormant forever.” Dr. Aguirre-Ghiso joins the SWCRF program on Tumor Dormancy under the leadership of Dr. Liliana Ossowski.

Beverly Emerson, Ph.D., Professor, The Salk Institute

P16 gene expression is inactivated in upwards of 80% of all human cancers, including pancreatic cancer, and well-known to be “silenced” by DNA methylation, a normal biological process that is heavily correlated with cancer development. Unfortunately, the mechanisms by which DNA methylation is deregulated in human cancers is poorly understood.

Dr. Emerson’s grant will enable her to build a biochemical model of the p16 gene using cloned genes and then generate specific DNA methylation. Ultimately, her research will strive to develop new, more selective therapeutics. Dr. Emerson will immediately collaborate in the SWCRF Overcoming Gene Repression Program.

“We want to create drugs to reverse DNA methylation and stop erroneous targeting,” Dr. Emerson offers, then adds, “As DNA methylation occurs early in cancer genesis, it may be used as a marker to help localize tumors and prevent metastases.”

Neil Rosen, M.D., Ph.D., Professor of Medicine and Cell Biology, Weill Medical College-Cornell University Medical College, Program Associate, Cell Biology, Memorial Sloan-Kettering Cancer Center

Abnormal B-raf signaling pathway occurs in the majority of human melanomas. This leads to dysregulated growth of the cancer cell. Dr. Rosen will apply his grant toward a more comprehensive understanding of how the various proteins involved in this growth circuit affect the biology of melanoma.

“What we’re trying to do is use new agents to explore the role played by B-raf in melanoma cells,” he points out. “We hope to move quickly into clinical trials and accumulate data to develop new

treatments that will interfere with mutated B-raf signaling pathway.”

David Tuveson, M.D., Ph.D., Assistant Investigator, Abramson Family Cancer Research Institute Assistant Professor, Cancer Biology and Hematology/Oncology, University of Pennsylvania

While mutations of the B-raf gene have been associated closely with melanoma, they also have been observed in benign cancers – requiring a comprehensive assessment of this oncogene that could potentially serve as a significant therapeutic target in malignancy. Dr. Tuveson’s grant will allow him to develop the first mouse model of melanoma using the B-raf gene.

The model complements Dr. Tuveson’s current correlative scientific work with investigators at the University of Pennsylvania, who are studying melanoma patients being treated with Raf kinase inhibitor. Only half of the clinical trial participants have responded to the drug, which inhibits several kinases including the B-Raf protein made hyperactive by the oncogenic mutation. Inhibition of B-raf function will lead to the discovery of biomarkers directly relevant to our translational scientific objectives with these clinical trials,” says Dr. Tuveson. Dr. Rosen and Dr. Tuveson will actively collaborate with scientists at Mount Sinai to develop a multi-disciplinary SWCRF melanoma program.

Golf Tournament

Thanks to Club member and longtime SWCRF supporter Mike Dritz, the 22nd Annual Invitational Golf Tournament was held at GlenArbor, in Bedford, NY on June 29th. The Tournament raised \$200,000.

The event was underwritten by our Golf Patrons, whose generosity enabled all monies raised to be used directly to support SWCRF funded investigators. They include: Lawrence Altman of Aspen, CO; Robert Cannon of Weston, CT; Eric Goldstein of Harrison, NY; Gary Jacob of Westport, CT; Abby Levine of Boca Raton, FL; Tony Shogren of Oyster Bay, NY and Jerry Wolff of Delray Beach, FL. Also, a special thanks to our corporate underwriter, SAC Capital Advisers, LLC, and to corporate sponsors DB Poster Associates and Bank of America.



Pearl Bernsohn and Dr. Jerry Wolff



Tom Gilbert and Honorary Board member Ed Scheurer



Board President, Dr. Tamar Spilo; past Board Chairman, Alan Safir and Dr. Samuel Waxman



Board Member Ed Sheldon and Joe Sweedler



Front Row (from left): Michael Prober, Eric Semler and Ricky Sandler; Back Row: David Sachs



From Left: Benjamin Marks, Andrew Fox, Alan Safir and Jeff Zucker



From Left: Bob Rohrlich, Steven Silberstang, Gene Singer and Hack Seymour



Joe Ades, David Kaplan, Eric Brophy and Steve Beberman



Bob Fishbein, David Moreinis and Abby Levine

A Hamptons Happening



Photo by Giles Ashford

The first-ever SWCRF Hamptons event was held at the 6-acre home of Marcia and David Lavipour on Saturday, July 31 in Bridgehampton. Nearly 300 people attended the fundraiser, which included a cocktail reception, silent art auction and raffle. Entertainment was provided by: pianist James Ilardi, mimes from the New York Entertainment Connection and music by the Marta Topferova Quintet.

The cover art of the invitation, the evening's program and a 40" x 30" color poster commemorating the event was designed by graphic artist Lon Kirschner. Flowers were provided by 1-800-Flowers, courtesy of designer/arranger Michael George. Auction displays were provided by Dean Denninger of Windmill Construction.

Gift raffle items included a private helicopter flight for 4 from the Hamptons to NYC from Blue Star Jets; a 2.4K "Diamonds by the Yard" 36-inch 18K yellow gold necklace donated by Donna and Simon Swaap; a 14K gold earrings and bracelet set with semi-precious stones donated by Sharyn Van Reepinghen; two VIP season passes to the 2005 Music Festival of the Hamptons donated by Eleanor Sage Leonard; a sable knitted scarf from the Maximilian Fur Salon at Bloomingdales, and two nights in the Garden View Room at the Sanctuary at Kiawah Island, from Kiawah Island Golf Resort and the Travel Siblings.

Members of the Planning and Benefit Committee who individually and collectively gave of themselves so generously and tirelessly were: Bonnie Cantor, Marcia Lavipour, Laurie Schaffran, Marion Waxman and Dena Weiner.

The event raised \$142,000 which will be matched dollar-for-dollar by the Skirball Foundation, for a total of \$284,000.



From left: Marcia Lavipour, Michael Nierenberg, Board Chairman; Dr. Samuel Waxman, Elin Nierenberg and David Lavipour



From left: Alana Zona, Rachel Lavipour and Ashley Goodman



Front row: Randy Abend, Dena Weiner, Board Vice President; Ruth Rozenholz; David Rozenholz; Back row: Chris and Dean Denninger



Marta Topferova Quintet



From Left: Carrie Tucker (Miss New York State 2000), Pratima Yarlagadda (Miss Indiana 1999) and Bridget Vezina (Miss USA First Runner-Up 2000)

Silent auction display before the guests arrived



(continued from page 2)

Scientific Director's Message

and, in combination with other targeted agents, prevent and treat head, neck and lung cancers. This clinical research continues.

For 25 years, overabundant EGF receptor has been linked with abnormal cell growth associated with common cancers. Developing monoclonal antibodies or specific drugs to block EGF receptor function has taken 20 years, with five years of clinical trials showing that EGF receptor inhibitors in combination with chemotherapy are effective in patients with advanced and resistant colon and lung cancer. This research resulted in two new FDA-approved cancer treatments. But recently, Dr. Jeffrey Settleman, a SWCRF investigator working with a group at Massachusetts General Hospital, reported that a specific mutation in the EGF receptor protein is required for therapeutic success. This new finding underscores the importance of continued research even after a drug is FDA-approved.

Today, five research groups from around the world are collaborating to develop drugs to block gene targets selective to the malignant blood cell. They are working under the auspices of the SWCRF program, Overcoming Aberrant Gene Expression in Blood Malignancies, which is supported by The Skirball Foundation. Basic science is being conducted at the Salk Institute, while translational, preclinical, and clinical studies are being performed at Mount Sinai, Albert Einstein, Brandeis University, the Leukemia Research Foundation in London, and the Shanghai Institute of Hematology. All good research may not result in breakthroughs, but clearly all breakthroughs require good research, like that supported by SWCRF, recently deemed by our external Scientific Review Committee to be of the highest quality. Fortunately, modern technology and research partnership with industry are decreasing the time it takes to answer complicated scientific questions. Still, given the inherent complexity in solving the mysteries of the cancer cell, it is reasonable that for many years I will continue to address the question, "Why do breakthroughs in the laboratory take so long?"

News Briefs

Appointments and Awards



- ◆ **Dr. Jonathan Licht**, SWCRF Associate Scientific Director, was recently named Associate Dean for Cancer Programs at the Mount Sinai Medical Center. In this newly created position, Dr. Licht will coordinate and integrate clinical care and research related to cancer throughout Mount Sinai.
- ◆ **Dr. Reuben Lotan**, MD Anderson Cancer Center, has been awarded a "bridge" grant for \$75,000 to continue his research collaboration within the SWCRF's "Institute Without Walls" on developing novel therapies for head and neck cancers. Dr. Lotan had been the first recipient of the David T. Workman Memorial Endowment Award in 2002. The one-year grant is renewable on an annual basis.

Research and Collaboration Highlights

- ◆ **Dr. James Herman**, Johns Hopkins, reported that silencing of a specific gene promotes the development of colorectal cancer thus offering a new site for targeted therapies (Nature Genetics, 2004). The effects of dietary folic acid and alcohol intake on the silencing of genes in colorectal cancer were reported by Dr. Herman and a group from the Netherlands (Cancer Research, 2003).

A new test to identify patients with lung cancer that will respond to EGFR inhibitors such as Gefitinib

- ◆ **Dr. Jeffrey Settleman**, Massachusetts General Hospital, has demonstrated that a specific mutation in the EGF receptor is predictive for response to the drug Gefitinib as a treatment in lung cancer (New England Journal of Medicine, 2004).

Bridge Grants

Bridge grants were awarded to two investigators to join the SWCRF Aberrant Gene Expression Program:

- ◆ **Ruibao Ren, Ph.D.**, Associate Professor, Brandeis University
His animal models for specific types of acute leukemia will be used to study targeted differentiation agents.
- ◆ **Ari Melnick, M.D.**, Assistant Professor, Albert Einstein School of Medicine
A site in an abnormal gene associated with a common form of lymphoma will be used to screen a large number of compounds to develop a targeted therapy.

(continued from cover)

Scientific Advisory Committee



Dr. Waxman presenting to Joan Safir a tee shirt, "An Artful Evening in Soho, 1986", as a memento of her long and outstanding leadership and philanthropy to the Foundation.



From left: Board members Gary Gladstein, Treasurer, Judi Gladstein, Marketing Committee Chairman, Costas Kondylis, and Alan Safir, past Chairman.

SWCRF "fills that important 20% hole that the National Institutes of Health (NIH) just doesn't cover."

written reports by each Foundation-supported investigator, SAC members summarized their findings. Their review assessed the quality of the research and evaluated new collaborations between investigators in SWCRF's network.

Committee members unanimously applauded the measurable progress of SWCRF's objective to build a coordinated global research effort to generate cancer cell selective treatments in the battle against cancer. Dr. Rauscher stated that SWCRF is a "unique example of a coordinated effort toward a common research goal with a defined theme across multiple institutions." He also noted that SWCRF "fills that important 20% hole that the National Institutes of Health (NIH) just doesn't cover." Dr. Goldman

concluded, adding that the "hole" refers to innovative ideas that need seed money, but are considered too high risk by the NIH.

Dr. Muggia and Dr. Weinstein stated that the Foundation is part of a revolution in cancer treatment, as well as a catalyst in transferring research-acquired knowledge into treatment advances. While 40 years ago patients were given toxic and non-targeted treatments, today they receive less cytotoxic therapies, thanks in large measure to early SWCRF-generated research that helped to pioneer a different way of reprogramming cells and investigating their genetic makeup and the mechanisms that cause them to go haywire.

Audience members agreed with



Two SWCRF funded investigators under the watchful eye of Dr. Einstein: From left: Dr. James Herman, Johns Hopkins University, and Dr. Albert Baldwin, University of North Carolina.

the Committee's comments. Dena K. Weiner, Vice President of the Board of Directors and Chairman of the lay Scientific Committee, said she was "bubbling with pride." Martin Blackman, President of The Skirball Foundation, offered that based upon what he heard, SWCRF is getting the "best bang for its buck in research." And Dr. Paul Klotman, Chairman of the Mount Sinai Department of Medicine, remarked that the success of the Foundation is due to Dr. Waxman's vision, and that the quality of its work stems from its "great scientists and science."

Second David T. Workman Memorial Lecture and Award

The Second David T. Workman Memorial Endowment Lecture and Award Presentation will take place on Monday, November 8 at the NY Academy of Sciences. The award recipient will be Dr. Michael Grever, Chairman of the Department of Internal Medicine, the Ohio State University Medical Center.

The Endowment memorializes David Workman and his special role on the SWCRF's board, and awards an outstanding researcher who is working on developing drug therapies that target cancers for which current treatments are inadequate. The two-year \$50,000 award will support research currently being conducted by Dr. Grever and his

colleague Dr. John Byrd. The two will share their clinical and research findings for chronic lymphocytic leukemia (CLL) at the lecture.

In CLL, one of the most common forms of leukemia among adults in the Western Hemisphere, non-functional white blood cells called lymphocytes accumulate in the bloodstream and interfere with normal immune function. Lymphocytes play important roles in immunity, but they can lead to cancer when they fail to undergo apoptosis (naturally programmed cell death). Despite palliative treatments, CLL remains difficult to treat. Drs. Grever and Byrd are developing new therapeutic options.

The Foundation's Newsletter is available by email. If you would prefer to receive our Report electronically, and to help us keep costs down, please send your email address to report@waxmancancer.org

HOLD THE DATE
"Collaborating for a Cure"
Benefit Dinner and
Silent and Live Auction
Thursday
December 2, 2004
Metropolitan Pavilion
Hosted By
Elin and Michael Nierenberg

NON-PROFIT ORG.
U.S. POSTAGE
PAID
NEW YORK, NY
PERMIT NO. 938

SAMUEL WAXMAN
CANCER RESEARCH FOUNDATION
150 FIFTH AVENUE, NEW YORK, NY 10128
TEL: 212-241-1760 FAX: 212-426-2273
WWW.WAXMANCANCER.ORG

