



## NCI awards \$1.3M for cervical cancer trial

IT'S A STRIKING EXAMPLE of translational research – the development of a drug in Yale Cancer Center laboratories leading to its clinical evaluation in patients. In this case, the drug is indole 3 carbinole and it's being tested in the prevention of cervical cancer.

David Austin, Ph.D., assistant professor of chemistry, first predicted that certain members of the indole family of compounds would suppress HPV infections, an important risk factor in nearly all cases of cervical cancer. With indole 3 carbinole already under investigation by the National Cancer Institute (NCI) for the prevention of other cancers, Austin proposed that it be tested in preventing cervical cancer. The NCI responded by awarding the Cancer Center a \$1.3 million grant to conduct a multi-institutional phase III trial of people with chronic, persistent genital HPV infections.

Albert Deisseroth, M.D., associate director of clinical research at the Yale Cancer Center, worked with Austin in developing the new compound. "This is an entirely new way of making drugs, based on the molecular structure of cancer-causing genes/proteins," he says. "With the information we are now able to obtain on the cellular level, we can design drugs that are targeted specifically toward the basic defect or change in cancer cells that makes them spin out of control."

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### DeVita leads renewal of war on cancer

Yale Cancer Center Director Vincent T. DeVita, Jr., M.D., has been selected by U.S. Senator Dianne Feinstein to serve as co-chair of a Senate advisory committee that will make recommendations for updating the National Cancer Act of 1971.

Comprising national leaders in the field of cancer, the committee will seek opinions from those throughout the cancer community with an eye toward developing new national cancer legislation to be introduced in Congress. "Our knowledge of cancer, cancer research and cancer control have changed substantially since the original National Cancer Act was enacted," notes DeVita. "I look forward to uniting the cancer community to formulate a new blueprint for the war on cancer."

The advisory committee will be working hand-in-hand with the National Dialogue on Cancer (NDC), of which DeVita is also a member. Spearheaded by former President George Bush, NDC is a forum that brings together key leaders and organizations in the public, private and nonprofit sectors with the mission of developing a real and lasting dialogue on the eradication of cancer.

### Dr. Mel's gift: A bestseller

WHEN HE LEARNED three years ago that he had multiple myeloma, Dr. Mel Goldstein could not even get out of bed. Today, while retired from his academic duties in meteorology at Western Connecticut State University, the popular local weatherman maintains a rigorous media schedule at NewsChannel 8, the *Hartford Courant* and several Connecticut radio stations.

As if that's not enough, he's now on the library and bookstore circuit, promoting his new book, "The Complete Idiot's Guide to the Weather." All profits from sales of the book are being donated by Goldstein to the recently-established Dr. Mel Goldstein Multiple Myeloma Research Fund at the Yale Cancer Center.

A relatively rare cancer of the bone marrow, multiple myeloma strikes about 14,000 Americans annually. More than 11,000 people die each year of the disease, but Goldstein credits the care he's received at the Yale Cancer Center with keeping him alive. He has undergone chemotherapy

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More than 125 fans attended a benefit luncheon at Hot Tomato's Restaurant in New Haven to kick off a book tour by Connecticut meteorologist Dr. Mel Goldstein. Many relished the opportunity to meet the popular TV weatherman and receive autographed copies of "The Complete Idiot's Guide to Weather."

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JEFF HACKETT



Dr. David Austin, a chemist (left) and Dr. Albert Deisseroth, chief of medical oncology, have teamed up to test a new compound designed to suppress HPV infections and prevent cervical cancer.

What's new



**Warren Shlomchik, M.D.**, a medical oncologist and transplant specialist from the University of Pennsylvania is the newest addition to the Yale Cancer Center's oncology team. Shlomchik's research focuses on the cellular determinants of graft versus host disease (GVHD), a life-threatening complication of stem cell transplantation. His recently published study in *Science* identified the trigger in the immune system of the transplant recipient that allows the donor T-cells to recognize the recipient's cells as foreign, and stimulates them to attack.

YCC Director **Vincent T. DeVita, Jr., M.D.**, has received the Mary Waterman Award from the Breast Cancer Alliance of Greenwich for his outstanding achievements in the fight against breast cancer. Named in memory of the Greenwich resident who founded the Breast Cancer Alliance, the award is specifically for the CMF protocol developed by DeVita and colleagues, which is widely used to treat breast cancer and prevent its recurrence. DeVita has also been selected by the Leukemia Society of America to receive a 50th Anniversary Commemorative Award, recognizing his role in helping to find the cure for leukemia and blood-related cancers. The YCC director has also been elected to the board of directors of the Association of American Cancer Institutes for a three-year term.

The Yale Cancer Center has again been selected to run the **Cancer Information Service** regional office for New England. A five-year, \$6.5 million contract with the National Cancer Institute funds the office, which provides more than 20,000 callers a year with free, personalized cancer information in understandable terms. The CIS can be reached by calling 1-800-4-CANCER.

The Cancer Center will begin an annual lecture series focusing on compassionate care of cancer patients, thanks to a \$50,000 endowment from YCC member **David Fischer, M.D.**, in memory of his wife. The Iris Fischer Lecture-ship will focus on quality of life issues integral to the total care of the patient.

YCC member **Tish Knobf, Ph.D.**, has been named an American Cancer Society Professor of Oncology Nursing. Presented to outstanding clinicians, educators and researchers in oncology nursing, the three-year award will fund her work with women who experience premature menopause as the result of chemotherapy.

**A second gift**

A second \$500,000 gift from the **Ted Mann Foundation** of Los Angeles to Dr. DeVita will continue funding research into lymphoma at YCC. Among the projects supported by the first donation is the lymphoma vaccine program of **Frank Hsu, M.D.** Clinical trials of the vaccine, which use dendritic cells to stimulate the immune system into attacking its own tumor, have shown promising results.

Genetic discrimination fears not unfounded



Ellen Matloff

FEAR OF DISCRIMINATION IN INSURANCE and employment often keeps those concerned they may be at risk for developing hereditary cancer away from the genetic testing that can – in some cases – save their lives.

These same fears are shared by experienced cancer genetic counselors, according to a study led by Ellen Matloff, M.S., director of the Cancer Genetic Counseling Shared Resource at the Yale Cancer Center. Most of the counselors in the study said they would go ahead with genetic testing, however, if certain safeguards were in place.

In a survey of nearly 300 active cancer genetic counselors, the vast majority (85% and 91%) said they would pursue genetic testing for BRCA (breast cancer gene) or HNPCC (hereditary nonpolyposis colon cancer gene) mutation if one parent or sibling was a known carrier of the mutation. However, 68% said they would *not bill* genetic testing charges to their health insurance company, and 26% said they would use an alias. In addition, 82% of counselors said that if tested positive, they would share the results with their physicians, but many would not want their carrier status documented in their medical records.

“Those closest to the issue still believe the benefits of genetic testing outweigh the risks,” notes Matloff. “But there are real risks, and this study underscores the need for better legislation in this area.” While advising caution in genetic testing, Matloff points out that there have been no documented cases of discrimination arising from the genetic counseling and testing program at the Yale Cancer Center. “We are very aware of and sympathetic to these concerns, and have in place a number of safeguards that protect patients and make them feel more comfortable.”

Study questions wisdom of breast-sparing surgery

WOMEN WITH CANCER-CAUSING GENES who choose lumpectomy and radiation therapy appear to have an increased risk of getting a second tumor in the conservatively treated breast five to 10 years after treatment.

The results of a 14-year study led by YCC member Bruce Haffty, M.D., associate professor of therapeutic radiology, suggest that breast cancer patients who carry either the BRCA1 or BRCA2 gene may be at higher risk for late relapses than those who do not harbor these mutations. The study also found that *early* relapse is not a concern for patients carrying one of the cancer-causing genes; they respond very well to treatment immediately following surgery, but begin developing second tumors up to ten years or more after the initial treatment.

“These findings are significant because drugs like tamoxifen or other estrogen reception modulators that prevent second tumors can perhaps be prescribed earlier,” says Haffty. “Some clinicians are beginning to recommend double mastectomies for women with BRCA1 or 2 mutations who have not yet been diagnosed with breast cancer, but more research with long-term follow-up is needed to make definitive treatment suggestions.”

Collaborating with Haffty on the research, which appeared in the *Journal of Clinical Oncology*, were YCC members Peter Glazer, M.D., Ph.D., Malcolm Beinfield, M.D., and Ellen Matloff, M.S.



Bruce Haffty

**Yale** CANCER CENTER

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**NCI** A Comprehensive Cancer Center designated by the National Cancer Institute

## Breast Cancer Awareness

MORE THAN 300 BREAST CANCER SURVIVORS, friends, and family attended Y-ME of Connecticut's 10th anniversary breast cancer symposium, "Survivorship for the New Millennium," hosted by YCC in honor of Breast Cancer Awareness Month. Noted surgeon, author and lecturer Bernie Siegel, M.D. spoke on "Living and Laughing and What Gets You Through." Other experts addressed some of the many wellness issues faced by breast cancer survivors. Y-ME of Connecticut is a statewide breast cancer support organization.

Also in October, the Yale-New Haven Hospital Auxiliary held a fashion show to benefit patients receiving treatment at the Yale Breast Care Center, as well as the purchase of Mammotome biopsy equipment which allows physicians to perform less invasive biopsies guided by ultrasound images. A number of YCC members, including Dr. Liane Philpotts, (below), modeled the latest styles.



# Community

### Kids' Holiday Cards

In between visits to specialists and chemotherapy treatments, young cancer patients, including Samantha (above), lent their artistic talents to help the Tommy Fund raise money for supportive services for children with cancer and their families. Four holiday greeting cards were created by pediatric oncology patients at Yale-New Haven Children's Hospital. Now available at all Connecticut Motor Club AAA offices in New Haven, Fairfield, and Litchfield Counties, Adams Super Food stores and the Atrium Gift Shop at Yale-New Haven Hospital, Tommy Fund holiday cards are sold in packages of 12.



## Research Notes

### New research tool

With a supplemental grant to YCC Director Vincent DeVita, M.D. from the NCI, the Yale Cancer Center is launching a DNA microarray sequencing facility which will offer state-of-the-art biotechnological analyses for scientists studying the molecular causes of cancer.

DNA microarrays provide a powerful and rapidly evolving technology that enables scientists to assess changes in the level of expression of a large subset of the 100,000 human genes on a scale unattainable by other methods. This technique can quickly produce a snapshot of the genes that are active in a tumor cell, which provides critical information in narrowing down the precise molecular causes of a cancer.

The \$249,000 grant, along with matching funds from the Yale School of Medicine, will help fund instrumentation for the facility. It will be operated jointly by the Yale Cancer Center and the HHMI

Biopolymer/W.M. Keck Foundation Biotechnology Resource Laboratory.

### YCC joins early detection research network

The Yale Cancer Center is among those selected by the National Cancer Institute (NCI) to become part of a network designed to discover and develop new biological tests for the early detection of cancer and biomarkers for increased cancer risk.

An initial investment of \$8 million from the NCI will fund the establishment of 18 Biomarker Developmental Laboratories across the country to identify, characterize, and refine techniques for finding molecular, genetic, and biologic early warning signals of cancer. The laboratories are part of the Early Detection Research Network, a research collaboration created to evaluate

biomarkers for common cancers, such as prostate, breast, lung, colorectal, and ovarian cancers.

The focus of the research at the Yale Cancer Center will be on cancers of the breast, colon and pancreas. Investigators, led by Deputy Director Jose Costa, M.D., will perform detailed mutational analysis of specific genes using a variety of technologies, and develop a new technology to detect and quantify point mutations at the cytologic level. "Ultimately, this work will benefit patients by the rapid creation of better tests to find cancer and the discovery of points in time at which to intervene to prevent the disease," Costa says.

Also as part of this NCI project, YCC member Barry Kacinski, M.D., Ph.D., professor of therapeutic radiology, was awarded a 5-year, \$1.8 million grant for the development of novel methods of accurately detecting early, rather than late-stage ovarian cancer in asymptomatic women at increased risk. The research will evaluate early genetic changes and aberrant mRNA expression as potential biomarkers.

## ◀ 1 From bench to bedside

Cancer-related viruses such as Epstein Barr or HPV produce oncoproteins, which kick off the process of reproduction. By inhibiting the proteins, the tumor cells stop replicating. HPV depends on the E2 protein to keep itself going, so indole 3 carbinol was developed specifically to disable that protein so crucial to the survival of the disease. “The beauty of this approach,” says Deisseroth, “is that the drug will not affect other cells in the body. It’s totally nontoxic and more effective than traditional cancer treatments.”

The clinical trial will test the drug in 200 people with chronic HPV infections who are at risk for cancer of the cervix or anus, but are not at the point where surgery is indicated. Because HPV warts are a major problem in people with

suppressed immune systems, half the study participants will be individuals who are HIV positive. The drug, or a placebo, will be taken daily for eight weeks, during which time participants will be examined weekly for signs of toxicity.

More than 10 million American women are infected with high-risk HPVs, and an estimated 15,000 American women are diagnosed with cervical cancer each year. While routine Pap screening has significantly reduced the rate of cervical cancer in this country, it remains a leading cause of cancer death in many other parts of the world. There are approximately 500,000 cases of cervical cancer worldwide each year — about one-third of them fatal.

Deisseroth credits the Cancer Center with providing the environment that brought together researchers from several different disciplines to collaborate on what he believes will be a success-

ful project. “If not for the Cancer Center, I would not have hooked up with David Austin in the first place. Animal testing was possible because of a rabbit model developed by YCC member Janet Brandsma, Ph.D. The Cancer Center provided funding to keep the project going, and the result is this promising clinical trial.”

## ◀ 1 Dr. Mel

and is currently continuing treatment with thalidomide — an old drug with potential new uses against cancer and other diseases. Goldstein, who since being diagnosed has always spoken publicly about his illness, hopes the research fund will “contribute to the understanding of this disease and benefit all multiple myeloma patients.”

The self-described “weather nut” says he always wanted to write a book, but until approached by the publisher, never dreamed it would be an “idiot’s guide.” A humorous compendium of information on meteorology for the laymen, *The Complete Idiot’s Guide to Weather* has proven popular not only locally, but with readers nationwide.

It is the number one seller on Amazon.com in the State of Connecticut, an number three nationwide on the Barnes and Noble science list. Never one to say no to a request, Goldstein has 20 book parties and signings on his calendar in December to promote the popular paperback.

### A CENTER OF EXCELLENCE

The Yale Cancer Center is among the first in the nation to be named an “HPV Center of Excellence” by the DIGENE Corporation, makers of the most sophisticated tests for detecting HPV. The designation is awarded to geographically diverse academic centers with a demonstrated level of excellence in gynecologic oncology and women’s health. Centers so named are also among the first in the country to offer the newest HPV DNA testing, which helps physicians identify women who are most at risk of having or developing cervical disease.

## COMING UP

### Patient Holiday Party:

The Yale Cancer Center is hosting its 3rd annual holiday party for patients and their families on Wednesday, December 8 from 5:30 to 7:30 p.m. in the Harkness Lounge of the Yale School of Medicine. All adult patients—past and present—are invited to attend. To R.S.V.P., please call Renee Moore at 203-785-2143.



A great holiday gift idea

### Dr. Mel’s Book Tour:

DECEMBER 5, 12:00 p.m., Walden Books,  
7 Backus Avenue, Danbury.

DECEMBER 12, 3:00 p.m., Walden Books,  
Westfarms Mall, Farmington.

## Yale CANCER CENTER

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