



University of Michigan
Health System

THE MICHIGAN DIFFERENCE

Transplant Center
University of Michigan
3868 Taubman Center
Ann Arbor, MI 48109-5391
Phone: 734-936-7491



New Beginnings
New Beginnings

Michigan Transplant News

New Beginnings

FALL 2008

INSIDE

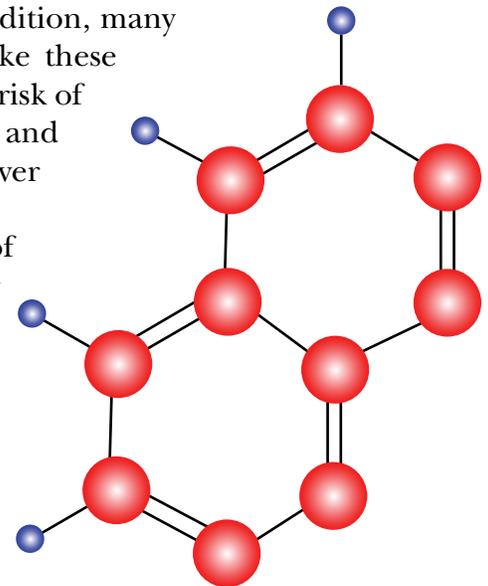
- Developing New Drugs 2
- Liver Tumor Clinic 3
- Leadership Changes in
Transplant Programs..... 4
- UM Heroes! 5
- Zingerman's – Faculty as
Servers and Busboys 6
- Remembering Heroes 7
- Michigan Donor Drive 8
- Robert Merion, M.D.
Receives Award 9
- Merion paves way for
paired organ donation.... 10

New Medications for Hepatitis C

Chronic hepatitis C virus (HCV) infection has emerged as a leading cause of cirrhosis and liver cancer in the United States and other parts of the world. Therefore, it is not surprising that HCV related liver disease has become a leading reason that patients have liver transplants. Almost half of all liver transplant patients in the United States have HCV. Although outcomes with liver transplantation continue to improve, patients with HCV almost always develop recurrent viral infection following transplantation identifiable by a blood test. The consequences of recurrent HCV vary widely but transplant recipients are at increased risk of developing more severe inflammation and scar tissue formation compared to other HCV patients.

The current approach to management of liver transplant recipients with recurrent HCV is to carefully balance the side effects of anti-rejection medications verses the risk of recurrent disease. Anti-rejection medications may include steroids, Cellcept®, Imuran®, tacrolimus or cyclosporine, or a variety of others. Since 2002, our approach has been to use Pegylated interferon injections given once a week in combination with daily antiviral tablets of ribavirin in highly selected patients with moderate to severe recurrent HCV. However, both of these medications have a number of potentially serious side effects that may require the doctor to lower the dose or stop the medicine. Not surprisingly, the success rate of antiviral treatment is lower in transplant recipients compared to non-transplant patients. In addition, many liver transplant recipients are unable to take these drugs at all and Interferon may increase the risk of rejection. Therefore, there is a need for safe and effective medications that can be given to liver transplant recipients with recurrent HCV.

Since the molecular structure of the Hepatitis C virus was identified over 15 years ago, a number of new targets for drug development have been discovered. Current research is directed toward developing drugs that inhibit certain parts of the machinery that allows the virus to



Developing New Drugs

New drugs undergo extensive testing in humans that includes at least three phases of testing before they are reviewed and approved for general use by the US Food and Drug Administration. New drugs are usually developed in laboratories and tested extensively in laboratory animals and model systems prior to being given to people. Clinical trials often include three separate phases. Phase 1 testing is done in small numbers of patients (i.e. < 100) to identify potential side effects and the amount of medication that is safe to give. Phase 2 testing is done in moderate sized studies of patients (i.e. 100 to 500 patients) to establish effectiveness of the medication and to further evaluate its safety. Phase 3 testing is done in larger studies (i.e. 500 to several thousand patients) to establish both the benefit to the patient and safety of the medication with prolonged use compared to commonly used treatments.

Table 1- Drugs in Development for Hepatitis C in 2008

DRUGS	STATUS
Protease Inhibitors	
Telaprevir (VX-950)	Phase 2 with Pegylated Interferon & ribavirin
Boceprevir (SCH-503034)	Phase 2 with Pegylated Interferon & ribavirin
TMC435350	Phase 1
Polymerase Inhibitors	
R1626	Phase 2 with Pegylated Interferon & ribavirin
R7128	Phase 2 with Pegylated Interferon & ribavirin
VCH-759	Phase 1 – Diarrhea side effect
GS-9190	Phase 1
Valopacitibine (NM283)	Discontinued due to side effects
Immunomodulatory Agents	
Albinterferon	Phase 3 with ribavirin
Controlled release interferon	Phase 2
GI-5005 (Immunotherapy)	Phase 1
Silibinin (Silymarin)	Phase 1 with Pegylated Interferon
Other Antiviral Agents	
Nitazoxanide	Phase 2 with pegylated interferon & ribavirin
Debio 025	Phase 1

For more information about clinical trials, you may wish to visit the following website: www.clinicaltrials.gov

New Medications for Hepatitis C continued from page 1

multiply (see Table 1). However, demonstrating benefit, minimizing side effects, and preventing resistance to these drugs has slowed their movement from the laboratory to patient use in the clinic. For example, the protease inhibitor Telaprevir or VX-950 is a new oral medication that was initially tested as a stand alone antiviral agent for HCV. Although it did stop the virus from multiplying, viral particles that were resistant to Telaprevir (VX-950) rapidly appeared within a few weeks. In addition, a number of side effects including skin rashes have been noted with patients who took this drug for a long time. Currently, Telaprevir (VX-950) is being tested in combination with Pegylated interferon and ribavirin in non-transplant patients and may allow for a shorter course of treatment with improved rates of eliminating the virus. However, finding the perfect balance between the amount of Telaprevir (VX-950) to give in combination with other drugs and for the optimal length of time has not yet been established in transplant recipients.

Other drugs in development for HCV target the intracellular manufacturing of viral particles. In addition, newer formulations of interferon that can be given every 2 weeks rather than weekly are under development as well as other drugs which target the host immune response (immunomodulators). However, before any of these drugs can be given to liver transplant recipients, the safety, dosing and side effects will need to be established in standard HCV patients. In addition, any potential interactions of these new drugs with anti-rejection medications will need to be studied prior to giving them to transplant patients. Despite the need for additional studies, many of us are hopeful that one or several of these new drugs will become available for use in transplant recipients in the next five years.

*– Robert J. Fontana, MD
Medical Director of Liver Transplantation*

Liver Tumor Clinic

A new multidisciplinary Liver Tumor Clinic was opened in the fall of 2007 to offer coordinated care to patients with tumors that arise in or have spread to the liver such as primary liver cancer, bile duct cancer, metastatic colorectal carcinoma, and various benign liver tumors. This weekly clinic is a unique program that combines expertise from multiple specialists in Hepatology, Surgery, Medical Oncology, Radiation Oncology, and Interventional and Diagnostic radiology. In addition, close collaboration with the Liver Transplant program can lead to the early identification of potential transplant candidates. As part of the University of Michigan NIH designated Cancer Center access to the latest approved and investigational therapies for liver tumors is available along with social work, nursing, and hospice services from the Cancer Center

Our mission is to offer timely, innovative, and compassionate care to all patients with known or suspected liver tumors. As a part of this mission, we aim to become a referral center of excellence for the development of new screening and imaging techniques, innovative multimodality treatments and improve the scientific understanding of the development and natural history of liver cancers. Patients referred to the clinic will be seen during a single visit by physicians from all of the appropriate disciplines in either the same week of referral or the following week. For patients with primary liver cancer and underlying liver disease, liver transplantation evaluation is available during the same visit.

Following a clinic evaluation, every case is reviewed at our weekly multidisciplinary Liver Tumor Conference. Following careful review of all radiological studies, pathologic information, prior treatments, and patient status, a detailed treatment plan is developed for each patient.

Contacts for appointments or scheduling:
Liver Tumor Clinic Coordinator
734-647-8916, 734-615-4484 (FAX)

Patients needing to speak with a nurse:
Liver Tumor Clinic Nurse
734-647-8902, 734-647-8689 (FAX)

Medical Professionals available in Liver Tumor Clinic:

- Hepatobiliary and Transplant surgeons
- Hepatologists
- Medical Oncologists
- Radiation Oncologists adept at state of the art stereotactic radiotherapy
- Interventional radiologists adept at state of the art chemoembolization and treatment with Theraspheres

Established Therapies for Liver Malignancies:

- Liver resection using the latest techniques including minimally invasive laparoscopic liver surgery
- Pre-operative portal vein embolization to allow for larger resections when margins or residual liver function is a concern
- Vascular resection/reconstruction techniques
- Laparoscopic and percutaneous radio frequency ablation
- Resection following chemotherapy for downstaging
- Transarterial chemoembolization (TACE)
- Yttrium90 intraarterial microspheres
- Novel methods of focal liver tumor irradiation
- Liver transplantation (for cirrhotic patients with primary liver cancer)
- Oral anti-angiogenesis drugs to treat advanced liver cancer
- Various investigational treatment protocols are routinely available for patients at all stages.

Leadership Changes in Transplant Programs

Shawn Pelletier, MD was appointed as Surgical Director of Liver Transplantation for adult patients. Dr. Pelletier is a gifted surgeon with a deep commitment to liver transplantation. His leadership, passion, and energizing new ideas will allow the program to continue to thrive. Dr. Pelletier is replacing Jeffrey D. Punch, MD, who led the program for over eight years. Dr. Punch will continue to be involved in the care of liver transplant patients. The change in leadership will allow Dr. Punch, in his role as the Director of the Transplant Center, to continue the development of the Transplant Center and to pursue his academic interests. Congratulations, Dr. Pelletier!



Randall Sung, MD was appointed as Surgical Director of Kidney Transplantation for adult patients. Dr. Sung brings a wealth of experience, knowledge, and passion to this position. In the past five years, he has performed more kidney transplants than any other surgeon within the program. We are fortunate to have his depth of talent and commitment to the program. Dr. Sung's expertise will allow the program to continue its pattern of growth as one of the largest kidney programs in the country. Dr. Sung is replacing John C. Magee, MD., who led the program since 2000. Dr. Magee will continue to care for kidney transplant patients. Congratulations, Dr. Sung!



John C. Magee, MD continues his role as Surgical Director of Pediatric Transplant for kidney and liver pediatric transplant patients. Dr. Magee has held this position since 2000. The shift in leadership of the adult kidney program was a direct result of Dr. Magee's exceptional academic success. The change will allow him to focus on his many other academic and administrative activities, including Principle Investigator of the Biliary Atresia Research Consortium, Surgical Director of the Pediatric Liver and Kidney Transplantation, Co-investigator for the Scientific Registry of Transplant Recipients, Chair of the ASTS Fellowship Committee, and many others. **Dr. Magee deserves recognition for his exceptional leadership of the adult and pediatric kidney programs and the pediatric liver transplant program for the past eight very hectic years. THANK YOU, Dr. Magee!**



A Vacation in Aruba Reveals UM Heroes!

One cold Saturday in early January, Doug, Joan & Jack Armstrong, Vicki Shieck and Chuck Moore boarded a flight from Detroit to Aruba for an annual vacation with family and friends. Their long flight was uneventful except for an extended wait at the Aruba airport for a gate to disembark the plane. Thus arriving late, this UM group would later be joined by an entire group of about 19 for a week of rest, relaxation and fun in sunny Aruba. After being welcomed at the airport by members of Doug's family, they made their way out of the airport, rented a car and made their way to an ocean front resort.

Arriving at the resort, bags were unpacked and plans were made for a restful evening of visiting and playing games with multiple members of the group who meet annually in Aruba. Pizza was brought in, they visited, they played games – they stayed up late, perhaps a bit too late considering their early a.m. departure and a long hectic day of travel.

On Sunday, Chuck slept in a little later than his usual 5 a.m., got up, went for a walk, stopped for a cup of coffee and returned to find that Doug and Vicki were already heading down to lounge at the pool. Chuck got some breakfast, changed to swim trunks and headed to the pool only to be greeted by Doug who wondered why he wasn't at church – which is Chuck's normal habit for a Sunday morning. Obviously, Chuck had forgotten what day it was. He glanced at his watch, excused himself, hurried back to his room to change clothes, and he made it to church just in time. After church Chuck returned, changed once more and headed back to the pool.

At the pool, Doug, Joan, Jack and Vicki were relaxing and discussing future activities for the day. Having already had such a busy morning, Chuck stretched out on a lounge chair to get a little rest and listen to what was being planned. Chuck had just gotten comfortable when Doug, who was facing the opposite direction, suddenly sprung from

his chair yelled "Chuck come on" and took off running towards the pool. Doug had apparently witnessed a commotion at the end of the pool as a child was being pulled from the water.

As they reached the end of the pool, they saw a pale flaccid little girl being laid on the concrete with a screaming crowd of onlookers starting to encircle her. They fought their way through the crowd and identified themselves to an arriving security officer who was attempting to gain control of the situation. Here they found a poorly positioned little blonde child with an individual making a feeble attempt at mouth to mouth resuscitation.

As the security guard was attempting to hold back the crowd and trying to make sense of the situation, Doug positioned himself at the head of the child and Chuck was at her feet while they also tried to gather information about what led up to this event. At first appearance she looked like a child who had experienced a seizure but there was no sign of respiration or pulse. Within seconds – although it felt like forever – Chuck realized her grandfather was hovering above him. Chuck pulled the grandfather down to obtain a few little tidbits of history to work with. He knew of no history of seizures, she had been eating near the edge of the pool, had choked and had fallen into the pool. No one knew if she had hit her head. Chuck started chest compressions as Doug controlled her airway. She immediately began to vomit as a result of the chest compressions. Chuck and Doug struggled with the family and onlookers to flip her over to clear her



Zingerman's – Faculty as Servers and Busboys

On March 11, 2008, a group of good-hearted transplant surgeons traded in their scrubs for aprons in Ann Arbor. The first-ever Zingerman's Roadhouse meal to benefit the Transplant Center took place with surgeons waiting tables. The special-menu event was the brainchild of Zingerman's Roadhouse owner and Chef Alex Young. Chef Alex and his staff were on hand to help the surgeons get accustomed to their new roles.

People were lined up at the door waiting to see their favorite doctor try to keep all the orders straight. The docs had a full house to contend with but did a great job serving drinks, appetizers, salads, main courses and even dessert. They soon figured out how to tag team and back each other up in order to keep all the drinks filled and bread and butter on the tables.

Besides a fabulous meal and the fun of watching the surgeons waiting tables, there was a lively auction. From autographed sports memorabilia to art work, many people took wonderful auction items home. Videos of Camp Michitanki entertained diners throughout the evening as well.

This event was such a great hit it is sure to be repeated. Keep yourself up to date on upcoming events such as this on the Transplant Center web site, www.michigantransplant.org.



Remembering the Heroes We Lost

Robert P. Kelch, M.D., U-M's executive vice president for Medical Affairs hosted an event to remember and honor the Transplant/Survival Flight Team members who lost their lives trying to save the life of a patient. To open the reception held in the Towsley Lobby on June 4, 2008, Dr. Kelch welcomed the many family members, friends and colleagues of our fallen heroes. In his brief comments Dr. Kelch spoke of our lost team, who they were, what they stood for, what they achieved and what they sacrificed. He spoke of loss and that we still hold David, Richard, Dennis, Ricky, Bill and Martin in our thoughts. He spoke of how we honor these men by continuing to save lives and caring for patients in the best way we know how.

In honor of their tremendous contributions, a permanent sculpture is being planned in their memory. A task force, selected by President Coleman and Dr. Kelch, working with families of the Transplant/Survival Flight team will

recommend an artist to create a sculpture that will be placed outside the front entrance of University Hospital on the east side of the main lobby. The task force plans to have the sculpture completed by June 2009.

At 5:00 p.m., the time of the crash of our plane, Carillonneur Steven Ball from the School of Music tolled the bells for six minutes – one minute for each team member lost. He was joined in this effort by nine other carillonneurs across the city. It was a moving memorial.

To view the reception, Dr. Kelch's remarks and the tolling of the bells, visit our website at <http://www.med.umich.edu/heroes2007/>.

We will remember David, Richard, Dennis, Ricky, Bill and Martin. They made a powerful and lasting mark on us and the lives of many others. We will honor them by continuing their work.



Michigan Donor Drive

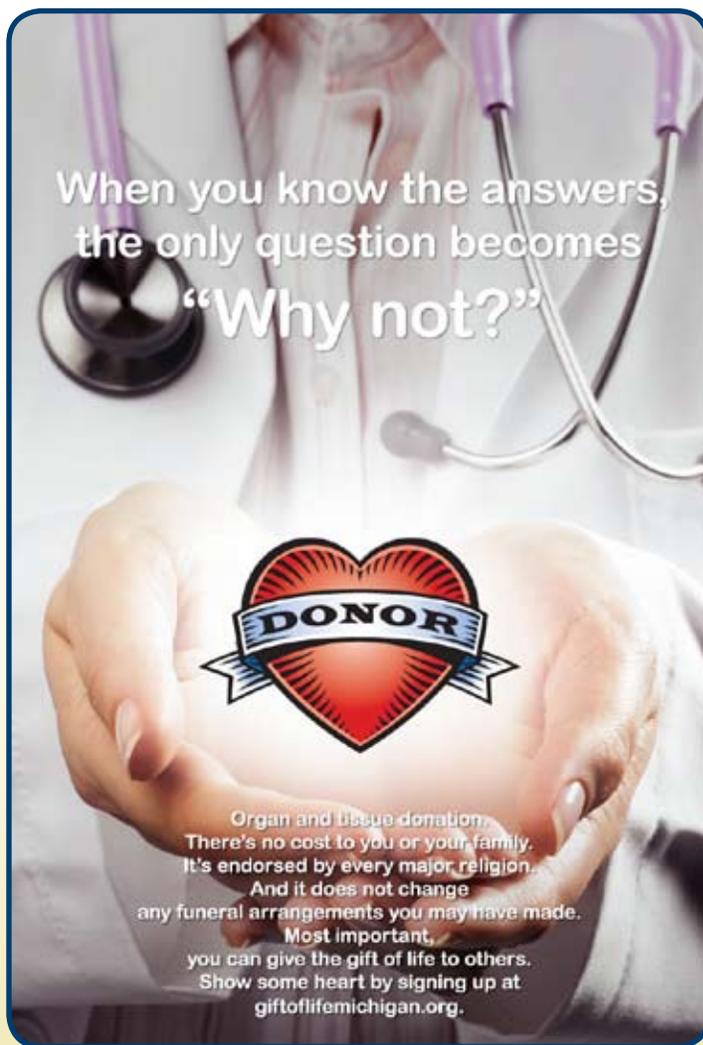
During Donor Awareness Week, the new donor awareness campaign called the 'Michigan Donor Drive' was kicked off within University Hospital. A booth was set up in the cafeteria to promote the new campaign. The campaign was also prominent during the annual Transplant Center and donor awareness booth in the triangle at University Hospital.

This campaign was very successful at University Hospital. In 2008, during the week of Organ Donor Awareness 453 individuals registered to be organ donors. This is more than double the 208 registrants from the previous year.

For more information or to register as an organ donor, please visit <http://www.giftoflifemichigan.org/showusyourheart/Default.aspx>



Michael S. Valdes, Associate Director for Operations and Ancillary Services



Michigan Donor Drive

Robert Merion, M.D. Receives Francis Moore Mentorship Award

Several of us wanted to draw your attention to a great recent honor. Bob Merion was one of the first recipients of the Francis Moore Mentorship Award by the American Society of Transplant Surgeons (ASTS). Bob was honored in a ceremony at the recent ASTS winter meeting (that coincidentally one of his many mentees, Dr. Randy Sung, ran). While Bob has clearly had an impact on everyone here, he has also had an impact as a mentor on several other leaders in transplantation around the country. Bob's remarks were characteristically thoughtful and humble.

This contribution aside, I was also impressed when one of the great curmudgeons of our day, while

making some comments after someone else's talk, warned of the evils he always finds associated with analysis of registry data (drawing unwarranted associations and inferences, failure to understand what the question is or what the data means, etc) then paused and said, "unless the work is done by the SRTR". Bob's impact on both knowledge and scientific thought in the community has been truly immense. Teaching an old dog a new trick is one thing but getting the whole pack to think and behave rationally is something else.

In a way he has mentored the entire transplant community.

-John Magee, M.D.

A Vacation in Aruba Reveals UM Heroes! continued From page 5



airway. Another security officer arrived with rescue equipment. It was quickly apparent they had brought only adult equipment. Doug utilized an adult face mask and modified it quickly to get the small patient some oxygen. The security guard who arrived with the equipment eventually took over the chest compression as Chuck searched the equipment for a stethoscope and small airway, but he only found the stethoscope. A quick listen revealed no airflow or heart sounds. Doug worked with the portable suction unit to clear her mouth and they again turned her to clear the airway before resuming the chest compressions and ventilations. The child then took a couple of gasping breaths and heart sounds could be heard. A strengthening pulse was felt by Chuck, and chest compressions were stopped while the child continued with short shallow breaths that gradually increased. Luckily, the ambulance arrived with proper equipment and at Chuck's insistence the child was transported immediately.

The young girl arrived at the hospital breathing on her own and was admitted for observation. Two days later, she returned to her family and the resort with a Welcome Home Balloon reception.

Chuck followed up daily on the little girl's condition and Doug followed through by meeting with security and resort management to ensure necessary pediatric equipment will be available in the future.

Thanks to two special members of our MICHIGAN team, this six year old girl was able to return to her home in the northeast United States after a very eventful trip to Aruba.

Chuck and Doug – you were the MICHIGAN DIFFERENCE in that situation!
Very nice work!

Merion helps pave way for paired organ donation

Thanks to the tireless efforts of a number of transplant surgeons and the American Society of Transplant Surgeons, the changeover to 2008 brings kidney transplant patients more options than ever to find a living donor. Robert Merion, M.D., Professor of Surgery, U-M Transplant Center, was one such physician recognized in the passage of legislation that allows paired organ donation, an organ matching process that provides a larger pool of potential living donors to transplant patients. To understand paired organ donation, let's say a man needs a kidney transplant. His sister offers to donate a kidney. This situation is ideal: an organ transplant is a better option than dialysis and a living donor is the best chance for success. However, what happens if the sister isn't a match? Merion says that many pairs of potential donors and patients are not matches, but they could work with others in similar situations to find an organ. This is called paired donation. Until now, it was unclear whether this process was legal, resulting in patients losing the chance for a life-saving transplant.

The problem was a term in the National Organ Transplant Act, "valuable consideration," which was originally included in the legislation to make it illegal to buy or sell organs. Merion wrote countless letters, visited Capital Hill and helped Senate staff craft messages that were medically accurate. On Dec. 31, 2007, President Bush signed a revised act into law, making it clear that paired organ donations and similar processes are allowed. "What I tried to do is put a human face on the issue," Merion says. "I have patients who could really benefit from paired organ donation. Every transplant that occurs saves someone's life and reduces the cost by getting the patient off dialysis." The new law will save money, with one economic analysis estimating a \$500 million cost reduction over 10 years. Merion says long-term transplant



Robert Merion, M.D.

costs are about \$10,000 per year compared to \$68,000 per year for dialysis.

Merion was recognized by Senator Carl Levin in his remarks on the floor of the U.S. Senate when the bill was presented for final passage. He noted Merion's "tireless advocacy" in the effort to educate Congress on the need for paired donation. Levin also presented the new legislation as a tribute to the six members of the U-M transplant team who passed away last June. "All of my colleagues who perished in that horrible crash were committed to organ donation," Merion says. All six of these fine men would have been extraordinarily proud to know that their names were being invoked to stimulate final passage of a bill that will provide the gift of life to so many others."

- U/M Applause March-2008



Transplant Center's Mission

The Transplant Center's clinical mission is to provide our patients with the best possible medical care in a setting that emphasizes excellence, compassion, accessibility, responsiveness and prompt delivery of care.

University of Michigan Transplant Center Contact Information

Liver Transplant Programs

Adult

Liver Transplant Clinic - Gastroenterology Division
1500 E. Medical Center Drive
3868 Taubman Center, SPC 5391
Ann Arbor, Michigan 48109-5391
Phone: 734-936-7491 (Local)
Phone: 800-395-6431 (Toll Free)
TTY: 800-649-3777
Fax: 734-936-2464

Pediatric

Liver Transplant Program - Pediatric
Medical Professional Building
1500 E. Medical Center Drive
Room D3256, SPC 5718
Ann Arbor, Michigan 48109-5718
Phone: 734-615-2462 (Local)
Phone: 877-543-7789 (Toll Free)
Fax: 734-615-2223

Heart Transplant Programs

Adult and Pediatric

Cardiovascular Center
200 North Ingalls Building, 8B02
Ann Arbor, Michigan 48109-5477
Phone: 888-287-1082

Kidney and/or Pancreas Transplant Programs

Adult

Kidney and Pancreas Transplant Program
1500 E. Medical Center Drive
3868 Taubman Center, SPC 5391
Ann Arbor, Michigan 48109-5391
Phone: 734-936-7491 (Local)
Phone: 800-333-9013 (Toll Free)
Fax: 734-647-3417

Pediatric

Kidney Transplant Program - Pediatric
C. S. Mott Children's Hospital
1500 E. Medical Center Drive
Room F6865, SPC 5297
Ann Arbor, MI 48109-5297
Phone: 734-615-2040 (Local)
Phone: 877-543-7789 (Toll Free)
Fax: 734-615-2042

Lung Transplant Program

Adult

Lung Transplant Program
1500 E. Medical Center Drive
3862 Taubman Center, SPC 5391
Ann Arbor, Michigan 48109-5391
Phone: 734-936-7491 (Local)
Phone: 800-333-9013 (Toll Free)
Fax: 734-936-6671

United Network for Organ Sharing (UNOS)

The United Network for Organ Sharing provides a toll-free patient services line to help transplant candidates, recipients, and family members understand organ allocation practices and transplantation data. You may also call this number to discuss a problem you may be experiencing with your transplant center or the transplantation system in general. The toll-free patient services line number is 1-888-894-6361.

Executive Officers of the University of Michigan Health System: Robert P. Kelch, Executive Vice President for Medical Affairs; James O. Woolliscroft, Dean, U-M Medical School; Douglas Strong, Chief Executive Officer, U-M Hospitals and Health Centers.

The Regents of the University of Michigan: Julia Donovan Darlow, Laurence B. Deitch, Olivia P. Maynard, Rebecca McGowan, Andrea Fischer Newman, Andrew C. Richner, S. Martin Taylor, Katherine E. White, Mary Sue Coleman (ex officio).

The University of Michigan, as an equal opportunity/affirmative action employer, complies with all applicable federal and state laws regarding nondiscrimination and affirmative action, including Title IX of the Education Amendments of 1972 and Section 504 of the Rehabilitation Act of 1973. The University of Michigan is committed to a policy of nondiscrimination and equal opportunity for all persons regardless of race, sex, color, religion, creed, national origin or ancestry, age, marital status, sexual orientation, gender identity, gender expression, disability, or Vietnam-era veteran status in employment, educational programs and activities, and admissions. Inquiries or complaints may be addressed to the Senior Director for Institutional Equity and Title IX/Section 504 Coordinator, Office of Institutional Equity, 2072 Administrative Services Building, Ann Arbor, Michigan 48109-1432, 734-763-0235, TTY 734-647-1388. For other University of Michigan information call 734-764-1817.