

## PHILADELPHIA INTERNATIONAL MEDICINE® NEWS BUREAU

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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.*

### **Temple University Hospital Expands its Transplant Program**

**Philadelphia** – Temple University Hospital has added pancreas transplant surgery to its abdominal organ transplantation services after receiving approval from the United Network for Organ Sharing (UNOS) and the Pennsylvania Department of Health.

Considered the only potential cure for Type 1 diabetes, pancreas transplants can help greatly enhance the quality of life for many of Temple's kidney transplant patients.

"A pancreas transplant can help preserve a new kidney by restoring normal sugar control and eliminating the need for insulin injections in patients with type I diabetes," said John A. Daller, MD, PhD, director of the Abdominal Organ Transplant Program. "It can also arrest or reverse many co-morbidities often associated with diabetes – such as vascular disease."

The new pancreas transplant team will be lead by Andreas Karachristos, MD, PhD, transplant surgeon and Serban Constantinescu, MD, PhD, transplant nephrologist.

Temple surgeons have already listed their first two patients on the national organ transplant waiting list.

A regional leader in transplantation services, Temple University Hospital performs transplants of the following solid organs: kidneys, lungs, hearts and pancreas. Since 1989, more than 1,500 transplants have been performed at Temple University Hospital.

### **Fox Chase Cancer Center Enters Partnership To Advance First Clinical Trials Of Novel Fluorescence Molecular Imaging Technologies**

Fox Chase Cancer Center and VisEn Medical announced a partnership to advance Phase I clinical trials of one of VisEn Medical's "smart" fluorescence activatable imaging agents to enable physicians to identify and characterize early stage disease in oncology patients. Olympus

Medical Systems Corp. will provide paired fluorescence laparoscopic imaging systems to enable the detection and evaluation of ProSense™ highlighted tumors in patients in the trials. The clinical trials will initially focus on ovarian cancer and are planned to begin in 2009 at Fox Chase Cancer Center.

To actively manage this potential or perceived conflict of interest, Fox Chase contracted with bioethicist Arthur L. Caplan, PhD, director of the Center for Bioethics at the University of Pennsylvania, for counsel. On the advice received, Fox Chase Cancer Center will take the following steps to manage any potential or perceived conflict of interest associated with the partnership:

- Utilize an independent Institutional Review Board (IRB) to review the research protocols and determine whether such research protocols adequately protect the human subjects
- Utilize an independent Data Safety Monitoring Board to review the data from the research
- Utilize an independent biostatistician to review the data from the research
- Find a Principal Investigator (PI) at the Center who has no fiduciary or management role at the Center
- Separate clinical and research discussions from business discussions between the Center and VisEn
- Separate clinical and research discussions from business discussions within the Center
- Disclose institutional financial interest to human subjects prior to obtaining consent to participate in the research
- Ensure that management oversight of the research is limited to only that extent necessary and consistent with the way management oversees all other research

Importantly, because Fox Chase Cancer Center's current president and CEO, Michael V. Seiden, MD, PhD, was involved in research related to ProSense while at Massachusetts General Hospital prior to his appointment at Fox Chase and maintains an ongoing interest in this research, he will act solely as the Center's CEO and will have no role in the continuing research beyond his normal role in overseeing the Center's research enterprise.

### **Jefferson, Ohio State Team Find Gene Signature Profile for Metastasis**

A common signature of tiny, specific pieces of non-coding genetic material known as microRNAs (miRNAs) may be directly involved in the spread of cancer to other parts of the body. Researchers at the Kimmel Cancer Center at Jefferson in Philadelphia and Ohio State University Medical Center in Columbus have identified such a signature, made up mostly of overexpressed miRNAs. The findings, reported at the annual meeting of the American Society of Clinical Oncology in Chicago, may represent a novel diagnostic tool in characterizing gene targets in metastatic cancer.

MiRNAs play a number of roles in biological regulation, including development and cell differentiation. When damaged, they can contribute to cancer by either turning on cancer-causing genes or by inhibiting tumor-blocking genes. The ways that MiRNAs are expressed have been used to profile tumor types in humans.

Because miRNAs are involved in cancer development and progression, scientists led by Raffaele Baffa, MD, associate professor of Urology at Jefferson Medical College of Thomas Jefferson University and Anne Rosenberg, MD, clinical professor of Surgery at Jefferson Medical College, in collaboration with a research team led by Carlo Croce, MD, director of Ohio State University's human cancer genetics program and professor and chair of the Department of Molecular Virology, Immunology and Medical Genetics, wanted to see if there was a specific gene signature that characterized metastasis. Using microarray technology to test many genes at once, they compared different organs – breast, lung, bladder and colon – to see if miRNAs were either increased or decreased in activity. They analyzed the miRNAs in both primary and metastatic tumors from 43 patients, including 13 breast cancers, 10 lung cancers, 10 bladder urothelial cell cancers and 10 colon cancers.

They discovered that some miRNAs are organ-specific. “Some are increased and decreased specifically in certain organs, telling us that these are commonly involved in the metastatic process,” says Dr. Baffa.

Because of the ups and downs in miRNA activity, “many miRNAs that are involved in metastasis are not necessarily specific for one organ, but rather are related to the cell acquiring the ability to spread.” The researchers also found a direct association between the alterations in some miRNAs and changes in target proteins.

Many of the miRNAs that were overexpressed in primary tumors had previously been

reported, he says, confirming that miRNA signatures are useful in classifying tissue origin. “Now we have to identify which of the miRNAs in the signature are the most important in facilitating metastasis,” Dr. Baffa says.

### **Penn Researchers Find Lou Gehrig’s Disease Protein Found Throughout Brain, Suggesting Effects Beyond Motor Neurons**

Two years ago researchers at the University of Pennsylvania School of Medicine discovered that misfolded proteins called TDP-43 accumulated in the motor areas of the brains of patients with amyotrophic lateral sclerosis (ALS), or Lou Gehrig’s disease. Now, the same group has shown that TDP-43 accumulates throughout the brain, suggesting ALS has broader neurological effects than previously appreciated and treatments need to take into account more than motor neuron areas.

“The primary implication for ALS patients is that we have identified a molecular target for new therapies,” says co-author John Q. Trojanowski, MD, PhD, director of Penn’s Institute on Aging. “The other implication is that new therapies for ALS now need to go beyond treating only motor neurons.”

Traditionally, ALS has been diagnosed based on muscle weakness and neurodegeneration of the upper and lower motor neurons that extend from the motor cortex to the spinal cord and brainstem motor neurons, which directly innervate voluntary muscles. For example, if you want to wiggle your big toe, the signal travels from the motor neuron in the cortex at the top of your head to a synapse on the lower spinal cord motor neurons in the lower back, which, in turn transmit the “wiggle” command by sending a signal to the muscles that move your big toe. Patients with ALS cannot wiggle their big toe or complete other voluntary muscle movements, including those carried out by their other extremities and eventually, by the diaphragm that moves air in and out of their lungs.

### **Women Who Gain Excessive Weight During Pregnancy More Likely to Have Overweight Children**

Children of mothers who gain more than the recommended amount of weight during pregnancy are more likely to be overweight at age seven, say researchers from The Children’s Hospital of Philadelphia and the University of Pennsylvania School of Medicine, in a study published in the American Journal of Clinical Nutrition. Children of mothers who are obese prior to pregnancy and gain excessive weight are at the greatest risk for overweight.

“The earliest determinants of obesity may operate during intrauterine life, and

gestational weight gain may influence the environment in the womb in ways that can have long-term consequences on the risk of obesity in children,” said study leader Brian Wrotniak, PT, PhD, of The Children’s Hospital of Philadelphia and the University of Pennsylvania. “Adherence to pregnancy weight gain recommendations may be a new and effective way to prevent childhood obesity, since currently almost half of U.S. women exceed these recommendations.”

The researchers reviewed data from a cohort of 10,226 participants enrolled between 1959 and 1965 in the multicenter National Collaborative Perinatal Project. It was initiated to investigate risk factors for cerebral palsy at 12 U.S. sites. This study looked at the children born at full-term gestation, and researchers evaluated socioeconomic and growth data during gestation, at birth and at age 7. Maternal data were collected at enrollment by using a questionnaire that included maternal pre-pregnancy weight, age and race. Maternal weight and height were measured at the time of delivery to determine gestational weight gain - the difference between the measured weight at delivery and the reported pre-pregnancy weight.

According to the Institute of Medicine (IOM), which makes recommendations for weight gain during pregnancy, the amount of weight women should gain during pregnancy depends on the mother’s weight status before pregnancy. Women at a healthy pre-pregnancy weight are encouraged to gain 25 to 35 pounds, while women who are overweight should stay between 15 to 25 pounds. Women who are underweight should gain more weight during pregnancy — between 28 and 40 pounds.

Of the women studied by the researchers, 11 percent gained excessive weight, 24 percent gained adequate weight and 65 percent gained insufficient weight. Today, said the researchers, these proportions would be very different, with almost one in two women gaining more weight than recommended during pregnancy.

The authors say that encouraging pregnant women to adopt healthy eating practices and engage in aerobic physical activity could help them achieve appropriate weight gain and also help prevent obesity in their children. They add that benefits would likewise result from healthy eating and exercise before becoming pregnant, as well as reducing postpartum weight retention before a subsequent pregnancy.

Using the IOM guidelines, children whose mothers exceeded the recommended weight gain were 48 percent more likely to be overweight than children whose mothers stayed within the recommended weight gain. The risk of overweight was similar for children born of women

who gained insufficient weight compared with mothers who gained appropriate weight during pregnancy.

The researchers add that more research is necessary to clarify whether the association between greater gestational weight gain and increased odds of overweight in offspring is causal, and whether it exists in today's environment of increasing obesity.

Dr. Wrotniak's coauthors were Justine Shults, Ph.D., of the Center for Clinical Epidemiology and Biostatistics (CCEB) at the University of Pennsylvania School of Medicine; Samantha Butts, M.D., M.S.C.E., of the Division of Infertility and Reproductive Endocrinology at the University of Pennsylvania School of Medicine; and Nicolas Stettler, M.D., M.S.C.E., of Children's Hospital and the Penn CCEB.

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