

DIRECTOR'S MESSAGE

JOHN S. KOVACH, MD



FROZEN TISSUE BANK: AN EXPANSION OF CANCER CENTER RESOURCES

As discussed in this issue of *News & Views* (page 3) Stony Brook University Hospital and the Health Sciences Center have created a state-of-the-art frozen cancer tissue bank needed for translational cancer research. The secrets to the causes of cancer, its unrelenting but often unpredictable behavior, and its sensitivity and resistance to treatment are all determined by acquired biochemical changes (mutations) in specific genes. Increasingly, the tools needed to reveal this information are becoming available at a cost compatible with academic resources. In addition to scientists and money, a critical element needed to crack the cancer conundrum is access to frozen samples of cancer tissue and the surrounding normal tissue in which the cancer arose.

Deciphering the human genome has revolutionized the ability to study the genetic changes that underlie the series of events that lead to cancer. Within a decade, the entire genetic profile of an individual may be obtainable at an affordable price and in a reasonable period of time. Detection of gene differences between diseased and normal cells will provide targets for therapies tailored to exploit variations specific to the disease. Genetic analyses may also allow determination of whether the mutations in cancer cells came about because of inborn or acquired (environmental) factors.

Indeed, the nature of the biochemical changes in acquired

gene damage may even implicate specific classes of environmental toxins as likely causes of disease. For example, the pattern of gene damage in lung cancers of smokers is highly suggestive of the effects of the toxins in cigarette smoke. There is also strong circumstantial evidence indicating that environmental factors contribute to the causation of other common cancers, such as breast cancer, for which a clear link to environmental toxins is not obvious from epidemiological studies. Knowledge of patterns of biochemical damage in genes known to be associated with specific cancers should help to determine whether the causes of the large differences in breast cancer incidence among different ethnic groups are linked to environmental factors. Patterns of gene damage in specific cancers may also provide clues as to whether a "cancer cluster," an unexpectedly high rate of a specific type of cancer in a defined geographic region, occurs because of a dominant toxin in the environment or by chance alone.

The day is not too far off when direct comparisons of entire genomes and proteomes can be made from such samples, providing insights as to the fundamental nature of the cancer cell and, hopefully, its causation.

The frozen tissue bank, established in the Department of Pathology under the direction of Dr Youjun Hu, will enhance the interactions of our clinical and basic cancer investigators at the interface of molecular pathology and epidemiology as they seek to conquer cancer.

TRANSPLANTATION PROGRAM JOINS NATIONAL DONOR NETWORK

During the fall of 2004, Stony Brook University Hospital's Blood and Marrow Stem Cell Transplantation Program attained membership to the National Marrow Donor Program (NMDP), a network of more than 500 leading medical facilities for marrow and blood cell transplantation. This permits the Stony Brook program to be a national stem cell collection center where blood and marrow stem cells can be sent to matched recipients around the country, many of whom are cancer patients.

Patients are referred through the NMDP, and patient referral is

generally regional. For example, when a matched donor resides on Long Island, or within the area, including southern Connecticut, the organization would contact the transplantation program at Stony Brook for the blood or marrow stem cells.

The NMDP, which connects patients, donors, physicians, and researchers to resources they need, facilitates an average of 200 transplants per month. For more about the NMDP, call 1-888-999-6743, or contact the organization online at www.marrows.org.

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400 PLUS ATTEND HOSPITAL GALA TO SUPPORT CANCER SERVICES

More than 400 Stony Brook University Hospital (SBUH) physicians and staff, corporate donors, and other supporters of cancer services gathered in November to "Celebrate Excellence" during SBUH and the School of Medicine's Second Annual Gala. Funds raised from the event will benefit the hospital's cancer programs.

Honored that evening were former Senator Alfonse D'Amato (on left) and Gardner "Pat" Cowles, III, for their previous support of cancer programs at Stony Brook and continued interest in the development of the Long Island Cancer Center. Senator D'Amato received the Advocate Award and Mr Cowles the Patron Award.

The event provided an opportunity for friends, colleagues, and community members to learn more about cancer programs at SBUH, as well as dine and enjoy the celebration.



HAPPENINGS

Winter 2004/2005 **Prostate Cancer Screening**
Contact: Cancer Helpline:
1-800-862-2215

Free prostate cancer screenings are offered each month at various Suffolk County locations by Stony Brook Urology, PC. Annual prostate cancer screenings are recommended for all men age 50 and older and those age 40 and older who are either African-American or have a family history of the disease. **Appointments for screening can be made by calling the Stony Brook University Hospital Cancer Helpline at 1-800-862-2215.**

January 3 **Look Good...Feel Better Program**
February 7 **6 PM to 8 PM**
Stony Brook University Technology Park
East Setauket
Contact: 1-800-862-2215

For women cancer patients undergoing treatment, this 2-hour beauty program includes tips on skin, hair care, and makeup, as well as demonstrations of wig, turban and scarf use. The program is facilitated by a licensed cosmetologist. Registration is required.

February 2 **Breast Cancer Education & Support Group**
Topic: "Stress Management & Massage Therapy"
Holiday Inn Express, Stony Brook
7 PM to 9 PM
Speaker: Patricia Cadolino, LMT
Contact: Shirley Calhoun, LCSW,
at 631-444-4970

Sponsored by the Carol M. Baldwin Breast Care Center, these lectures feature information on the diagnosis, treatment, and recovery from breast cancer, as well as other issues pertaining to the disease. The support group is for people who have already been diagnosed with breast cancer.

March 5 **GIFT for Kids**
Stony Brook University Hospital
Galleria (HSC Level 3)
9:30 AM to 2:30 PM
Contact: Linda Bily (631) 444-2390
/Cynthia lombardo (631)444-8035

GIFT for Kids is a program for children and teenagers whose mother, father or primary caregiver has been diagnosed with breast cancer and is undergoing treatment. The program is an addition to the GIFT (Giving Inspiration, Fighting Together) Program that provides support to women diagnosed with cancer by offering educational materials, comforting amenities and emotional support. GIFT for Kids includes group discussions, recreational therapy, lunch, entertainment, and take-home educational materials. Registration is required.

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CREATION OF FROZEN TISSUE BANK ENHANCES LICC RESEARCH

A new frozen cancer tissue bank jointly created by Stony Brook University Hospital (SBUH), the School of Medicine, and the Long Island Cancer Center (LICC) is a building block for advancing cancer research at Stony Brook. Operational as of December 1, 2004, the tissue bank provides cancer investigators with normal and abnormal human tissue and blood for a host of investigations on the nature and cause of human cancers.

Youjun Hu, MD, Assistant Professor of Pathology, directs the development of the frozen tissue bank and is working with cancer surgeons to attain tissue. Patients play the key role in developing the tissue bank by consenting to researchers' use of excess tissue after cancer surgery.

"I am delighted the department has been able to establish at Stony Brook this new resource that will allow our cancer patients to contribute to advances in the study and treatment of cancers by banking tissue specimens," says Jay Bock, MD, PhD, Acting Chair, Department of Pathology.

All tissue samples to be stored are derived from material not needed for clinical purposes. Although such samples are ordinarily discarded after pathologic diagnosis, retention of specimens in a tissue bank still requires informed consent from each patient, which is obtained by the patient's surgeon. Patient confidentiality is maintained by assignment of an identifying number for each sample. The tissue bank database is also constructed to provide investigators with specific demographic and clinical information without disclosing patient identity.

Federal Grant for Instrumentation

Purchases of advanced technology equipment for the frozen tissue bank jump-started the program. These purchases were made possible by a \$300,000 grant to the LICC obtained through the efforts of Congressman Tim Bishop.

Two essential instruments purchased are a customized tissue array device and a laser microdissection apparatus. The tissue array device places many small samples of tissue on a single microscope slide. This allows a scientist to rapidly assess the characteristics of hundreds of different cancer cases, such as the reactivity of new antibodies, efficiently and at reduced costs. This type of cancer investigation is important because it expedites the search for molecular markers that may be useful for early cancer diagnosis, prediction of clinical course, and as targets for new therapies.

The laser capture microdissection apparatus consists of a microscope linked to an automated dissecting system that can precisely isolate small numbers of purified populations of cells, even single cells. These cells can then be studied in a pure state uncontaminated by the many normal cells in which the cancers arise.

Freezing Versus Fixative

Because of its large volume of cases, Stony Brook's Department of Pathology is poised to build a sizeable frozen tissue bank for cancer investigation. The department has archives of more than 200,000 samples of tissue specimens collected during the past 24 years.

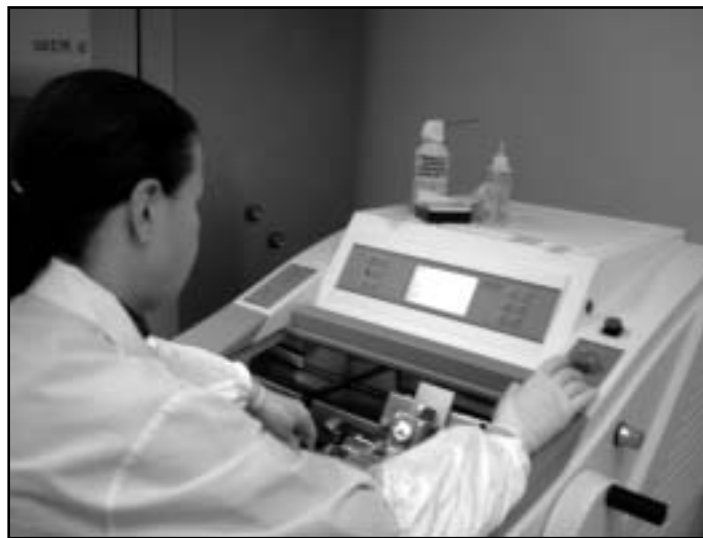
However, these samples were placed in a fixative to preserve the tissue for histologic study under the microscope, a standard practice of all hospitals. Tissue preserved within this fixation process, however, greatly increases the difficulty in carrying out

molecular studies because the fixative chemically reacts with many cellular elements. The great advantage of maintaining samples of tissue in a frozen state is the preservation of biochemical structure of genes and their products. Studies of these genes and their products are necessary in order to uncover the mysteries of the causes of cancer.

Based on the most common cancers surgically treated at SBUH, Dr Hu expects to receive tissue primarily from breast, colon, ovary, thyroid, and lung tumor cases. Nevertheless, samples of all cancers will be placed in the tissue bank. Many samples of a wide variety of cancers will help to construct a tissue bank at Stony Brook that will be an invaluable resource for cancer investigators.

“This new resource will allow our cancer patients to contribute to advances in the study and treatment of cancers”

—Jay Bock, MD, PhD, Acting
Chair, Department of Pathology



Histologist Camille Kutcher prepares frozen tissue section slides in a cryostat (a frozen chamber), one of the steps necessary to verify tumor diagnosis within the tissue section and preserve and prepare it for molecular study. Stony Brook University Hospital's Department of Pathology will house the frozen tissue bank, available for cancer researchers.

INVESTIGATOR TESTING A SUPER POTENT ASPIRIN AS PREVENTATIVE FOR COLON CANCER

By Greg Filiano

It is never easy to predict treatment results in people based on results in laboratory animals. But Basil Rigas, MD, Professor of Medicine and Chief of the Division of Cancer Prevention in Stony Brook's Department of Medicine believes that the use of an aspirin derivative, called nitric oxide-donating aspirin, or nitroaspirin, for the prevention of colon cancer might be similarly as effective in people as it is in laboratory animals. Dr Rigas, who joined Stony Brook University Hospital's Department of Medicine in 2004, has tested the use of nitroaspirin on animals for the past 4 years. He has consistently found that for many mice with colon cancer, tumor growth is inhibited and adverse effects are almost non-existent.

These results are compelling enough for Stony Brook University Hospital clinicians from the divisions of Gastroenterology, Medical Oncology and Surgical Oncology to begin working with Dr Rigas to test nitroaspirin as a preventive agent against colon cancer in high-risk patients. Dr Rigas received \$3.2 million from the National Cancer Institute (NCI) to conduct his studies. This funding supports a trial on humans to test the effectiveness and safety of nitroaspirin as a preventive treatment on up to 240 patients at high risk for colon cancer.

Traditional aspirin and other non-steroidal anti-inflammatory agents (NSAIDs) have previously been shown to reduce colon cancer recurrence in high-risk patients. But Dr Rigas emphasizes that there are two glaring problems with using aspirin in such patients – it is effective in only half who take it, at best, and the adverse effects are many. These include allergic reactions, gastrointestinal bleeding, and kidney damage – all of which can even be fatal.

Alternatives to aspirin, a class of arthritis pain drugs called COX-2 inhibitors that inhibit an enzyme involved in the inflammatory process, are reported to have fewer adverse effects than aspirin and also have inhibitory effects on the development of colon cancer. But the recent withdrawal of one of these NSAIDs (Vioxx) from the market – because of its added risk for heart attack or stroke – has placed suspicion on the safety of all COX-2 inhibitors for long-term use.

Nitroaspirin as Possible Alternative

"The use of nitroaspirin does not appear to depend on COX-2 to take effect," says Dr Rigas. "And unlike regular aspirin, nitroaspirin

has been modified to release nitric oxide, which has been shown to have numerous positive effects within the cardiovascular and respiratory systems in people," he explains, adding that the drug holds great promise for cancer prevention.

Martin Karpeh, MD, Chief, Division of Surgical Oncology, says that there are many studies testing pharmacological agents for preventing colon cancer. Although it remains to be seen if nitroaspirin is effective and safe in preventing colon cancer in people, Dr Karpeh contends that its use is one of the most promising colon cancer prevention methods under investigation. He cites Dr

Rigas' lab results as the leading evidence in support of the nitroaspirin approach.

Encouraging Lab Results

Dr Rigas' laboratory results have shown that nitroaspirin is hundreds of times more potent than traditional aspirin in inhibiting the growth of colon cancer cells in cell cultures and is effective in preventing colon cancer in laboratory animals as well. He and his research team have used laboratory animals that are engineered to have a high risk of developing colon tumors. In groups of mice with colon cancer, nitroaspirin was given daily for three weeks. Some mice were untreated. On average, the treated groups displayed a 59% reduction in tumors. In a similar study with rats, tumor growth

was inhibited by approximately 75%. In addition, new tumors did not grow in the animals. And according to Dr Rigas, there were no indications of any toxicity, including bleeding in the animals.

While promising, there is a long road of research to be completed before nitroaspirin becomes a preventive agent for colon cancer, if at all. Once testing in high-risk patients begins, Dr Rigas and Stony Brook colleagues will monitor the growth of tumors at the earliest possible stage, during the formation of precancerous lesions. By using a technique called magnifying endoscopy – which requires an instrument that is part microscope, part endoscope – researchers will get a 150-fold magnified view of such lesions.

Use of nitroaspirin, or any agent, that inhibits growth of colon cancer tumors at such an early stage could halt the disease process in its tracks. Considering this possibility, and because experts believe colon cancer takes years to develop, a safe chemopreventive agent against colon cancer would be the ideal way to treat a disease that is a leading cause of cancer death in the United States.



Basil Rigas, MD, is studying nitroaspirin as a chemopreventive agent against colon cancer in laboratory animals. Supported by a \$3.2 million grant from the National Cancer Institute, Dr Rigas is collaborating with Stony Brook University Hospital physicians to test this potent form of aspirin as a preventative drug in people.

LESS INVASIVE LAPAROSCOPIC SURGERY IS OPTION FOR COLON CANCER PATIENTS

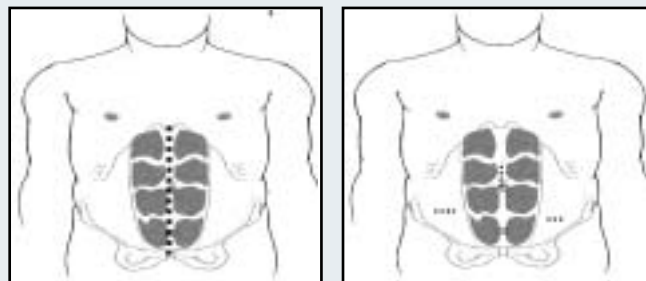
Open colectomy is the standard form of surgery for colon cancer patients, but laparoscopically assisted colectomy is gaining momentum as an alternative that is just as effective but is less invasive, leading to a quicker post-operation recovery time. Patients undergoing laparoscopic surgery for colon cancer may also experience less pain post-surgery than those who have open colectomy.

For David Rivadeneira, MD, Assistant Professor of Surgery, Division of Surgical Oncology, and a board certified colon and rectal surgeon, these are significant reasons for patients to consider the procedure as an alternative to open colectomy. When he joined the Long Island Cancer Center in 2003, he brought 10 years of laparoscopic surgery experience to his new practice. Since then, many of Dr Rivadeneira's colon and rectal cancer patients have opted for the procedure, and he reports that results in these patients have been extremely favorable.

Use of a laparoscope, a lighted viewing tube that is inserted into the abdominal cavity, has been effectively used for years for gallbladder removal, during appendectomies and other procedures. The laparoscope is connected to a video camera for viewing. In laparoscopically assisted colon cancer surgery, several small incisions – usually less than one inch – are made in the abdomen, and the lighted laparoscope is inserted into one of them to guide the surgery. The effectiveness of laparoscopic surgery for removing parts or the entire colon continues to be debated, but recent evidence indicates that it is a viable option for some patients.

A Multi-Institutional 5-Year Study

In May 2004, it was reported in the *New England Journal of Medicine* that after nearly five years of follow-up in hundreds of patients who had either conventional (open colectomy) or laparoscopic surgery for colon cancer, patients who had laparoscopic colectomy recovered more quickly and had a shorter duration of pain medication. Patients who had open colectomy had a median hospital recovery time of 6 days and took pain medications for a median of 4 days. Patients who had laparoscopic colectomy had a



Abdominal incisions for traditional colectomy can be as long as 10 to 12 inches (at left) but with laparoscopic surgery, each small incision is usually less than 1 inch (at right). This helps to minimize patient trauma and enhance recovery for most patients.

median hospital recovery time of 5 days and took pain medications for 3 days.

A total of 872 patients at 48 institutions in the United States and Canada participated in the study. Individuals were randomly assigned to receive open colectomy or laparoscopic colectomy. The median follow-up time was 4.4 years.

Survival rates were similar in both groups after three years (86% for laparoscopic, 85% for conventional), as was the cancer recurrence rate (16% for laparoscopic, 18% for conventional). The principal investigators of the multi-institutional study concluded that because recurrence rates were similar between both groups – thereby validating the effectiveness of the procedure to remove cancerous colon tissue – the laparoscopic approach is an acceptable alternative to open colectomy for colon cancer.

Dr Rivadeneira believes that the study results clearly indicate that laparoscopic colectomy is an acceptable alternative to open colectomy and that it may even have some advantages over conventional surgery for many patients. This year he spearheaded an educational program for surgeons who seek to gain expertise in laparoscopic procedures for colon and rectal surgery. The workshops, sponsored by Stony Brook University's School of Medicine, are one-day courses for Stony Brook University and area surgeons.

NATIONAL LEADER IN COLON AND RECTAL CANCER SURGERY JOINS STONY BROOK

Stony Brook University Hospital has recruited another expert in colon and rectal cancer surgery with the addition of Marvin L. Corman, MD, a nationally known surgeon and author of a book on the topic that is considered by many as the gold standard in its field. As Professor of Surgery, Division of Surgical Oncology, Dr Corman will center on management of diseases of the small bowel, colon, rectum and anus, including colon, rectal and anal cancer.

By joining surgeons Martin S. Karpeh, MD, Chief, Division of Surgical Oncology, and David Rivadeneira, MD, Assistant Professor, Division of Surgical Oncology, Dr Corman places the Long Island Cancer Center as a leading regional institution in the curative treatment of gastrointestinal cancers. This surgical team uses minimally

invasive laparoscopic surgery for some colon cancer patients and employs sphincter-saving surgical methods when possible.

In October 2004, the fifth edition of Dr Corman's textbook, *Colon & Rectal Surgery*, was published. The book is an instructional, up-to-date guide on the diagnosis and treatment of all disorders affecting the anus, rectum and colon.

Dr Corman has served as president of the American Board of Colon and Rectal Surgery, and he is regional vice president of the International Society of University Colon and Rectal Surgeons. Most recently he was Vice Chairman of Surgery and attending colon and rectal surgeon at North Shore-Long Island Jewish Medical Center in New Hyde Park, as well as Professor of Surgery at Albert Einstein College of Medicine in New York.

NEW HEAD OF HEMATOLOGY/ONCOLOGY

Ted Gabig, MD, has been named Chief of the Division of Hematology/Oncology, the newly consolidated division that will help build the collaborative clinical and research efforts of physicians within the previously named Divisions of Neoplastic Diseases and Hematology. He will also serve as Deputy Director of the Long Island Cancer Center (LICC) at Stony Brook University.

John S. Kovach, MD, Director of the LICC, says that Dr Gabig's medical and administrative expertise will serve the new division well as the LICC continues its expansion. Dr Gabig oversees a diverse division that now includes 14 full-time faculty members.

"The consolidation will have an immediate impact on the cancer program, as it serves to grow the faculty, complement the research skills of cancer specialists, and foster collaboration with basic scientists to grow translational research programs," says Dr Gabig. This approach will center on the prevention and early detection of cancer, with gastrointestinal cancers and lung cancer the immediate focus.



*Ted Gabig, MD
Chief, Division of
Hematology/Oncology*

Dr Gabig came to Stony Brook from the North Shore-Long Island Jewish Health System where he was Vice President for Cancer Services. From 1992 to 2002 he was Director of Hematology and Oncology in the Department of Medicine at Indiana University. In addition to his clinical experience, Dr Gabig is involved with research on identifying new biomarkers for cancer.



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