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For immediate release:

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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.

Oleh Haluszka, MD, Appointed Chief of Gastroenterology

Oleh Haluszka, MD, has been appointed chief of Gastroenterology at Temple University Hospital. Previously, Dr. Haluszka was director of Gastrointestinal Endoscopy at Fox Chase Cancer Center, where he was named one of Philadelphia Magazine's "Top Doctors" last year.

Dr. Haluszka was one of the first 11 doctors in the U.S. to do double-balloon enteroscopy. This procedure was the first to visualize the entire GI tract in real time. Once inserted the double-balloon enteroscope travels through the GI tract like a conventional endoscope until reaching the small bowel. There it begins using a "push and pull" method, inflating and deflating the balloons in succession to advance the scope, to explore the small bowel.

Prior to his tenure at Fox Chase, Dr. Haluszka was director of GI endoscopy and assistant professor of medicine at the University of Maryland. He also served as medical consultant for the White House medical department.

"I am excited about my new posts at Temple, where the practice and research of gastroenterology diseases and disorders are already superior," said Dr. Haluszka. "I plan to focus on maintaining the strength of the program while adding a major emphasis on therapeutic endoscopy."

His proficiency in therapeutic endoscopy is central to the diagnosis of a large diversity of intestinal problems. He also specializes in interventional endoscopy procedures, ranging from treatment techniques for patients with early forms of intestinal cancer to symptom relief via palliative procedures.

“With a combination of new techniques and new technologies, Temple will become a tertiary-care center of excellence in endoscopy,” said Dr. Haluszka. “Our goal will be to establish a very seamless referral pattern and, when appropriate, get patients back in the hands of their referring doctors.”

Dr. Haluszka was director of endoscopy at the Naval Medical Center in San Diego, CA, staff gastroenterologist at the U.S. Naval Hospital and clinical instructor in medicine at the University of California. He was a Navy medical officer upon entering medical school and promoted to captain in the U.S. Naval Reserve medical corps.

He completed his internship and residency in internal medicine at the U.S. Naval Hospital in San Diego, where he held a two-year fellowship in gastroenterology. Dr. Haluszka was also an endoscopy fellow at the Medical College of Wisconsin in Milwaukee. A board-certified gastroenterologist, Dr. Haluszka earned his medical degree at the Uniformed Services University of the Health Sciences in Bethesda, Md., and has his bachelor's degree from Dartmouth College.

Among Dr. Haluszka's clinical and research interests are therapeutic endoscopy for cancer and other diseases of the pancreas, bile ducts, liver and gallbladder; and treatment for gastrointestinal bleeding. He is proficient in new techniques for gastrointestinal stenting, which uses an endoscope to open gastrointestinal passages where a wire tube is placed to keep them open.

Dr. Haluszka has published over 50 research papers and abstracts and has presented several invited lectures, including serving as a speaker at the International Course in Gastroenterology and Digestive Endoscopy in La Paz, Bolivia, and a lecturer at the World Conference of Interventional Oncology in Philadelphia, PA.

His professional memberships include the American College of Gastroenterology and the American Society of Gastrointestinal Endoscopy.

New Gene Therapy to Reverse Heart Failure Ready for Clinical Trials

A promising gene therapy developed, in part, at [Thomas Jefferson University's Center for Translational Medicine](#) to prevent and reverse congestive heart failure is on the verge of clinical trials, after years of proving itself highly effective in the lab and a large animal study.

Reporting in the online July 20 issue of *Science Translational Medicine*, cardiology researchers have demonstrated feasibility, the long-term therapeutic effectiveness and the safety of S100A1 gene therapy in a large animal model of heart failure under conditions approximating a clinical setting.

“This is the last step you have to take to finish a very long line of research,” said [Patrick Most, M.D.](#), adjunct assistant professor of medicine at Thomas Jefferson University, and lead author of the study who now heads the Institute for Molecular and Translational Cardiology at the University of Heidelberg, Germany. “The reversal of cardiac dysfunction in this pre-clinical heart failure model in the

pig by restoring S100A1 levels in practically the same setting as in a patient is remarkable and will pave the way for a clinical trial.”

The therapy works by raising diminished levels of the protein S100A1, a calcium-sensing protein in the diseased heart muscle cell, to normal. Previous research suggests this will prevent against heart failure development, particularly in people who have had a heart attack.

According to Dr. Most, “the therapeutic profile of S100A1 is a unique one as it targets and reverses the underlying causes of heart failure: progressive deterioration of contractile performance, electrical instability and energy deprivation.”

About six million people in the United States have heart failure, and it results in about 300,000 deaths each year.

Work on S100A1 started bench side 15 years ago with Dr. Most and [Walter J Koch, Ph.D.](#), now director of the Center for Translational Medicine in the Department of Medicine in [Jefferson Medical College](#) of Thomas Jefferson University, who, with his team, have moved the research closer to bedside ever since.

Five years ago, Jefferson researchers showed that increasing levels of the protein above normal helped protect mouse hearts from further damage after simulated heart attacks. The hearts worked better and had stronger contractile force.

“We have pursued a completely different path over the years,” said Dr. Most. “We have set up a translational pipeline and don’t stick to just one model system. We took it step by step, and did whatever was necessary to go to the next level. We realized early on that a mouse is not a man. You need to design target-tailored translational research strategies and work in human-relevant model systems to take molecular discoveries from bench to bedside.

“With such a translational roadmap at hand, we are in the unique position to accelerate future development of molecular therapies.”

In their latest study in *Science Translational Medicine*, Drs. Koch and Most and their team of researchers used a pig model—this type more closely resembles human physiology, function and anatomy—to determine the effectiveness and safety of the S100A1 gene therapy. Researchers were also able to administer it with certified catheters and delivery routes, just as a human patient would receive it. “We’ve shown its effectiveness in the lab. It worked in mice and rats, then pigs and now it’s ready for humans,” Dr Most adds.

Heart failure was induced in the pigs, and at 14 weeks showed significantly decreased S100A1 levels. Treatment, however, with the gene therapy prevented and reversed development of heart failure by restoring the S100A1 protein levels or getting them above normal.

“This therapy gets to the core of the disease,” said Dr. Koch, who received the “Outstanding Investigator Award” for 2011 by the International Society for Heart Research for his work in heart failure gene therapy. “They are not just beta blockers or ancillary drugs, which only block the damage. This therapy makes the heart beats stronger and overcomes the damage from previous heart attacks. It’s the next great thing in heart failure.”

This is the final set of preclinical data needed to apply for investigational new drug status with the U.S. Food and Drug Administration and advance to a phase I clinical trial.

Researchers say one of the next steps is to find industry or private partners to help fund the work, as well as recruit eligible patients to enroll in the clinical trial.

“With National of Institutes of Health money in jeopardy, this work could be translated faster with funds from other sources,” said Dr. Koch. “It could fund both ongoing research with other targets using our translational roadmap and to take this particular target for heart failure into humans.”

Fox Chase Researchers Identify New Mechanism Used by Cells to Reverse Silenced Genes

Scientists at Fox Chase Cancer Center have discovered a new mechanism used by cells in the body to turn on silenced genes. This process is critical in preventing the development of cancer—suggesting the possibility of new therapies that might target the specific changes underlying the disease. The findings will be published online in the journal *Cell*.

The process investigated by [Alfonso Bellacosa, MD, PhD](#), associate professor at Fox Chase, and his colleagues, is called methylation, in which the cell chemically tags genes to turn them off. More specifically, the cell silences a gene by adding a chemical compound known as a methyl group; without that methyl group, the gene remains active.

It's a process of great interest to scientists, Dr. Bellacosa explains, because methylation is a key part of normal gene regulation – but, when it silences the genes that normally suppress tumors, it results in cancer. Indeed, some cancer drugs work by demethylating—meaning, removing methyl groups from DNA. But those drugs will demethylate DNA non-specifically, he says, causing side effects and other problems.

Now, Dr. Bellacosa and his team present the first direct evidence that demethylation can be, in fact, an active process, controlled by a specific protein – along with clues about how to act on it in a targeted way.

The researchers found that one protein called thymine DNA glycosylase or TDG—known to help repair DNA—is also responsible for removing methyl groups from DNA. Studies with mice that lacked TDG activity indicated the gene was needed for survival. Looking closer at the mouse embryos that didn't

survive, they saw that the methylation was all awry – genes that would normally be demethylated weren't, and remained silenced.

TDG needs a second protein to demethylate DNA, says Dr. Bellacosa—so future therapies might be devised to direct this machinery to turn on specific anti-cancer genes, for instance. “Since we now know there are proteins that actively affect demethylation, then we can imagine a new type of cancer therapy that demethylates specific genes. We would have a more precise and more targeted type of therapy.”

What's also exciting, explains Dr. Bellacosa, is the discovery that the cell uses tools that normally repair DNA for a very different purpose: reversal of gene silencing by demethylation. “It's a totally new concept – that DNA repair has this additional new function.”

Beside cancer, this knowledge may also be applied to other diseases with alteration of methylation. He cautions, however, that scientists still have not figured out how to target therapy to specific genes, so any benefits to this discovery are years away. “This is a very fundamental study that gets at the process by which genes are turned on or turned off,” he says. “We may be several years away from taking full advantage of this new knowledge. But we will get there.”

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 education to international physicians, administrators and other practitioners. PIM is owned by the Fox Chase Cancer Center, Temple University Hospital, and Thomas Jefferson University Hospital. It holds service agreements with the Alfred I. duPont Hospital for Children, St. Christopher's Hospital for Children, Kennedy University Hospitals, Wills Eye Institute and Jefferson Home Care Network. As the international department of several Philadelphia-area hospitals, international patients gain access to physicians and hospitals rated among the best in the world through one telephone call. You can reach PIM by calling 1-215-563-4733; fax, 1-215-563-2777; or e-mail, physicians@philadelphiamedicine.com. You can find out more about PIM through its Website at www.philadelphiamedicine.com.