Rare Patients May Hold Key to Transplantation Without Immunosuppression

By Jeffrey B. Matthews, PhD

For decades, the concept of immune tolerance has tantalized researchers and patients alike, promising safer, more effective and long-lasting protection from transplant rejection with only a short-term or intermittent treatment schedule.

Now the secrets to transplantation without immunosuppression may well lie with a handful of rare kidney transplant recipients whose immune systems seem to be naturally tolerant to their graft.

Exceedingly rare, these individuals have maintained good kidney function, despite the fact that they have discontinued all immunosuppressive therapy. What is it about the immune systems of these “naturally tolerant” patients that allow them to achieve what scientists have been attempting to accomplish for decades? Is it possible to reprogram other recipients’ immune systems to behave in the same, tolerant fashion? These are the questions to be addressed in a new study sponsored by the Immune Tolerance Network (ITN) and headed by Emory University transplant surgeon Dr. Kenneth Newell.

The study will compare naturally tolerant patients with a variety of other groups of kidney transplant recipients, including those who have discontinued immunosuppressive therapy but rejected their transplant.

“We are aiming to learn as much about these individuals’ immune systems as possible,” says Newell. “We’ll be looking at how they differ in terms of their genes, and how the various cells in their immune systems interact to create tolerance to their transplant.”

One of the goals of the ITN team is to identify a genetic, cellular or biochemical marker that will tell physicians that a particular patient might safely reduce their immunosuppressive drug dosage or even be safely taken off immunosuppressive therapy.

“If we can come up with a series of biomarkers that predict tolerance, then we can go to certain patients and say ‘You have a 95 percent chance of being tolerant so maybe it’s worth trying to wean you off these drugs’,” muses Dr. Newell, who believes that this could be the most likely and most immediate result of his study.

However, the Atlanta-based surgeon also harbors a more ambitious plan for the study, hoping that differences noted between the naturally tolerant and “normal” recipients might change both the way we view transplant rejection and how it is treated.

“I’m almost sure we are going to come out of this with a better understanding of how the immune system works and how it makes the decision to reject or tolerate a transplant,” says Newell. “Just maybe, we’ll find something new, something that can be changed through a drug or gene therapy to create tolerance.”

Right now, however, Newell is focused on the more immediate task of finding as many naturally tolerant patients as he can.

With the ITN’s help, Dr. Newell is reaching out to transplant surgeons and specialists around the world to construct the first “Tolerant Kidney Transplant Registry,” a database of all naturally tolerant patients from across the globe. It’s a demanding task, but one that has captured the imagination of Dr. Newell and collaborators from institutions in the U.S., England and France.

“It’s really a worldwide manhunt for these patients. There are so few, and, many times, there isn’t even a record that the patient has discontinued therapy.”

In some cases, the physician may recommend discontinuation of immunosuppressive therapy due to extreme side effects or other complications. This is usually done very slowly over a long period of time. In other cases, recipients disregard doctors’ orders and stop taking their medications. For the overwhelming majority of patients, however, this leads to the loss of the transplant.

Newell emphasizes that it is extremely rare that a patient will stop adhering to their immunosuppressive therapy and not reject their transplant. Doing so, he says, can have catastrophic consequences and “will almost certainly lead to the loss of their graft.”

If you would like more information on the ITN Registry project headed by Dr. Newell, or know someone who may be naturally tolerant, please visit www.immunetolerance.org/registry or call 866-752-6245 for more information.

About the Author
Jeffrey B. Matthews, PhD, is the Director of Communications for the Immune Tolerance Network.

Study Eligibility
The ITN Registry of Tolerant Kidney Transplant Recipients is seeking kidney transplant patients who:

• Have been off all immunosuppressive medications for one year and,
  i) have good kidney function, or
  ii) who may have impaired or gradually declining renal function (believed to be unrelated to rejection)

• Have good kidney function on only minimal immunosuppression

• Are recipients from identical twin donors.

Contact the ITN Registry at www.immunetolerance.org/registry or toll-free at 866-752-6245 for more information.