

MARCIA: A New Test for the Earlier Detection of Breast Cancer



Dr. Jose Costa, Deputy Director of Yale Cancer Center.

THE MARCIA ISRAEL-CURLEY LABORATORY for the Earlier Detection of Breast Cancer was established in 1997 with a gift from Mrs. Israel-Curley to further early diagnostic efforts. The past four years of research have yielded three significant advances in the earlier detection of breast cancer, which will be tested beginning in 2002.

"Thanks to the generosity of Mrs. Israel-Curley, we were able to set up a lab devoted to the earlier detection of breast cancer and have access to the Early Detection Research Network of the National Cancer Institute," Dr. Jose Costa acknowledged. Dr. Costa is the Deputy Director of Yale Cancer Center and Principal Investigator of the lab. The lab has also received significant support from The Breast Cancer Alliance of Greenwich.

Dr. Costa, Dr. Paul Lizardi, Co-Principal Investigator of the lab, and their research associates are now working to perfect these advances in breast cancer detection. "We hope to carry on the investigations and begin to apply them to patients in an effort to explore how precise the tests are in determining the risk for breast cancer," Dr. Costa said. They have named the new technology *Mutation Analysis of Recombinase-Circularized Amplicons (MARCIA)*, a combination

of the three tests developed in the Marcia Israel-Curley Laboratory for the Earlier Detection of Breast Cancer.

Researchers have based their studies on the use of cell samples from nipple aspirates or breast duct lavage. Using these methods, the cells can be obtained from the patient without invasive procedures. These samples can then be analyzed with exquisite sensitivity and specificity for cancer-causing, genetic alterations.

Yale Cancer Center researchers have developed techniques, which enable mutations to be detected in the small samples. Throughout the past year, they have made progress in the following areas: establishing feasibility of Mutational Load Distribution Analysis (MLDA), designing an advanced method for Whole Genomic Amplification, and inventing a method to use mass spectrometry to detect mutations.

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Dr. Paul Lizardi, Co-Principal Investigator of the Marcia Israel-Curley Lab for the Earlier Detection of Breast Cancer.

The Cancer Information Service – 25 Years at Yale

FOR THE PAST 25 YEARS, the Cancer Information Service (CIS) has provided the latest, most accurate information about cancer to patients, their families, and the public. The Cancer Information Service provides callers with the reliable, science-based information they need to become active participants in their own health care — from prevention, to early detection, to treatment and survivorship. The CIS serves callers through 14 regional offices located throughout the United States. Yale Cancer Center is proud to be the parent institution of the New England CIS.

As the CIS celebrates 25 years of service they have focused on two newer components: outreach programs and research initiatives. By working with local, state, and national partners, the CIS aims to help make educational programs on cancer prevention, detection, and treatments more effective. Hilarie Campbell, MPH, Partnership Program Coordinator, concentrates on locating community organizations that are currently working to educate the public on cancer and helping them to make their programs more effective. "My CIS training allows me to reach the community and empower the public with knowledge, so that they may make informed decisions about their health," Ms. Campbell said.

The National Cancer Institute funds the 14 regional offices of the CIS under a contract agreement. In the most recent renewal grant a research

initiative was added to the requirements of each CIS office stating they should work to become "research laboratories for communications." The New England Region has embraced this request and is currently using new grant money to study the relationship between the information processing styles of callers and the method in which the information is disseminated. Dr. Peter Salovey, Chair of Yale's Department of Psychology and a member of the Yale Cancer Center, and Linda Mowad, R.N., Director of the New England CIS, have created three fully-funded, peer-reviewed initiatives that use the call center as a research laboratory.

Ann Bradley, an information specialist and assistant supervisor with the New England CIS, is celebrating her 25th anniversary as well. She began as a volunteer when the office opened in 1976 and answered the first phone call into the office. Ms. Bradley later became a full-time employee of the office and has continued her work since her partial retirement in 1994. "As I celebrate my 25th anniversary with the CIS, I reflect on how fortunate I've been to be associated with so many dedicated people and to have been a small part of such a dynamic and rewarding program," Ms. Bradley said.

Trained cancer information specialists at the Cancer Information Service are available to answer your questions Monday through Friday from 9:00 am to 4:30 pm at 1-800-4-CANCER (1-800-422-6237).



STAFF BRIEFS

Elizabeth Bradley, Ph.D. has been named Director of the Health Management Program School of Epidemiology and Public Health.

Karina Brierley, MS joined the Cancer Genetic Counseling Program on July 1, 2001. Karina received her bachelors degree in Neuroscience from Bowdoin College, and her masters in Genetic Counseling from Brandeis University, graduating summa cum laude from both institutions. We welcome her to Yale Cancer Center.

Danbury Hospital, a member of the Yale Oncology network, dedicated its new **Praxair Cancer Center** in May. **Dr. Vincent T. DeVita, Jr.**, Director of Yale Cancer Center, served as keynote speaker for the dedication.

Dr. Daniel DiMaio, Director of the Molecular Biology Research Program, was one of three professors who received mentoring awards from the Yale Graduate School of and Sciences in May. The three award winners were chosen out of 38 nominees based on letters from grateful students.

Lauren Hackett, M.P.A. has been named Deputy Director of Administration for Yale Cancer Center.

Dr. Peter Salovey, Chair of the Department of Psychology, has received the Cancer Information Service 25th Anniversary Award in the category *Partner in Research*.

The American Cancer Society has elected **Linda Mowad, R.N.**, Director of the Cancer Information Service, as Chief Medical Officer of the ACS New England Division. Ms. Mowad is the first nurse to be elected to this position in the history of the ACS.

Yale CANCER CENTER

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A Comprehensive Cancer Center
Designated by the National Cancer Institute

Breast Cancer Alliance Honors Dr. Gina Chung With first ever Young Investigator's Award

DR. GINA CHUNG, a third year clinical postdoctoral fellow at Yale Cancer Center, has been awarded the first ever Young Investigator Award by the Breast Cancer Alliance, Inc. in Greenwich, CT. The award, given to encourage careers in breast cancer medicine and research, will sponsor Dr. Chung's research with \$75,000 over a two-year period. The Breast Cancer Alliance, Inc. strives to raise funds for breast cancer research on a national level as well as for breast cancer-related services in Fairfield County, CT.

The Breast Cancer Alliance, Inc. chose Dr. Chung as their first Young Investigator stating, "our Medical Advisory Board and Board of Directors felt that Dr. Chung embodied all of the qualifications we were looking for to merit this two-year fellowship."

Dr. Chung is working to decipher the wnt signaling pathway of the cell in an effort to determine the specific influences that create abnormalities within a cell. The signaling pathway is the consequence of both external and internal influences including hormones, proteins, and environmental factors on the cell. Using tissue microarray technology, which enables several hundred tissue specimens to be analyzed simultaneously on one slide, Dr. Chung is able to evaluate the signaling pathways of numerous patient samples. Specifically, Dr. Chung is studying the effects of β -catenin, a protein already implicated in the development of breast cancer, and its affect on the signaling pathway by assessing the levels and localization of the protein in the cell.

Using tissue microarray, Dr. Chung can evaluate the tissue samples of hundreds of breast cancer patients and compare them with clinical records using the tumor registry. In an attempt to discover the correlation between the expression of β -catenin and the risk of breast cancer relapse, Dr. Chung will compare the patient's history with their tissue sample as well as against the history and samples of other patients.

"I feel my research is one attempt to bridge the gap between the study of malignant cells and the care of cancer patients," Dr. Chung said. The goal of her research is to reveal a more specific therapy to reduce the risk of relapse of breast cancer based upon the tissue sample differences between patients who have and have not relapsed.

Dr. Chung works under the direction of David Rimm, M.D., Ph.D., director of the Tissue Microarray Shared Resource at Yale Cancer Center. Dr. Chung also attends to breast cancer patients in the outpatient clinic two days a week.



ANITA TELLIER

Dr. Gina Chung.

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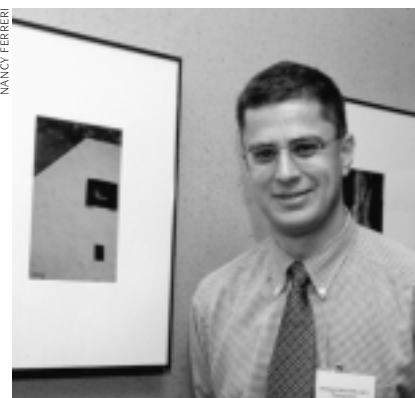
Mutational Load Distribution Analysis allows the DNA present in the nipple aspirate or duct lavage samples to be identified and mutated DNA to be pinpointed. The ability to recognize mutated DNA provides for the possibility that tumors can now be intercepted in the making. Researchers working to decipher DNA samples using MLDA are prepared to begin validating their promising results in a larger population.

Due to the minimal amount of sample collected from the nipple aspirate and duct lavage procedures, a novel method of whole genomic amplification has been developed in the Marcia Israel-Curley Laboratory for the Earlier Detection of Breast Cancer. Whole genomic amplification enables the genomes of the collected cells to be converted into the equivalent material present in a million cells. This conversion permits scientists to repeat tests without exhausting the sample supply.

Under the direction of Dr. Lizardi, researchers have also concentrated on the study of the proteins created by DNA sequences present in the samples. Using computerized models to analyze the DNA sequences, the resulting proteins can be deduced giving researchers a considerable advantage in the detection of breast cancer.

MARCIA will now be tested in a larger population in an effort to validate their results before publication.

NANCY FERRELL



Dr. Ghassan Abou-Alfa, a former member of the Yale Medical Group, stands with his photography exhibit in the Yale Physicians Building *Art Place*. A portion of the proceeds from the sale of the works by Dr. Abou-Alfa will be donated to cancer research at Yale Cancer Center. Dr. Abou-Alfa is currently practicing oncology at Memorial Sloan-Kettering Cancer Center.

Dr. Ghassan Abou-Alfa.

Breast Cancer Research Foundation Funds \$224K Grant



Dr. Michael DiGiovanna.

MICHAEL P. DIGIOVANNA, M.D., PH.D., Co-Director of the Breast Cancer Research Program at Yale Cancer Center, has been awarded a grant from the Breast Cancer Research Foundation to study the Herceptin targeted cell surface receptor, HER2. Herceptin is a breast cancer treatment used for patients where HER2, a protein found on the surface of cancer cells, is overexpressed.

The amount of HER2 protein in the tumor is measured in the laboratory to determine whether a patient might benefit from treatment with Herceptin. Patients whose tumors test strongly positive for HER2 protein overexpression are more likely to benefit. The discovery that HER2 exists in both an active and inactive state led Dr. DiGiovanna to write a grant proposal to fund research on the activity of HER2 and the correlation between the activity of the protein and the patient's response to treatment with Herceptin.

Dr. DiGiovanna will concentrate his research on clarifying two issues in breast cancer treatment, first, whether the activity of the HER2 protein affects the tumor response to Herceptin and secondly, whether the activity affects the tumor's response to taxol or taxol/doxorubicin combinations. Tumors that have expressed high levels of HER2 do not always respond to treatment with Herceptin. Studies have determined that only 14% of breast cancer tumors are controlled using Herceptin alone. Dr. DiGiovanna is hoping to predict a patient's response to breast cancer treatment based upon the activity of the HER2 protein, as opposed to the level of HER2, creating individualized treatment for every patient.

"The Breast Cancer Research Foundation will allow us to explore how HER2 activity impacts the response to all of the types of treatment used for breast cancer patients. This is logistically challenging research that requires collaborative efforts with other groups involved in testing therapies for breast cancer patients. I am extremely grateful for this funding from the Foundation, which will allow me the freedom to conduct this clinically important translational research," Dr. DiGiovanna said.

Evelyn H. Lauder established the Breast Cancer Research Foundation in September 1993. To date, the Foundation has committed nearly \$30 million in grants to support outstanding breast cancer research nationwide. Dr. DiGiovanna's grant will support his research, as well as the addition of a Research Associate, beginning October 2001.

Matloff wins Grant to Assess Health of Women in Menopause

ELLEN MATLOFF, MS, Director of the Cancer Genetic Counseling Shared Resource at Yale Cancer Center, has been awarded a \$250,000 grant from the Susan G. Komen Foundation for her research proposal focusing on the health of menopausal women. The grant, entitled *Menopausal Therapy in Women at Increased Risk for Breast Cancer: Does a Personalized Risk Assessment and Counseling Intervention Aid in Decision-Making?*, will investigate the impact of risk assessment counseling and the use of a personalized decision aid on women making menopausal therapy decisions. Menopausal Therapy can consist of hormone replacement therapy, tamoxifen, raloxifene, or no treatment at all.

Research has discovered that the majority of women make an arbitrary decision when choosing menopausal therapy. Based on this information, this study will assess the benefit of personalized risk assessments and counseling for women entering menopause. Ms. Matloff, along with Kristen Shannon, MS, of Massachusetts General Hospital, Nananda Col, MD of Harvard University, and Anne Moyer, Ph.D. of Stony Brook University, will begin their study October 2001 and begin recruiting patients in the Spring of 2002. Sixty women will participate in this study, forty women at Yale-New Haven Hospital and twenty at Massachusetts General; those eligible will need to be newly menopausal and cancer-free, with at least one first-degree relative with breast cancer.

Participants in the study will be split into two groups, one of which will receive counseling, the other will receive no intervention — the current standard of care. Counseling subjects will receive information, support, and a personal risk assessment based on a Markov decision model. This model is a statistical paradigm designed to incorporate the individual's personal health history (including lipid profile, bone density results, blood pressure, etc.) and family history to determine if they are at greater risk for breast cancer, cardiac disease, or osteoporosis. Based on the results of the Markov model and the patient's health assessment, an educated decision on Menopausal Therapy can then be made.

The study, which will take two years to complete, has been fully-funded by the Susan G. Komen Breast Cancer Foundation. Through grants, like the one Ms. Matloff has received, the Foundation and its affiliates have distributed over \$240 million to

eradicate breast cancer as a life-threatening disease by advancing research, education, screening, and treatment, since they began their program in 1982.

"I am very grateful to the Susan G. Komen Foundation for awarding our program this generous grant, and am excited to have the opportunity to work on this research, which I believe will help women make more informed decisions about postmenopausal therapy," Ms. Matloff said.



Ellen Matloff, MS.

Dr. Brian J. Druker, Founder and Director of the Leukemia Center at Oregon Health & Science University spoke to faculty and students at a special Cancer Center seminar in May. Dr. Druker developed the drug Gleevec to treat Chronic Myeloid Leukemia (CML) patients, which was approved by the Food and Drug Administration on May 10, 2001. CML involves an acquired genetic abnormality in the DNA resulting in mutated DNA in the stem cells. The mutation generates a larger percentage of white blood cells creating CML. Gleevec, manufactured by Novartis, gained worldwide recognition as the first effective molecular targeted cancer therapy and is currently

being tested on several other cancer types. Dr. Druker focused his discussion on the future of cancer research; he closed his talk stating, "Scientific discoveries come out of the background of huge amounts of knowledge, to think about the future you need to look at the past." Dr. Druker's visit was co-sponsored by Yale Cancer Center and Novartis.



Dr. Brian Druker.

National Marrow Donor Awareness Month

NOVEMBER IS "National Marrow Donor Awareness Month" and in recognition, Yale-New Haven Hospital, the Yale Cancer Center, and the New England Marrow Donor Program will take an active role in recruiting more donors onto the National Marrow Donor Program Registry. Each year, more than 30,000 people in the United States will be diagnosed with life-threatening diseases that can only be cured by a marrow, blood stem cell, or umbilical cord blood transplant. Nearly 75 percent of these patients will need an unrelated volunteer donor for their transplants.

Although joining the registry requires only a simple blood test to register a donor, becoming a volunteer donor is a serious commitment. Those who join the Registry are asked to remain committed to donating for any patient who is found to be a match to their blood sample through age 60.

For more information, please contact Sue Faraone at (203) 785-3142.

To join the registry, please attend one of the following Drive locations:

Monday, November 12 • 5-8 pm

Estrella de Jacob Church
506 Howard Avenue, New Haven

Tuesday, November 13 • 11am-4:30 pm

Joseph Slivka Center for Jewish Life
80 Wall Street, New Haven

Wednesday, November 14 • 12-4 pm

Yale University
Dwight Hall

Wednesday, November 14 • 12-6:30 pm

Harkness Ballroom, Yale School of Medicine
367 Cedar Street, New Haven

Wednesday, November 14 • 5-8 pm

Casa Otonal Community Center
148 Sylvan Avenue, New Haven

Thursday, November 15 • 11:30am-3:30 pm

Quinnipiac University
Alumni Hall, Hamden

Thursday, November 15 • 12-4 pm

University of Bridgeport
Student Social Room

Thursday, November 15 • 5-8 pm

St. Rose of Lima's Church
115 Blatchley Avenue, New Haven

Friday, November 16 • 11am-4:30 pm

Yale-New Haven Hospital
Grace Building Lounge

Monday, November 19 • 11:30am-2:30 pm

Yale School of Public Health
60 College Street, Room 608,
New Haven

Tuesday, November 20 • 12-4pm

Gateway Community College
Long Wharf Campus Cafeteria

UPCOMING EVENTS

October 24, 2001 Dr. Vincent T. DeVita, Jr., Director of Yale Cancer Center, will speak at the Bruce Museum in Greenwich, CT addressing the topic, *Hope Not Hype: What Can We Give Cancer Patients Today?*. By invitation only, for information please call Mary McCarthy at (203) 785-5257.

October 26, 2001 Yale-New Haven Hospital Mammography Van will be at the Grace Building, at the corner of Park and North Frontage Roads, New Haven.

For more information please call (203) 688-8824.

November 3, 2001 Y-ME Breast Cancer Symposium

Treatment Issues and Survivorship Strategies

Harkness Auditorium, Yale School of Medicine. 8:00 AM

For information please call Barbara Oliver at

(203) 483-8202.

December 5, 2001

Yale Cancer Center Holiday Patient Party

Harkness Lounge, Yale School of Medicine. 5:30 PM

For information please call Allison at (203) 737-2439.



Yale-New Haven Hospital has been listed in the *U.S. News & World Report's* Special Edition on America's Best Hospitals in 12 of 17 ranked specialties, including, cancer, gastroenterology, geriatrics, gynecology, hormonal disorders, kidney disease, orthopedics, otolaryngology, psychiatry, respiratory diseases, rheumatology, and urology.

Yale

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