Liver Transplant Research at the Comprehensive Transplant Center

Hepatitis C: Approximately 2.25% of the world’s population is infected with hepatitis C virus (HCV), with about 4 million people in the United States infected. HCV slowly causes the liver to become cirrhotic, which leads to end-stage liver disease (ESLD), eventually requiring liver transplantation. The standard of care (SOC) for treating HCV has changed over the last 15 years ranging from single agent interferon dosed three times a week to current FDA-approved triple-therapy using pegylated interferon, ribavirin and a protease inhibitor. There are six genotypes of HCV: 1-6. The prescribed duration of treatment and sustained virological response (SVR) rates vary from genotype to genotype with genotypes 1, 4, 5 & 6 requiring the longest duration of treatment and being the most difficult to treat.

Triple therapy has improved response rates from about 50% in genotype 1 patients to about 80%. HCV always returns post-transplant if SVR was not obtained prior to transplantation. With organ shortages one of the big problems in the post liver transplant arena is how to treat HCV infected patients. Triple therapy trials have crossed-over from the HCV hepatology population to the post-liver transplant population. About 40% of the liver transplants performed at Northwestern are in patients with ESLD from HCV. The CTC has been chosen as a site with Dr. Josh Levitsky in charge of the pioneering trial using triple therapy in the post-transplant population. It is hoped that response rates will mirror those seen in the non-transplanted HCV infected population.

Hepatocellular Carcinoma: Hepatocellular carcinoma (HCC) is the 5th most common cancer worldwide. Cirrhosis is the most common risk factor for HCC and it is the leading cause of death in patients with cirrhosis. Hepatitis B virus (HBV) is an oncogenic virus and patients with HBV can have HCC without cirrhosis. While there are numerous treatments for HCC, none has proven to be more effective than another. There are various liver-directed standards of care to treat HCC: Radioembolization (Y-90 Therasphere or Serospheres), Transarterial Chemoembolization (TACE), Chemoembolization or Chemotherapy. Sorafenib is the first FDA approved oral medication to treat HCC. A recently completed study at the CTC is currently examining using Y-90 ± sorafenib. Ideally, understanding the biological behavior of each individual’s tumor(s) and the genetics of the individual may be the key to unlocking which treatments may be best for each patient. Researchers at the CTC, led by Transplant Hepatologist, Dr. Laura Kulik, have several studies in place looking at biomarkers and genetics/proteomics of the patient’s tumor tissue and blood along with patient outcomes hoping to design individual treatments specific to each patient and each tumor’s genetic signature.

Tolerance and Immunosuppression Minimization/Withdrawal: Being able to transplant organs from genetically distinct individuals and not require long-term use of immunosuppression would be the “Holy Grail” of organ transplantation. Calcineurin inhibitor (CNI) based immunosuppression, while needed comes with problematic side-effects. Over time the very drugs that may be used to keep a liver from rejecting can damage kidneys requiring a transplant for end-stage renal - disease. Teaching the body to recognize a foreign organ as its own is referred to as tolerance. Ongoing studies, led by Dr. Levitsky and in conjunction with the Immune Tolerance Network (ITN) and his own investigator-initiated studies inside the CTC, are currently looking at gradually training the immune system to recognize a foreign liver as one’s own. Minimization of immunosuppressive is another way to limit exposure to the long term side-effects of CNIs. In addition, new types of immunosuppressive drugs that are not CNI based are being studied in a prospective manner.

Biomarkers: Studying biomarkers in liver transplant recipients and liver cancer patients may allow doctors to personalize immunosuppressive therapies and other treatments to the individual. Along with collecting samples from patients locally over the last few years, Dr. Levitsky is in charge of a large prospective NIH-funded study (CTOT) to evaluate gene and protein biomarkers of acute rejection, hepatitis C recurrence and chronic kidney disease in liver recipients. The overall goal is to be able to eventually use these biomarkers to predict, diagnose and follow transplant complications more specifically and effectively. In addition, Dr. Kulik, lead physician on the HCC biorepository studies, is encouraged that one day doctors will also be able to predict, based on biomarkers, which cancers will return post-transplant and how aggressive they will be once they return. For such studies, Dr. Kulik collects blood pre-and post-liver cancer treatment, as well as tumor and surrounding liver tissue during liver resection or liver transplant surgery.

Other Studies: Currently, ongoing NIH-funded studies include the Adult-to-Adult Living Donor Liver Transplant Study, which is in its 10th year and is overseen by Dr. Michael Abecassis. This study is the first of its kind with multiple living donor liver transplant centers studying the physical and psychological outcomes of donors that donate up to two-thirds of their livers. On the flip side, recipients are studied for their long-term physical outcomes and complications from living donor transplant surgery versus transplant patients that received deceased donor livers. Dr. Daniel Ganger is continuing as the site PI for a long-standing study of patients presenting with acute liver failure (ALF Study Group), also NIH-funded.