

SAMUEL WAXMAN CANCER RESEARCH FOUNDATION

REPORT

Fall 2006

Research Giants Tackle the Challenge of Melanoma

Summer tans have faded, but sun exposure sometimes linked to melanoma, the deadliest of skin cancers, is still taking its toll. If found early, melanoma has an excellent cure rate. However, a lesion that is no bigger in diameter than a pencil eraser and only one sixth of an inch deep can be life-threatening. According to American Cancer Society estimates, 7,910 Americans will die of melanoma in 2006. While the mortality rate for melanoma increased by 50% between the 1970's and 1980's and appears to be leveling off now, this cancer still presents a formidable research challenge.

A recently-funded \$1 million program grant from the Samuel Waxman Cancer Research Foundation (SWCRF) is funding a collaboration of eminent California scientists to pursue the hope offered by using gene therapy against melanoma.

Nobel-prize winner David Baltimore, who is President Emeritus and Robert Andrews Millikan Professor of Biology at Cal Tech, says, "Certain diseases – infectious diseases like AIDS and malaria, but predominately certain cancers – are just not handled well by the immune system. I started thinking about three years ago that it should be possible to reprogram the immune system so it

Institute Without Walls

Collaborating to Cure Melanoma

Collaboration is enriching the search for the key to curing melanoma. University of California, Los Angeles scientists are at the core of the process with a clinical trial, immune monitoring and in vivo imaging. Researchers at UCLA, California Institute of Technology, Children's Hospital of Los Angeles, University of Southern California and the University of Connecticut also collaborate in some or all of these research activities.

would respond the way we want it to rather than the way it chooses to." Doctor Baltimore chose to focus on this cancer "because we know more about the immunology of melanomas than almost any other cancer." Connecting with a clinical group with similar interests and priorities has been "extremely exciting" to Dr. Baltimore, and to his colleagues, James Economou and Owen Witte.

Genetically modifying the T cells (T Lymphocytes or "killer cells") our immune systems produce to fight cancer is at the heart of the matter. These cells need receptors that specifically recognize antigens on the surface of the melanoma cells. When T-Cells that would not otherwise function to kill cancer are molecularly modified, they will

(continued on page 5)

Inside

- 2 From the Chairman & Scientific Director
- 3 Melanoma Diagnosis Outcomes
- 6 Special Events
- 7 Scientific Advisory Committee Meeting
- 8 Meet Our Investigators
- 10 David Workman Memorial Award

From the Chairman & Scientific Director



Michael Nierenberg

With Fall upon us and our major fundraiser around the corner, we thought we would give you an update as to what we are doing at the SWCRF.

The Foundation has grown tremendously over the past few years as our generous donors have embraced our efforts to overcome cancer by creating a collaborative team of world-class scientists to translate cancer research discoveries from the bench to the clinic. Our *Institute Without Walls* focuses on uncovering genetic causes of cancer and delivering specifically tailored, minimally toxic treatments to cancer patients.

Your donations have enabled us to expand our reach and focus on research in brain, breast, liver, lung, pancreatic and prostate cancer, blood malignancies and melanoma. This month, a new wing will be dedicated to the Foundation at the Shanghai Institute of Hematology/RuiJin Hospital, Shanghai Second Medical University in China.

Each dollar given to the foundation is leveraged up to 5 fold with support from other peer reviewed grants from prestigious institutions like the National Institutes of Health. This puts the current value of SWCRF's 50 funded scientists at almost \$23 million - a large impact by any standard.

I would also like to invite you to our fall events. On November 14th, the David Yurman Boutique will be celebrating the Foundation's 30th anniversary by donating a portion of all proceeds to SWCRF. On November 16th, we will be presenting Dr. Douglas Lowy and Dr. John Schiller of the NIH the David Workman Memorial Award for their critical research resulting in the development of the Human Papilloma Virus vaccine to prevent women from the HPV infection that leads to cervical cancer. On November 30th, we look forward to seeing you at our annual Collaborating for the Cure Gala where John Fogerty will be the featured entertainment.

We remain extremely dedicated to finding a cure for half of all men and a third of all women in America who will be diagnosed with cancer in their lifetimes. With virtually no family being spared by this disease your continued support is critical.

— Michael Nierenberg



Samuel Waxman, M.D.

Fortunately, malignant melanoma is the rarest form of skin cancer. Common varieties of skin cancer are unique in that they seldom if ever recur in the same spot or metastasize. Melanoma, on the other hand is predictably unpredictable. If found early, often in a maze of benign "beauty marks" and moles, it can be cured surgically. However, at a later date, based on the genetic makeup of the melanoma, it may be surgically cured, rapidly spread and/or remain dormant and recur many years later. The oncologist continues to seek a way to prevent and treat recurrence of melanoma. However, conventional chemotherapy has had limited success.

The SWCRF Melanoma Research Program is briefly described in this Newsletter. It involves 6 laboratories and multiple disciplines. The BRAF mutation causes a cascade of abnormal signals that appear to be necessary for the development of 80% of melanomas. Inhibitors have been developed and are in clinical trial. However, the benefits thus far are disappointing. Thus, experts like Dr. Neal Rosen are digging more deeply into the signals and have discovered an escape pathway that protect melanoma cells from BRAF inhibitors. New inhibitors are now in design.

Dormant melanoma cells are responsible for the uncertainty associated with the cure of melanoma. The SWCRF Program on Tumor Cell Dormancy collaborates with the Melanoma Research Program to facilitate the development of treatments to prevent regrowth of melanoma cells. The Melanoma Research Program has collaboration with other SWCRF investigators working in stem cells and drug resistance.

Educating the immune system to attack melanoma cells has held the imagination of scientists for almost a century. Promising studies in animals and anecdotal reports in patients using non-specific immune stimulants and vaccines have generally failed to have impact. Why invest in this approach at this time? New technology using gene therapy to carry melanoma recognition genes to the human stem cell and then to the immune system and a way to image an activated immune system has been developed by an out-

(continued on page 4)



SAMUEL WAXMAN
CANCER RESEARCH
FOUNDATION

OFFICERS OF THE BOARD

CHAIRMAN
Michael Nierenberg

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

SECRETARY
Laurie L. Schaffran

TREASURER
Gary Gladstein

BOARD OF DIRECTORS

Lawrence Altman
Peter Claman
Judi Gladstein†
Eric Goldstein
Clifford Greenberg
Linda Herman
Costas Kondylis
Leslie Elliot Krause
Abner Levine
Mildred Levine
Thomas Marano
Edward Sheldon
Howard Shlafmitz
Tony M. Shogren
Clifford Sterling
Spencer Waxman
David T. Workman*†

CHAIRMAN'S COUNCIL

Philip Brudner
Robert E. Fischer
Arminio Fraga
Richard Mazer

HONORARY BOARD

Maureen Cogan
Martin L. Coyne
Mary Kantor
Susan W. Rose
Alan P. Safir*
Joan A. Safir*
Edwin C. Scheurer
Alfred Seaman*
Michael A. Wiener
Zena Wiener

SCIENTIFIC DIRECTOR
Samuel Waxman, M.D.

ASSOCIATE SCIENTIFIC DIRECTORS
Ethan Dmitrovsky, M.D.
Jonathan Licht, M.D.

SCIENTIFIC ADVISORY COMMITTEE

I. David Goldman, M.D.
Franco M. Muggia, M.D.
Frank J. Rauscher III, Ph.D.
I. Bernard Weinstein, M.D.
Max S. Wicha, M.D.
Stuart Yuspa, M.D.

EXECUTIVE DIRECTOR
Merle Duskin Kailas

*Chairman Emeriti
†deceased

SWCRF REPORT

WRITER/EDITOR
Carol Ardman

DESIGNER
Barbara Taff

Melanoma Diagnosis Outcome

Playing the Hand That's Dealt

It's a moment everyone dreads. You see or feel something suspicious, or during a physical exam. And then the verdict comes in. It happened to Richard Gambino and to Ron Gelb. Both were diagnosed with potentially deadly melanoma. While they had the chance to live, they displayed extraordinary courage and equanimity while facing

Richard Gambino, a thirty-eight-year-old professor at Queens College, learned the tumor in his chest was malignant two days before Thanksgiving in 1977 and underwent surgery the next Monday. Bad news turned worse. Five lymph nodes examined after the operation were cancerous. "It had metastasized," he says.

While recovering from the procedure, Mr. Gambino's physician, Sam Waxman, introduced him to a woman even younger than he who also had melanoma and who had already undergone the eighteen-month course of chemotherapy Mr. Gambino would begin as soon as he was strong enough. She became his mentor and friend.

Mr. Gambino remembers the weeks of chemotherapy as "horrific," and he says he randomly went through the grief cycle described by Elizabeth Kubler-Ross in her classic book, *On Death and Dying*. Miraculously, though his friend and mentor did not

live, he did survive. "Nobody can tell me why I'm alive," he says now, alluding to the riddle of why some patients with similar case histories live and others die.

His near-death experience changed Mr. Gambino and made him less susceptible to upsets over the small things. "Now it's deep in the past," he says. "I'm thankful."

"I'm here for the manicure and the pedicure," Ron Gelb quipped to the nurse when he entered a Boston hospital for a major operation that involved moving his cheekbone and removing part of his palate to try to excise the dangerously malignant tumor. Mr. Gelb stubbornly held onto his sense of humor, ignored the specter of death and fought mucosal melanoma for the next year and a half, until he was forty-two.

"Ron was very positive. We knew numbers weren't good but chose not to listen to that. We chose to fight. We were hopeful until the end," says his wife

BOARD

berg

NTS

er

er

fran

in

TORS

nan

n†

in

berg

in

/lis

use

e

ne

no

lon

nitz

ren

ng

nan

an*

†

UNCIL

er

er

ja

er

ARD

an

ne

r

ie

*

*r

rer

in*

ner

r

CTOR

y, M.D.

DIRECTORS

y, M.D.

M.D.

COMMITTEE

y, M.D.

a, M.D.

II, Ph.D.

in, M.D.

v.D.

A.D.

CTOR

ailas

riti

RT

OR

in

f

Outcomes

at's Dealt

scious, or during a checkup the doctor finds it.
and to Ron Gelb when they were in their prime.
e they had the opposite outcomes, both men
ty while facing down a killer.

Nanci, who lives in Western Massachusetts with their four children, ranging in age from fourteen to six.

"He left words to us reminding us to enjoy each and every day, that life is short, that you fill it with those you love, that you laugh and pursue your dreams, because they have the potential to come true," says Mrs. Gelb.

The fight against melanoma that Ron Gelb waged included taking part in clinical trials and experimental protocols. Even as he was dying, he was looking toward the future, when people in his situation would have a better chance.

Nanci Gelb agrees that's what's important. "Knowledge is increasing. Through collaborations, there are more possibilities for breakthroughs," she says. "As this journey continues, the battle must still be fought. But winning is within reach. Everyone has the opportunity to be involved - whether it's by making a charitable donation, working as an advocate or giving of your time to patients. That is how we make a difference."

In Memory of our Devoted Director
Judith Schnelwar Gladstein
 September 10, 2006
Her wisdom was instrumental in the
Foundation's growth;
her courage and determination
a testament to her strength.

Scientific Director *(continued)*

standing group of physician/scientists. Collaborating with an exceptional clinical research group, they have created a unique opportunity to put this concept to test. Moreover, the talents within this group will be available to share their disciplines with other SWCRF investigators working in other forms of cancer.

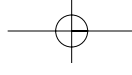
Although, the SWCRF is a relatively small organization, our program in melanoma research is a highly focused and collaborative program. The science is excellent and I am confident that future Newsletters will highlight remarkable breakthroughs by this group. As always, this can only happen with your support. *- Samuel Waxman*

SWCRF Rated #1 Cancer Charity in America

For 30 years, the Foundation has been instrumental in developing new drugs to successfully treat cancer and has supported and trained more than 160 scientists by awarding over \$55 million in grants. 89% of every dollar raised by the public and foundations goes directly to research. For that reason, The Foundation has been recognized recently by Charity Navigator as the #1 cancer research charity in America in its financial management and organizational effectiveness.

Charity Buzz

SWCRF recently teamed up with charitybuzz, an online auction firm that will manage our Gala's silent and live auctions this year. This is a very exciting opportunity for us as it expands our reach via the internet. Auction donations will be featured for two weeks before the event and will be offered for auction both on the internet site and live at our gala. This year, we are also doing a full public relations blitz to maximize our media exposure. We encourage you to visit the website at www.charitybuzz.com and to bid on a prize that can be associated with one of the most successful benefits in New York City. Last year, we raised a record \$2.8 million for cancer research, and we hope that, with your help, we will be even more successful this year.



Melanoma *(continued from cover)*

be able to identify and kill the cancer cells, and researchers will be able to observe the process.

“Waxman Foundation support is important to our research because it will be the first use of a lentiviral vector, which is a newer and more efficient gene transfer vehicle than used in the past,” says James Economou, Director the Human Gene Medicine program, Deputy

oper of the PET scan.

“By funding our team of investigators The Waxman Foundation has said that trying to translate our understanding of the basic biology of the immune response into new cancer therapeutics is serious,” says Owen Witte, Howard Hughes investigator and Professor of Microbiology, Immunology and Molecular Genetics at UCLA.

mental Therapeutics, is developing drugs to selectively inhibit one of the pathways required for the abnormal growth of malignant melanoma.

“In melanocytes a circuit that is commonly used for cell growth is comprised of the RAS protein which activates the RAF protein, which activates the MEK protein, which activates the MAP kinase protein,” Dr. Rosen explains. “In melanomas,

SWCRF is funding its investigators to translate the basic biology of the immune response into new cancer therapeutics

Director of the UCLA Jonsson Comprehensive Cancer Center and Professor of Surgery. “We’re also thinking about introducing the T cell receptor into blood stem cells but we need to do more pre-clinical animal studies first.”

“The second novel feature is that we will be putting in a gene that also allows us to visualize these cells in a PET scan (Positron Emission Tomography) so we can vaccinate patients and after we get these cells bring them in and do a PET scan. This will allow us to see where the modified cells are and how they’re behaving, instead of doing surgical biopsies. We can make sure the cells are following the model we’ve developed in animals. In the lab the researchers can already watch engineered T cells attack melanoma a few days after being injected into mice. That’s incredibly cool,” says Dr. Economou, who has also worked closely with Michael Phelps, the devel-

Dr. Witte is working with Drs. Baltimore and Economou to use the PET scan to follow the genetically engineered T lymphocytes. “This particular version we’re working on depends on introducing what we call a “reporter” gene, he says. “That will be introduced into the same T-Lymphocytes that we’re using for the therapeutic T Cell receptor gene. The reporter gene will allow us to concentrate a radioactive probe inside of the T Cells – vastly small amounts of probe with very high activity so it doesn’t damage T Cells or cause any other problem. We can visualize these cells and count them. And we’re getting ready to work to test this in people.”

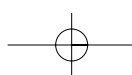
Broken Pathways

While colleagues in California are genetically modifying cells to fight melanoma, Dr. Neal Rosen, member of the Memorial Sloan-Kettering Department of Medicine and head of Develop-

mutations in the genes that encode the RAS protein and the BRAF protein commonly occur. When these proteins are mutated the pathway that leads to unregulated growth and is important for the development of melanomas is activated and cannot be turned off.”

Research in Dr. Rosen’s lab is concentrating on three drugs that inhibit this in malignant melanoma. All are in early clinical testing or being readied for testing in humans. One drug effective in melanoma models inhibits the MEK protein and arrests the growth of melanomas with the BRAF mutation. Another causes the destruction of the BRAF protein. The third drug that will be used in clinical trials late in 2006 inhibits the BRAF protein itself.

Dr. Rosen hopes to collaborate with Dr. Waxman in the future, “Our goal,” he says, “is to develop clinical strategies that will work.”



Special Events

24th Annual Golf Tournament

Event Chair Robert Fishbein and members of our Golf Tournament Committee were the hosts of this year's 24th Annual Golf Tournament held at Brae Burn Country Club on Monday, May 22nd. Their leadership efforts led to a total raised of \$200,000.

The event was underwritten by very generous sponsors Owl Creek Asset Management L.P. and the Jeffrey Altman Foundation, Edward Ricci, Bank of America and Satellite Asset Management L.P. and by our Tournament Patrons Lawrence Altman, Laurie and Robert Fishbein, Eric Goldstein, Linda and Gary Jacob, Mildred and Abner Levine, Tony Shogren, and Jerome Wolff.

Photos by Roland Thomasset



Center, Event Chair, Robert Fishbein with Scott Crocombe and Craig Leoce from Satellite Asset Management.



From left: Dolly Draizin, Barbara Steiner, Dale Claman and Nancy Strong.



From left: Board Member, Eddie Scheurer, Michael Dritz, Martin Gregge and Tom Gilbert.



From left: Peter Mack, Peter Workman, Dr. Samuel Waxman and David Taub.



From left: David Kaplan, Bob Rotanz, Board Chair, Michael Nierenberg and Howard Rubin.



From left: Bob Green, Jay Green, Harry O'Keefe and Ron Pinto.



From left: Norman Kramer, Board Member, Gary Jacob, Dennis Herman and Sam Giarusso.

3rd Annual Hamptons Happening

The Third Annual Hamptons Happening – a silent art auction and gourmet food tasting, was held on Saturday, July 8th at the home of Robyn and Kenneth Joseph on Georgica Pond in Wainscott. Nearly 450 guests were treated to delicacies from over 20 restaurants. 95 pieces of art were donated by galleries, artists and individuals. More than \$225,000 was raised, thanks to the dedication of event co-chairs Laurie L. Schaffran and Marion Waxman, who were tirelessly supported by Committee Members, Jocelyn Brandeis, Vira Capeci, Cecile Cohen, Dean and Kris Denninger, Elena Prohaska Glinn, Ed Greenblat, Kenneth and Robyn Joseph, Marcia Lavipour, Gale Meisenberg, Thomas Mikolasko, Lora Reichman, Dena K. Weiner and David Rozenholc, Clifford and Kristin Sterling, and Janet Tekworth. The Junior Committee Co-Chairs were Ruth Abend and Joanna Steinberg.

Palm Bay Imports and the Taub Family helped underwrite the four tents, and our very generous sponsors included Costas Kondylis, Leslie Elliot Krause, David and Marcia Lavipour, H. Robert Marcus and Audrey Flack, Elihu and Susan Rose, Andrew Sabin, Harvey and Karen Silverman, Robert Wechsler, and Albert J. and Ele Wood.

We look forward to seeing you at our fourth annual Hamptons Happening next July.

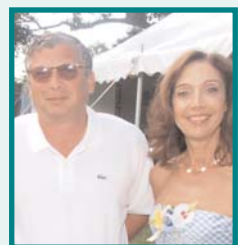
Photos by Richard Lewin



From left: Dena K. Weiner, Marion Waxman, Dr. Samuel Waxman, Robyn Joseph, Laurie Schaffran and Marcia Lavipour.



From left: Katerine Tekworth, Ruth Abend, Chris Brody, Lexi Kipper, Sara Meisel, Lauren Kepriss and Randy Abend.



Kenneth and Robyn Joseph.



Marion Waxman and Andrew Sabin.



Robert Marcus and Audrey Flack.



Kristin and Clifford Sterling.

Scientific Advisory Committee Commends 'Quality of Science'

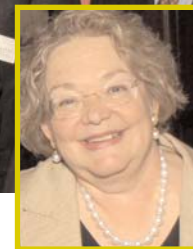
SWCRF grantees received wide-ranging praise from the Scientific Advisory Committee (SAC), which met on May 8, 2006. After a meeting which included presentations and a review of written materials, committee members commended the overall "quality of science" at the meeting and singled out individual grantees for praise. The Committee recognized "Excellent progress, promising work and uncovering a very novel mechanism." There was also enthusiastic acknowledgment of grantees "translating laboratory studies into the clinic and making an important discovery."

In addition, the Committee report lauded future funding plans, acknowledging "the success the Foundation has had in promoting symbiotic relationships that increase the power of each dollar spent... an enviable accomplishment at a time of reduced federal spending on cancer research." Congratulations were offered because the Foundation has been honored nationally for its record of efficiency in the use of research dollars.

"Our 2006 scientific review was a great success," says Dena K. Weiner, Vice President of the SWCRF and Chairwoman of the Scientific Advisory Committee. "This was not only because of the innovative science presented by our researchers, but also because of their collaboration. The 'Institute Without Walls' has achieved its goal of collaboration. It is bigger and more interactive than ever before, and therefore more exciting."



From left: Stuart Yuspa, M.D., Franco M. Muggia, M.D., Samuel Waxman, M.D., I. Bernard Weinstein, M.D., Frank J. Rauscher III, Ph.D., I. David Goldman, M.D.



Dena K. Weiner, Chair Science Committee.



Al Baldwin, Ph.D., UNC Chapel Hill speaking with Kathy Sarna representing The Three Strohm Sisters Family Foundation.

Committee Members

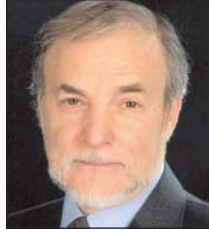
I. David Goldman, M.D. Professor of Medicine and Molecular Pharmacology, Director Albert Einstein College of Medicine, Cancer Research Center; **Franco Muggio, M.D.** Ann Murnick & David Cogan Professor of Oncology, Director of Medical Oncology, Kaplan Comprehensive Cancer Center; **Frank J. Rauscher, III, Ph.D.**, Professor and Chairman Molecular Genetics Program, Deputy Director, Wistar Institute Cancer Center; **I. Bernard Weinstein, M.D.**, Froe Jensen Professor of Medicine, Columbia University; **Stuart Yuspa, M.D.**, Chief, Laboratory of Cellular Carcinogenesis and Tumor Promotion, Deputy Director, Center for Cancer Research, National Institutes of Health, The National Cancer Institute.

(continued on page 9)

Meet Our Investigators



Nabeel M. Bardeesy, Ph.D



Stephen Baylin, Ph.D



Anthony J. Capobianco, Ph.D



James Economou, M.D., Ph.D.



Shai Izraeli, M.D.



Ari Melnick, M.D.



Terry Van Dyke, Ph.D

SWCRF Institute Without Walls Adds New Researchers

The Institute Without Walls received an impressive 70 individual and 21 program grant applications for its 2006 funding cycle. A panel of 33 investigators conducted an intensive peer review of each proposal based on a process employed by the National Institutes of Health and awarded five new individual and two new program grants.

The grants cover a period of up to three years. After the second year of funding, grantees must demonstrate collaboration with other SWCRF investigators and receive a positive review from the Foundation's external Scientific Advisory Committee. Grantees will then become eligible for a third year of funding and for future bridging grants.

Individual Grant Recipients

Nabeel M. Bardeesy, Ph.D., Assistant Professor of Medicine, Massachusetts General Hospital Cancer Center

Pancreatic cancer is a leading cause of cancer mortality for which no suitable therapies exist. There are stem cells in pancreatic cancer which are similar to stem cells found in many normal human tissues. Normal stem cells are responsible for replacing cells that die over an individual's lifespan while cancer stem cells are required for the unregulated growth of tumors. Dr. Bardeesy's lab believes that understanding these rare tumor cells and what controls their growth and survival will provide significant new insights relevant to pancreatic cancer treatment. An important pathway called the Notch pathway may regulate the abnormal growth of pancreatic stem cells. The lab will use new drugs to block the Notch pathway with the hope of killing these stem cells while having minimal effect on normal stem cells.

Stephen Baylin, Ph.D., Professor, Oncology and Medicine Department of Oncology/ Cancer Biology, The Johns Hopkins University

Epigenetic therapy is designed to recover the function of genes that are silenced in cancer.

Shutting down (silencing) of genes occurs frequently and is a complex problem which results in abnormal growth differentiation and tumor cell death. However, recovering their function by designing new drugs is a clinical reality. Dr. Baylin's lab has discovered a new class of enzymes that can shut down gene function in two powerful ways. The lab will develop new compounds to inhibit this enzyme and study its anti-tumor effects.

Anthony J. Capobianco, Ph.D. Associate Professor, Molecular and Cellular Oncogenesis Program, The Wistar Institute

Research in the Capobianco lab is directed towards understanding how deregulation of members of the notch signaling pathway leads to the formation of cancer. The lab's aim is to develop and analyze a therapeutic agent which restores the normal function of this pathway which can be directed towards treating blood malignancies. The lab will use mouse

models of leukemia which are genetically engineered to evaluate the effect of specific inhibitors in order to screen for new treatments.

Shai Izraeli, M.D., Head of the research section of Pediatric Oncology and a senior lecturer at Sackler Medical School, Sheba Medical Center & Tel-Aviv University

There is a high level of the ERG gene in many patients with leukemia, Ewing sarcoma (childhood bone cancer) and prostate cancer. Dr. Izraeli has recently discovered that normal levels of the ERG gene are required for the development of normal blood cells. The lab's current goal is to study why high ERG levels are associated with cancer cells and then to decipher the signals governing ERG gene functions. The lab will then focus on how to revert ERG function from causing the growth of cancer to normal development.

Terry Van Dyke, Ph.D., Professor of Genetics at University of North Carolina Chapel Hill, Lineberger Comprehensive Cancer Center.

Dr. Van Dyke's lab focuses on the most common brain tumor in humans, glioblastoma multiforme (GBM), for which there is currently no effective treatment. Dr. Van Dyke's lab is interna-

tionally known for establishing mouse models of human cancer which mimic the human disease. The lab has developed a preclinical mouse model of GBM and will study a major pathway responsible for the aggressively invasive properties of this cancer. These studies, not possible in humans, will likely lead to the identification of new therapeutic targets for the development of effective treatments in humans and will provide a better understanding of this aggressive and devastating disease.

Program Grant Recipients

Albert Einstein College of Medicine of Yeshiva University, University of Toronto, University of Maryland, Baltimore.

Primary Investigators/ Institutions:

Ari Melnick, M.D., Assistant Professor, Developmental & Molecular Biology

Gilbert Privé, Ph.D., Senior Scientist, Associate Professor, Department of Biochemistry

Alexander MacKerell, Ph.D. Professor, School of Pharmacy, Pharmaceutical Sciences

This research team has developed computational tools to design highly specific and non-toxic cancer drugs based on their atomic-level mapping of cancer causing proteins. The first part of the project focuses on a cancer protein called BCL6, which is involved in causing a majority of B-cell lymphomas in the USA. The investigators have already shown that inhibition of BCL6 by the drugs they have developed kills lymphomas without toxicity. The current work will refine and identify new classes of BCL6 inhibitor

that can be tested in clinical trials to improve the outcome for patients with lymphomas. In the second part of their project, the team has shown that another protein called kaiso is required for the survival of several different tumor types. Kaiso does this by shutting down genes that would otherwise allow cancer cells to die or stop growing. The investigators have identified the molecular "Achilles heel" of kaiso and are designing drugs that will block the actions of kaiso without affecting normal cells. This work is expected to lead to a new class of drugs that could potentially benefit patients with several different kinds of tumors. This group of scientists with expertise in computational chemistry and drug design, structural biology and cancer causing proteins offers an important resource for many other SWCRF investigators working towards the development of drugs that target cancer causing proteins.

University of California, Los Angeles, California Institute of Technology, University of Southern California, Children's Hospital of Los Angeles and the University of Connecticut.

Primary Investigators/ Institutions:

James Economou, Professor of Surgery, Professor of Microbiology, Immunology and Molecular Genetics Director, UCLA Human Gene Medicine Program, Deputy Director, UCLA Jonsson Comprehensive Cancer Center

Owen Witte, Professor of Microbiology, Immunology and Molecular Genetics. Director, Institute for Stem Cell Biology and Medicine

David Baltimore, President Emeritis, Millikan Professor of Biology, California Institute of Technology

Please see article on Page 1 of this Report.

(continued from page 7)

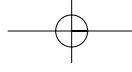
Scientific Advisory

Outstanding Grantee Performances

Jonathan Licht, MD, Northwestern University Feinberg School of Medicine, received accolades from the SAC for his work with transcriptional functions and targets of the MMSET Protein in the t(4:14) myeloma. Publishing 5 papers in the past year, Dr. Licht has provided "convincing evidence that the MMSET protein is a global histone methyl transferase and regulator of transcription." The SAC feels his plans for future investigation are "excellent and well designed."

The SAC recognized **Ari Melnick, MD,** Albert Einstein College of Medicine for "excellent progress in providing evidence that the Kaiso protein is an essential repressor of methylated tumor suppressor genes in colon cancer." Because he is skilled in techniques related to chromatin structure and "epigenomics," he could act as an important resource or leader for other SWCRF investigators. Dr. Melnick was also commended for having made "remarkable connections for collaborative work for Chip-Chip and structural biology work, as well as for research connected with BMI-1 and PRC complexes.

William Weiss, MD., PhD., University of California, San Francisco has made the "important discovery" that inhibition of p13-kinase signaling destabilizes the Myc protein and thereby inhibits growth and causes apoptosis in neuroblastoma cells in which N-Myc is amplified. Future plans in this "superb project in translational research" include screening for and developing P13-kinase inhibitors for use in treatment of children with neuroblastoma.



David Workman Memorial Award

Mount Sinai Medical Center's Goldwurm Auditorium, located at 1425 Madison Avenue, will be the setting for our Third David Workman Memorial Award and Lecture, to be presented on Thursday, November 16, 2006. The David Workman Memorial Endowment was established to honor the memory of David Workman and his 20 years of commitment and dedication to the Samuel Waxman Cancer Research Foundation. The Endowment provides a \$50,000 grant to enable the clinical development of novel selective therapies for poorly treatable forms of cancer.

SWCRF 2006 honorees are two National Institutes of Health (NIH) scientists whose

research resulted in the clinical development of the Human Papilloma Virus (HPV) vaccine against cervical cancer, the first HPV vaccine to be approved by the FDA. The vaccine protects women against strains of a widely transmitted infection of HPV that causes cervical cancer. Cervical cancer strikes more than 14,000 U.S. women each year, killing more than 3,900, and is more prevalent in developing countries.

Dr. Douglas Lowy and Dr. John Schiller, world-renowned scientific investigators from the NIH and the third recipients of the David Workman Memorial Award, will share their clinical and research findings on the HPV vaccine against cervical cancer. Past

recipients included Dr. Waun Ki Hong and Dr. Reuben Lotan of MD Anderson Cancer Center of the University of Texas as well as Dr. Michael Grever, Chair, Department of Internal Medicine, Ohio State University.

The program will start at 5:00 PM with the award ceremony and lecture followed by a cocktail reception. Dr. Dennis Charney, Dean of Scientific Affairs, at the Mount Sinai Medical Center and Dr. Samuel Waxman will pay tribute to David Workman's life and work and introduce the recipients of the Workman Memorial Award.

This event is made possible by a grant from Merck & Co.

Help us keep costs down, please send your email address to report@waxmancancer.org

HOLD THE DATES

"Collaborating for a Cure"
Benefit Dinner and
Silent and Live Auction
Featuring John Fogerty
Thursday, November 30, 2006

David Yurman Boutique, NYC
Celebrate SWCRF's 30th
Anniversary
Tuesday, November 14, 2006
6-8 PM

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

**SAMUEL WAXMAN
CANCER RESEARCH FOUNDATION**
1150 FIFTH AVENUE, NEW YORK, NY 10128
TEL: 212-241-1760 FAX: 212-426-2273
WWW.WAXMANCANCER.ORG

