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PHILADELPHIA INTERNATIONAL MEDICINE® NEWS BUREAU

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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.

Temple University Hospital is One of the First in the Region to Implement "Bio-Artificial" Liver

Philadelphia — Temple University Hospital is among a select group of hospitals in the United States to use an investigational "bio-artificial" liver that can potentially replicate the organ's complex functions by passing a patient's blood through an external device containing live liver cells.

The investigational device, called an ELAD (Extracorporeal Liver Assist Device®), may help patients with liver failure become healthy enough for transplant, or, possibly, extend the lives of those who are unable to receive a transplant.

Temple successfully used the "bio-artificial" liver on a female patient on February 7. The patient is scheduled to be discharged later this week, according to Santiago J. Munoz, MD, medical director of Temple University Hospital's Liver Transplantation Program and the hospital's principal investigator for the Phase II/III clinical trial.

If proven successful, ELAD® therapy can help doctors address one of the main challenges of liver failure: keeping the patient healthy enough to undergo transplant surgery until a compatible donor organ can be found. In cases where the liver damage is less severe, the hope is that an ELAD® intervention may be able to take some of the load off the liver, enabling it to regenerate on its own.

Unlike kidney failure, in which patients can maintain organ function through dialysis, no comparable intervention has been successfully developed for the liver because of the complex series of functions the organ carries out.

"The idea behind the ELAD® has existed for more than two decades," said Dr. Munoz. "Earlier devices did little more than pass blood through a filter, which, at most, could only attempt to clean the

blood. For the first time, new technology allows us to use actual living cells to not only remove toxins, but also perform higher liver functions such as the synthesis of proteins.”

The ELAD[®] is connected to a patient via a major blood vessel, such as the femoral vein in the leg or the jugular vein in the neck. Blood is processed through a series of four cartridges containing about a pound (440 grams) of human liver cells, which can perform the liver's intricate functions outside the patient's body.

The ELAD's[®] specialized cells were originally harvested from a liver cancer tumor, because, unlike ordinary liver cells, these “immortal cells” have the ability to reproduce indefinitely while still retaining their functionality. The cells are shielded from the patient by a series of membrane filters, which have been designed to allow only the patient's blood and liver by-products to pass through.

Temple is one of 17 sites in the United States actively enrolling patients in this clinical trial.

Penn Researchers Find Genetic Link to Leukemias with an Unknown Origin

Although leukemia is one of the best studied cancers, the cause of some types is still poorly understood. Now, a newly found mutation in acute myeloid leukemia patients could account for half of the remaining cases of adult acute leukemia with an unknown origin.

“The molecular biology of leukemia has been studied for the last 20 years and we thought we had found most of the common genes for leukemia,” comments senior author Craig B. Thompson, MD, director of the Abramson Cancer Center of the University of Pennsylvania. “Now we’re able to point to a distinct type of mutation for half of the remaining leukemias for which we didn’t know the cause and between one-quarter and one-third of leukemias in older patients.” The findings are described online this week in *Cancer Cell*.

Using samples from a Penn tissue bank of acute myeloid leukemia (AML), Dr. Thompson and colleagues found that AML patients have increased levels of a molecule called 2HG. AML is a quick-moving, deadly cancer that starts in the bone marrow and soon moves into the blood. The increased amounts of 2HG stem from a mutation in one of two related metabolic enzymes, IDH1 or IDH2.

Screening for elevations in 2HG in the tissue bank, the team found that *IDH1* and *IDH2* mutations are observed in over 23 percent of the AML patients studied. A shared feature of cancer-related *IDH* mutations is increased production of 2HG.

What’s more, the *IDH* gene mutations are the first known cancer mutations that result in the creation of a protein with a new enzymatic activity. Most cancer-causing mutations make the mutated protein either overactive or inactive in performing its normal function. In contrast, the mutations in the IDH proteins give these enzymes the blueprint to create a new molecule not normally produced by cells.

Interestingly, the researchers also found that *IDH2* mutations are more common than *IDH1* mutations in AML.

Other gene-related causes of leukemia include breaks and reformations in chromosomes called translocations.

The ease with which the researchers were able to detect *IDH* mutations in tumor samples, and the ability to identify patients with these mutations due to the presence of increased 2HG gives hope for better detection of AML and suggests that blocking the production of 2HG might reverse the ability of the mutant genes to maintain the leukemic cells.

“If we’re able to block tumors from producing 2HG, perhaps we would be able to stop the patient’s leukemia,” states Dr. Thompson. Exactly why 2HG production leads to leukemia is not yet clear. It does not appear to act like other cancer-causing metabolites which induce further mutations. One possibility raised in the manuscript is that 2HG accumulation may block the ability of the leukemic cells to differentiate into normal blood cells.

The research was funded in part by grants from the National Cancer Institute and the Abramson Family Cancer Research Institute.

Jack Jallo, MD, PhD, FACS, Joins the Department of Neurological Surgery at Jefferson

Jack Jallo, MD, PhD, FACS, recently joined the Department of Neurological Surgery at Jefferson Hospital for Neuroscience, and was named a professor at Jefferson Medical College of Thomas Jefferson University.

Dr. Jallo received his medical degree from The George Washington University School of Medicine & Health Sciences in Washington D.C. in 1990, where he also earned a bachelor of science degree in 1986. After receiving his medical degree, Dr. Jallo spent the next seven years of medical training at Temple University Hospital in Philadelphia, including a Fellowship in Neurotrauma and Critical Care from 1996-1997. While at Temple, Dr. Jallo also earned a PhD in Physiology in 2003.

Prior to joining Jefferson, Dr. Jallo was in the Department of Neurosurgery at Temple from 1997-2009. While there, he served as director of Neurosurgical Intensive Care, director of Functional Neurosurgery, and director of the residency program in Neurosurgery. In 2003, Dr. Jallo was promoted to associate professor of the Department of Neurosurgery, and was given a second appointment as an associate professor in the Department of Orthopedics Surgery.

Dr. Jallo is board certified by the American Board of Neurological Surgeons and is a Fellow of the American College of Surgeons. He is also a member of several national honor societies including Alpha Omega Alpha and Phi Beta Kappa. He is a member of the American Association of Neurological Surgeons, Congress of Neurological Surgeons and the American Medical Association. Locally, Dr. Jallo

is a member of the Philadelphia County Medical Society, the Pennsylvania Medical Society and the Pennsylvania Neurological Society. Dr. Jallo has an extensive list of published research in leading medical journals, authored and co-authored 18 book chapters, and edited two text books of neurosurgery. His research has been funded through industry grants and through the National Institutes of Health.

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