

Yale Cancer Center

centerpoint

MAGAZINE



Pinpointing
Oncogenes to
Destroy Cancer

winter | spring 2011



features

2 Finding a Pathway to Survive

Lorraine Romano's journey through cancer treatment led her to find expertise at Yale in 2009. She had a partially matched stem cell transplant and nearly two years later, she has traveled her path to recovery.

4 Making Cancer Quit Cold Turkey

Yale Cancer Center researcher, Frank Slack, discovered that stopping the expression of an oncogene may lead to complete regression of tumors. His work has demonstrated oncogene addiction in lymphomas with microRNA21.



On the Cover

Frank Slack, PhD, Director of the Yale Cancer Center Genetics and Genomics Research Program

Peter Baker **photographer**

departments

1 Director's Letter

7 Advances

Breakthrough Research from Yale Cancer Center

8 Prevention

The Key to Smoking Cessation

10 Forefront

Yale Launches Cancer Biology Institute

12 Training

Educating the Next Generation of Epidemiologists

14 Giving

Join the Momentum to Fund Cancer Research

16 Meet the Physician

Q&A with Dr. Roy Herbst

17 New Faces

Appointments at Yale Cancer Center

director's letter

yale cancer center

Thomas J. Lynch, Jr., MD
Director

Kevin Vest, PT, MBA, FACHE
Deputy Director, Administration and
Clinical Affairs

Renee Gaudette
Director, Public Affairs and Marketing

art + production

Tia Phillips
Art Director

Sharon Peck
Production Director

contributors

Writers
Emily Fenton
Steve Kemper
Colleen Shaddox

Photographers
Peter Baker
pbakerphoto.com

Design
Imagemark Publishing and
Design Studio, Wilton, CT
imagemark.net

submit your ideas...

Do you have an idea for a story
you'd like to see featured
in Centerpoint Magazine?
Submit your ideas to:
renee.gaudette@yale.edu

Yale Cancer Center
centerpoint
MAGAZINE

Centerpoint Magazine is published
two times a year by Yale Cancer Center
to inform the public and the Center's
friends, volunteers, donors, and staff
on current items of interest at Yale
Cancer Center.

Yale Cancer Center
333 Cedar Street, PO Box 208028
New Haven, CT 06520-8028
yalecancercenter.org

©Copyright 2011, Yale Cancer Center.
All rights reserved. No part of this
periodical may be reproduced by
any means, prints, electronic, or any
other, without prior written permission
of the publisher.

Editorial Office
Yale Cancer Center
157 Church Street
New Haven, CT 06510-2100
renee.gaudette@yale.edu

Yale Cancer Center has experienced a period of tremendous growth and progress over the last year. I began my tenure in April of 2009 and have had the pleasure of recruiting several top scientists and clinicians to continue to strengthen the outstanding basic science and clinical care here at Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven.

Smilow Cancer Hospital began full operation a year ago with the consolidation of Yale's inpatient and outpatient cancer services into one facility, making it the most comprehensive, single destination for cancer services in the Northeast. Since the opening of Smilow, we have welcomed 23 new faculty members to our membership, including three outstanding leaders in the cancer community – Lieping Chen, Roy Herbst, and Yossi Schlessinger. The leadership that these senior recruits bring to Yale, and the energy and excitement that has been added to our clinical and research teams, is immeasurable.

Lieping Chen's laboratory research on cell surface molecule pathways and their impact on innate and adaptive immunity will ensure Yale continues to push the frontiers in cancer immunobiology. His laboratory has made seminal contributions to the development of cancer therapeutic monoclonal antibodies against CD137, PD-1, and B7-H1, which are all currently in clinical trials.

In 2010, Yale made significant investment in the understanding of the biology of cancer with the opening of a Cancer Biology Institute, led by Yossi Schlessinger. Yossi is a world-class scientist with an unparalleled track record of turning new targets into medicines that help cancer patients live longer. I am confident that his leadership will enable the Institute to become one of the world's great centers for understanding the fundamental nature of cancer and finding ways to defeat it.

I am pleased that Roy Herbst will join Yale Cancer Center in March as Chief of Medical Oncology and Associate Director of Translational Research. Roy's focus will be to unite our basic and clinical research efforts to ensure we are quickly moving breakthroughs in cancer research to benefit our patients through clinical trials.

I am eager to share the new ideas and advances that will emerge in 2011 as our new faculty members integrate with the strong basic research teams at Yale in the next issue of Centerpoint.

Sincerely,



Thomas J. Lynch, Jr., MD, Director, Yale Cancer Center

Physician-in-Chief, Smilow Cancer Hospital at Yale-New Haven

PETER BAKER





Finding a Pathway to SURVIVE

Emily Fenton **writer** Peter Baker **photographer**

Lorraine Romano with her dog, Bella.

Lorraine Romano's long journey of treatment and recovery began more than ten years ago when she found an enlarged lymph node that was biopsied and showed low-grade lymphoma. Treatment for low-grade lymphoma with conventional therapy is quite effective but the lymphoma ultimately returns and subsequent remissions after treatment generally become shorter over time. This is what occurred with Lorraine,

and in April of 2009 she received another round of standard treatment. After the treatment, Lorraine's blood counts began to plummet and quite surprisingly, her blood counts did not recover. Because her counts remained so low, she could not continue to receive therapy for the lymphoma and she required frequent transfusions. Several bone marrow studies showed that her bone marrow had stopped functioning without obvious cause.

Lorraine's life became dominated by the frequent need for blood transfusions and periodic hospitalizations for infection. The issue with her bone marrow was compounded by the fact that her lymphoma was continuing to grow and could not be safely treated. The only way that both problems could be treated was with a stem cell transplant.

It was recommended that she see Dr. Dennis Cooper, Director of the Stem Cell Transplant Program at Smilow Cancer Hospital at Yale-New Haven, for an evaluation. Unfortunately, Lorraine did not have a family match who could serve as a donor. Susan Faraone, RN, Yale's allogeneic bone marrow transplant coordinator, found potential matches through the National Marrow Donor Registry but none of the possible matches were fully compatible.

"From the time that my blood counts failed to recover, I was working on borrowed time. It was three months before a donor was found and I am very thankful they found one when they did. I was receiving transfusions every other day and at times, I felt very weak and had several infections," Lorraine explained.

Lorraine received what is known as a partially matched stem cell transplant since a fully matched donor was not found. The most severe complication resulting from a stem cell transplant is graft-versus-host disease (GVHD), which can cause intense rash, abdominal pain, diarrhea, and liver dysfunction due to an attack by the donor's immune system against the patient's tissue.

"Our transplant physicians had initiated a clinical trial for partially matched transplants after realizing that the patients that were receiving partially matched stem cell transplants were encountering serious GVHD effects. Under the direction of Dr. Stuart Seropian, the prophylaxis used after transplant to prevent GVHD was changed and since then we have not seen any severe cases of GVHD, and are quite pleased with the results," Dr. Cooper said.

Before the transplant occurred, Lorraine was started on a con-

ditioning regimen developed by Dr. Francine Foss to treat the lymphoma. This involved chemotherapy and total body irradiation. The expertise of the entire transplant team combined to provide Lorraine with a unique treatment plan customized for her.

"To my knowledge, there is no other center that is using the

"I am blessed that I was not brought down by this disease and I was able to persevere. I was not done playing an active role in the life of my family."

same method for preventing graft-versus-host disease after a partially matched stem cell transplant. GVHD is a serious problem for this type of transplant and to be able to control it better provides us with more options and has made a huge difference in the lives of our patients," Dr. Cooper said.

In Lorraine's case, it allowed her to receive the transplant that she desperately needed. She has passed the one-year mark since her transplant, and has no evidence of disease. She continues to take immunosuppressants to prevent the occurrence of GVHD, and once a month she is monitored through the Bone Marrow Transplant Day Hospital at Smilow Cancer Hospital by transplant-specialized nurse practitioners, physicians, and a dietician.

"I am blessed that I was not brought down by this disease and I was able to persevere. I was not done playing an active role in the life of my family," Lorraine said. Lorraine is back working full time and is happy to be involved in the lives of her children again. She explained that family and friends are a crucial part to getting through cancer treatment, but also having trust in the knowledge and expertise of those caring for you.

microRNA21
microRNA21
microRNA21
microRNA21
microRNA21
microRNA21

Making Cancer **Quit** Cold Turkey

Colleen Shaddox **writer** Peter Baker **photographer**

A cancerous tumor might contain 50,000 mutations. Professor of Molecular, Cellular & Developmental Biology Frank Slack found that turning off a single oncogene – microRNA21 – was enough to cause tumors to completely regress in mice in just a few days. The study was the first to establish a phenomenon being referred to as “oncomiR addiction,” though Slack said that “dependency” might be a better term. In his experiments, lymphomas could not survive without this particular microRNA. “Their ‘cold turkey’ is to die,” he said. He recently published these findings in the journal *Nature*.

Slack cautioned that treating cancer in humans is a far more complex endeavor than treating it in mice. There is no certainty that the therapy will have human applications, which would take years to develop. But the finding is promising because microRNA21 has already been found in unusual levels in many common human cancers and because scientists already know how to stop its expression.

“Frank’s cutting edge research provides convincing evidence that microRNA21 can drive tumorigenesis and is necessary for maintaining tumors in an animal model,” said Curtis C. Harris, MD, Chief of the Laboratory of Human Carcinogenesis at the National Cancer Institute. “These preclinical studies support the potential of targeting certain microRNAs in cancer prevention and therapy.”

MicroRNAs were not discovered until 1993. As the name implies, they are small RNAs. At about 20 nucleotides long, they are so minute that for most of human history we lacked the technology to detect them. Scientists found microRNAs have the ability to regulate genes, meaning they signal genes to become active or remain dormant. Only in the past six years have some microRNAs been shown to play a role in cancer. Slack’s research focuses on these and other microRNAs. He is trying to answer fundamental questions about how microRNAs function while also looking at ways to harness them to address cancer and aging.

microRNA21



Frank J. Slack, PhD, Director of the Yale Cancer Center Genetics and Genomics Program and Professor of Molecular, Cellular & Developmental Biology.

In the case of these overabundant microRNA21, Slack explained, a potential cancer therapy could involve “binding” the microRNA to stop its activity. MicroRNA function by fitting together with given spots on the genome – much like the pieces of a puzzle. That action can be stopped by introducing another agent that is a perfect fit for the microRNA, thus blocking it from latching onto the genome. Academic medical centers and private biotech firms are active in developing these synthetic puzzle pieces, said Slack.

Many of his experiments use *Caenorhabditis elegans*, transparent roundworms that are a favorite of scientists because they are so easy to manipulate.

“It was a risky program because we didn’t have any prior indication, except that the microRNA was over-expressed in cancers,” said Slack.

He spent four years on the project, which was funded by the James S. McDonnell Foundation and Yale Cancer Center. It

microRNA21



answered two key questions: Is microRNA21 an oncogene? And can tumors survive without it?

While microRNA21 is over-expressed in many cancers, that does not mean it causes cancer. Slack tested this by working with mice genetically engineered to over-express microRNA21 but otherwise perfectly normal. They went on to develop an aggressive disease reminiscent of pre B-cell lymphoma and displayed clinical symptoms of lymphoma/leukemia, including enlarged lymph nodes, enlarged spleens and labored breathing. This demonstrated that the over-expression of microRNA21 was not simply a sign of their disease; it was the cause. The tumors could be transplanted to mice without the genetic modification and continued to grow. This indicates that the tumors were malignant.

When he “shut off” microRNA21, the tumors shrank rapidly, in large part due to apoptosis, programmed cell death. The tumors literally could not live without microRNA21. His next step is to determine if a treatment to knock out microRNA21 has any toxicity in mice. Slack’s hope is that in three to four years the research will lead to clinical trials in humans and to targeted cancer therapies. Though much work remains to make that happen, the progress of microRNAs from a newly discovered factor to a potential drug target has been rapid.

“Some of the most amazing discoveries have been basic science discoveries,” said Slack, who added that as technologies are developed to do biology on ever-smaller subjects more such discoveries would follow. “We have to keep looking. We’re exploring a part of the cell that was dark before,” he said. He recalled how in the 1980s and 90s, scientists believed that many parts of the human genome served no purpose and deemed these regions *junk* DNA. But as microRNA research illustrates, close examination can prove that unlikely bits of biology can be overwhelmingly useful.

“Maybe there’s no junk in the genome,” said Slack. “We just have to keep looking.” ↻



Insulin Levels Found to Affect Breast Cancer Survival

J Clin Oncol. 2011 Jan 1;29(1):32-9.

Women treated for breast cancer who have elevated levels of circulating insulin face substantially higher mortality rates than their peers with lower levels, according to a new study authored by Melinda Irwin, PhD, Co-Director of the Yale Cancer Center Prevention and Control Program.

Patients with amounts of an insulin marker known as C-peptide greater than 1.7 ng/mL were at a two-fold higher risk of breast cancer death compared with women with C-peptide levels lower than that. Women with type 2 diabetes had an even greater risk of breast cancer death compared with women without type 2 diabetes.

Cellular Toolkit for DNA Repair Found by Yale Researchers

Nature. 2010 Sep 2;467(7311):108-11.

Yale researchers have identified key mechanisms used to repair breaks in DNA strands, a fundamental question in biology with implications for cancer research. Chromosomes are constantly under assault from environmental threats such as radiation and, as a consequence, suffer breaks in strands of DNA. If left unrepaired, these DNA breaks can lead to the development of cancer. The process of break repair is so complex it has baffled scientists for decades.

The Yale team, led by Patrick Sung, PhD, Chair of the Department of Molecular Biophysics and Biochemistry, identified 10 proteins crucial to the process and outlined how those proteins interact to initiate the repair of the breaks.

Exercise is Associated with Reduced Risk of Endometrial Cancer

Cancer Causes Control. 2010 Nov 26.

Women who routinely perform moderate- to vigorous-intensity exercise for 2.5 hours or more weekly have a significantly reduced risk of endometrial cancer, new research by the Yale School of Public Health has discovered.

This association was particularly pronounced among active women with a body mass index (BMI) less than 25, where the reduction in risk was 73 percent compared with inactive women with a BMI greater than 25. Although body mass index showed a strong association with endometrial cancer, even women who were overweight, but still active, had a 52 percent lower risk.

Breast Milk Protein Linked to Poorer Breast Cancer Survival in Younger Women

Proc Natl Acad Sci U S A. 2010 Jun 22;107(25):11405-10.

In a study that sheds light on why breast cancer may be deadlier for premenopausal women, a research team led by John Wysolmerski, MD, Professor of Endocrinology at Yale School of Medicine, has linked breast cancer survival with levels of a transport protein that regulates milk production in mammary glands.

During breastfeeding, a great deal of calcium must be transported from the circulation into milk. This is accomplished through mammary cells that express the plasma membrane calcium-ATPase 2 (PMCA2). The research showed that persistent PMCA2 expression in breast cancers lowers calcium levels inside malignant cells, allowing them to avoid cell death. Further, the researchers associated these excessively high PMCA2 levels with poorer outcomes in breast cancer.

Cancer's 'Addiction' Spurs New Treatment Hopes

Nature. 2010 Sep 2;467(7311):86-90.

Cancer can call upon a bewildering array of genetic tricks to wreak havoc, but Yale researchers, led by Frank Slack, PhD, Director of the Yale Cancer Center Cancer Genetics Research Program, show that the disease can become dependent upon a tiny gene that allows it to adapt and proliferate. The identification of such an "oncogene addiction" within a tumor means that researchers have a potentially new and valuable therapeutic target with the potential to cripple the deadly disease.

Ancient Chinese Herbal Recipe Eases Side Effects of Chemotherapy

J Chromatogr A. 2010 Sep

10;1217(37):5785-93.

A combination of Chinese herbs in use for more than 1,800 years reduced the gastrointestinal side effects of chemotherapy in mice, while actually enhancing the effects of the cancer treatment, Yale Cancer Center researchers report. The formula used in the experiment consists of four herbs, called PHY906, and is based on an herbal recipe called Huang Qin Tang, used historically to treat nausea, vomiting and diarrhea.

Yale Study Finds Hospice Saves Money, Improves Care for Cancer Patients

J Clin Oncol. 2010 Oct 1;28(28):4371-5.

The cost of care for cancer patients who stopped hospice care was nearly five times higher than that for patients who remained with it, according to a study led by Elizabeth Bradley, PhD, Professor of Epidemiology and Public Health. Patients who stop hospice are also far more likely to end up needing emergency department care, ICU care and to be hospitalized.



PETER BAKER

Benjamin A. Toll, PhD

So Much to Gain

Using Research to Help Cancer Patients Kick the Habit

*Quit smoking and you'll get fewer colds.
Keep smoking and you'll get more colds.*

Those messages contain similar objective information, but the first is likelier to persuade a smoker to quit. Assistant Professor of Psychiatry Benjamin Toll's research focuses on finding better ways to help people stop smoking. Much of it has explored how "gain-framed" messages, emphasizing the benefits of quitting rather than the dangers of continuing, can boost quit rates.

As Toll develops a smoking cessation program for patients at Smilow Cancer Hospital, there are plenty of gains to emphasize. "Smoking cessation will make their cancer treatments more effective, reduce the risk of future cancers and extend their lives," said Toll. The National Cancer Institute has become a strong supporter of smoking cessation

programs for cancer patients, said Toll, and that represents a new understanding of how critical smoking cessation is during cancer treatment.

For example, research led by Susan Mayne, PhD, Professor of Epidemiology, showed that head and neck cancer patients who continued to smoke after diagnosis had an 80 percent higher mortality rate than those who quit after diagnosis – regardless of either group's previous smoking history.

Before such findings, clinicians sometimes hesitated to ask cancer patients to quit cigarettes during an already stressful time, said Frank Detterbeck, MD, Chief of Thoracic Surgery. Today clinicians see the enormous benefit to helping their patients quit. But as knowledge about smoking cessation grows, the field is becoming highly specialized. "You really need a dedicated smoking cessation program to implement an evidence-based approach for our patients," said Detterbeck.

The cessation program is offered to all patients with head and neck or lung cancers. Individualized treatment plans will include a combination of counseling and drug treatment. Eventually the service will be extended to patients with other forms of cancer, beginning with breast cancer. The smoking cessation staff will work with other departments to schedule

appointments that dovetail with existing cancer treatment sessions.

Much of Toll's research builds on Prospect Theory, which states that focusing on dangers made people more likely to choose a riskier option.

Toll recently tested a real-world application of this theory by doing messaging training with workers at the New York State Smokers' Quitline, a free telephone smoking cessation service. Some workers used "gain-framed" messages stressing the benefits of quitting and sent out printed materials that did the same. Callers who had received the gain-framed messages had a higher quit rate after two weeks, but not at a three-month follow up. His results were recently published in the *Journal of the National Cancer Institute*. To follow-up, Toll will explore ways to extend the early benefit of gain-framed messaging. He was also pleased that the study demonstrated the practicality of training Quitline workers in evidence-based techniques. Quitlines exist in all 50 states.

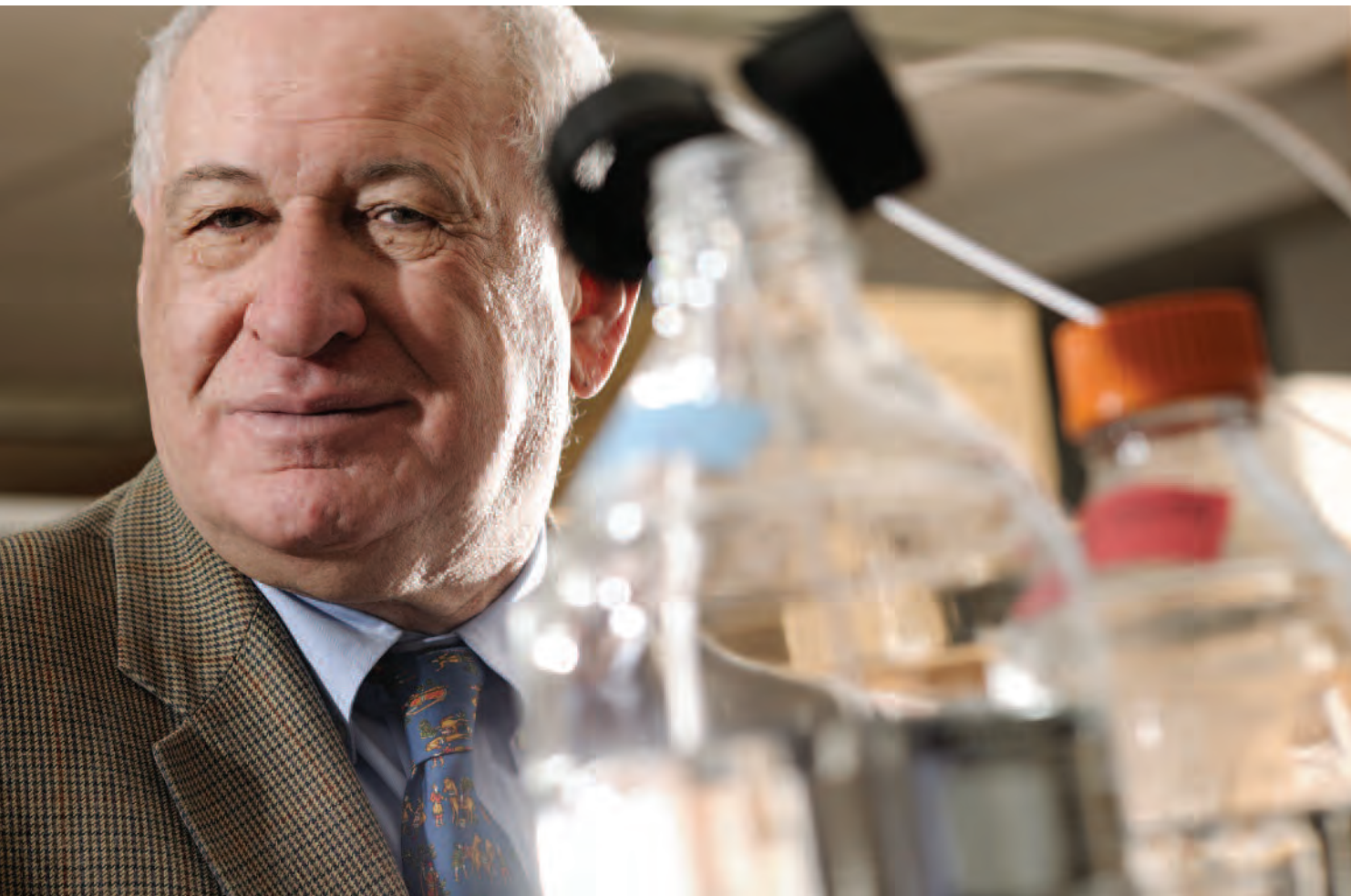
Earlier Toll had looked at the role gain-framed messaging could play in combination with bupropion, a prescription anti-depressant used in smoking cessation. All volunteers in the study were given bupropion, and all saw factually equivalent videos about the effects of smoking. One group's video was gain-framed. The other

"With the growing number of options in smoking cessation, a patient's particular circumstances will often determine the best plan of action."

group watched a loss-framed video, emphasizing the negative effects of smoking. The group with the gain-framed messages had a higher quit rate.

Toll's research has also explored the effectiveness of other drugs in supporting cessation, the problem of weight gain during smoking cessation and many other factors involved in the highly complex act of kicking the habit. With the growing number of options in smoking cessation, a patient's particular circumstances will often determine the best plan of action. As with cancer treatment, Toll said that smoking cessation treatment must be "personalized."

Offering smoking cessation also fits in the emphasis on long-term health as initial cancer treatments become more successful, said Mayne. "We're looking at everything patients are doing and what we can do to help them enjoy a better survivorship down the road," she said. ☺



PETER BAKER

Joseph Schlessinger, PhD

Understanding the Biology of Cancer

The search for the best person to run the new Cancer Biology Institute eventually came full circle. In December, Joseph Schlessinger, PhD, the William H. Prusoff Professor and Chairman of the Department of Pharmacology at Yale School of Medicine, was named the Director of the new institute. He will also continue as Chairman of Pharmacology.

Offered congratulations, Schlessinger laughed and said, “Yes, for working harder. At my age [65], all my peers in Europe are retiring and I’m starting a new career.”

The Cancer Biology Institute will join four other new research centers on Yale’s West Campus. The institute represents an ambitious expansion of Yale’s commitment to cancer research. Over the next several years, Schlessinger will guide the hiring of 150 research scientists and 11

principal investigators, each of whom will have a lab in the institute.

The plan’s bold scope invigorated Schlessinger. “I like to start things from scratch,” he said. “I started three companies that are doing very well, and I have built a lot of institutions in my life.”

A building needs a strong foundation. Schlessinger believes that his first and most important task is to find the right three senior people. These will in turn help him attract eight junior people. Each member of this core group will staff his or her own lab with research scientists.

“I’m going to hire people who will be so good that they are not going to face problems with the current financial environment with NIH. Every scientist I recruit will be like an entrepreneur,” said Schlessinger. “He or she will have to raise their own money, have their own program, be totally independent. They will be recruited to do what they do best, and what they want to do. I will just provide an environment where they can reach their full potential.”

He stressed that finding the right people requires patience. To fully staff the institute might take four or five years.

Schlessinger has a reputation for choosing transformative scientists. “I came to Yale nine years ago,” he said, “and under my leadership the Department of Pharmacology is now ranked among the

top three programs in the United States by the National Research Council. They want me to repeat that at the Cancer Biology Institute.”

Schlessinger was born in Croatia and educated in Israel. After stints at Cornell and the National Cancer Institute, he worked at Israel’s Weizmann Institute from 1978 to 1991. His next stop was New York University’s School of Medicine, where he was Chair of the Department of Pharmacology and directed the Skirball Institute of Biomolecular Medicine. He came to Yale in 2001.

He has also co-founded three biotechnology companies devoted to the discovery of cancer drugs: Sugem (now owned by Pfizer), Plexxikon, and Kolltan. He has been a pioneer in targeted cancer drugs. One of these, Sutent, was approved by the FDA in 2006 for kidney and stomach cancers. Another, PLX4032, developed by Plexxikon, targets melanoma and colorectal cancer, and has been very successful in clinical trials. Schlessinger is a member of the National Academy of Sciences and the Institute of Medicine. Among many honors, he was awarded the Pezcoller Prize last year from the American Association for Cancer Research.

The institute, he said, “will be a tremendous boost” to cancer research at Yale. It and the other new centers on West Campus will add missing components of

basic research. Schlessinger ticked them off: cancer genetics, cancer genomics, quantitative aspects of cancer, molecular mechanisms, systems biology, chemical biology, bioengineering, microbiology. All these disciplines will be focused on understanding the causes of cancer and devising new therapies to overcome it.

“To give good care,” said Schlessinger, “we need to improve the basic side of science. Developing research drives so much of cancer treatment. The more you understand targeted therapies, the faster you’re able to bring them to the clinic. This will benefit the clinicians, who will get better training and have better options, and so will the patients at the hospital.”

Schlessinger pointed out that the concentration of research centers on West Campus will create a critical mass of people working on cancer, and that the centers will cross-pollinate. “When you do science, your mind is fertilized not only by the questions you are addressing,” he said, “but is inspired by working in another discipline. It’s very good to mix people, to have a place where they can have lunch and talk.” These expanded opportunities will, in turn, attract the best graduate students from all over the world.

Schlessinger is confident that once all of these elements are in place, the Cancer Biology Institute will become one of the top such research centers in the world. ☞



Susan T. Mayne, PhD

Partners in Training

Yale Cancer Center and The National Cancer Institute

“I don’t think it can be overstated how much this program can accelerate your progress, and truly set you on a trajectory that’s hard to realize at other institutions,” said H. Dean Hosgood, MPH ’05, PhD ’08, and now a Research Fellow at the National Cancer Institute (NCI).

Hosgood was describing his participation in a one-of-a-kind partnership between Yale Cancer Center and the NCI. Pre-doctoral students in the program do their course work in epidemiology and public health at the Yale School of Public Health and then take their qualifying exams, like all PhD candidates. But at that point they move to the NCI where they immerse themselves in research on their dissertations while also joining the NCI research teams. The students typically finish their dissertations after two years at the NCI, and then receive a PhD from Yale. There’s no program like it in the country.

“It gives the trainees access to phenomenal resources,” said Dr. Susan Mayne, who conceived and directs the program. She is also Associate Director for Population Sciences at Yale Cancer Center and a Professor of Epidemiology and Public Health.

Hosgood agrees. “For cancer epidemiology, the NCI has the largest bio-repositories of specimens, the largest studies, and the best designed studies in the entire world,” he said. “And through this program that Susan developed, students are privileged enough to gain access to these incredible resources.”

Hosgood did his dissertation on the molecular epidemiology of lung cancer susceptibility to indoor air pollution from solid fuel use. The NCI has been studying the issue for decades. “By joining the NCI, I really accelerated my career,” he said. I might have been able to study this topic somewhere else, but it would have required at least five or ten years to build the beginning of a research portfolio. Even then, the portfolio would have only been a small fraction of what I have been able to access through the NCI.”

The origins of the program go back nearly ten years. One of Mayne’s doctoral students needed large data sets to answer certain questions for her dissertation. The NCI was the obvious resource. Mayne had collaborated and published with

many of the investigators there, so she approached the institute about giving the student entry. They were happy to oblige, as long as they had some oversight. The experiment worked and was repeated by several more students. Eventually the partnership was formalized in 2003, with funding from the NCI. In 2008 it was refunded for another five years.

The program is extremely competitive and typically awards two fellowships each year, one in nutritional epidemiology and cancer (Mayne’s area) and one in environmental epidemiology and cancer, based out of the Division of Environmental Health Sciences at Yale, which is led by Dr. Tongzhang Zheng. Like Mayne, Zheng has collaborated with many investigators at the NCI. These contacts help to cushion the trainees’ transition from Yale to the NCI.

Stephanie M. George, MPH ’07, PhD ’10, and now a post-doc at the NCI, considers the strong co-mentoring as the program’s greatest strength. A corollary benefit, she added, is that working closely with the NCI scientists lets the student plug into invaluable networks of interdisciplinary scientists. “I am interested in the roles that nutrition and physical activity play in the study of cancer at a population level,” said George. The ability to develop large networks of collaborators who are interested in the same research area but

have different perspectives is really amazing to be exposed to as a pre-doc.”

Yale and the National Cancer Institute also benefit from the partnership. Mayne noted that the program’s graduates are likely to be future leaders in the field, which burnishes Yale’s reputation for training leaders in cancer research, and leads to better applicants. One benefit that Mayne didn’t foresee is that the program has fostered increasing collaboration between Yale faculty and investigators at the NCI.

For the National Cancer Institute, the key benefit is a pipeline to bright, well-trained young scientists. So far, most of the trainees have stayed at the National Institutes of Health.

The program is too new to measure its public benefits, but there are signs. Each year, the American College of Epidemiology gives an award to the best doctoral student paper. “In both 2008 and 2009,” said Mayne, “the top paper award nationally went to our trainees. That’s an unbelievable measure of success.”

She added that all of the trainees are working on important questions in cancer. “The work they’re doing is hopefully translating into lives saved. When I look back after my career,” she continued, “I think one of my biggest impacts will be the number of people we’ve trained who are doing phenomenal work and contributing to the public betterment.”



PETER BAKER

John Wareck

Joining the Momentum

John Wareck's family has lived and worked in the New Haven area for three generations. His grandfather emigrated from Russia in 1901 and started an auto business here. Over the years the family has developed a long-standing relationship with Yale. His father graduated from Yale University in 1952, and both of John's daughters were born at Yale-New Haven Hospital. When his parents were diagnosed with cancer, they were both treated at Yale. John's father was diagnosed with pancreatic cancer in the early 1990's and his mother with breast cancer a few years ago. Unfortunately, his father was diagnosed at a late stage and succumbed to the disease, but thankfully his mother is in remission today.

John's history of giving is a long one. He can remember back to his childhood and donating money to local charities. He has given to the Yale Golf Course where his

father played while in school, and to the Yale medical community over the years. "It's good to make a habit of giving; if you start when you are young then it becomes easier to give as you get older. Personally it makes me feel involved and invested in something. Every bit helps and it's gratifying to know that I am a part of the bigger picture. It makes me happy to know that I can help solve

"If I can give to just one researcher, or one doctor, and help them try to cure cancer, that's enough. It is a great feeling knowing that I am playing a role in helping them with cutting edge research to help fight this disease."

some of the challenges that others are facing," John said. His family has realized the importance of supporting cancer research and patient care first hand. His support of Momentum Fund is motivated by these personal experiences. Gifts to Momentum Fund provide essential funding for Yale Cancer Center and Smilow Cancer Hospital to pursue powerful new cancer therapies and personalized medicine.

Having a real estate business located in New Haven, John is rooted in the community and understands the importance of giving locally. He is pleased that Yale Cancer Center is one of the foremost research facilities and happens to be in his 'backyard.' John is excited about the joint efforts of Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven in pursuing the most promising cancer research and providing the most effective patient care. "It is wonderful to have all the experts in one place enabling them to work more efficiently. Now there is a beautiful building that people can see and know that even by giving a little, they can

be a part of something that is making such a dramatic difference," said John. "It's hard to imagine not giving to and supporting the work being done at Yale Cancer Center and Smilow Cancer Hospital, because they support us and we need to give that support in return."

Pancreatic cancer is still a tough disease to fight, but John feels that if the advanced cancer treatments and personalized patient care available now were options when his father was diagnosed, maybe his father could have been saved. There is hope for John in knowing that now people with late-stage pancreatic cancer have a chance at a future, and that's what giving is all about, the future. For him, it was easy to begin the wonderful habit of giving; all it takes is one donation to make a difference.

"My experience with giving has been tremendous. If I can give to just one researcher, or one doctor, and help them try to cure cancer, that's enough. It is a great feeling knowing that I am playing a role in helping them with cutting edge research to help fight this disease," John explained. ↻



Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven have joined forces to create *Momentum Fund*, which provides essential funding for breakthrough cancer research and compassionate patient care by combining the gifts of many donors. This support is critical to ensure that new research can be pursued without delay, promising treatments are aggressively developed and patient care is continuously enhanced. The generous support of *Momentum Fund* donors accelerates ongoing work and helps to launch important new research projects and programs.

The support of the community is integral to the success of *Momentum Fund*. We value the efforts of our donors, volunteers, and advocacy spokespeople. There are many opportunities for members of the community, cancer survivors, and those passionate about cancer research and patient care to become involved in the efforts of *Momentum Fund* and to support our mission.

Individual contributions as well as organized efforts to raise funds through events all can have an impact. Events such as movie nights, walk-a-thons, and birthday parties can be a fun and effective way to direct donations to support *Momentum Fund*.

FOR MORE INFORMATION ON HOW YOU CAN HELP, VISIT OUR WEBSITE AT MOMENTUMFUND.ORG





Q+A

meet the physician

Roy S. Herbst, MD, PhD

Chief of Medical Oncology and
Associate Director of Translational Research

What is your first priority when you begin your tenure at Yale?

My first priority is to spend time meeting the faculty in the section of medical oncology and throughout the cancer center and the medical center. I really want to better understand what is going on at Yale Cancer Center and Smilow Cancer Hospital and appreciate people's interests and agenda so that I can best facilitate translational research. The extraordinary basic and clinical research at Yale is exciting and I plan to strive to bring them closer together to develop more protocols and treatments that can be translated to patients as quickly as possible.

What are your goals during the first year at Yale?

My primary goal is to enhance the medical oncology clinical research to raise the bar and bring the best therapies possible to care for patients with advanced solid tumors. I am very excited to focus on the development of novel therapeutics for all cancer types, for we are truly in the era of personalized medicine, where understanding each patient's tumor biology can potentially have a positive impact on their successful treatment. I am eager to work with the leadership of the new Cancer Biology Institute to develop a system where we can quickly access the newest and most personalized and effective therapy for our patients using the most current genomic technology for target identification and assessment of prognosis.

What area of translational research has the most promise for patients in the next 5 years?

I think our ability to biopsy a tumor and then use the tumor tissue to sequence the DNA and look at the RNA transcripts will afford extraordinary potential to understand the biology of each patient's tumor and to link it with appropriate therapies. Therefore, it is important that we build both our basic biology and pathology services to support clinical care. We are also working to develop new therapeutic trials and novel approaches to study them. I am quite excited about the ability to measure cytokines and identify proteins in blood cells. These liquid biopsies might offer the opportunity to follow patients' tumors in real time, while also allowing for early detection of disease and the implementation of more effective and less toxic therapies.

How do you explain the importance and value of clinical trials to your patients?

Clinical trials are important for a number of reasons. By participating in a clinical trial patients have the opportunity to obtain some of the most novel therapies available for any given tumor. I am especially excited to help build a Phase I drug program where Yale, which was the home of the first use of chemotherapy, can again emerge as a leader in drug discovery.

One of the goals of federally designated centers, like Yale Cancer Center, is to offer clinical trials to provide patients with the best possible care, while also having the ability to then verify and validate the therapies that can and should be pursued in the future. One of the studies that I will bring to Yale is the BATTLE trial, Biomarker-based Approaches of Targeted Therapy for Lung Cancer Elimination, which I implemented with my team at MD Anderson Cancer Center. This is a study where patients have a biopsy performed before their treatment and the results of that biopsy are used to determine the most effective and least toxic therapy for advanced lung cancer.

Anees Chagpar, MD

Yale Cancer Center and Smilow Cancer Hospital at Yale-New Haven were pleased to welcome Anees B. Chagpar, MD to the position of Director of the Yale Breast Center at Smilow Cancer Hospital in September. Dr. Chagpar focuses her clinical research on molecular expression and biomarkers in breast cancer and has served as the principal investigator for several clinical studies analyzing sentinel node biopsy, new therapeutic options, and hormonal therapies for patients.

Previously, Dr. Chagpar served as an Associate Professor in the Department of Surgery at the University of Louisville and Director of the Multidisciplinary Breast Program at James Graham Brown Cancer Center in Louisville, KY. She received her medical degree from the University of Alberta and earned a Masters of Science degree from the University of Saskatchewan and a Masters of Public Health degree from Harvard School of Public Health. Dr. Chagpar completed the Susan G. Komen Interdisciplinary Breast Cancer Fellowship at MD Anderson Cancer Center.



Lieping Chen, MD, PhD

Internationally known for his work in cancer immunobiology, Lieping Chen, MD, PhD has been appointed Director of Cancer Immunology at Yale Cancer Center. His laboratory work is focused on the understanding of molecular, biochemical, and structural aspects of cell surface molecule pathways and their functions in the control of innate and adaptive immunity and subsequent development of cancer.

Throughout his career, Dr. Chen has played a leading role in the discovery and characterization of costimulatory molecules in the B7-CD28 and the TNF receptor/ligand superfamilies. His laboratory has made seminal contributions to the development of cancer therapeutic monoclonal antibodies against CD137, PD-1, and B7-H1, which are currently in clinical trials.

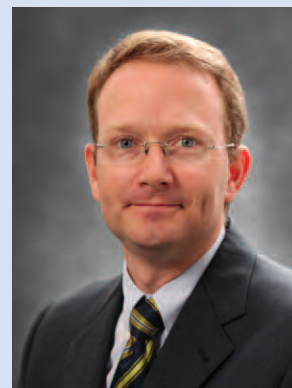
Prior to his appointment at Yale Cancer Center, Dr. Chen was a Professor of Oncology and Dermatology at Johns Hopkins University School of Medicine. He is a co-founder of the Amplimmune Biotechnology Company based in Bethesda, Maryland.



Mark Faries, MD

Mark Faries, MD, FACS was appointed to the position of Associate Professor of Surgical Oncology at Yale School of Medicine last fall. Dr. Faries specializes in the surgical treatment of melanoma and is an integral member of the Yale Cancer Center and Smilow Cancer Hospital Melanoma Program. He brings extensive experience in tumor immunology and melanoma metastases, adding to the strength of the translational research in melanoma currently underway at Yale.

Dr. Faries splits his time between patient care and research through the Yale Cancer Center Immunology Research Program. Before joining Yale Cancer Center, he was an Associate Member of the John Wayne Cancer Institute and Director of their Translational Tumor Immunology Lab. A graduate of Haverford College, Dr. Faries received his medical degree from the Cornell University Medical College. He completed his internship and residency at the Hospital of the University of Pennsylvania and his fellowship at the John Wayne Cancer Institute.



Howard Hochster, MD

Howard S. Hochster, MD joined the faculty of Yale Cancer Center in July as a Professor of Medicine in Medical Oncology, Medical Director of the Gastrointestinal Cancers Program, and Associate Director of Clinical Research. His clinical research concentrates on the study of new treatments, and combinations of therapies, for patients with advanced and relapsed colorectal cancer. Dr. Hochster is a leader in translational research in development of targeted agents for GI cancers and has led national, pivotal clinical trials in the use of Bevacizumab and Cetuximab in colorectal cancer.

Previously, Dr. Hochster was a Professor of Medicine at New York University School of Medicine in the divisions of Medical Oncology and Clinical Pharmacology and Director of the Gastrointestinal Cancer Program at the NYU Cancer Institute. He is a fellow of the American College of Physicians and a member of the American Society of Internal Medicine, American Society of Clinical Oncology (ASCO), and American Association for Cancer Research.



333 Cedar Street, P.O. Box 208028
New Haven, CT 06520-8028

“I try to think back to
my life before cancer, and it is
almost impossible. It changed the way I
live each day. Everyday I look at my family,
my wife, my two daughters, and our new son
Robert, and I am so thankful that I am still
here to be a husband and father to them.”

Robert—Esophageal Cancer Survivor

Yale Cancer Center aims to be a global leader in cancer care, research, and education. Over 350 scientists and physicians at Yale Cancer Center collaborate to make the discoveries that advance the prevention and cure of cancer, while providing the very best in clinical cancer care to our patients at Smilow Cancer Hospital at Yale-New Haven in a supportive, patient-centered setting.



Yale Centerpoint Magazine
Issue: Winter/Spring
Date: 1.21.11.v8_2:01p

COVERS

cover 1 (FRont) Research image, cover line i	cover 2 (inside FRont) t able of contents ii	cover 3 (inside BAck) Department new FAcEs Appointments 17	cover 4 (BAck) ycc, sch logos, indicia 1/2pg in house ad iv
--	---	--	--

Masthead Depart. DiRect LetteR 1	Feature (survivor) Lorraine - Lymphoma a begins 2	Feature (survivor) Lorraine - Lymphoma ends 3	Feature (Research) oncomiR Addiction begins 4	Feature (Research) oncomiR Addiction ends 5	Feature (Research) oncomiR Addiction ends 6	Department ADvAnces Research highlights from ycc 7	Department PRevention Tobacco Cessation begins 8	Department PRevention Tobacco Cessation ends 9	Department FoReFRont West Campus begins 10	Department FoReFRont West Campus ends 11	Department tRAining ePh/nci t raining begins 12	Department tRAining ePh/nci t raining ends 13	Department giving Momentum Fund begins 14	Department giving Momentum Fund ends 15	Department Meet the PhysiCIAn Roy Herbst 16
--	---	---	---	---	---	---	--	--	--	--	---	---	---	---	---

Cover

Survivor Image
 one cover line

Table of ConTenTs

with imagery_3-4 images
 -survivor_Lorraine
 -research_Frank S
 -giving_John Wareck
 1 page

fea tures

Survivor Story
 Lymphoma Patient
 3 pages
 imagery: Lorraine_opener
 Research Story
 oncomiR Addiction
 2 pages
 imagery: Frank Slack_opener plus 1
 follow up

dep artments

Masthead/Letter from the Director
 1 page
 imagery: Tom Lynch

 Advances
 1 page
 (Journal Clips/News from YCC)
 imagery: NA

 Prevention
 (Tobacco Cessation Story)
 2 pages
 imagery: Ben Toll-call center
 opener

 Forefront
 (West Campus/Cancer Biology
 Institute Story)
 2 pages
 imagery: Dr. Yossi Schlessinger

 Training
 (EPH/NCI Story)
 2 pages
 imagery: Susan Mayne (in-house)

Giving (Momentum Fund)

Donor story on John Wareck
 2 pages
 imagery: John Wareck_opener
 Meet the Physician
 1 page
 Photo with Q&A
 imagery: Roy Herbst

New Faces
 1 page
 (Recent Appointments)
 imagery: 4 headshots



Waiting on Edit / Imagery



In ART / edit



In PRODUCTION / approved