

Pioneering research aims to improve the number and quality of donor livers for transplantation



More than three decades after progressing from an experimental therapy to an accepted clinical treatment, liver transplantation has become a common procedure in the United States with more than 6,000 surgeries occurring each year. A number of advances have led to higher survival rates, including refinement of surgical procedures and the efficacy and strategic use of immunosuppressant medications. Despite these gains, work continues to further improve survival rates, lower organ rejection rates and increase the number of transplant candidates who receive livers.

More than 16,000 Americans are on a waiting list for a liver transplant with roughly 10 percent of candidates dying before a liver becomes available. A number of factors have contributed to the disparity between donor organs and transplant candidates. More donor organs today are obtained from an aging population and thus may be of lower quality than organs from younger and healthier donors. Approximately 10 to 15 percent of donor livers are discarded prior to transplant due to inferior quality. Moreover, the demand for liver transplantation has soared as the qualification criteria have expanded to include more conditions that were previously excluded from consideration.

Expanding the pool of viable donor livers

“About 90 percent of liver transplant patients survive more than one year,” says Jerzy Kupiec-Weglinski, MD, PhD, director of the Dumont-UCLA Transplantation Center. “But problems still exist. Many thousands of patients die on the waiting list because they cannot get a transplant.”

Long-term failure rates have improved little over the past two decades, he adds. Ischemia-reperfusion injury impacts failure rates, particularly in organs from older or sicker donors. “What we’re trying to do is use the time between organ retrieval and transplantation to rejuvenate the organ to make it better, to prevent the ischemic damage to the organ,” Dr. Kupiec-Weglinski says.

“At UCLA we have a very strong interaction between the academic and clinical enterprises. The department recognizes the importance of basic and translational research. We have a proven record of taking a novel therapeutic idea and translating it successfully from the bench to the bedside. As a current example, we are at the forefront of donor liver rejuvenation research — applying therapeutic techniques to donor organs that would currently be declined for use due to poor quality.”

At UCLA, which has the largest program in liver transplantation in the world, pioneering research is under way aimed at extending the number of donor livers by treating suboptimal organs prior to transplantation and by preventing cellular damage to donor organs during the sensitive time period between retrieval and transplantation.

Understanding the nature of suboptimal organs

Ischemia-reperfusion injury (IRI) in the liver is a major complication in transplantation surgery, responsible for a significant rate of both short-term and long-term complications. This under-studied problem is thought to entail two interrelated phases: local ischemic insult followed by inflammation-mediated reperfusion injury. The cascade of cell damage can ultimately lead to the death of hepatocytes and poor liver function.

UCLA researchers have performed in vitro cell culture studies to investigate the signaling pathways involved in IRI. The findings suggest that preventing activation of T lymphocytes and macrophages is important to promoting optimal hepatocyte function and liver quality. Specific modalities, including the use of monoclonal antibodies, have been developed that upregulate specific signaling pathways preventing IRI while promoting cell protection. Additional studies at UCLA and elsewhere now suggest that upregulation of the SIRT1 pathway is a promising strategy to rejuvenate the donor organ through DNA repair.

Ongoing research is centered on donor livers that have been deemed unsuitable for transplantation due to inferior quality. The organs undergo perfusion with a SIRT1 activator over a six- to eight-hour time frame to assess whether such treatment rejuvenates the organ to a degree that it can be transplanted. The goal of the research is to assess whether organ rejuvenation increases the number of livers available for transplantation and improves both short-term and long-term survival rates.

Translational research

Ischemic injury and related inflammation is a common culprit in many disease processes, including the rejection of other types of transplanted organs and in cardiovascular disease. UCLA researchers are exploring whether treatments to curtail damage in donor livers may apply to preventing cell death in other medical conditions.

UCLA has recently been awarded two National Institutes of Health grants as well as a grant from the W.M. Keck Foundation to pursue liver transplantation rejuvenation. As the most experienced liver-transplantation program in the Western United States, UCLA serves patients from California and throughout the Southwest and acts as a tertiary referral center for other transplant programs faced with particularly challenging cases. Since its inception in 1984, UCLA surgeons have performed more than 5,500 liver transplants. The program's innovations have facilitated life-saving expansion of the organ pool by refining indications for donor-recipient matching, the use of split donor livers and living donation, as well as ongoing work to extend the criteria for donor livers.

Participating Physicians

Ronald W. Busuttil, MD, PhD

Chairman, Department of Surgery
Chief, Division of Liver and Pancreas Transplantation

Liver Transplant Researchers

Jerzy Kupiec-Weglinski, MD, PhD

Professor, Surgery, Pathology and Laboratory Medicine

Director, Dumont-UCLA Transplantation Research Center

Haofeng Ji, MD

Adjunct Assistant Professor, Department of Surgery, Liver and Pancreas Transplantation

Bibo Ke, MD

Adjunct Associate Professor, Department of Surgery, Liver and Pancreas Transplantation

Yuan Zhai, PhD

Associate Professor, Department of Surgery, Liver and Pancreas Transplantation

Adult Liver Transplant — Surgery

Vatche G. Agopian, MD

Elaine Cheng, MD

Douglas Farmer, MD

Fady M. Kaldas, MD

Gerald S. Lipshutz, MD, MS

Hasan Yersiz, MD

Ali Zarrinpar, MD, PhD

Adult Liver Transplant — Hepatology

Gina Choi, MD

Francisco A. Durazo, MD

Mohammed El Kabany, MD

Steven-Huy Han, MD

Sammy Saab, MD, MPH, AGAF

Contact Information

Department of Transplantation Services
Division of Liver and Pancreas Transplantation

Dumont-UCLA Transplant and Liver Cancer Centers

Pfleger Liver Institute
200 UCLA Medical Plaza
Los Angeles, CA 90095

(310) 825-8138

transplants.ucla.edu