

## DiGiovanna and Stern Lead Breast Cancer Research Program

IN AN EFFORT TO COMBINE THE WORK of both basic scientists and clinical researchers in the fight against breast cancer, Yale Cancer Center has named Michael DiGiovanna, M.D., Ph.D. and David Stern, Ph.D. Co-Directors of the Breast Cancer Research Program. "We are emphasizing a disease-oriented program, bringing together different disciplines to create a synergistic approach to breast cancer care and research," DiGiovanna said. The Yale Breast Care Center is comprised of clinicians, basic researchers, and epidemiologists producing a program involving several areas of cancer research.

DiGiovanna and Stern represent both facets of the Breast Care Center. DiGiovanna is an attending physician and researcher focusing on translational research and Stern is a basic scientist. Together they typify the cross section of the members of the Breast Cancer Research Program. They will focus the members of the Center on early detection, identification of patients at high risk for recurrence and ways to diminish that risk, and identification of new means to treat resistant disease.

DiGiovanna and Stern have established two primary objectives for

the Breast Care Center in order to build a strong program at Yale Cancer Center. In recognition of the increased need for communication between basic and clinical researchers, they aim to stimulate and encourage interaction between investigators within the Center and nationally. The Breast Care Center sponsors speakers from other centers, provides representation at national meetings on breast cancer, and its members collaborate in research endeavors with cooperative groups on a national scale.

With increased communication and collaborative research, the program directors are working to strengthen the institutional infrastructure to promote translational breast cancer research. Yale Cancer Center has several shared resources, including the clinical trials office, the tissue microarray facility, and flow cytometry, all of which are to bring basic research to the clinic.

"It is especially important in this era to have communication among researchers. The basic science aspect of cancer research has matured and has elucidated pathways that are destined to become clinical therapeutic targets," Stern concluded.

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### HOW TISSUE MICROARRAY WORKS



The Tissue Microarray Shared Resource at Yale Cancer Center, directed by David Rimm, M.D., Ph.D., enables researchers to analyze several hundred tissue samples within a single paraffin block, providing highly efficient evaluation and assessment of the samples. The diagram pictured above shows the production of the tissue microarrays. The arraying device first obtains a core of tissue from a given patient and secondly, transfers the core to the recipient block. The recipient block, containing samples from hundreds of patients, can then be used to assess patterns of marker expression within a population of patients. One advantage of this technology is that samples are handled identically. Tissue microarrays provide a method for rapid, large-scale molecular analysis of thousands of tissue specimens, therefore providing a powerful technique for evaluating newly discovered molecular alterations in cancer research.

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### Chênevert Joins Board

Louis Chênevert, President of Pratt & Whitney in East Hartford, CT, a unit of United Technologies Corporation, has joined Yale Cancer Center's Director's Advisory Board. Chênevert joined Pratt & Whitney in 1993 and was named President in April 1999.

The Director's Advisory Board is comprised of members of the corporate and foundation sectors as well as private advocates who are dedicated to raising public awareness of the Center and expanding fundraising opportunities.



# Survivin Gene New Detector for Bladder Cancer

THREE YEARS AFTER the initial identification of the gene Survivin by Yale University School of Medicine scientists the gene has been linked to the detection of bladder cancer when recognized in urine analysis testing, in a study published in the *Journal of the American Medical Association*. Dario Altieri, M.D., a professor of Pathology, member of the Yale Cancer Center, and lead investigator in this study, explained the importance of their research, "the use of the gene Survivin in the detection of bladder cancer is attractive to both patients and doctors; currently the only diagnostic tool for bladder cancer is a cystoscopy and biopsy, both of which are invasive and expensive procedures."

Bladder Cancer is the sixth most common cancer in the United States. Early detection of the disease, like many types of cancer, automatically creates an increased rate of survival. When bladder cancer is detected early, and has only affected the superficial cells in the bladder and is treated, the 5-year survival rate is 93 percent. The study, a collaboration between the Department of Surgery (Urology) and the Department of Pathology at Yale University School of Medicine, investigated the relationship between the detection of survivin in urine and the diagnosis of bladder cancer.

Dr. Altieri, Dr. Robert Weiss, a Professor of Surgery as well as a mem-

ber of Yale Cancer Center, and Dr. Shannon Smith, an Associate Research Scientist, led the study at Yale University School of Medicine. Urine samples were collected from volunteers with several types of cancer, including bladder cancer as well as healthy volunteers. The study revealed that Survivin was not detected in normal volunteers (0/16), or those with prostate, renal, vaginal, or cervical cancer (0/29) but was in those with new

## When bladder cancer is detected early the survival rate is 93 percent.

onset or recurrent bladder cancer (31/31), establishing urine Survivin as a new molecular marker for the detection of bladder cancer.

Dr. Altieri noted that they have applied to the National Cancer Institute's (NCI) Early Detection Research Network (EDRN) to initiate a more extensive study, which will validate their results using a greater number of patients at several other NCI designated Cancer Centers in addition to Yale Cancer Center. The first phase of the application process has concluded; Dr. Jose Costa, Deputy Director of the Cancer Center, will introduce the study to the EDRN for funding once the formal application has been completed.

## Oncology Nursing Council Focuses on Nursing Care

IN A JOINT EFFORT to advance the nursing care of cancer patients at Yale-New Haven Medical Center, oncology nurses at Yale Cancer Center, Yale-New Haven Hospital, and Yale School of Nursing have formed an Oncology Nursing Council. Nurses representing various departments and subspecialties of the Medical Center meet monthly, creating a concerted effort to support the clinical nursing environment. "The group formed in response to the recognized need for a more cohesive organization of oncology nurses throughout the facility," Council Chair Constance Donovan, R.N. added.

The current focus of the group is on the recruitment and retention of the nursing staff. This summer will mark the first Clinical Internship Series, a three-month program for new graduates and registered nurses who have recent clinical experience and are interested in specializing in oncology nursing. In addition, the Council will support more nurses to become nationally certified by the Oncology Nursing Society. To aid those taking the exam, they will offer study sessions for review of the test material; Yale-New Haven Hospital reimburses the testing fee to all nurses who

have passed the exam.

The Council is also working to create an Oncology Nursing Resource Directory, which will list all oncology nurses in the medical center and their specialties, allowing nurses to consult one another for expertise in a particular area. Furthermore, they will work to revise the Nursing Care Protocols and Standards to create an updated, evidence based guide giving nurses the "most recent suggested and scientifically based practices, as opposed to traditional procedure," Donovan explained. Oncology Nursing Education Forums will begin on April 2nd, continuing the mission of the Council to update and inform the oncology nurses throughout the Yale-New Haven Medical Center.

The initiatives of the Council all work to support their long range goal of supporting the research efforts of clinical nursing, adding to the scientific base of nursing practice at Yale-New Haven Medical Center. Ultimately, Donovan noted, "the aim of the Council is to develop nurse practices, which effectively contribute to the overall interdisciplinary care of patients with cancer."



ANITA TELLIER

### Yale CANCER CENTER

Director  
Vincent T. De Vita, Jr., M.D.  
Associate Director, Administration  
Lauren Hackett  
Associate Director, Development and Community Affairs  
Judith Winslow  
Editor  
Renee Moore  
Design  
Jeanne Criscola/Criscola Design

Yale-New Haven Hospital  
Yale University School of Medicine  
P.O. Box 208028  
New Haven, CT 06520-8028  
<http://info.med.yale.edu/ycc>



A Comprehensive Cancer Center designated by the National Cancer Institute

# Dr. Vincent T. DeVita, Jr., Appointed Medical Director of Oncology

IN A JOINT APPOINTMENT by Yale School of Medicine Dean David Kessler and Joseph Zaccagnino, President and Chief Executive Officer of Yale-New Haven Hospital, Dr. Vincent T. DeVita, Jr., M.D. was named the Medical Director of Oncology, an extension of his current responsibilities as Director of Yale Cancer Center. Dr. DeVita will work closely with both the hospital administration and clinical chiefs as well as with the department chairs in the school in an effort to supervise all oncology services at the Yale-New Haven Medical Center.

With the aim of enhancing and expanding the clinical oncology services offered, Kessler and Zaccagnino agreed Yale's Comprehensive Cancer Center will "become the focus for the basic and clinical research that is such an integral part of a modern oncology program. Dr. DeVita will lead a clinical cancer facilities planning

effort and will coordinate key clinical recruitment efforts in support of an integrated oncology initiative," Kessler and Zaccagnino explained in a letter announcing the appointment.

The new organizational structure for the Oncology Clinical Services combines the strengths of both the hospital and school. The unification will seek to enhance the services offered to oncology patients and their families at Yale-New Haven Medical Center.

## In a joint appointment by Yale School of Medicine & Yale-New Haven Hospital

The addition of a Clinical Services Cabinet, chaired by the Medical Director of Oncology, has been included in the Yale Cancer Center governance to oversee the changes in Oncology Services at Yale-New Haven Medical Center.



Breast Cancer Alliance Board Members Kenny Mettler and Carol Santora with Advisory Board Member Dr. Dickerman Hollister.



Dr. Jose Costa, YCC Deputy Director, Lucy Day, Breast Cancer Alliance Board Member, and Dr. Dario Altieri, Professor of Pathology.



Breast Cancer Alliance President Janie Weyl

## Breast Cancer Research Funded Greenwich Breast Cancer Alliance Supports YCC

THE BREAST CANCER ALLIANCE, INC. has awarded two Yale Cancer Center scientists with grants to support their research in a continuing effort to find methods of earlier detection and a cure for breast cancer. Dr. Jose Costa was given a research grant to support his Earlier Detection Project, in search of the answer to this question, "How can we know when a tumor is about to arise anywhere in the breast?" In a second grant to Yale Cancer Center, Dr. Barbara Burtness was given funds to support her Clinical Trial for Dose Dense Doxorubicin/Docetaxel for Locally Advanced Breast Cancer.

Dr. Costa, in collaboration with Dr. Paul Lizardi and Dr. David Ward, are working with a newly developed biomarker called "Breast Mutational Load Distribution Analysis" (MLDA), which assesses tissue for the risk of breast cancer using nipple aspirates. The biomarker tallies the number of mutations present in a tissue and reflects the speed of growth of groups of cells concealing mutations in cancer genes. Drs. Costa, Lizardi, and Ward are now looking to study groups of patients with known risks to link MLDA to known increases in risk, confirming their theory and allowing the MLDA process to be used in the earlier detection of breast cancer.

The Clinical Trial funded under the direc-

tion of Dr. Barbara Burtness will use intensive chemotherapy prior to surgery to reduce the number of cancerous lymph nodes to less than four. The trial involves measuring the state of the disease throughout treatment in order to guide the prescription of chemotherapy. The goal of the trial is to determine the intensity and duration of treatment necessary for an increased chance of cure of micrometastatic disease.

The Breast Cancer Alliance's mission is to "raise funds for breast cancer research on the national level, to raise funds for breast cancer-related services in the Fairfield County area, and to educate women on the importance of the early detection of breast cancer." The organization, currently led by Janie Weyl, President for the year 2001, is comprised of breast cancer survivors, their friends, and health-care professionals. At their October 20, 2000 annual benefit luncheon and fashion show, sponsored by Neiman Marcus, they raised over \$700,000 to support their mission. In turn, the Alliance awarded a record \$700,000 in grants to researchers from various institutions to aid their investigations into the causes and cures for breast cancer; Yale Cancer Center has received \$380,000 in research funding from the Alliance over the past four years.

# HPV Testing Recommended for Early Diagnosis of Cervical Cancer

YALE UNIVERSITY School of Medicine’s “Human Papillomavirus (HPV) Center of Excellence,” researchers are emphasizing the importance of HPV testing in women. The Center designated by the Digene Corporation, manufacturer of the Hybrid Capture II HPV Test, is the only one of its kind in Connecticut. While many doctors in Connecticut are taking advantage of the Center’s Resources, the Department of Pathology is looking to expand the number of tests performed each year, to provide the most efficient and most effective early detection of cervical cancer precursors.

HPV is the most common sexually transmitted disease in the United States, with 5.5 million people diagnosed each year, and is the major risk factor for the development of cervical cancer. Recent studies have shown that HPV is present in 99.7% of cervical cancer cases worldwide. In 1999, it was estimated that 12,800 cases of invasive cervical cancer were diagnosed in the United States, and that 4,800 women would die from cervical cancer.

Detection of HPV allows patients to be carefully monitored for the development of cervical cancer; when detected at the premalignant stage, invasive cervical cancer is one of the most successfully treatable diseases with a 5-year survival rate of 91%.

## HPV is the most common sexually transmitted disease in the United States ... and is the major risk factor for the development of cervical cancer.

The Hybrid Capture II HPV Test is a DNA test that detects HPV infection of the cervix. Only women with “high risk” types of HPV are at risk of developing cervical cancer. The Pap test screens cervical cancer, 5-10% of Pap tests show “borderline” lesions containing atypical squamous cells of undetermined significance (ASCUS). Most borderline lesions are transient and not associated with cervical cancer. However, about 7% of women with borderline lesions have high-grade lesions, which can be determined only by biopsy.

The HPV test is recommended for women with ASCUS. If the HPV test is negative, then the woman is not at risk of cervical cancer and she does not need the costly and invasive biopsy procedure. In the general population, about 60% of women with ASCUS are negative for cancer-associated HPV. Without HPV testing, most ASCUS patients return for repeat Pap testing at four to six month intervals and are then sent for biopsy if the ASCUS lesion does not clear.

Janet Brandsma, Ph.D., Yale Cancer Center member and Director of the HPV Center of Excellence at Yale explained, “We believe that the HPV Hybrid Capture Test should be performed automatically for patients with borderline Pap test results. Substantial data demonstrate that this is a highly effective means to determine which patients will benefit from referral for biopsy.”

# HPV Genes Linked to Cervical Cancer Cell Growth

YALE CANCER CENTER researchers have identified a previously unidentified function of two viral genes in cervical cancer. Infection with high-risk human papillomaviruses (HPVs) is essential for the development of cervical cancer, a leading cause of cancer death in women worldwide. The HPV expresses two proteins, the E6 and E7 proteins, that stimulate cell growth. By identifying the biochemical property that makes cells cancerous, in this case the E6 and E7 proteins, scientists are able to develop molecular approaches to combat this disease.

The most recent research at Yale demonstrates that the HPV E6 and E7 proteins are continuously required for the growth of the cancer cells, even many years after the initial infection. Once the viral genes are turned off, the cancer cells enter a permanent, non-growing state making these viral proteins targets for therapy.

Yale Cancer Center and School of Medicine Department of Genetics members, Dr. Daniel DiMaio, Director of the Molecular Virology Research Program, and Dr. Edward Goodwin collaborated on this study along with a team of researchers in Korea headed by Dr. Eun Hwang, a former researcher in DiMaio’s laboratory.

The group has developed the methods to turn off expression of the HPV E6 and E7 genes in cervical cancer cells growing in the laboratory. When these viral genes are turned off, the cancer cells rapidly stopped growing and entered senescence, the stage at which normal cells can no longer grow. If inhibition of the viral genes has the same effect in patients, it will prevent the cancer from further growth. “We are optimistic that it may be possible to induce senescence in cancer cells as a means of treatment,” Dr. DiMaio said.

The approach, developed at Yale, suggests a new way to treat or prevent cervical cancer. One goal of continuing research is the discovery of medicines that interfere with HPV protein function and thereby induce senescence. Testing of vaccines that may prevent HPV infection is currently in place, however, even if vaccines work, there will remain a need for effective medicines for women who are already infected or who do not receive or respond to the vaccines. “Successful treatment or prevention of virally-induced tumors is an important goal,” DiMaio pointed out, “they account for 15% of cancers worldwide.”



ANITA TELLIER

## Amgen Sponsors Visiting Professorship

Dr. Victor Giannini, Clinical Research and Education Manager at Amgen, Inc., and Ms. Linda Craig, Amgen’s Professional Sales Representative at Yale presented a donation to Dr. Vincent T. DeVita, Jr. to support a Visiting Professorship for Yale Cancer Center. Amgen hopes to continue their relationship with Yale Cancer Center in the future by establishing and sustaining a yearly professorship.

# Local Students Plan Terry Fox Run to Benefit Yale Cancer Center

ON THE MORNING OF SUNDAY, MAY 20, 2001, Choate Rosemary Hall, a coed boarding/day preparatory school in Wallingford, CT, will sponsor the first Terry Fox Run to be held in the State of Connecticut, to benefit Yale Cancer Center. Omar Itum, a junior at Choate from Saudi Arabia, has initiated and is coordinating the 5K run/walk in conjunction with several community service clubs, area public and private high schools, local churches, and the staff of Choate Rosemary Hall.

“This is an excellent opportunity to bring our community together, people of all ages, cultures, and backgrounds, and to help those who have suffered, or are currently suffering, from the devastating effects of cancer,” Itum enthused. Choate’s Spring Fest weekend will take place simultaneously creating an exciting Sunday full of events for students and families, beginning with the race and drawing to a close with a concert.

The Terry Fox Foundation sponsors runs throughout the world to raise funds for cancer research. In 1977, Terry Fox was diagnosed with bone cancer in his right knee. Although his leg was amputated, Terry pledged to

run across Canada to raise money and awareness for cancer research in a journey dubbed The Marathon of Hope. Terry’s 1980 run raised \$24.17 million, to date the foundation has raised \$270 million worldwide. Terry died in June 1981, leaving a foundation working to “maintain the heroic efforts and integrity that Terry Fox embodied.”



Omar Itum, Committee Chair and Tara Korde, Committee Member

Itum and volunteers have begun to recruit sponsors for the race expressing in a letter sent to local businesses, “Together, we can make this day a success—together, we can save a life.” Corporate sponsorship levels are as follows: Corporate Member, \$80+, Corporate Benefactor, \$200+,

## This is an excellent opportunity to bring together those who have suffered the devastating effects of cancer.

Chairman’s Club, \$600+, and Executive Club, \$1000+. All sponsors will be recognized the day of the race on a donor wall and all contributions will directly benefit research at Yale Cancer Center.

### TERRY FOX RUN REGISTRATION

Donation of \$10 for Students and \$15 for Adults is suggested for Pre-registration.

#### To Register

Log on to <http://crh.choate.edu/Terryfoxrun/>  
Or call Charlotte Murphy at (203) 697-2252

#### To Donate to the Run

Please make checks payable to Choate Rosemary Hall, Terry Fox Run  
Charlotte Murphy  
Director of Communications  
Choate Rosemary Hall  
333 Christian Street  
Wallingford, CT 06492

## Dr. Rachel Remen Brings Lessons on Healing to Yale

RACHEL NAOMI REMEN, M.D., the author of *The New York Times* bestseller *Kitchen Table Wisdom: Stories that Heal* and most recently *My Grandfather’s Blessings: Stories of Strength, Refuge, and Belonging* will address the art of healing at several events on April 30th and May 1st during a visit to YCC. Remen, a well-respected physician, professor, therapist, and author, has become a leader in the field of psycho-oncology. She is the Co-founder and Medical Director of the Commonweal Cancer Help Program. Yale Cancer Center will host Dr. Remen for two days, which will include lectures, booksignings, and a Brown Bag Luncheon with Dr. Remen open to the public.

Dr. Remen writes to encourage inner strength and to address spiritual issues such as suffering, meaning, love, faith, courage, and miracles, in cancer patients. Her perspective on healing results from her professional background as well as her 45-year personal history with Crohn’s Disease, a disease affecting the intestinal track of the digestive system. She is currently on tour promoting her newest book, *My Grandfather’s Blessings*. Dr. Remen’s writings are enlightening for the reader, in an excerpt she writes, “Every life serves a purpose which is both simple and profound. We are here to grow in wisdom and to learn to love better...all people are on a spiritual path.”

Yale Cancer Center invites area cancer patients, their families, and Medical Center staff to join Dr. Remen at a Brown Bag Luncheon on Tuesday, May 1, 2001 from 12:30-2:00 in Harkness Lounge at Yale School of Medicine. Dr.



Remen will focus her discussion on the inner strength and healing of cancer patients using techniques and materials from her two books. The lunch is free but reservations must be made by calling Allison McConomy at (203) 737-2439.

Two booksignings will also be held during Dr. Remen’s visit, both of which are open to the public. On Monday, April 29th Dr. Remen will appear at R.J. Julia Book-sellers in Madison, CT at 7:00 PM. Her

books will be available for purchase and signing and Dr. Remen will speak to guests. For more information please call Linda at (203) 245-3959. Dr. Remen will also appear for a booksigning at the Center for Hope in Darien, CT on Tuesday evening, May 1st, at 7:00 PM. For more information on this event, please contact Janet at the Center at (203) 655-4693.

Dr. Remen’s visit was funded by a gift from Reverend Albert P. Nielson in memory of his wife, who visited the Commonweal Cancer Help Program during her battle with cancer. Reverend Nielson is a graduate of Yale College ‘52 and has sponsored Dr. Remen’s trip to Yale Cancer Center in response to the impressive work of Dr. Remen.

## UPCOMING EVENTS

**April 21, 2001.** La Cassa Magica, The Country Club of Fairfield, 6:00 PM.

**April 30, 2001.** Booksigning with Dr. Rachel Remen, RJ Julia Booksellers, Madison, CT, 7:00 PM.

**May 1, 2001.** Brown Bag Luncheon with Dr. Rachel Remen, Harkness Lounge, 12:30 PM. Call Allison at (203) 737-2439 for more information.

**May 1, 2001.** Booksigning with Dr. Rachel Remen, The Center for Hope, Darien, CT, 7:00 PM. For more information please call Janet at (203) 655-4693.

**May 20, 2001.** Terry Fox Run, Choate Rosemary Hall, Wallingford, 9 AM. For more information please call Charlotte Murphy, (203) 697-2252.

**June 10, 2001.** Cancer Survivor's Day, Harkness Courtyard, 2 PM.

**June 12, 2001.** Discussion on Peripheral Neuropathy, CH 201, 6:30 PM. For more information please call Bonnie Indeck, LCSW, at (203) 688-6573.

## Survivorship and Communication with your Healthcare Team

On Saturday, May 5, 2001 from 9 AM to 3 PM, Yale Cancer Center will host a unique program for cancer patients and their families in an effort to help answer questions commonly asked by cancer patients. The panel, comprised of oncologists, nurses, social workers, patients, and a representative from the Connecticut Commission on Insurance, will speak on a variety of topics related to cancer care as well as address questions from the audience. The conference is sponsored by Yale Cancer Center, the Leukemia & Lymphoma Society, and Ortho Biotech. The conference is free and will include breakfast and lunch. To reserve a place, please call Betsy Kunz at (203) 379-0445.

## Support Groups

Open to all patients, please call for more information.

STEM CELL TRANSPLANT .....688-6573  
Bonnie Indeck, LCSW

WOMEN WITH CANCER .....688-5962  
Pat Scholl, LCSW

LOST CHORD CLUB .....688-2257  
Eileen Cain, LCSW

BRAIN TUMOR .....688-7528  
Angela Thomas, LCSW

PARENTS OF CHILDREN WITH CANCER ...688-7519  
Connie Nicolosi, LCSW

TEEN ONCOLOGY SUPPORT .....688-7519  
Connie Nicolosi, LCSW



Dr. Richard Payne, Chief of Pain and Palliative Care Service at Memorial Sloan—Kettering Cancer Center, presented the first Iris Fischer Lectureship for the Humanities in Medicine Program at Yale University School of Medicine on November 16, 2000. Dr. Payne, shown here with Dr. David Fischer, a member of Yale Cancer Center, and benefactor who donated the lectureship in memory of his beloved wife, Iris, spoke both on the difficulties of assessing pain and the importance of addressing and treating emotional and physical pain in cancer patients. "Patients who are in pain should be treated effectively...being able to help is one of the reasons I entered the field of cancer—pain treatment."

**Yale** CANCER  
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Yale-New Haven Hospital  
Yale University School of Medicine  
P.O. Box 208028  
New Haven, CT 06520-8028

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