

SAMUEL WAXMAN CANCER RESEARCH FOUNDATION

REPORT

Fall 2007

Using Epigenetic Tools, Eminent SWCRF Researchers Pursue Colo-Rectal Cancer Cure

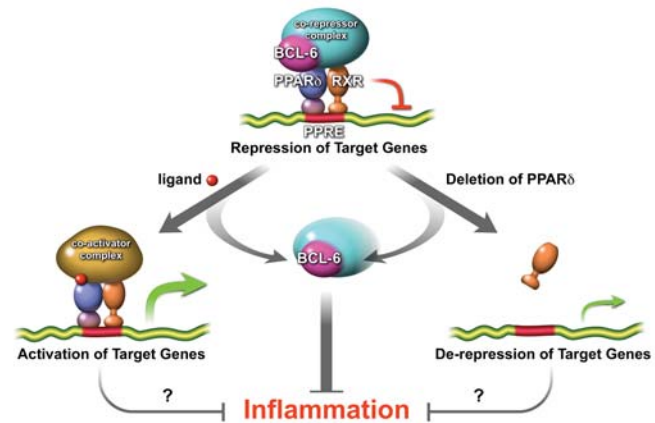
For most of us, screening for colon and rectal cancer includes diagnostic tests during check-ups, and after the age of fifty, a regular colonoscopy. Though usually these procedures are no big deal, sometimes they do reveal a problem.

The National Cancer Institute estimates that there will be 152,760 new cases of colon and rectal cancer in 2007, and that 52,180 Americans will die of these two diseases combined. Those big numbers are increasing, partly because of “lifestyle” factors, especially diet – our Western diet which is so high in fats (lipids).

Whether you develop colo-rectal cancer depends on your family history and your personal history – for example, your age, weight, alcohol and cigarette consumption, Crohn’s or inflammatory bowel or other disease and diet.

A number of eminent SWCRF researchers are hot on the trail of a cure for these epithelial cancers, which are similar to other dangerous carcinomas, such as lung and ovarian. They’re working with epigenetics, which some believe will produce an across-the-board payoff. These investigators don’t want to permanently modify DNA. They want to use epigenetics to change gene expression temporarily, so “silenced” genes that ordinarily

Turning on Silenced Genes



A direct link between lipid metabolism and inflammation exists. Chronic inflammation is known as a cause for cancer. The nuclear receptor PPARdelta complexes with RXR and BCL-6. Together, these act as a switch that responds to dietary lipids and regulates inflammation. Two receptor states are shown here. One follows treatment with a drug (ligand) for PPARdelta. The other occurs after loss of PPARdelta. Both can release BCL-6, which affects PPARdelta target genes. These dictate therapeutic effects of this receptor. Research is now underway to study how best to use this receptor to control inflammation and treat colon and rectal cancers.

stop cancers from growing can be “turned on” to do their job without lasting alterations to their DNA. Aberrant silencing of tumor suppressor genes has a critical role in the initiation and progression of most, if not all, tumors. As science-oriented as this is, it is also related to our everyday lives.

“We have obesity, reduced exercise, high-fat diets, and these lead to metabolic disease and a whole series of complications – high blood pressure, hyper lipidemia (high cholesterol), high blood sugar, chronic body-wide inflammation and a greatly increased risk for cancer,” says Dr. Ronald Evans, Howard Hughes Medical Investigator, The Salk Institute for Biological Studies. “The link between high-fat diet and colon cancer is well documented. Also, there is a large amount of data that

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Foundation News

Message from the Scientific Director

Colon cancer is the focus of this Newsletter. This disease develops in several steps from benign polyps to aggressive cancer and spreads, each step due to abnormal gene expression. Diet and intestinal inflammation also play important roles. Colon cancer can be familial or sporadic, and both are preventable by timely colonoscopic examinations. Colon cancer remains a major cause of human suffering and death and yet should be even more preventable than it is currently. Oncologists are in great need of a new treatment approach for this disease, since present-day therapies have not significantly altered the mortality rate in advanced disease.

The genetic alterations associated with each stage of colon cancer have been a model for understanding the genetic and epigenetic step-wise development of many other forms of cancer. This understanding has resulted in a more scientific basis for cancer treatment and enabled the beginning of the 21st century cancer treatment revolution, which we are now experiencing. The merging of conventional chemotherapy with these treatments is just at the beginning and appears to improve therapeutic outcome.

The SWCRF has funded a group of scientists to form the world's best program on understanding the abnormal epigenetic expressions which cause colon cancer, the role of inflammation and a plan for the development of targeted epigenetic therapy for prevention and treatment. The Dr. Evans and Drs. Casero, Baylin, Belinsky programs have identified compounds that can target abnormal epigenetic components in colon cancer.

In addition, the SWCRF is forming a drug discovery program with facilities to move these experimental compounds into substances suitable for drug development. The melding of basic science, translational research and drug discovery will enable the SWCRF Institute Without Walls to partner with academic institutions, philanthropy and industry. This partnership will constitute a holistic team to facilitate the collaboration for a cancer cure.

Sincerely,



Samuel Waxman, M.D.



Dr. Dennis S. Charney, Dean, Mount Sinai Medical School presenting the award to Dr. Samuel Waxman

Samuel Waxman Named Distinguished Professor by Mount Sinai School of Medicine

In September, The Mount Sinai School of Medicine honored oncologist and professor of medicine, Samuel Waxman, M.D., conferring on him the new title of "Distinguished Service Professor." The award was presented at the Twenty-Second Annual Convocation ceremonies.

The Distinguished Service Professor title recognizes faculty who have dedicated their careers to Mount Sinai, and have had a major impact on the educational experience of students, the clinical care of patients and quality of research and scholarship. The select cadre of Distinguished Service Professors has given decades of outstanding service to the School and Hospital as master clinicians, researchers and educators.

Chinese Health Minister Pledges Cooperation with SWCRF

The former director of the Shanghai Institute of Hematology, and a researcher in the SWCRF Institute Without Walls, Dr. Zhu Chen has been appointed Health Minister of China. He is a molecular biologist and an expert on leukemia and was once a visiting professor in Medical Oncology at Mt. Sinai, where he was mentored by Sam Waxman.

"I appreciate your guidance at the beginning of my career. I'll do my best to support the SIH and SWCRF," Dr. Chen said in a recent email to Sam Waxman. "I wish we become life-long friends and colleagues forever. I'm looking forward to develop the Sino-American cooperation model in the cancer research field."

Before his new appointment, Dr. Chen was Vice President of the prestigious Chinese Academy of Sciences. During the Cultural Revolution, he spent five years working in the rice-growing province of Jiangxi and attending a medical vocational school. He returned to Shanghai, where he was born, and did graduate work. He received a Doctorate of Science at the Institute of Hematology, University of Paris.

"Good thing a new generation who have a wide global vision is emerging," Dr. Chen wrote. "This will enhance our capacity for international cooperation."



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SWCRF REPORT

WRITER/EDITOR - Carol Ardman
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Colon Cancer: How Bob Quinlan F

Bob Quinlan felt a little strange sometimes, and once in a while he feared he had a physical problem. But he was in his prime. He was forty-three years old, happily married with two kids, a house in the suburbs and a good job managing the insurance program for a major bank in New York City. For about eight months he tried to ignore some rather disquieting symptoms. His stomach made “crazy” noises at night, he felt “bloated,” his digestive system didn’t seem to be working perfectly. Occasionally he ran a low-grade fever.

His physician didn’t know exactly what might be wrong, but he thought it could be an infection in Bob’s prostate. Antibiotics were prescribed. The pills seemed to control Bob’s fevers, but as soon as he stopped taking the medication, his temperature reappeared.

“I didn’t have a lot of pain, but I kind of knew something was wrong,” Bob says now. “I went back to the doctor several times.”

Regular colonoscopy, the examination of the lining of the large intestine for polyps, tumors or areas of inflammation or bleeding, is usually recommended beginning at the age of fifty. Bob was too young for a colonoscopy by that standard, but he did have other risk factors for colo-rectal cancer. Though his parents were both living and his three older siblings were healthy, an aunt on his father’s side had died of pancreatic cancer at the age

of thirty-four. More striking, his mother’s two sisters and brother had all died of some form of cancer. “My uncle was only sixty-one when he died of colon cancer,” Bob says.

“I was kind of young, but they did the colonoscopy. That’s when they found the tumor.” The tumor, which was malignant, was the size of a grapefruit. “I went into a state of panic,” Bob says.

When someone gets news of a serious illness, the first thing on the agenda is to find the right specialist and choose the best possible treatment. Bob’s internist and the radiologist who had done the colonoscopy both recommended a general surgeon who had a specialty in vascular surgery. Ironically Bob’s wife had visited this very man to consult about a varicose vein. He certainly didn’t seem like the right surgeon to perform an important, risky operation.

“It was very upsetting,” Bob says. “I called my sister, who is a nurse, a couple of neighbors who are also nurses and anyone and everyone I thought could help. Then I spoke to another close friend, Miriam Aronson. She said, ‘Stop the presses. I have the person who is going to take care of you.’”

That person was her uncle, Dr. Samuel Waxman. A few days later Bob was sitting in his office. “Dr. Waxman already had copies of the films of my colonoscopy,” Bob says. “He was very efficient and quickly came up with a plan for what to do and how to do it. He scheduled everything. I went around the corner and had another CT scan. I had blood work done.”

Sam Waxman recommended minimally invasive surgery to remove the tumor and set up an appointment with Dr. Barry Salky, Chief of Laparoscopic Surgery at Mt. Sinai. “There was no question

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Bob Evicted an Unwelcome Guest

about it," Bob says. "Dr. Salky had the credentials. He was the one who was going to do the surgery. My wife and I went and saw him. He told us the procedure, the timeline, how it would work."

Two weeks later, on December 21, 2005, Dr. Salky operated. "Everything went smoothly. The hospital and nurses were great," Bob says. But he didn't linger. Only three days later, on December 24, Bob's wife, his father, his brother and son chauffeured him home in a Chevy Suburban. He was sore and he felt ill, and that ride was an unforgettable ordeal, but it was great to be alive and to be home for the holidays.

The operation was behind him, but Bob's encounter with cancer was not. As soon as he was back on his feet, Dr. Waxman designed a chemotherapy program for him. Basically he said, 'I'm going to kick the s**t out of you to get rid of the cancer once and for all. If it gets to be too much, let me know.' His attitude from day one was, 'I'm going to beat the hell out of you but you're going to be fine.'

Fortunately Bob was young, he was strong and he was ready to do whatever was necessary. Under Dr. Waxman's watchful eye, he endured over eight months of intense chemotherapy. It wasn't easy, physically or emotionally. On top of dealing with the nausea and the weakness, the medications pooled in Bob's extremities so that his fingers and toes were numb, his feet sore and dry. He was sensitive to cold so that it was painful even to hold a can of chilled soda. But Bob continued to work during the entire eight months.

"Dr. Waxman said if I sat at home and thought about the next treatment I wouldn't want to have it. It would be better to con-

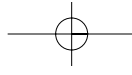
tinue to work. They were great about it at the bank," says Bob. Still, it can't have been easy to go for a treatment at two in the afternoon, then fight the crowds at Penn Station to get on the Long Island Railroad, commute to his home, and get up for work the next morning and do it again.

"I couldn't have gotten through it without Carmen," Bob says, referring to the nurse in Dr. Waxman's office who administers the chemotherapy and who supplied emotional support as well as medication. During the first round of treatments I was given two different drugs at the same time. One was pumped in through an IV and when that was done they took a needle and injected a dose of the nasty stuff," Bob says.

In time, however, the eight months passed, and with them the feeling of living in a nightmare. "I don't have big, ugly scars, because of the laparoscopic surgery. The numbness in my fingers and toes has gone away," Bob says. But there have been some changes. "I take better care of myself," he says. "I eat better, play lacrosse as I always did and coach my kids, who are active in sports."

His advice to others? "I'm on a mission to tell all my friends – to tell everyone. If you have a family history of cancer, especially colon cancer, it doesn't matter how old you are. Have a colonoscopy. If your doctor won't recommend it, find another doctor."

As for his doctor, Sam Waxman, "He's working to find a cure, to make more progress. He's in his office every Tuesday, seeing people, helping people. Then he's in his lab searching for a cure. I commend him for that."



(continued from cover)

Colo-Rectal Cancer Cure

suggests inflammation is linked to many cancers. It is not surprising that patients with inflammatory bowel disease, ulcerative colitis and similar illnesses have an increased risk for colo-rectal cancer."

Hormones and Fats

Working at the "crossroads between lipid metabolism and inflammation," Dr. Evans has chosen to study genetic "switches" -- hormone receptors that control genes in response to dietary lipids. "Many of the dietary lipids that we take in have a certain hormonal property to them," says Dr. Evans. "They

are combining their expertise with the unified goal of developing new agents and strategies to target the aberrant epigenetic silencing of genes, striving to understand gene chromatin that is associated with that silencing and how to manipulate the chromatin to re-express the genes. Steve Belinsky, Senior Scientist, Lovelace Respiratory Research Institute, Albuquerque, New Mexico, describes his overall goal as identifying better ways to treat both primary cancers, including colon and lung (his specialty) and also to develop primary and secondary prevention.

genes that have been silenced? This is a highly innovative approach to test novel therapies and will give us a better index of whether these therapies will work in humans."

The way Dr. Robert Casero, Professor of Oncology at the Johns Hopkins University School of Medicine, entered the field of epigenetics was associated with the discovery of lysine specific demethylase1 (LSD1), which plays an important role in epigenetic gene regulation. "Its activity is typically associated with the down regulation of gene expression," says Dr. Casero.

Aberrant silencing of tumor suppressor genes has a critical role in the initiation and progression of most, if not all, tumors. As science-oriented as this is, it is also related to our everyday lives.

instruct the body by controlling fat receptors known as PPARs. Two types of PPARs act as molecular switches inside cells to control fat burning and fat storage. These molecular switches not only manage metabolism, but they also control inflammation. So they are in charge of what triggers the problem and they're also in charge of the problem itself."

Dr. Evans is, in effect, trying to kill two birds with one stone by working with the genome. "It's logical," he asserts. "We're working with the body's essential regulators of lipid metabolism and inflammation." Initially Dr. Evans' lab will be working with mice, inducing colo-rectal cancers and then looking for agents that can change gene expression and eventually stop the development of cancer.

At the same time, three other labs

Secondary prevention is keeping a tumor that has been removed from returning. "Our approach is to target the silencing of genes by a process called gene promoter hypermethylation, an event that can be reversed by special types of therapy."

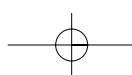
Experimental Therapies

Using orthotopic methods, human lung tumor cells are instilled into a rat's lung. They grow there into lung tumors which can be tested with experimental therapies for re-expressing the genes that have been silenced by methylation. "This technique simulates the human setting," says Dr. Belinsky. "A human lung cancer patient has issues of delivery of the drugs to the tumor, and this process allows us to look at drug-delivery and response more easily. That means, do we re-express the

"When LDS1 activity is high, typically what happens is that the chromatin of the genes it's targeting is demethylated at a specific site—histone 3, lysine 4 (H3K4). That leads to a closed conformation chromatin in that promoter region and turns off the transcription of that gene.

"My lab's expertise and goal is actually targeting the demethylase enzymes associated with inappropriate silencing of genes, which can, in turn, lead to cancer," Dr. Casero says, and mentions Dr. Patrick Woster of Wayne State University in Detroit as a collaborator in the project. "We want to specifically inhibit LSD1 in tumor cells and then allow reactivation of these genes – and there are preliminary and published data that suggest this is not only possible, but that we can do it, at least in culture."

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Special Events

25th Annual Golf Tournament

Honorary Event Chair Tony Shogren and members of our Golf Tournament Committee were the hosts of this year's 25th Annual Golf Tournament held at The Creek Country Club on Thursday, June 7th. Their leadership efforts led to a total raised of over \$250,000.

The event was underwritten by Freestyle Marketing, North Fork Bank and Thacher Proffitt & Wood LLP. Janet and Edward Ricci were the event's brunch sponsors; the Steak and Lobster Beach Reception was sponsored by Allison and David Sachs. Patrick Mucci, Jr. sponsored our \$1,000,000 Hole-In-One. The Foundation also acknowledges with gratitude our most treasured Tournament Patrons Lawrence Altman, Eric Goldstein, Jay Green, Gary Jacob, Abner Levine, Tony Shogren, David Taub and Jerome Wolff, M.D.

Photos by Michael Molinoff



Tony Shogren, Honorary Chair



David Ehrlich, Clifford Greenberg



Dr. Samuel Waxman thanking golf pro Roberto Borgatti



(L to R) Peter Brunell, Mitch Winter, SWCRF Board Chair Michael Nierenberg, Kevin Genis



(L to R) Lana Sperling, Barry Sperling, Caryn Stoll, Joy Sperling



(L to R) David Sachs, Mitchell Jacobson, Bart Osman, Brad Tolkin

FOURTH ANNUAL HAMPTON'S HAPPENING RAISIES NEARLY A QUARTER OF A MILLION DOLLARS FOR CANCER RESEARCH

4th Annual Hamptons Happening

The Fourth Annual Hamptons Happening took place on Saturday evening, July 14th at the home of Robyn and Kenneth Joseph on Georgica Pond in Wainscott. It was attended by more than 400 guests and raised \$240,000.

Restaurants that participated included: Alice's Teacup, Blue Water Grill, Brandt Beef, davidburke&donatella, DuFour Pasty Kitchens, Ichiban Sushi, il Buco, Il Cantinori, La Masseria, Leo's Latticini, Orsay, Periyali, The Seafood Shop, and Spoonbread. Palm Bay Imports was our beverage sponsor along with Acqua Panna and Pellegrino.

Our very generous benefactors were the Naddisy Foundation, Linda and David Taub and Spencer and Bettina Waxman. Sponsors included The Golieb and Axelrod Families, Leslie Elliot Krause, Marcia and David Lavipour, Audrey Flack and H. Robert Marcus, Murphy and Durieu, Susan and Elihu Rose, Diane Saatchi, Andrew Sabin, Riva and Alan Slifka and Robert Wechsler.

Benefit Co-Chairs were Laurie Schaffran and Marion Waxman. Committee members included: Meg Axelrod, Vira Capeci, Dean and Kris Denninger, Robyn Joseph, Marcia Lavipour, Gale Meisenberg, Thomas Mikolasko, Diane Spilker, Clifford Sterling, Helen Taylor Ginns and Dena K. Weiner. Joanna Steinberg was the Junior Committee Chair.

Photos by Michael Molinoff



Benefit Committee (L to R) Robyn Joseph, Laurie Schaffran, Marion Waxman, Marcia Lavipour, Meg Axelrod, Merle Kailas



Millennial Society (L to R) Amanda Lullo, Tim Norton, Joanna Steinberg, Kyle Widrick, Jake Sokol, Scott Schaffran, Rachel Katz, Matthew Dunne, Leslie Steinberg



(L to R) Jayson Hicks, Thomas Mikolasko, Malcolm Price, Toffer Grant



Robyn Joseph, Diane and Marc Spilker

(continued from page 5)

Colo-Rectal Cancer Cure

Striving for Less Toxicity

In Dr. Casero's lab, in collaboration with Dr. Steve Belinsky, and in the lab of Steve Baylin, professor at the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, different parts of cell chromatin are being attacked with different inhibitors with the goal of achieving additivity or synergism. With additivity one medication might work 20% and another might also work 20%, giving a combined efficacy of 40%. With synergy, the combined effect might be 60%. That, of course, is preferable. But if additivity can be achieved with low doses, there is less toxicity.

Dr. Stephen Baylin, Director of the Cancer Biology Program and the Chief of the Tumor Biology Lab at Johns Hopkins University School of Medicine, is working with Dr. Casero on ways to obstruct SIRT1. "We have observed in cell culture how interfering with SIRT1 can lead to re-expression of a group of abnormally silenced genes," he says. "What we'd like to do now is verify that and take it further with mouse systems – trying to do it in the whole animal."

Another goal is to use Dr. Casero's LSD1 in mouse models that would predict whether the same effect – the anti-tumor effect – can be achieved first in animals and then, eventually, in the clinic. "We're also interested in whether inhibiting both these molecules would give an additive or synergistic effect," says Dr. Baylin. We're looking for composite strategies to re-express these genes."

Conventional chemotherapy is often extremely toxic. In order to eradicate a tumor, sometimes it's necessary to put the patient at risk. One of the essential hopes of the scientists doing epigenetic research is that they can come up with more gentle drugs which would be a boon to an older, more vulnerable population. Says Dr. Evans, "The challenge is killing the tumor but not the host."

These SWCRF investigators represent the country's leading program for the development of epigenetic therapy for colo-rectal cancer.

Drug Discovery Program Initiated

Expanding its reach and concentrating on another critical area of cancer research, the SWCRF's Institute Without Walls has established the Drug Discovery Program. The rationale for this new program is the simple, bold thesis that cancer is caused by abnormal gene function. Aberrant gene expression is often due to abnormal non-DNA or epigenetic components which are good targets for drug development.

"The Institute Without Walls is made up of the most expert scientists, working closely together in the fields of epigenetic therapy and stem cell research," says Sam Waxman. "Several areas have been identified where we believe drugs can be developed in the future."

The Center for Molecular Therapeutics at the Massachusetts General Hospital Cancer Center, directed by SWCRF investigator Dr. Jeffrey Settleman, is hosting the initial component of the Drug Discovery Program with SWCRF support. "We're very excited about having the opportunity to work with other Waxman-funded investigators to incorporate their promising new anti-cancer compounds in our screening program to identify potential anti-cancer activity," he says.

Dr. Settleman, is researching ways to match individual cancer patients with particular targeted drug therapies to maximize the likelihood of a positive clinical response. The Center's broad objective is to identify molecular genetic features of a tumor that predict responsiveness to various molecularly targeted therapies. These therapies have been approved for clinical use, are in early clinical development, or are still undergoing pre-clinical analysis.

The Center has collected more than 1100 human cancer cell lines derived from human tumors of virtually every tissue, including breast, brain, colon, lung, pancreas, kidney, stomach, skin, and blood. State-of-the art technologies are maintaining and propagating this large

collection of cell lines, as well as screening the collection for sensitivity to drugs and for other targeted inhibitory compounds in assays of proliferation and cytotoxicity.

Screening is conducted using robotically assisted automated technology. "It's largely automated, but there is a manual component," says Dr. Settleman. "When we put cells on plates in culture to add drugs and make measurements – the actual plating of cells we need to do manually under very sterile conditions. The part where we analyze huge numbers of cells and drugs is done by robot. The plates get processed and fed into a machine that reads the effect of the drug on the cells, and that information is displayed in a form so we can easily spot the drugs that have interesting activity.

"Drug sensitive" cell lines are further analyzed to identify shared molecular features in the responsive cell lines. The molecular features include:

- potential mutations in the gene encoding the drug target,
- amplification of particular genes as assessed by comparative genomic hybridization (CGH) array technology,
- gene expression signatures, as assessed by microarray profiling,
- specific phospho-protein alterations

The SWCRF core facility at the Massachusetts General hospital is already testing the efficacy of seven candidate compounds in 500 different cell lines with investigators Reuban Lotan, Ph.D., from the University of Texas, Julio Aguirre-Ghiso, MD, Suny Albany, and Ethan Dmitrovsky, M.D, Dartmouth Medical School.

Two additional facilities for the Drug Discovery Program are currently being explored.

Meet Our Grantees



Dr. Frank Rauscher



Dr. Robert A. Casero, Jr



Dr. Ronald Evans



Dr. Curt Civin



Dr. Craig Jordan

Institute Without Walls Adds Five New Research Projects

Five new investigative teams have been awarded grants from the SWCRF. This brings the total researchers world-wide to 60. The Institute Without Walls is intended to promote a global collaborative approach to cancer research. SWCRF is unique in that the research it supports is not disease-specific but concept-driven, and researchers must agree to collaborate with their SWCRF peers on all research projects funded by the Foundation.

"We are very pleased to expand the scope of our cancer research activities with the funding of these additional five new research initiatives this year. We know these worthwhile projects, in collaboration with our collective efforts over the years, will contribute to the improvement of treatment and outcome of cancer patients," said Dr. Sam Waxman.

Prospective research teams submitted 70 detailed proposals for this highly selective and competitive award process of which only five were chosen. All the proposals were peer-reviewed. The peer review consisted of assessing the merits of the work and the potential for building collaborative programs in epigenetic therapy, tumor dormancy and cancer stem cells. The final grantees were chosen by utilizing the NIH scoring system. All funded programs will be reviewed annually by an independent, external committee of eminent scientists.

This year's grantees are from John Hopkins University, The University of Rochester Medical Center, The Salk Institute for Biological Studies, The University of New Mexico, and The Wistar Institute.

Newly funded research will be conducted in the following areas:

Dr. Frank Rauscher, Professor and Chairman, Molecular Genetics Program The Wistar Institute, Philadelphia

"Targeting the Sumoylation Machinery for the Relief of Gene Silencing and Differentiation Therapy"

Mechanisms whereby the human body can silence the vast majority of genes (in particular tissues) therefore affecting tissue-specific gene expression. In order to understand this process, we must identify the critical mechanisms the cell uses to maintain gene silencing and therefore define the cellular "software" that does that. This research will do so by analyzing a new protein, SUMO, which is intimately involved in human gene silencing.

Dr. Robert A. Casero, Jr., Professor, Johns Hopkins Kimmel Cancer Center, (Project Leader), Dr. Stephen B. Baylin, Professor of Oncology and Medicine, Johns Hopkins Kimmel Cancer Center; Dr. Steven Belinsky, Senior Scientist Lovelace Respiratory Research Institute, University of New Mexico

"Novel Therapies Targeting Epigenetic Silencing of Tumor Suppressors"

A specific epigenetic component that malfunctions in colo-rectal cancer has been identified and inhibitors are being tested in this program. (See article, page 1)



Dr. Ronald Evans, Investigator, Howard Hughes Medical Institute, Professor, The Salk Institute for Biological Studies

"Pharmacogenetic Targeting of the Nuclear Hormone Receptors PPARdelta/gamma in Colo-rectal Cancer"

The nuclear receptor family called PPAR plays an important role in inflammation thought to effect the development of colon cancer. (See article, page 1)

Dr. Curt Civin, Samuelson Professor of Cancer Research, Johns Hopkins Kimmel Cancer Center; Dr. Craig Jordan, Associate Professor, University of Rochester Medical Center

Dr. Civin and Dr. Jordan will collaborate with others in the SWCRF to understand how to reprogram leukemia stem cells and eliminate the root cause of acute leukemia.

"MicroRNAs Regulating Acute Leukemia"

Research will determine the micro-RNAs as expressed in purified populations of acute leukemia stem cells. Understanding how micro-RNAs regulate stem cells may elucidate general mechanisms in stem cell biology and cancer and have a broad potential impact on cancer therapeutics.

"Differentiation Therapy and Epigenetic Modulation of Human Leukemia Stem Cells"

Understanding the effects of mir-155 and mir-16 in leukemias may provide new specific molecular targets for leukemia drugs and other treatments that will attack the crucial leukemia stem cells which sustain the patient's leukemia.

Scientific Advisory Committee Impressed With Science, Recommends Enhancements

The SWCRF Annual Scientific Meeting was held in New York City on May 7 and 8. The purpose was to present the latest discoveries of funded investigators, to encourage collaborations between them through workshops, and to select the next programs and projects for Foundation support. This meeting was attended by an internationally distinguished panel made up of the Foundation's Scientific Advisory Board (SAB), investigators and friends.

The SAB evaluates the quality of research and productivity of programs, projects and collaborations. They also advise the Scientific Director on strategies for enhancing Foundation investment in bench to bedside (translational) research. The SAB made recommendations for improving the review process and direction of research.

"We are impressed by the quality of the science in this year's presentation, and by people seeking funding" said Stuart Yuspa, who chairs the SAB.

The SAB identified three areas of substantial strength for the Foundation: molecular targets, epigenetics, and stem cells and tumor dormancy. "We see a consolidation of strength in those areas," said Dr. Yuspa. "They are at the forefront of current investigation."

In its role as advisor to the SWCRF Scientific Director on strategies for improving the review process and direction of research programs, the SAB recommended modifications in the Annual Meeting to assure standardization of progress reports and scientific presentations. They pro-



Top: (L to R) Dena K. Weiner, Chair, Board Science Committee, Dr. I. Bernard Weinstein, Dr. I. David Goldman
Bottom: Dr. Franco Muggia and Dr. Samuel Waxman

posed clarification of policies for "Bridge" and "Continuation" grants. These are the ways to provide support for productive SWCRF investigators beyond their initial funding period. These policies are now in effect. A standardized progress report format has been requested of grantees. Given the Foundation's sizable growth, the Annual Scientific Meeting will be streamlined by alternating years when grantees present to the SAB. This recognizes there are deciding points in the funding cycle.

The SAB will have an even more active role in reviewing new grants to assure their alignment with the Foundation's missions, using conference calls and SAB input on reviewers' critiques for each grant recommended for funding by the primary peer-reviewer committee. They will provide oversight on prioritization of

applications for funding.

The SWCRF has a rigorous peer-review system not only to monitor progress of grantees, but also to evaluate new applications for funding. Proposals are judged by respected experts in cancer biology, many of whom are already funded by the SWCRF. Proposals are carefully scored as are those submitted to the National Institutes of Health based on scientific merit and on potential for collaborative research.

Encouraging collaborations was the aim of the workshops held on the second day of the Annual Scientific Meeting. The most recent discoveries were presented as were the newest core facilities. Taken together, these activities reflect the Foundation's mission to create an "Institute Without Walls" by assembling an international team of highly collaborative scientists.

Scientific Advisory Committee

I. David Goldman, M.D.

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Frank J. Rauscher, III, Ph.D.

Professor and Chairman, Molecular Genetics Program; Deputy Director, Wistar Institute Cancer Center, Philadelphia, Pennsylvania. Editor-in-Chief, *Cancer Research*

Barbara L. Weber, M.D.

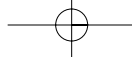
Vice President, Discovery and Translational Medicine, Oncology GlaxoSmithKline

I. Bernard Weinstein, M.D.

Frode Jensen Professor of Medicine, Columbia University, New York, New York

Stuart H. Yuspa, M.D.

Chief, Laboratory of Cancer Biology And Genetics, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, Maryland



One Million Dollar Challenge Grant Received from the Skirball Foundation

The Samuel Waxman Cancer Research Foundation recently received its second \$1,000,000 Challenge Grant from The Skirball Foundation to support programs in Hematological Malignancies and Tumor Dormancy. At this year's "Collaborating for a Cure" live auction, Sotheby's Executive Vice President, C. Hugh Hildesley will be asking our guests to help us meet this million dollar challenge by "bidding" in support of our programs.

We hope that you will join us on Thursday, November 29th at the 69th Regiment Armory located on Lexington Avenue at 26th Street. Meeting this challenge means we will jump-start our evening with a \$2,000,000 success story!

SAVE THE DATES

"Collaborating for a Cure"

**Thursday, November 29
6:30 PM**

**69th Regiment Armory
Lexington Ave @ 26th Street**

**Dr. Samuel Waxman Speaks on
Dormancy in Breast Cancer**

**Monday, December 3
6 PM**

**JCC – 7th Floor
Amsterdam Ave @ 76th Street**

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

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CANCER RESEARCH FOUNDATION**

