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For immediate release:

In this month's edition

1. Fox Chase Researchers Find Estrogen May Help Precancerous Cells Spread in Oral Cavity
2. New Lung Procedure at Temple University Hospital Saves Lives
3. Daniel M. Quirk, MD, MPH, Joins Jefferson's Division of Gastroenterology and Hepatology
4. Temple University Hospital Helps Investigate a Novel Treatment for Type-1 Diabetes

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.

Fox Chase Researchers Find Estrogen May Help Precancerous Cells Spread in Oral Cavity

PHILADELPHIA—Head and neck cancer is the sixth most common type of cancer and is on the rise in some demographic groups, including young women without any known risk factors. Now, researchers at Fox Chase Cancer Center report that estrogen may increase the movement of precancerous cells in the mouth and thus promote the spread of the disease within the oral cavity. The new results, which are reported in the January issue of *Cancer Prevention Research*, may lead to novel chemoprevention strategies in the future.

Margie Clapper, PhD, co-leader of the Cancer Prevention and Control Program at Fox Chase Cancer Center, and colleagues reported earlier this year that estrogen metabolism changes after smoke exposure in the lungs and may contribute to lung cancer. To find out if this female hormone influences development of head and neck cancer, Ekaterina Shatalova, PhD, a postdoctoral fellow and first author on the paper, examined the impact of estrogen on precancerous and cancerous cells.

They found that estrogen induces the expression of an enzyme called cytochrome P450 1B1 (CYP1B1), which is responsible for breaking down toxins and metabolizing estrogen. Interestingly, CYP1B1 induction occurred only in precancerous cells, which are neither normal nor cancerous; estrogen did not induce CYP1B1 in cancer cells.

With closer investigation, the team found that depleting the expression of CYP1B1 diminished the ability of precancerous cells to move and divide, as compared to similar cells with normal levels of CYP1B1. Estrogen also reduced cell death in the precancerous cells, irrespective of the amount of CYP1B1 present.

“In the future we would like to find a natural or dietary agent to deplete the CYP1B1 enzyme and see if we can prevent oral cancer at the precancerous stage,” said Dr. Shatalova.

“Our previous studies showed that the CYP1B1 enzyme sits at the hub of changes which occur in the lungs after smoke exposure. We were now able to look at its role in a more direct fashion by removing it from precancerous cells of the oral cavity,” Dr. Clapper says. “We found that cells lacking it move slower. CYP1B1 could be a wonderful target in precancerous lesions of the head and neck, because by attacking it, we might stop these lesions from progressing or moving to a more advanced stage.” In addition, patients diagnosed with head and neck cancer are at a high risk of developing a second primary tumor, which is associated with poorer overall survival. Finding a way to reduce these subsequent tumors could improve patients’ survival.

Co-authors on the study include Andres J.P. Klein-Szanto, Karthik Devarajan, and Edna Cukierman, all of whom are at Fox Chase Cancer Center.

New Lung Procedure at Temple University Hospital Saves Lives

Temple University Hospital can provide ambulatory extracorporeal membrane oxygenation (ECMO) in awake, spontaneously breathing patients as a life-saving bridge to transplantation.

ECMO is the use of total cardiopulmonary support for patients in severe respiratory failure. “Think of it as an artificial heart and lung,” says Abeel Mangi, MD, surgical director of the Temple Lung Transplant Program.

Patients who undergo traditional ECMO become bed-bound due to the placement of the cannulas, or tubes, that are used to link the mechanical oxygenators that remain outside the body with the patient's own circulatory system. “Access needs to be through a larger artery or vein, so most doctors use the femoral artery, located in the groin area,” says Dr. Mangi. “But that prohibits the patient from getting up and walking around, and that is undesirable. In addition, uniformly, patients are intubated and on the mechanical ventilator.”

As a result, Dr. Mangi modified the procedure to use the large blood vessels under the clavicle (or collar bone) as his point of access which allows patients to get up and walk around after the procedure. Such mobility reduces or eliminates the deconditioning and diaphragmatic weakness associated with total immobility. Another dramatic twist to the procedure is that it is performed while the patient is awake, sitting upright, and breathing spontaneously.

Forty-seven-year-old Tamar Ellensworth is a walking testament to Dr. Mangi's expertise with ambulatory ECMO. After coming to Temple with severely failing lungs in late-August of 2009, Ellensworth underwent ambulatory ECMO, and, just two days later, received a double-lung transplant. Today, she goes to a gym everyday to work out on a treadmill and elliptical machine to keep her new lungs healthy.

Daniel M. Quirk, MD, MPH, Joins Jefferson's Division of Gastroenterology and Hepatology

Anthony J. DiMarino, MD, William Rorer Professor of Medicine and chief of the Division of Gastroenterology and Hepatology in the Department of Medicine at Thomas Jefferson University Hospital, announces the appointment of Daniel M. Quirk, MD, MPH, as an associate professor.

Dr. Quirk received his medical degree from the Brown-Dartmouth Program in Medicine in Providence, Rhode Island in 1991. He earned a Bachelor of Science degree from Providence College in 1987. Dr. Quirk completed both a medical internship (1991-92) and a residency (1992-94) at The Johns Hopkins Hospital in Baltimore. He completed a clinical research fellowship in gastroenterology at Massachusetts General Hospital in Boston (1994-97) where he also earned a masters degree in Public Health from the Harvard School of Public Health in 1997.

During his tenure at Brown University School of Medicine, Dr. Quirk was on active staff at both Rhode Island and Roger Williams hospitals. He was named a clinical instructor in 1997; after two years he was promoted to clinical assistant professor in 1999, for which he served until 2008 when he was promoted to clinical associate professor. He also served as director of Endoscopic Ultrasonography at Rhode Island Hospital and as director of Translational Research in the Division of Gastroenterology at Brown University.

Dr. Quirk is Board Certified by the American Board of Internal Medicine and is a Diplomate of Gastroenterology. Among his many affiliations, he is a member of the Massachusetts Medical Society and the American Gastroenterological Association. He has been acknowledged by his peers as a "Top Doc" in gastroenterology both by Rhode Island Monthly and Philadelphia's Main Line Times.

Temple University Hospital Helps Investigate a Novel Treatment for Type-1 Diabetes

Temple University Hospital (TUH) is participating in an international, randomized clinical trial to evaluate the safety and effectiveness of an investigational drug (Otelixizumab) in delaying the progression of disease in newly-diagnosed (90 days or less) patients with Type 1 diabetes.

"We are currently participating in this important trial, called DEFEND-2, which holds a great deal of promise as a potential one-time treatment to delay or slow the progression of diabetes in a defined

subset of the patient population,” said TUH principal investigator Elias S. Siraj, MD, associate professor of medicine and director of clinical endocrinology at Temple University Hospital.

Diabetes is the name given to disorders in which the body has difficulty regulating high blood glucose level. There are two major classes of diabetes: Type 1 and Type 2. Type 1, previously known as juvenile diabetes or insulin-dependent diabetes, is a disease in which the immune system mistakenly signals the body’s T-cells to attack and destroy its own insulin-producing cells (beta cells) in the pancreas. The resulting decrease in the production of natural insulin means that patients must monitor their glucose levels frequently and give themselves insulin by injection or pump to control blood-sugar levels.

According to Dr. Siraj, the DEFEND-2 trial [Durable-Response Therapy Evaluation for Early or New-Onset Type 1 Diabetes] is a follow-up study on the DEFEND-1 trial, in which Temple also participated. Those studies have come on the heels of smaller, earlier studies that have also used Otelixizumab, an investigational monoclonal antibody, as a therapeutic tool to modulate the immune system’s response to diabetes. “Essentially, the drug targets a receptor in T-cells to impede the T-cells’s ability to destroy insulin-producing pancreatic beta cells,” explains Dr. Siraj. After receiving a single, 8-day course of infusions of Otelixizumab, study participants will be carefully monitored and assessed for improvement in their insulin-secretion. The drug will be administered as an addition to insulin, diet, and other standard treatments.

Temple University Hospital has a well-established, multidisciplinary diabetes program, within its Endocrinology Division, that handles thousands of patient visits each year. The program’s physicians, researchers, nurses and nurse practitioners, and allied-health professionals offer patients state-of-the-art therapies for the management of diabetes, including diabetes education, as well as the opportunity to participate in a rich variety of clinical trials designed to advance the treatment of diabetes.

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