

EMBARGOED FOR RELEASE until August 20, 2015 – 5:00 PM (ET)

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ANTIBODIES IN THE BLOOD PROVIDE CLUES TO KIDNEY TRANSPLANT RECIPIENTS' LIKELIHOOD OF REJECTION

Presence of certain antibody types may indicate the need for aggressive anti-rejection therapy

Highlights

- Among kidney transplant recipients, patients with mostly IgG3 donor-specific HLA antibodies had a higher likelihood of organ rejection soon after transplantation.
- If rejection occurred in those with mostly IgG4 antibodies, it was usually much later after transplantation.

Antibody-mediated injury is the leading cause of kidney failure following transplantation.

Washington, DC (August 20, 2015) — The dominant antibody type present in the blood of transplant recipients may indicate their likelihood of experiencing organ rejection, according to a study appearing in an upcoming issue of the *Journal of the American Society of Nephrology* (JASN). The findings may help doctors identify patients who need aggressive treatments to safeguard the health of their new organ.

Transplant recipients who receive a kidney, heart, or lung often develop an immune response to the foreign tissue in the form of antibodies referred as donor-specific HLA antibodies. Some patients may already have these antibodies before their transplant because they have been exposed to blood products or previous transplants. Although the presence of donor-specific HLA antibodies in a recipient is usually not a good sign, not all patients who have them experience a poor outcome.

Through a collaboration of two transplant centers in France and the United States, Carmen Lefaucheur, MD, PhD (Saint-Louis Hospital, in Paris) and his colleagues designed a study to determine the greatest risk for losing a transplanted organ based on the characteristics and function of donor-specific HLA antibodies. Their study included 125 kidney transplant patients with donor-specific anti-HLA antibodies detected in the first year post-transplant.

The researchers found that the presence of certain donor-specific HLA antibodies—namely IgG3 and IgG4 subclasses—correlated with distinct patterns of antibody-

mediated injury to the transplanted organ. Patients with mostly IgG3 donor-specific HLA antibodies had a higher likelihood of organ rejection soon after transplantation. If rejection occurred in those with mostly IgG4 antibodies, it was usually much later after transplantation.

“Our clinical investigation may help in the future to identify the patients that will require interventions to prevent the loss of a transplanted organ,” said Dr. Lefaucher. “Also, based on what we learned in this investigation, more studies will be initiated to further elucidate why some patients seem to maintain good outcomes while others demonstrate accelerated deterioration of the transplanted kidney in the presence of circulating donor-specific HLA antibodies.”

In an accompanying editorial, Stanley Jordan, MD (Cedars-Sinai Medical Center) noted that if the findings are supported by additional studies, they could be of great help in counseling patients and possibly avoiding costly immunotherapy to reduce what appear to be largely benign donor-specific HLA antibodies. “Lefaucher *et al.* are to be commended for this important work, which further enlightens our understanding of the natural history of immunodominant donor-specific HLA antibodies and their effect on allograft pathology and outcomes,” he wrote.

Study co-authors include Denis Viglietti, MD, Carol Bentlejewski, Jean-Paul Duong van Huyen, MD, PhD, Dewi Vernerey, Olivier Aubert, MD, Jérôme Verine, MD, PhD, Xavier Jouven, MD, PhD, Christophe Legendre, MD, Denis Glotz, MD, PhD, Alexandre Loupy, MD, PhD, and Adriana Zeevi, PhD.

Disclosures: One Lambda donated reagents but was not otherwise involved in either the conduct of the study or the preparation of the manuscript.

The article, entitled “Immunoglobulin G Donor-specific anti-HLA Antibody Subclasses and Kidney Allograft Antibody-mediated Injury,” will appear online at <http://jasn.asnjournals.org/> on August 20, 2015.

The editorial, entitled “Donor-Specific HLA Antibody IgG Subclasses Are Associated with Phenotypes of Antibody-Mediated Rejection in Sensitized Renal Allograft Recipients,” will appear online at <http://jasn.asnjournals.org/> on August 20, 2015.

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