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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.

Thomas Jefferson University Hospital Designated Live Donor Liver Transplant Center by UNOS

Thomas Jefferson University Hospital has been designated a Live Donor Liver Transplant Center by the United Network for Organ Sharing (UNOS), the organization that administers the nation's policies on organ transplantation and procurement.

Cataldo Doria, MD, PhD, FACS, director of the Division of Transplantation at Thomas Jefferson University Hospital (TJUH), and associate professor of surgery, Jefferson Medical College (JMC) of Thomas Jefferson University, will lead Jefferson's LDLT team as primary surgeon. The UNOS-approved team will also comprise Stephen P. Dunn, MD, division chief of general surgery and solid organ transplant surgery at A.I. duPont Hospital for Children, and professor of surgery and pediatrics at JMC; Carlo Ramirez, MD, transplant specialist at TJUH, and assistant professor of surgery at JMC; and Adam Frank, MD, transplant specialist at TJUH, and assistant professor of surgery at JMC.

"We are extremely pleased to be able to offer living donor transplantation as another leading-edge, potentially life-saving treatment to our liver patients here at Jefferson," said Dr. Doria. "LDLT does not replace traditional deceased donor transplantation, but it will allow us to transplant more patients from the UNOS waiting list."

At this moment, there are approximately 17,000 people on the UNOS liver transplant waiting list, and the numbers are steadily increasing due primarily to cirrhosis, or scarring of the liver, which is most

commonly cause by Hepatitis C. Advancements in surgical techniques, immunosuppressant drugs, and protocols have also made more patients candidates for liver transplantation than ever before. However, only about one-third of these patients will receive deceased donor organs.

“Adult-to-adult living donor transplantation provides another, extraordinary option to these patients with end-stage liver disease,” added Dr. Doria.

LDLT is a procedure in which a healthy, living person donates a portion of his or her liver to another individual with end-stage liver failure. Up to 70 percent of the donor’s liver may be safely removed and transplanted into the recipient, immediately after the recipient’s diseased liver has been entirely extracted. After separation and transplantation, the two portions of the liver regenerate to nearly normal size for both the donor and the recipient. (The liver is the only organ in the body capable of fully regenerating itself.)

Thomas Jefferson University Hospital has a tradition of outstanding success in the treatment of patients with all forms of acute and chronic liver disease. Initiated in 1984, Jefferson’s is the longest continuously active Liver Transplantation program in the Philadelphia area. Today, Jefferson’s team offers patients a comprehensive approach by combining a range of dedicated specialists who help each individual with their medical, psychological, and financial needs—step-by-step, from initial evaluation, through surgery and recuperation.

For Children With Heart Disease, a Risk of Attention and Behavior Problems

Philadelphia – Researchers from The Children’s Hospital of Philadelphia found that for children who had undergone surgery for complex congenital heart disease as newborns, there was a higher risk for inattention and hyperactivity.

The researchers, who reported their findings in the April issue of *Pediatrics*, studied a group of 109 children, aged five to 10, who had undergone cardiac surgery for complex congenital heart disease at Children's Hospital when they were newborns. Of that group, 53 children--nearly half of them--were receiving remedial services at school, and 15 percent were in special education classrooms.

Based on questionnaire responses from their parents and teachers, although the majority of the children with CHD scored in the normal range, the rates of high-risk scores for inattention and hyperactivity were three to four times greater than those found in the general population.

Previous studies at The Children's Hospital of Philadelphia and other centers found that school-aged children with complex CHD tended to have normal cognitive abilities but were at risk for problems in visual and motor skills, as well as impairments in speech, language and executive functioning (executive functioning refers to capacities for attention, planning, decision-making and problem-solving).

Each year, over 10,000 newborns in the U.S. have CHD severe enough to require surgery before they are one year of age. Advances in medical and surgical treatments have steadily improved survival rates for even the most complex conditions. One such condition is hypoplastic left heart syndrome, in which a

severely underdeveloped left ventricle is unable to pump enough blood to the body. A series of three surgeries during the newborn and infant period is needed to correct this heart defect. Children with this and several other congenital heart conditions were included in the study.

"As survival rates have improved," said the research team, "the important longer-term issue is quality of life for patients and their families as they reach school age and beyond. We hope our findings will help raise awareness among parents, teachers and physicians about the children's risk of neurodevelopmental problems." The next step for researchers is to conduct larger, multicenter studies, with more formalized diagnostic tools, and to develop formalized follow-up protocols for these children. Such follow-up programs are currently being designed at Children's Hospital.

Survey Names Fox Chase Cancer Center a Top Spot for Postdocs to Stop

A survey released by *The Scientist*, a prominent life sciences magazine, places Fox Chase Cancer Center among the top ten best places to work for postdoctoral researchers. Fox Chase was the top ranked institution in the Northeast region and ranked seventh overall in the U.S.

Postdocs gave Fox Chase high marks when asked about factors relating to remuneration and compensation, quality and breadth of training, funding, institutional factors, and quality of family and personal life. Their positive impressions of Fox Chase as an employer mirror the high value the organization places on postdoctoral contributions to its research programs.

"At Fox Chase, we recognize that postdocs are our lifeblood," says Maureen Murphy, Ph.D., director of postdoctoral training programs at Fox Chase Cancer Center. "Unlike other universities and research institutions, our postdocs do not compete with graduate, medical and undergraduate students for attention, training and resources."

The survey yielded responses from 3,086 postdocs at 82 U.S. institutions and 17 international institutions. Respondents were asked to assess their postdoc experience according to 44 criteria in 11 different areas by scoring positive statements. Answers were scored on a 1 to 5 scale with 5 = "Strongly agree," 1 = "Strongly disagree" and 3 = "Neither agree nor disagree." The criteria included statements relating to the lab's principal investigator, colleagues, department or division and the institution.

According to the survey, Fox Chase postdocs gave high ratings to the relationships they have developed with Fox Chase faculty, responding positively to questions regarding mentorship and communications. "I think we are justifiably proud of how we treat our postdocs and this survey reflects that," Murphy says.

"By choosing Fox Chase, our postdocs have made an investment in us as the place where they want to begin their careers," Murphy says. "We try to reward this investment by creating an environment where they can enrich their professional lives – by providing unique resources such as seminars and workshops – along with their personal lives – by providing benefits, such as housing and daycare."

Penn Researchers Discover 'Modus Operandi' of Heart Muscle Protein

Researchers at the University of Pennsylvania School of Medicine have discovered that a protein called leiomodulin (Lmod) promotes the assembly of an important heart muscle protein called actin. What's more, Lmod directs the assembly of actin to form the pumping unit of the heart. The findings appear in *Science*.

"Very little was known about Lmod when we began this study," says lead author Roberto Dominguez, PhD, associate professor of physiology. "It appeared that this protein was present in muscle cells but this had not been demonstrated directly and nobody knew what it did," explains Dominguez. "We compared the amino acid sequence of Lmod with the sequence of another protein called tropomodulin [Tmod] that was already known to bind actin filaments in muscle cells. We found that one part of Lmod was very similar to Tmod, but Lmod was a bigger protein than Tmod and contained unique features that made us suspect that it could assemble the actin filaments of the heart muscle. This is exactly what we found."

The results answer a question that scientists studying the heart have long asked: What controls the assembly of the pumping unit of the heart?

Actin is the most abundant protein in most animal cells and forms long polymers, or filaments, that make up the cell skeleton. In the cells that make up muscles and the heart, interactions of actin filaments with motor proteins produce the contractions that pump blood through the body.

Actin spontaneously forms polymers in test tubes, but living cells use nucleator proteins to control the time and place where actin filaments form. "For a long time, physiologists have wondered what serves as the nucleator protein in cardiac muscle cells," says co-author Professor Thomas Pollard, PhD, of Yale University. "It was very satisfying after all these years to discover that Lmod can serve as the nucleator protein to initiate the forming of actin polymers in heart muscle cells."

Lmod also directs actin filaments to the sarcomere, the part of the heart that controls contractions or pumping. When Lmod was knocked down in cardiac muscle cells by an RNA silencing technique, the sarcomeres became completely disorganized and could not direct muscles to contract.

Proper localization of Lmod in heart cells is critical, because even moderately elevated levels promote the formation of abnormal actin bundles in the nuclei of cardiac muscle cells where actin does not belong. A similar disorganization of actin bundles is characteristic of a disease of skeletal muscle weakness called intranuclear rod myopathy. Although this disease is caused by a mutation in a skeletal muscle-specific actin gene, the similarity in appearance suggests that mutations in Lmod could cause the same type of disease in cardiac muscle cells.

The Penn team is currently studying how the heart regulates the level of Lmod and how Lmod might be relevant to cardiac muscle disease. In addition, the team is attempting to crystallize Lmod in order to study its structure directly.

Malgorzata Boczkowska of Penn and David Chereau of Boston Biomedical Institute are co-first authors of this study. Other key contributors are Pekka Lappalainen and Aneta Skwarbek-Maruszczyńska of the University of Helsinki; Ikuko Fujiwara of Yale; David B. Hayes of Boston Biomedical Institute; and Grzegorz Rebowski of Penn. The study was supported by grants from the National Heart Lung and Blood Institute and the National Institute of General Medical Sciences.

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