www.waxmancancer.org Launched

Featuring a fresh look and much information, the Foundation's new website has been launched. Please visit the site for the latest research developments, news about upcoming events, and information on how to support the work of the Foundation.

The development of the new site would not have been possible without the help of our dedicated Website Committee. The Foundation is particularly grateful to Jerry Pickholz, Lori Skrobola, Board President Dr. Tami Spilo, and Board member Spencer Waxman. ◆

Design by Barbara Taff / Studio 8 Design www.studio8.com
Written by Allison Kidd

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

NON-PROFIT ORG.
U.S. POSTAGE
PAID
STATEN ISLAND, NY
PERMIT NO. 169

Samuel Waxman Cancer Research Foundation

REPORT

FALL / WINTER 2003

Independent Scientific Review Committee Praises Foundation's Progress

From left: Dr. Rauscher, Dena K. Weiner, Science Committee Chair, Dr. Samuel Waxman, Scientific Director, Dr. Wicha, Dr. Yuspa, and Dr. Muggia

2003 Scientific Advisory Committee:

FRANCO M. MUGGIA, M.D., DIRECTOR, DIVISION OF MEDICAL ONCOLOGY, KAPLAN COMPREHENSIVE CANCER CENTER, NEW YORK UNIVERSITY.

FRANK J. RAUSCHER, III, PH.D., DEPUTY DIRECTOR, WISTAR INSTITUTE CANCER CENTER, UNIVERSITY OF PENNSYLVANIA. EDITOR-IN-CHIEF, *CANCER RESEARCH*.

MAX WICHA, M.D., DIRECTOR, UNIVERSITY OF MICHIGAN COMPREHENSIVE CANCER CENTER.

STUART YUSPA, M.D., DEPUTY DIRECTOR, CENTER FOR CANCER RESEARCH, NATIONAL INSTITUTES OF HEALTH.

Citing breadth and depth of research, the Scientific Advisory Committee (SAC), an external, independent committee, commended the Foundation for the expansion it has undertaken over the past several years at the annual SAC Meeting, held on June 9.

During the day, the Committee reviewed presentations and written material by each Foundation supported investigator in order to assess the quality of the research being conducted, and to evaluate new collaborations between investigators. Board members and friends of the Foundation received a summary of the Committee's findings and engaged in a question and answer session (at a meeting) held at The Lotos Club that evening.

The expansion of the Foundation's research focus, while maintaining an

continued on p. 5

New Laboratory Space at Mount Sinai for the Waxman Foundation

The Foundation supported investigators at The Mount Sinai Medical Center will move to larger, recently renovated laboratories this Fall. The five new laboratories are located on the 24th floor of the Annenberg building, the primary building of the Mount Sinai School of Medicine. The Foundation's investigators will share the floor with other investigators within the Division of Hematology and Oncology of the Department of Medicine.

In addition to being larger, the new labs are much closer to the School's research infrastructure, including the Microscopy Core and the Microarray Core. The 24th floor contains many shared departmental

continued on p. 5

Inside

Scientific Director's Message

Dear Friends,

During this year, the Foundation has experienced enormous growth. Our "Institute Without Walls" - once a vision - now comprises an international and national network of more than 24 leading cancer investigators. The Institute, only two years old and burgeoning, is the organizing principle around which we will accelerate our research efforts in collaborating for a cure.

How does the Institute work? Academic medical institutions are pre-selected and asked to submit one application. The investigator's proposal must demonstrate scientific expertise as measured by peer-reviewed National Institutes of Health (NIH), research grants and productivity, commitment to develop targeted therapies and a willingness to collaborate with others in the Institute. Priority is given to:

- Proposals addressing promising new areas of study, where funding may serve as the first step in obtaining long-term funding from the National Institutes of Health and other major granting agencies.
- Studies that will directly impact the understanding of the mechanisms of the disease and/or the clinical treatment of individuals with cancer.

Research must be in one of the following areas:

- Development of transcription based therapy-agents that defeat gene repression in cancer.
- Development of new therapies/pathways to overcome defective differentiation and/or encourage selective death (apoptosis) of cancer cells.

All applications are evaluated by the Foundation's Grants Review Committee, comprised of members of the Scientific Advisory Committee and independent, outside reviewers. Final review and approval rests with the Board of Directors. Funding of awards is based on the priority score awarded each application, the recommendations of the Grants Review Committee and the Scientific Advisory Committee.

Based upon peer review of nearly 50 highly competitive applications received in this year's cycle, two were funded for three years.

Recognizing that there is a need to maintain formative collaborations, the Institute will further "cement" currently sponsored studies by continuing to fund some of the most promising sponsored programs to serve as catalysts and "bridges" between Foundation investigators. Our goal is to continue funding investigators so that within the next three to five years, we increase the number to 50.

We have long believed that working together is the most effective way to facilitate cancer research from the laboratory to the patient and that partnerships can successfully exist between government, academia, nonprofit institutions, the pharmaceutical industry and you, our supporters and advocates.

It is a privilege to see the enthusiasm, hope, commitment and generosity by the leadership of the Foundation and its many friends are at an all time high. Now will be the time when you will see the Foundation make a stronger and more visible impact on developing new, targeted cancer selective therapies. Collaborative research is the vital link to finding treatments. Your involvement and support make this all possible.

– Samuel Waxman

REPORT
Samuel Waxman Cancer Research Foundation

FOUNDED IN 1976, THE FOUNDATION IS A NOT-FOR-PROFIT ORGANIZATION DEDICATED TO THE SUPPORT OF BASIC AND CLINICAL RESEARCH ON THE CAUSES OF CANCER AND TO DEVELOPING LESS TOXIC, CANCER CELL-SPECIFIC TREATMENTS.

News Briefs

Chemotherapy and Waxman Foundations Linked Together Again

The Ezra M. Greenspan Chair in Clinical Cancer Therapeutics at the Mount Sinai School of Medicine has been awarded to Dr. Jonathan Licht, Associate Scientific Director of the Foundation. Dr. Licht is also Vice Chairman of Research in the Department of Medicine and Director of the Division of Hematology/Oncology.

The Chemotherapy Foundation established this Chair in recognition of Dr. Greenspan's leadership as its founder, chairman and medical director, and his pioneering work in developing innovative cancer therapies. A professorial chair represents an endowment of $2 million.

The Chemotherapy Foundation has been involved in the work of the Waxman Foundation since its inception. In fact, a grant from the Chemotherapy Foundation in 1976 helped initiate Dr. Samuel Waxman's research dedicated to finding and developing targeted cancer therapies. The Chemotherapy Foundation has remained a major supporter of the Waxman Foundation over the past 27 years, and now plays an important role in Dr. Licht's research career as well. ◆

Dr. Paul Klotman, Professor and Chairman of the Department of Medicine, awards the Greenspan Chair to Dr. Jonathan Licht

In recent months, important findings have been reported by Foundation sponsored investigators. Highlights include:

- **Dr. Jeffrey Settleman**, MGH-Harvard, has found a means of specifically inactivating the Ras gene. The Ras gene is the most commonly detected cancer-causing gene, and plays a causative role in approximately one-third of all human tumors. This study could lead to the development of a drug that effectively treats human tumors that carry altered Ras genes.[1]

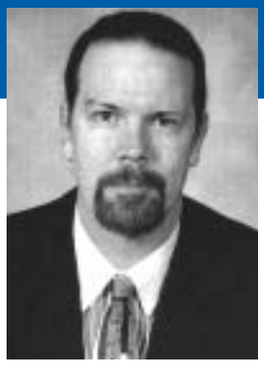
- **Dr. Albert Baldwin**, University of North Carolina, has shown that the oncogene Ras activates the transcription factor NF-kB only in a limited manner, activating a subset of NF-kB-dependent genes while suppressing others. The findings will allow for a better understanding of oncogenic mechanisms controlled by Ras. This identifies another pathway for therapeutic blocking of mutant Ras.[2]

- **Dr. Doris Germain**, Mount Sinai Medical Center, has developed and characterized a new mouse model of breast cancer that accumulates cyclin D3 in their mammary glands, and has found that 100% of these mice develop cancer. Cyclin D3 is found to be abnormally elevated in 15% of breast cancers and its presence is associated with low survival rates. This development provides an animal model that mimics this 15% of breast cancers with elevated D3 and will allow for testing of particular drugs on these cancers.[3]

- **Dr. Rafael Mira-y-Lopez**, Mount Sinai Medical Center, has reported that CRBP, a vitamin A receptor, safeguards the normal mammary epithelium against the transforming effect of oncogenes and a mechanism whereby CRBP prevents breast cancer development. He previously reported that the CRBP gene is blocked in 25% of breast cancers. Treatment strategy to restore CRBP function is in development and may help prevent the development of breast cancer.[4]

- **Dr. Ethan Dmitrovsky**, Dartmouth Medical School, reported the identity of retinoic acid target genes in the lung using gene profiling (DNA microarray analyses). These species are potential targets for lung cancer therapy or chemoprevention.[5]

[1] Fischbach MA, Settleman J. Specific biochemical inactivation of oncogenic Ras protein by nucleoside diphosphate kinase. Cancer Research 63 (14): 4089-94, 2003 Jul 15.
[2] Hanson J, Anest V, Reuther J, Baldwin A. Oncoprotein suppression of TNF-induced NF-kB activation is independent of Ras-controlled pathways. Journal of Biol. Chem. 278, 34910-34917, 2003.
[3] Prikmaier A, Dow R, Ganiatsas S, Waring P, Hendley J, Germain D. Alernative mammary oncogenic pathways are induced by D-type cyclins; MMTV-cyclin D3 transgenic mice develop squamous cell carcinoma. Oncogene 22: 4425-4433, 2003.
[4] Submitted to Journal of Cell Biology: Farias EF, Ong DE, Ghyselinck NB, Kuppumbatti YS, Mira-y-Lopez R. The cellular retinol-binding protein type I enforces mammary epithelial morphogenesis through retinoic acid receptor activation and phosphatidylinositol-3 kinase inhibition.
[5] Ma Y, Koza-Taylor P, DiMattia D, Hames L, Fu H, Dragnev K, Turi T, Beebe J, Freemantle S, Dmitrovsky E. Microarray analysis uncovers retinoid targets in human bronchial epithelial cells. Oncogene, 22: 4924-4932, 2003.



Meet our Investigators

Longstanding Collaborator: **Paul Fisher**

At the first International Conference on Differentiation Therapy, a biannual conference that the Waxman Foundation has co-sponsored since its inception in 1986, a mutual colleague introduced Drs. Paul Fisher and Samuel Waxman. Both had an intense interest in the potential of differentiation therapy to treat cancer. What has since developed is a long collaboration with the Foundation, with Dr. Fisher receiving grants for each of the past 14 years.

Paul B. Fisher, M.PH., Ph.D., is Professor of Clinical Pathology, Director of Neuro-Oncology Research and a Michael and Stella Chernow Urological Cancer Research Scientist at the College of Physicians and Surgeons of Columbia University.

Dr. Fisher's laboratory is primarily interested in understanding the molecular basis of cancer development and progression by studying malignant melanoma. He has pioneered the use of molecular approaches (such as subtraction hybridization; Fig. 1) to identify and clone genes displaying altered expression as a result of differentiation therapy, which causes the malignant melanoma cells to revert into more normal cells that lose their cancerous properties. By identifying genes associated with and possibly causative of cancer reversion, including genes promoting cancer (oncogenes) and inhibiting cancer (tumor suppressors), Dr. Fisher hopes to develop targeted therapies that inhibit oncogene or restore tumor suppressor activity in melanoma cells, leading to the targeted death of the cancer cell. The therapeutic strategies developed using melanoma

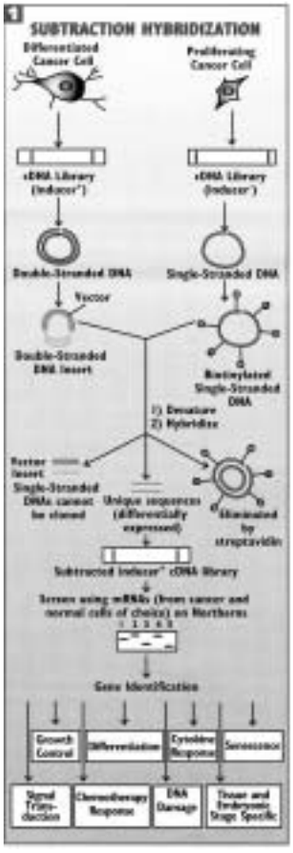


Figure 1

models could have broader relevance for other forms of cancer, and Dr. Fisher has expanded his research studies to include prostate, breast, pancreatic, colorectal, and brain cancers.

Dr. Fisher considers one of his most important research discoveries to be the identification of a novel gene that selectively kills cancer cells without harming normal cells. This gene, referred to as melanoma differentiation associated gene-7 (mda-7), because of its isolation from differentiating melanoma cells, is in fact a novel cytokine (a secreted protein associated with the immune system), now named interleukin-24 (IL-24). Mda-7/IL-24 protein is secreted from both normal and cancer cells following infection with a replication incompetent adenovirus expressing this gene. The cytokine nature of this protein is very relevant to cancer therapy, since mda-7/IL-24 not only kills initially infected cancer cells, but also because the secreted protein also affects tumor cells at a distance, inducing a 'bystander killing effect'. In principle, this unique cytokine will be secreted throughout the body and, as a result, will be able to target metastases (the spreading of cancer) that have developed at a distance from the original tumor. This is particularly important for the treatment of advanced cancers, as most cancer fatalities are the result of metastases.

The cancer-killing drug developed from this research is now in Phase II clinical trials at the M.D. Anderson Cancer Center in Houston and the Samson Clinic in Dallas. A Phase II trial is a second tier evaluation of a therapeutic to define optimal dose and potential efficacy as a therapy worthy of future testing for real clinical benefit compared to other approaches in treating a disease state.

In addition to a longstanding collaboration with Dr. Waxman, Dr. Fisher is actively involved in partnerships with other Foundation supported researchers. He is a participant in the exchange program with the Shanghai Institute of Hematology (SIH) on a program involving neuroblastoma, a rare and aggressive childhood cancer that originates in the nervous system. In addition he has begun communications with Dr. Albert Baldwin at the University of North Carolina, Dr. Reuben Lotan at the M.D. Anderson Cancer Center, a recipient of the Foundation's prestigious David Workman Memorial Endowment Award, and Dr. Yongkui Jing at the Mount Sinai School of Medicine, all of whom conduct research on signal molecules responsible for cancer development in various types of the disease. ◆

New Laboratory Space

continued from page 1

facilities, including a tissue culture room, cold room (for conducting procedures requiring low temperatures, and storing reagents and tissue samples), instrument room and dark rooms (for developing films). The proximity to these high quality research facilities will allow for streamlining the research process.

The Foundation's independent Scientific Advisory Committee, given the opportunity to view the new facilities, reported that they were pleased to learn of the move, and noted it "will be of significantly improved quality and quantity and should enable the continued development of research programs at Mount Sinai."

For many years, limited space has been a hindrance to the expanding research programs supported by the Foundation. However, with more room and more modern facilities, the Foundation's investigators at Mount Sinai – Drs. Doris Germain, Yongkui Jing, Rafael Mira-y-Lopez, Liliana Ossowski, and Samuel Waxman - will be able to hire additional research staff.

The proximity to other investigators in the field will facilitate collaborative interactions, one of the primary goals of the Foundation. According to Dr. Ossowski, "The main benefit is the potential for more collaborative [research] with the Hematology/Oncology Division. There are several excellent scientists, two of them newly recruited, that will become close colleagues."

A formal dedication of the new Waxman Foundation laboratories will be held next year, and naming opportunities are available. Please contact Ann Jackowitz, Executive Director, if you would like further information. ◆

Independent Scientific Review

continued from page 1

emphasis on selectively targeting malignant cells, was cited as a major development. The Committee applauded the Foundation for working in multiple forms of cancer, including leukemias, prostate, uterine, ovarian and breast cancers, and for expanding its research into both therapeutic and prevention trials. Clinical trials, such as these, are the final step in the development of cancer therapies.

Following the Scientific Review, a workshop was held on June 10th in which Foundation investigators discussed developments in their research and forged new collaborative relationships.

For a copy of the Scientific Advisory Committee's Report, please contact the Foundation office at (212) 241-1760 or swcrf@waxmancancer.org. ◆

From left: Drs. Reuben Lotan, M.D. Anderson Cancer Center, James Herman, Johns Hopkins Medical Institute, and Paul Fisher, Columbia University

From left: Corrine Barsky, Board member, Joan Safir, Chairman Emeritus, Laurie Schaffran, Board Secretary

From left: Dale and Peter Claman, Board member, and Dr. Yongkui Jing

From left: Cynthia and Tony Shogren, Board member, and Alan Safir, Chairman Emeritus

Fundraising News

21st Annual Golf Tournament a Success

There were 85 players and many dedicated volunteers who helped raise over $245,000 at the Foundation's 21st Annual Golf Tournament, held on June 16th at Sunningdale Country Club. This year, the day was dedicated to the memory of Shumer Lonoff. Mr. Lonoff, who played an integral role in supporting the annual tournament, was an avid golfer and served as Treasurer of the Foundation's Board.

Dr. Martin Goldstein made Tournament history by hitting a hole-in-one and driving home a new Land Rover, generously donated by Land Rover Larchmont. Other prizes included tickets to the 2004 U.S. Open at Shinnecock Hills Golf Club and a getaway to the Four Seasons Resort in Palm Beach, FL.

Our thanks to the Golf Committee, chaired by Ed Sheldon and co-chaired by Gary Jacob, Abby Levine and Ed Scheurer, and Golf Patrons Lawrence Altman, Paul Bernstein, Robert Cannon, Eric Goldstein, Gary Jacob, Abby Levine, Ed Sheldon, Tony Shogren and Dr. Jerry Wolff who helped to make the event fun and successful. ◆

Dr. Martin Goldstein celebrates his hole-in-one

From left: Robert Fischer, Board member, Alan Safir, Chairman Emeritus, Dr. Samuel Waxman, Benjamin Marks, Robert Zimmer

From left: Dr. Samuel Waxman, Michael Sokol, Kenneth Sherman, Charles Schaffran, and Mark Abehouse

Edie Scheurer and Mildred Levine

From left: Myron Wald, Dr. Samuel Waxman, Mark Hill, Ed Scheurer, Honorary Board member, and Ryan Kenny

From left: Dan Brodsky, Peter Claman, Board member, Dr. Samuel Waxman, Martin Levine, and Joshua Muss

Philanthropy for the Future

Mildred & Abby Levine

For over twenty years, the Foundation has been fortunate to include Mildred and Abby Levine among its strongest supporters. This relationship has included service on the Board of Directors, the establishment of a challenge grant for prostate cancer research, and serving as an annual patron of the Foundation's golf tournament. Yet it is with an eye to the future, and not to the activities of the past, that the Levines look to make a difference.

A desire to improve the world for future generations has led the Levines to become active philanthropists. Whether it be the survival of Israel, to which they are also strongly dedicated, or the improvement of medical treatments, Abby and Mildred feel strongly that their own good fortune should be shared with others.

The Levines became involved in the work of the Foundation after Abby was diagnosed with lymphoma in 1982. Upon the recommendation of a friend, he scheduled a visit with Dr. Samuel Waxman, whom he lovingly calls "his guru," and was successfully treated for the disease. Mildred and Abby were eager to support a golf tournament that had just been organized by their friends, David Workman, Alan Safir and others, to support the research conducted by Dr. Waxman.

The Levines have continued to sponsor the Tournament every year since. Rather than play golf at the Tournament, Abby prefers to ride around with Dr. Waxman in order to serve as an ambassador of the Foundation, speaking with players and sharing his belief in cancer differentiation therapy, the driving force behind the Foundation's research.

However, nothing demonstrates their commitment to engaging others in the work of the Foundation better than the Abner and Mildred Levine Challenge Grant, established to fund research on the use of arsenic trioxide to treat prostate cancer. By personalizing the cause for their friends and family, Abby and Mildred saw a challenge grant as the most effective way to raise the funds necessary to help find a cure. To date, the Levine Challenge Grant has raised nearly $250,000 to support this important research.

In their commitment to a future of improved cancer therapies, the Levines have not only worked actively on behalf of the Foundation, but also maintained a personal relationship with Dr. Waxman, who notes, "I look constantly to Mildred and Abby for advice on how to develop the Foundation. They have been an invaluable source of strength and wisdom."

Abby and Mildred are blessed and thankful to have celebrated their 60th wedding anniversary this October. ◆

New Directors Elected to Board

Clifford Greenberg and **Leslie Elliot Krause** have been elected to serve on the Foundation's Board of Directors.

Mr. Greenberg is Vice President and Portfolio Manager of Baron Capital's Small Cap Fund, and is a graduate of Cornell University and Columbia University Law School. Together with his wife, Alyssa, Mr. Greenberg has served on the Benefit Committee of the Foundation's annual Dinner and Auction, and has been active in increasing awareness of the Foundation's presence and mission. In addition, he serves on the Board of Directors of the United Jewish Appeal, and is active in its Wall Street Division. Mr. and Mrs. Greenberg live on Long Island with their daughter and two sons.

Mr. Krause is a longtime supporter of the Foundation, and brings extensive expertise in advocacy and philanthropy for leukemia research. He serves on the National Board of the Leukemia and Lymphoma Society, and is President of its New York City chapter. Mr. Krause is a personal injury attorney in Manhattan, and earned an MBA from Baruch College, a JD from Brooklyn Law School, and an LLM from New York University School of Law. He is the parent of a survivor of leukemia.