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Press Release

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STUDY IDENTIFIES GENES INVOLVED IN TOLERANCE FOLLOWING KIDNEY TRANSPLANTATION

Highlights

- In tissue samples from patients who received kidney transplants without the need for chronic immunosuppression, researchers found increased expression of many genes associated with the regulation of certain immune cells.
- The findings provide an improved understanding of transplant organ acceptance and rejection.

Achieving organ tolerance after transplantation is a major challenge.

Washington, DC (November 30, 2017) — A new study provides insights on the mechanisms that allow an individual's immune system to accept, rather than reject, a donor kidney. The findings, which appear in an upcoming issue of the *Journal of the American Society of Nephrology* (JASN), point to markers that could be monitored to asses and track the health of organs following transplantation.

Immunosuppressive therapy is effective at inhibiting acute rejection. However significant morbidities are associated with the life-long use of immunosuppression. Hence, the "holy grail" of transplantation is to achieve tolerance, a state of acceptance of the donor organ without the use of chronic immunosuppression.

A team led by Lorenzo Gallon, MD (Northwestern University) and Valeria Mas, PhD (University of Virginia) studied patients in whom tolerance was induced by creating at state of persistent donor chimerism. "Chimerism" is a state in which bone marrow stem cells from two genetically different individuals coexist. The infusion of donor bone marrow cells in organ transplant recipients can lead to chimerism, which subsequently leads to tolerance for any other tissue or organ from the same donor.

In their recent report, the researchers examined peripheral mechanisms by which these patients developed donor-specific tolerance. By analyzing gene expression in tissue samples obtained from the kidneys of tolerant patients, the investigators found lack of any active immune responses to donor tissue at the molecular level in tolerant kidneys compared against controls kidney samples of patients undergoing standard immunosuppression. Furthermore, the researchers found a significant upregulation of

genes involved in pathways linked to B cell receptor signaling and activation suggesting an active immune regulation of B cells in the chimeric (tolerant) kidney transplant recipients when compared with other transplant recipients without acute rejection undergoing standard immunosuppression.

“We have shown for the first time molecular pathways occurring in the transplanted organs of chimeric tolerant patients,” said Dr. Gallon. “The data generated from this study can help not only longitudinally monitoring our tolerant patients but also could help identify those patients on chronic immunosuppression (the vast majority of the kidney transplant recipients) whose kidneys might have increased expression, due to very low levels of chimerism, of the genes we identified and could therefore be potentially considered for minimization of their immunosuppression.”

Study co-authors include James Mathew PhD, Sai Vineela Bontha PhD, Catherine Dumur PhD, Pranav Dalal MD, Lakshmi Nadimpalli MD, Daniel Maluf MD, Aneesha Shetty MD, Suzanne Ildstad MD, and Joseph Leventhal MD PhD.

Disclosures: Dr. Ildstad has equity interest in and is the CEO of Regenerex, LLC, a start-up biotech company. Dr. Leventhal receives grant support from Regenerex, LLC and Novartis Pharmaceuticals. All other authors have no conflicts of interest to declare.

The article, entitled “Intragraft Molecular Pathways Associated with Tolerance Induction in Renal Transplantation,” will appear online at http://jasn.asnjournals.org/ on November 30, 2017, doi: 10.1681/ASN.2017030348.

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