

SAMUEL WAXMAN CANCER RESEARCH FOUNDATION

# REPORT

Spring 2007

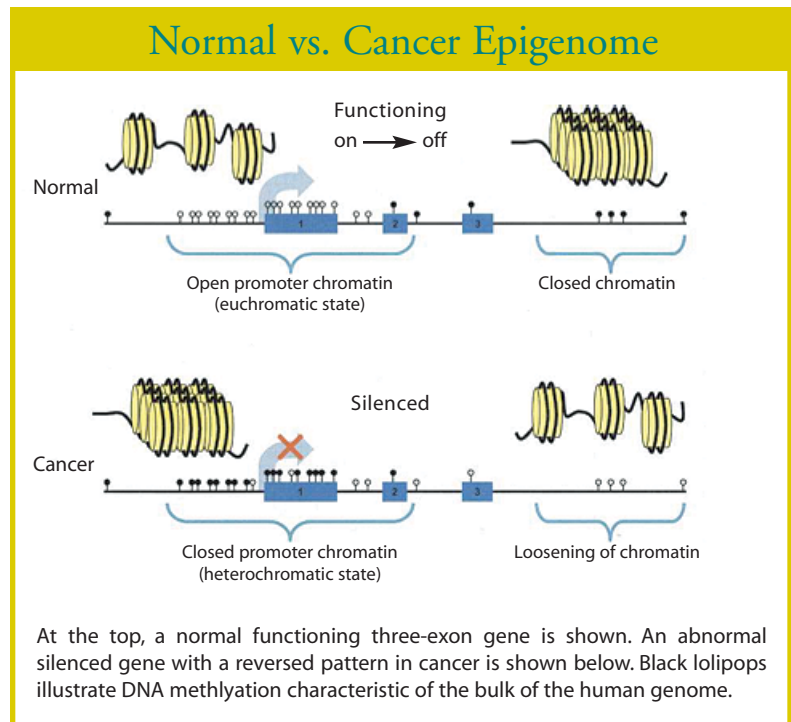
## Epigenetic Therapy: Promising New Focus on Blood Malignancies

*A Way to Reverse Abnormal Gene Controls that Cause Cancer*

**F**or decades the general public has been aware that genetics can play an important role in cancer and its treatment, but most people have never heard the word epigenetics — a “hot” field of cancer research that presents another rich avenue of possibility.

Genetics is the study of heredity and variation of genes, which are made up of DNA. Investigating the human genome has, among other things, helped to uncover cancer-related mutations in human DNA, producing tools for the discovery of treatments. However, gene therapy to replace mutated cancer-causing genes has been difficult to develop.

Epigenetics, the study of the control of gene expression by non-DNA components, is another exciting area of opportunity for scientists looking for ways to overcome abnormal gene expression in blood malignancies such as leukemia. This work also has profound implications for the treatment of solid tumors, since these controls are reversible and correctable without gene replacement. Genes that have been “switched



off” or “silenced” or are overly active due to these non-DNA components are common in all forms of cancer. Genes can be “turned on” by pharmaceutical agents so the genes function normally, or are “off”, causing cancer cells to differentiate and direct them to die with minimal toxicity to normal cells.

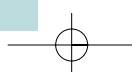
### Long-Term Work Moves Forward

Scientists have been examining gene expression for years, but now there is significant progress in the effort to figure out how to manipulate those expressions with drugs. As Dr. Samuel Waxman explains it, in the past several years the FDA has approved 3 epigenetic drugs that can “change the behavior of malignant genes by drugging the proteins that control them.” These promising new drugs are less toxic than

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## From the Chairman & Scientific Director



**Michael Nierenberg**  
Chairman of the Board

*The opening years of the 21st century brought new approaches to the prevention, diagnosis and treatment of the many forms of cancer that together constitute one of the greatest threats to human health. To respond, the Samuel Waxman Cancer Research Foundation has dramatically expanded the number of collaborative institutions and scientists participating in our Institute Without Walls.*

*Traditionally, our support has come from our very dedicated private contributors. We are now trying to galvanize significant private sector support to sustain our increased grantmaking by launching a new initiative this year inviting corporations to partake in our expanding growth by joining our Corporate Council. The Corporate Council is the channel that marshals creative forces to bind physicians, scientists, and the biotechnology and pharmaceutical industries to help capitalize on intellectual property, experiments, clinical trials and accomplishments of the distinguished scientists and research institutions who collaborate and that we support throughout the globe.*

*The Samuel Waxman Cancer Research Foundation stands apart in two significant ways. First, we require a collaborative approach functioning as an Institute Without Walls and providing an innovative framework for research that brings together world-class biomedical investigators with a critical mass of technology. Second, we intend to launch a major growth campaign in order to reach our goal by 2010 to have on-going support for 100 investigators in the search for a cure.*

*The SWCRF research expenditure is \$4.8 million for fiscal year 2006-07 and we are working to double that in the next five years. We project that the total programmatic impact of collaborative research in the Institute to be \$25 million or a return of five-fold on the Foundation's investment by the leverage of other sources of funding our grants generate.*

*Last year's Collaborating for a Cure gala raised a record \$4 million for cancer research, a tremendous achievement which was recognized in Crain's New York Business. Our annual events are a demonstration of the energy, dedication and personal investment of the leadership of the Foundation and you, our committed supporters. Please help SWCRF in our efforts to generate the research that will increase the number of cancer survivors, prevent the disease and ultimately eliminate it from our lives. The scientists who work toward that goal appreciate your trust and support.*

– Michael Nierenberg



**Samuel Waxman, M.D.**  
Scientific Director

*Recently I have been giving a series of talks to groups of people like yourself – sharing my excitement about the new “21st Century Cancer Therapies”. I thoroughly enjoy telling about the first 21st century cancer vaccine which blocks human papilloma virus infection, the cause of most cases of cervical cancer. This is an amazing breakthrough, which took more than two decades of hard work and will save hundreds of thousands of lives throughout the world. You may recall that the SWCRF gave the David Workman Memorial Award to Doug Lowy and John Schiller for wonderful work on the vaccine.*

*Three 21st century drugs have been recently approved by the FDA to treat leukemia, myelodysplastic syndrome and lymphoma. These drugs are designed to target the epigenome which consists of several proteins that control how a gene functions. Epigenetic therapy with these drugs is appealing since this part of the defective gene switch can be reversed whereas attacking the genome where there may be a total loss of a gene or a mutation is not reversible unless one can successfully deliver gene therapy to the cancer cell. In 1989, SWCRF investigators reported the first successful epigenetic therapy for acute promyelocytic leukemia (APL). The epigenetic drug used was retinoic acid and then afterwards arsenic trioxide. Correcting the abnormal epigenome of APL was the basis of differentiation therapy which changed a highly fatal leukemia to a disease that is 90% curable disease. It is estimated that more than 50,000 lives have been saved with this treatment which is standard world-wide. This breakthrough started with laboratory experiments in 1970 and continues in the 21st century.*

*Pier Paolo Pandolfi, in an introduction to a book on APL published this year, wrote the following:*

*“The APL breakthrough demonstrates that cancer can be defeated in universities and other academic institutions by an international effort by government and philanthropic support”. The APL model will continue to be the paradigm of SWCRF as we go forward with you as partners to conquer other forms of cancer.*

*Treatments of other acute leukemias have not done as well and still rely on skillful use of chemotherapy and bone marrow transplantation, which also cure many people. Combinations of drugs that target the epigenome described in this Newsletter by Steve Gore are showing benefit when conventional chemotherapy has not. There is every reason to*

(continued on page 5)

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SWCRF REPORT  
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# Acute Myeloid Leukemia

## *Mark Fizulich's Journey*

**At the end of 2005, Mark Fizulich was riding high. He had met and proposed to the woman of his dreams. He was enjoying everything about his sales job in credit derivatives at financial giant Bear Sterns. "I worried about things like what good restaurant to take my clients to, and how to choose exactly the right wine," he says.**

**M**ark (he's one of those people everyone calls by their first name) was healthy, high energy and athletic. He had gone to college on a basketball scholarship, double-majoring in business administration and economics, and continued to dribble and dunk with pals as a hobby. He didn't really pay much attention when he got the first couple of headaches, or when a basketball buddy told him he wasn't looking so good. "I thought I was just a little tired, or that I might have a sinus infection," he says. The idea that he had Acute Myeloid Leukemia, subtype 8/21, could not have been further from Mark's mind.

### Receiving the News

A visit to the doctor on a Thursday showed he had no fever and his sinuses were fine. A blood test was done. On Friday Mark planned to fly to Florida with his fiancée. He got an urgent call when the plane was already on the runway, waiting for takeoff. The doctor wanted Mark to cancel his trip and go to the hospital immediately for blood transfusions and treatment. "I flew to Florida, since I couldn't get off the plane, and had the transfusions there," he says.

On Monday, Mark returned to New York and went directly to a hematologist. It must have been shocking to learn that his blood levels were dangerously low, but Mark isn't the type of person who would mention that. He's a just-the-facts man – forthcoming and completely without self-pity.

A little later, having learned that he had leukemia but knowing almost

nothing about the disease or what to do, Mark talked to his friends at work, hoping they had information. That's where the SWCRF came in.

### SWCRF Connection

When he heard about Mark's illness from colleagues at Bear Stearns, SWCRF's Chairman Michael Nierenberg went into action. He offered the global resources of the Foundation to help Mark. Then Bear Stearns Chairman Alan "Ace" Greenberg contributed to the SWCRF and appealed to his co-workers to donate too.

Ironically, when Dr. Sam Waxman got the call about Mark, he was in Atlanta attending a conference with leading hematologists. Also, several SWCRF investigators in Dr. Waxman's lab and Dr. Zhu Chen, director of The Shanghai branch of the Institute Without Walls, and his colleagues had been working on treatments for Mark's specific disease, bringing out a paper called "Cell Death and Differentiation" at almost the same time.

### Three Rounds of Chemotherapy

Soon Mark was conferring with Dr. Waxman about what leukemia is, how it works and about treatment options. After meeting with doctors at Mt. Sinai in New York City, Mark was admitted. The Mt. Sinai team recommended three rounds of high-dose chemotherapy. "A piece of my 8th chromosome breaks off and a piece of my 21st chromosome breaks off and they touch each other and create a leukemia cell," Mark says, explaining his disease process. "The type of AML I have – 8/21 – actually has longer survival rates than some of the other seven subtypes. The three rounds of chemotherapy cures some people forever."

Until April of 2006, Mark was in and out of the hospital, receiving chemotherapy during one-week stays, going back to New Jersey

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where he lives, returning to Mt. Sinai for blood draws and to receive blood products like platelets. His leukemia went into remission.

"In June I went back to work," he says, finessing the time and effort it took to recover from the high-dose treatment. Again he seemed to be riding high. Another three months passed without a problem. At the end of September Mark got married. Then, just when he was beginning his new life with his bride, when he returned from his honeymoon, he discovered he had relapsed. The leukemia had come back.

Mark was readmitted to Mt. Sinai for more chemotherapy. But once a person has had chemotherapy and it hasn't produced a permanent cure, doctors are reluctant to continue it. They recommended high doses of chemotherapy followed by a bone marrow transplant. Again Dr. Waxman stepped in to help. Following treatment at Mt. Sinai, Mark decided to go to Seattle, to the Fred Hutchinson Cancer Research Center, where bone marrow transplant was pioneered.

### Bone Marrow Transplant

Mark and his family went out to Seattle. It turned out that his sister was a genetic match — a one in four chance — and a good donor for the bone marrow cells that could save Mark's life. "I had three days of full body radiation before the transplant," he says. "And after that I had chemotherapy that wasn't like what I had before in New York. The earlier chemotherapy didn't destroy the cells in my bone marrow forever. This did."

The actual transplant took place this past January. According to Mark's description, the bone marrow cells that he received from his sister had no trouble migrating to where they were needed and taking up residence — engrafting. In the process, his blood type changed and became her blood type. His bone marrow is now identical to his sister's.

When Mark spoke to us for this article, he was recuperating in an apartment near the hospital in Seattle. It was day 59 of the recommended 100 days of monitoring after the transplant. "I'll probably be out here through April," he said, "I'm counting the days."

Then, on March 9, after more tests, Mark's family sent a joyful message to all his supporters in spite of low blood pressure and fever that were sending him back to the hospital. It said: "Our prayers were answered again. Mark's bone marrow has normal cells with NO signs of disease. We have a formal meeting with doctors tomorrow to go over what could be making his levels go down, but relapse has been ruled out."

Recent SWCRF-sponsored research at the Shanghai Institute of Hematology shows that a drug derived from TCM was used successfully to treat a mouse genetically engineered to have 8/21 leukemia, with minimal toxicity. Work of this type may offer a new option for treating Mark's form of leukemia.

## Everything You Wanted to Know About Bone Marrow Transplants

**A** bone marrow transplant (BMT) is a difficult, lengthy, complex, costly and somewhat risky procedure usually performed on patients who have leukemia, lymphomas and other life-threatening illnesses, when conventional chemotherapy is no longer effective.

The procedure begins with finding a donor whose cells match the genetic make-up of the patient's as closely as possible - preferably a parent or sibling; if the match is not good enough, the new bone marrow cells may be rejected — a condition known as graft-versus-host-disease (GVHD).

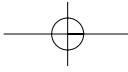
Once a donor has been found, the BMT progresses for both the patient, whose own diseased bone marrow and malignant cells elsewhere are destroyed with very high doses of chemotherapy in preparation for the transplant, and for the donor, whose bone is harvested for stem cells and for infusion into the patient.

The patient has already received several days of very strong chemotherapy and/or radiation to kill cancerous cells and to make room for the transplant.

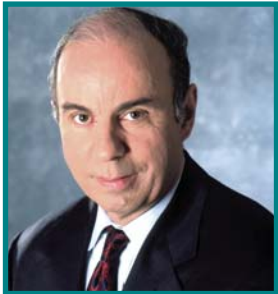
The BMT itself is done in the patient's hospital room in a process much like a blood transfusion. Once the new blood cells enter the patient's body, they migrate, taking up residence in the places where they are needed. During the first few weeks, if everything goes well, the new cells "engraft" and begin producing normal blood cells. While this is happening, however, the patient is suffering extreme flu-like symptoms of weakness, fever, chills and nausea. The patient needs blood transfusions and infusions of blood platelets to prevent bleeding, and medication to stave off the possibility of GVHD and other complications.

This is all emotionally stressful, and serious medical complications are not rare. Also, the patient's immune system is severely compromised from the previous chemotherapy and elaborate precautions are necessary to prevent infections of all kinds. Hopefully frequent blood tests may finally show that the engraftment is producing new normal red blood cells, white blood cells and platelets.

The patient is ready to leave the hospital a few weeks later and begin recovering nearby while returning to the hospital often for monitoring, transfusions and other care. There is still a risk of infection, so when the weakness and feeling of illness subside, the patient may leave the house but must take care not to catch even a slight cold. During this time some patients wear surgical masks when venturing outside. Initial recovery takes at least two months. Even then, there is still a long road for the transplant patient. The new blood marrow cannot function normally for up to a year. There is general agreement that a successful BMT can greatly improve a person's quality of life, and for many it can eliminate the disease.



## Welcome to New Board Members



Thomas A. Conway

**Thomas A. Conway** has been the Chief Financial Officer of Thirteen/WNET for twelve years and also oversees all of the corporate and foundation program underwriting activities. Prior to that, he was the CFO at Madison Square Garden Corporation, ESPN and the Entertainment Channel, now better known as A&E. Mr. Conway serves on the Boards of PBS Sponsorship Group and National Public Broadcasting Inc.



Bernard Sillins

**Bernard Sillins** was involved with family owned and leased hotels for several decades and is now the owner of several apartment buildings throughout New York City. His company BTP Real Estate LLC owns and manages properties. Mr. Sillins is a Board Member of the Robert Sillins Family Foundation. The Robert Sillins Foundation made a \$50,000 grant to the Samuel Waxman Cancer Research Foundation to be used for research in Israel. We thank Mr. Sillins, a new member of our Chairman's Council, for making this generous gift available to our Institute Without Walls.



David Taub

**David Taub** is President and CEO of Palm Bay Imports, Inc., a business he and his father, Martin, founded. Since 1978, Palm Bay Imports has had a portfolio of imported wines and spirits that spans four continents and continues to expand. He also is on the Board of the Parker Jewish Institute Foundation and Hillel of New York, a member agency of the UJA-Federation of New York, and is actively involved in a family program at the Holocaust Museum in Washington, D.C. for New York area college students. He is also on the Board of The Atlantic Center for the Arts, New Smyrna Beach, FL.

## SWCRF Forms Corporate Council

The Samuel Waxman Cancer Research Foundation announces its newly formed Corporate Council. Companies who join at the \$10,000 membership level will be given a guided tour of Dr. Waxman's laboratory at the Mount Sinai Medical Center and have access to our world-wide network of investigators at our Annual Scientific Review reception on May 7th at the St. Regis Hotel. Corporate Council members will receive prominent recognition on our website and in SWCRF newsletters, e-bulletins and press releases.

Additionally, all Council members will receive an award at either our Annual Scientific Review or our Annual Golf Tournament. Our charter members include Costas Kondylis & Partners, LLP, Elie Tahari, Ltd., ITOCHU International, Inc., Orda Management Corporation and The Trump Organization.

For further information, please contact Mark Silverstein, Director of Development, at 212.241.1760.

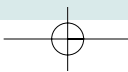
## From the Scientific Director *(continued from page 2)*

*believe that there will be a way to combine the two and increase the chance for controlling or even eradicating cancer.*

*Abnormal epigenetic function leads to abnormal signals that drive the abnormal growth, differentiation and cell death characteristic of the cancer cell. Inhibiting these abnormal signals has lead to a plethora of drugs recently approved for use or in clinical trial. Another 21st century treatment is Sorafenib, a drug designed to block two cancer cell dependent pathways. Initially released for the treatment of kidney cancer, it has just been reported to have impact on survival in patients with advanced liver cancer. As*

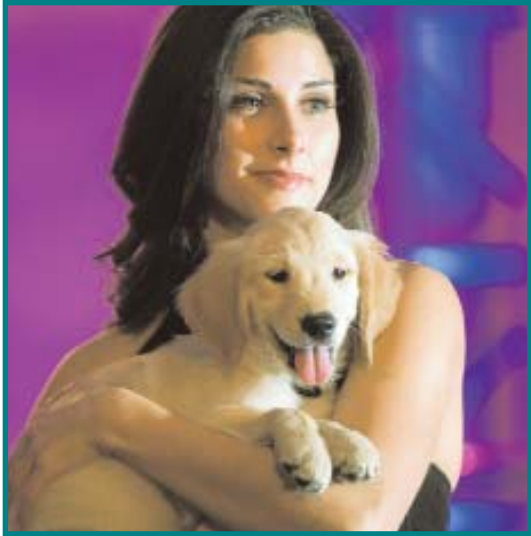
*described in this Newsletter, the SWCRF funded a collaborative research program in liver cancer that will contribute to expanding the scientific base for developing targeted treatments. These signal pathways and the epigenetic makeup of the cancer-forming stem cell are being investigated by several scientists supported by the SWCRF. My prediction is that there will be a unique epigenome in cancer stem cells which will provide the next 21st century treatments for eradicating the cancer stem cell by causing its differentiation and subsequent death.*

*Samuel Waxman*



# Special Events

## 9th Annual SWCRF Gala



Cutest guy in the room

**M**ore than 1,000 people attended our 9th annual gala raising a record \$4 million. Our evening began with entertainment by Bill Evans Soulgrass Band, followed by a sumptuous dinner. This year, an additional air of excitement was added as the silent auction and the live auction led by C. Hugh Hildesley, Executive Vice President of Sotheby's were conducted simultaneously at the event and on the Web via charitybuzz.com. After dinner, John Fogerty and his band treated our guests to an extraordinary performance. The evening was topped off with the Knockout Drops rocking all into the wee hours of the morning. The event was a powerful display of the energy and commitment of our supporters as collaborative partners in the search for a cure.

Photos by Rebecca Weiss; Chris London



Howard Rubin, Kristin Sterling, Mitch Winter, Wes Edens



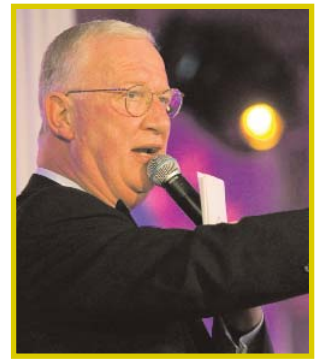
Adrienne and Robert Kantor, Dr. Samuel Waxman



Michael and Elin Nierenberg, William Baldwin



Dena Weiner, and Spencer Waxman



C. Hugh Hildesley, Executive Vice President of Sotheby's North and South America & Senior Director of Sotheby's Canada



Gary Jacob, Joseph R. Gannascoli, Merle Kailas and Clifford Sterling



Samuel Waxman and Gary Gladstein

**Our many thanks to the companies and individuals who made the Samuel Waxman Cancer Research Foundation's 2006 "Collaborating for a Cure" Benefit Auction and Dinner such a special event.**

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# Special Events

## 3rd Annual David Workman Memorial Award Ceremony

**F**riends and family of David Workman gathered at Mount Sinai Hospital on November 16th for the third David T. Workman Memorial Endowment Lecture and presentation of the Workman Memorial Endowment Award to two National Institutes of Health scientists Drs. Doug Lowy and John Schiller whose research resulted in the clinical development of the HPV vaccine against cervical cancer.

The evening reception and dinner at the Metropolitan Museum was a tribute to David Workman's 20 years of dedication to the Foundation. Formally established in 2003, the Workman Award is a \$50,000 grant to enable the clinical development of novel selective therapies for poorly treatable forms of cancer.

This year's Workman Award will support the research of Drs. Lowy and Schiller on developing an experimental non-human primate model for HPV infection. This event was made possible by a grant from Merck & Co. which developed Gardasil, the first HPV vaccine to be approved by the FDA.



Dr. Samuel Waxman presents the David T. Workman Memorial Award to Douglas Lowy, M.D. and John Schiller, Ph.D. from the National Institutes of Health.



Merle Duskin Kailas, SWCRF Executive Director, thanks Margaret McGlynn, President, Merck Vaccines, for its support of the David Workman Memorial Award

## Young Professionals Group Plans "Cruise for a Cure"

### SWCRF Announces the Formation of the Millennial Society

**A** group of passionate young professionals who are committed to supporting the innovative research of Dr. Samuel Waxman and the Foundation's Institute Without Walls have joined together to form the Millennial Society.

Joanna Steinberg, Chair of the Millennial Society, explains that it will "demonstrate the power of philanthropy that goes beyond monetary donations to leverage the skills and expertise of fresh young individuals. Our committee is a prime example of application of talent benefiting a greater cause." The group aims to establish a network of young, creative, intellectually agile independent thinkers who are leaders in their respective fields. The Millennial Society considers it a duty to give back and lead lives of leadership and service.

Its inaugural event this season will be held on Thursday, June 14th from 7:30- Midnight. CRUISE FOR A CURE, will be held on the Majesty, which will depart from Chelsea Piers. "It will be the ultimate kick-off to summertime fun in New York," says event Vice Chairman Bryan Rodman, "and will include live music, a luxury raffle and dancing under the stars."

Please email: [millennialsociety@wax-mancancer.org](mailto:millennialsociety@wax-mancancer.org) for more information.

## Epigenetic Therapy

(continued from cover)

conventional chemotherapy, and because of that, offer hope of gentler treatment, especially for cancer victims who are over sixty.

The SWCRF's pioneer program for studying ways to overcome aberrant gene expression in blood malignancies with epigenetic therapy is a collaboration of fifteen labs from Shanghai to Boston, funded in part by a million dollar challenge grant from the Skirball Foundation.

"Through epigenetics we can orchestrate gene expressions into a symphony of information," says Dr. Waxman. Researchers in the lab and the clinic are just as enthusiastic.

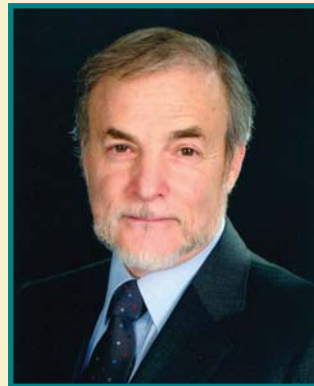
Dr. Stephen Baylin, Director of the Cancer Biology Program, and the Chief of the Tumor Biology Laboratory at Johns Hopkins, studying DNA methylation, a chemical process thought to be influential in controlling gene expression, has discovered a new way to manipulate genes epigenetically. "When the DNA methylation happens at the start site of these genes it becomes associated with a process where a number of changes in chromatin – the DNA and proteins that are bound to it – occur," he says. It is at that intersection that Dr. Baylin and his colleagues discovered a new step – a protein called SIRT1 – that is a known gene-silencing protein in yeast.

"What we discovered is that this protein is associating with the start site of these genes, along with the DNA methylation, and there are inhibitors. When we blocked the activity of this protein, the genes came back on and didn't lose their DNA methylation. We're trying to take this further to see how rich it's going to be," he says. This exciting work is being supported by the SWCRF.

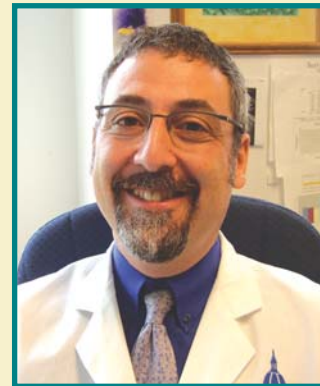
### The Long Reach of Research

In his lab in London Dr. Arthur Zelent, reader in biochemistry and a leader of the transcriptional controls in leukemia team at the Institute of Cancer Research, concentrates on trying to find answers to why acute myeloid leukemia generally responds poorly to treatment with retinoic acid as opposed to acute promyelocytic leukemia, which responds well. "We're working with the hypothesis that this lack of responsiveness of acute myeloid leukemia to retinoic acid is due to abnormal epigenetics. These epigenetic events, which represent an additional layer of information and cellular memory to that encoded in the DNA sequence, Dr. Zelent thinks lead to inhibition of expression of effector molecules (for example, retinoic acid receptors) that could mediate responsiveness to retinoic acid. "The idea now is to use this knowledge to develop a process to restore the expression of these molecules," he says.

(continued on next page)



Stephen Baylin



Steven Gore

## Scientists in the Spotlight: Stephen Baylin and Steven Gore

One doctor – that's Stephen Baylin – works in the lab. "What we do relates strongly to one of the major interests of the Waxman Institute," he says. "That's an interest in Differentiation. We don't work it in the completely classical way, but that's the idea behind what we're doing. We're trying to manipulate cancer cells – not exactly in a way that's going to kill them, but in such a way that it is going to cause an immature cell to grow up (and then die) or cause it just to stop."

For Dr. Baylin, it's Petri dishes and animal models, pipettes and microscopes, and that's the environment in which he thrives. However, without application, Dr. Baylin's work would remain entirely theoretical.

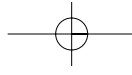
That's where Dr. Gore comes in. Patients suffering from serious, sometimes potentially fatal illnesses come to him in search of help.

The two scientists sit down together in a combined effort. They discuss the science of what's been produced in the lab to see if it's reasonable to take it to the clinic. And then, "All of these studies in the clinic need correlative lab studies to determine not only whether the patient is getting better, but to learn whether a drug is working the way we think it is," he says.

Dr. Gore is excited about the clinical work on epigenetics he's participating in now. It has already been reported in abstract form to ASH (the American Society of Hematology) and some data are scheduled for presentation at a meeting of the American Association of Cancer Researchers in April. And he has hopes for what the large study now in progress will eventually reap.

"This (study) will enable us to see whether in fact the excellent clinical responses we observed with Azacitidine and MS 175 are due to the fact that they're used in combination. We've got a bunch of really wonderful lab correlative studies we're planning to do to try to understand in a bigger site whether what has happened really depends on reversal of methylation and gene expression, or whether something else is going on.

"Hopefully this will lead us to our next generation of drugs and the next generation of clinical trials."



### Future Applications

But all research is not confined to the lab. When Dr. Steven Gore, Associate Professor of Oncology at the Johns Hopkins University School of Medicine started conducting clinical trials with epigenetic drug combinations in the late '90s, patients had no trouble taking the first medication, Azacitidine, but needed a one-liter infusion pump to deliver the other component, Sodium Phenylbutyrate. Since then, Dr. Gore's work has come a long way. Clinical data from studies combining Azacitidine and a new epigenetic drug MS 275 have been tremendously encouraging. So encouraging that a national study has been opened for patients with Myelodysplastic Syndrome, Acute Myeloid Leukemia and a related disease, looking at dosage, as well as conditions of methylation and gene expression. The study is currently running simultaneously at more than 100 institutions. Similar clinical trials are in process in many common forms of cancer.

Both laboratory scientists and those whose work takes them into the clinic are unabashed in their enthusiasm for the potential of epigenetic therapy. Dr. Zelent sums it up: "We all focus on the particular models we develop, but the mechanisms we study are general. Much of what we're learning about leukemia and other blood malignancies can, and is, being extended to solid tumor cancers. The whole field has been stimulated to look into these anticancer agents that target epigenetic controls across the board."

## SWCRF Funds Research Leading to "Major Advance" in Stopping Liver Cancer

It has been called a silent epidemic. An estimated 4.1 million Americans and as many as 500 million world-wide carry the Hepatitis C virus (HCV), a blood-borne infection that can become chronic, eventually resulting in serious or fatal liver problems including cancer. Hepatitis C is responsible for about 90% of primary malignant liver tumors in adults in the Western world. The incidence of liver cancer has almost doubled in the United States in the last decade and now stands at 2.5 cases per 100,000 people. This number is expected to rise as people who contracted Hepatitis C years ago and have not been diagnosed begin to suffer its damaging effects.

Now the SWCRF can report "remarkable progress" in learning about liver cancer caused by the Hepatitis C Virus. Based on work funded by the SWCRF, led by Dr. Joseph Llovet of Barcelona, Spain, and headquartered at Mount Sinai Medical Center in New York, major strides have been made in understanding this usually fatal cancer and how it develops. Dr. Llovet was the lead investigator of a randomized clinical trial of 600 patients with advanced liver cancer that was so successful it was ended so those patients who were receiving a placebo could be given access to the treatment. The drug used in the trial — Sorafenib — is the first proven to significantly improve survival rates and is considered a "major advance" in the field.

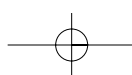
This work is supported by the SWCRF Beverly Yaffe Memorial Fund and by the Mark Family Fund. Dr. Llovet, working with Sam Waxman, among others at Mount Sinai, has led a multidisciplinary, international team studying gene patterns in 150 liver samples, each of which contained 40,000 genes. The analysis of these millions of genes allowed researchers to separate the samples into four groups: normal, precancerous, early and late-stage liver cancer.

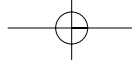
These significant findings give physicians tools to diagnose precancer in those suffering from Hepatitis C, before the liver cancer actually develops. Because of this it may be possible to remove the problem area surgically, saving lives that would otherwise have been lost. Also vitally important, the gene patterns will allow researchers to identify defects that can be used to develop new targeted treatments.

The results of this groundbreaking work have been published in two major medical journals — *The Journal of Gastroenterology* (2006) and the *Journal of Hepatology* (2007). And work continues. The number of samples studied for gene patterns is being increased so that researchers can select fewer genes to measure for the purpose of prevention, early treatment and new drug development. In addition, a specific overexpressed gene pattern which results in signals to increase the growth of liver cancer has been identified.

An undertaking as large as this has called for huge resources. Dr. Llovet brought together research laboratories in the Division of Liver Disease, Oncology, Transplant Surgery, and Bioinformatics at Mount Sinai Medical Center. Through the SWCRF Institute Without Walls he collaborated with a wide-ranging group of scientists from Dana Farber Cancer Center, MIT, Albert Einstein School of Medicine, University of Barcelona and the Tumor Institute in Milan, Italy.

Dr. Llovet, who is Associate Professor of Medicine/Director, HCC Research Program, Division of Liver Diseases, Mount Sinai School of Medicine, New York, and Professor of Research at Barcelona Clinic Liver Cancer Group, Liver Unit, Hospital Clinic Barcelona, commenting on the successful clinical trial, said, "These results point to new potential treatment options for those patients suffering from this devastating disease."





## HOLD THE DATES: Special Events Calendar 2007

**Monday, May 7, 2007**  
**Annual Scientific Meeting**  
St. Regis Hotel  
5:30 pm

**Thursday, June 7, 2007**  
**25th Annual Golf Tournament**  
The Creek Country Club  
Come win the \$1 Million prize for a "hole in one."

**Thursday, June 14, 2007 - 7:30 PM**  
**Cruise for a Cure - New York City**  
SWCRF Young Professionals

**Saturday, July 14, 2007**  
**4th Annual Hamptons Happening**  
Gourmet Tasting Stations  
and Silent Auction

Auction will open for bidding on: [charitybuzz.com](http://charitybuzz.com)  
beginning in June.

**Thursday, November 29, 2006**  
**10th Annual**  
**"Collaborating for a Cure"**  
Benefit Dinner  
Silent and Live Auction

Help us keep costs down, please send your email address to: [swcrf@waxmancancer.org](mailto:swcrf@waxmancancer.org)

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