PHILADELPHIA INTERNATIONAL MEDICINE® NEWS BUREAU

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February 26, 2009

For immediate release:

In this month's edition

Editors note: Research, new techniques and improved facilities by Philadelphia International Medicine hospitals and physicians may lead to new ways to treat some of our most challenging diseases. Below are just some examples from our hospitals.

NCI-Penn Collaboration Finds Targeted Immune Cells Shrink Tumors in Mice

Philadelphia – Researchers have generated altered immune cells that are able to shrink, and in some cases eradicate, large tumors in mice. The immune cells target mesothelin, a protein that is highly expressed, or translated in large amounts from the mesothelin gene, on the surface of several types of cancer cells. The approach, developed by researchers at the University of Pennsylvania School of Medicine and the National Cancer Institute (NCI), shows promise in the development of immunotherapies for certain tumors. The study appears online in the *Proceedings of the National Academy of Sciences*.

Expression of mesothelin is normally limited to the cells that make up the protective lining (mesothelium) of the body's cavities and internal organs. The protein is abundantly expressed by nearly all pancreatic cancers, many ovarian, and non-small-cell lung cancers. The precise biological function of mesothelin is not known for certain, it is thought to play a role in the growth and metastatic spread of the cancers that express it.

"Since tumor cells are derived from the body's normal cells, the immune system often fails to recognize tumor molecules as dangerous or foreign and counteract against them," said Ira Pastan, MD, chief of the Laboratory of Molecular Biology in NCI's Center for Cancer Research, a study collaborator. Even though it is possible to genetically engineer immune system cells to recognize molecules on tumor cells, most of the molecules found on tumor cells are also found on normal cells. But, Dr. Pastan notes, "mesothelin is a promising candidate for generating tumor-targeting T cells, given its limited expression in normal tissues and high expression in several cancers."

Previous laboratory research has shown that certain immune system cells, called T cells, can kill tumor cells that express mesothelin. In addition, studies in both animals and humans have shown that antibodies directed against mesothelin protein can shrink tumors.

To study the effects of the engineered T cells on tumor tissue, the researchers implanted human mesothelioma cells underneath the skin of mice. About six weeks later, when tumors had formed and progressed to an advanced stage, the engineered T cells were administered to the mice. Direct injection of the T cells into tumors or into veins of the mice resulted in disappearance or shrinkage of the tumor.

"Based on the size of the tumors and the number of cells administered, we estimate that one mesothelin-targeted T cell was able to kill about 40 tumor cells," said study leader Carl H. June, MD, Professor of Pathology and Laboratory Medicine and director of Translational Research at Penn's Abramson Cancer Center. "This finding indicates that small doses of these cells may have potential in treating patients with large tumors. Clinical trials are being developed to investigate this approach in patients with mesothelioma and ovarian cancer."

Temple University Hospital Introduces Laser-Assisted Lead Extraction

Electrophysiologist Bindi K. Shah, MD, recently performed Temple University Hospital's first laser-assisted extraction of an implantable defibrillator lead.

Leads are insulated wires that can range in length from 45 to 90 centimeters. They are connected to implantable devices such as pacemakers or defibrillators, and deliver electric pulses to help the heart maintain its rhythm. Over time, scar tissue can form over these leads, binding them to blood vessel and heart walls. At times, leads must be removed or replaced because they get infected or are faulty.

During a typical laser lead extraction, Dr. Shah explains, an incision is made overlying the pacemaker or defibrillator and the device is removed from the patient.

Next, the lead is freed from the tissue in the chest and it is cut to expose the inside coils. A Lead Locking Device is threaded through the lead to secure it in place. Then, a sheath with an excimer laser is carefully guided along the length of the lead, cutting it free from any scar tissue that has grown around it. Dr. Shah reports that the procedure was a success, and the patient was discharged the next day. Prior to the advent of the laser extraction method, patients faced a high risk of major complications from the procedure. "The new technology has reduced the complication rate to less than 2 percent," said Dr. Shah.

Biomarker Predicts Disease Recurrence in Colorectal Cancer

Findings published in the *Journal of the American Medical Association* by researchers at Thomas Jefferson University show that the presence of a biomarker in regional lymph nodes is an independent predictor of disease recurrence in patients with colorectal cancer.

Detection of the biomarker, guanylyl cyclase 2C (GUCY2C), indicates the presence of occult metastases in lymph nodes that may not have been identified by current cancer staging methods, according to Scott Waldman, MD, PhD, chairman of the Department of Pharmacology and Experimental Therapeutics at Jefferson Medical College of Thomas Jefferson University and Hospital.

According to Dr. Waldman, who is also the Samuel M.V. Hamilton Professor of Clinical Pharmacology in the Department of Medicine at Jefferson Medical College, colorectal cancer that has metastasized, or spread, to the regional lymph nodes carries a worse prognosis and a higher risk for recurrence.

"One of the unmet needs in colorectal cancer is an accurate staging method to determine how far the disease has spread," said Dr. Waldman, who is also director of the Gastrointestinal Malignancies Program at the Kimmel Cancer Center at Jefferson. "The current standard method, histopathology, is imperfect since it only involves looking at a very small sample of the regional lymph nodes under a microscope. There is no way to know whether occult metastases are present in the rest of the tissue."

Dr. Waldman and his colleagues conducted a prospective, multicenter study of 257 patients with colorectal cancer that had no metastases identified in the lymph nodes (node-negative) according to current standards. They analyzed the lymph nodes for GUCY2C expression using a technique called reverse transcriptase-polymerase chain reaction (RT-PCR). This technique, according to Dr. Waldman, amplifies the sensitivity to detect cancer cells compared to histopathology.

The majority of patients – 87.5 percent – had lymph nodes that were positive for GUCY2C. Among those patients, 20.9 percent developed recurrent disease. By comparison, only 6.3 percent of the patients whose lymph nodes were negative for GUCY2C developed recurrent disease.

The patients were followed for a median of 24 months for disease recurrence or death. Indeed, patients who expressed GUCY2C had a shorter time to recurrence and a shorter disease-free survival. The prognostic value of the marker persisted even after a multivariate analysis that took other known prognostic factors into account.

According to Dr. Waldman, 20 to 30 percent of patients diagnosed with node-negative colorectal cancer experience disease recurrence within five years. This is approximately the same rate of recurrence as that for some categories of patients diagnosed with node-positive disease. These observations suggest that there are occult metastases in the lymph nodes of node-negative patients at the time of diagnosis. GUCY2C specifically identifies these occult metastases that indicate risk for recurrent disease.

"Beyond predicting disease recurrence, detecting this biomarker could be useful for identifying patients who might benefit from treatment with adjuvant chemotherapy, which is specifically given to patients with node-positive disease," Dr. Waldman said.

Fox Chase Receives Magnet Status for the Third Time in a Row

Fox Chase Cancer Center, the first acute care hospital in Pennsylvania and specialty hospital in the country to receive Magnet status, has been designated for the third time in a row — now making it the first hospital in Pennsylvania to have achieved two successful Magnet renewals. This designation is the nation's highest form of recognition for nursing excellence and is one of the benchmarks used to measure the quality of care patients receive.

"Our success in achieving our third Magnet designation highlights our ability to sustain magnet excellence over the past decade. Each designation period since 2000 has required us to remain focused on nursing excellence, innovation and collaboration to insure that we remain committed to fostering excellence in nursing practice and patient care," says Joanne M. Hambleton, RN, MSN, NE-BC, vice president of nursing and patient services at Fox Chase. "Achieving this status three times in a row demonstrates Fox Chase Cancer Center's sustaining commitment to nursing and to the needs of our patients. I could not be prouder of the individual and group contributions of our entire staff."

The Magnet Program provides a framework to recognize excellence in: the management philosophy and practices of nursing services; adherence to standards for improving the quality of patient care; leadership of the chief nurse executive in supporting professional practice and continued competence of nursing personnel; and attention to the cultural and ethnic diversity of patients and their significant others, as well as to the care providers in the system.

Published research has shown that hospitals with Magnet designation have positive outcomes for patients, nurses and the workplace. Patients receiving care at Magnet hospitals have been recorded as experiencing lower mortality rates, greater satisfaction, and shortened hospital stays.

"We are very proud of our outstanding nursing staff and their achievement in earning this prestigious status for the third time in a row," says Michael V. Seiden, MD, PhD, president and CEO of Fox Chase. "The fact that only 2 percent of hospitals in the country have received Magnet re-designation speaks to the magnitude of this accomplishment."

The Magnet Nursing Recognition Program was established in 1993 by the American Nurses Credentialing Center (ANCC). Institutions applying for Magnet status must pass a rigorous review, designed to demonstrate superior nursing and excellence in patient care. Magnet status is valid for four years, after which the recipient must reapply.

Philadelphia International Medicine is an organization that provides medical and patient support services to international patients. It also provides continuing medical education and health care training and

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