Genes identify transplant rejection

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Acute rejection after kidney transplantation occurs in about 15%–20% of patients despite immunosuppressive therapy. Rejection is usually heralded by an increase in the patient's serum creatinine (a marker of kidney function), and a kidney biopsy is then performed to confirm whether rejection is taking place. However, elevated creatinine is not sufficiently sensitive to identify all early rejection or specific enough to prevent some unnecessary kidney biopsies, so a noninvasive means of identifying acute rejection is needed.

In the Assessment of Acute Rejection in Renal Transplantation study published this week in *PLOS Medicine*, Silke Roedder, Tara Sigdel, senior author Minnie Sarwal (Department of Surgery, University of California San Francisco, San Francisco, California, United States of America), joint first author Nathan Salomonis (University of Cincinnati), and colleagues developed a 17-gene set to analyze patients' peripheral blood samples to determine which patients were at risk of acute rejection of their kidney transplants. The authors used 558 peripheral blood samples from 438 adult and pediatric renal transplant patients from eight renal transplant centers in the United States, Mexico, and Spain and enrolled between 2005 and 2012 to develop a quantitative real-time polymerase chain reaction (PCR) test. They developed the test in 143 samples from adults with and without acute rejection as determined by kidney biopsy, and then finalized and validated the test in three cohorts of patients.

The ability of the test to identify acute rejection in the final validation cohort was measured using the statistical approach of area under the

curve. With 0.5 being equal to pure chance and 1.0 being perfect identification, the area under the curve for the test was 0.93 (95% CI 0.86–0.99). The authors conclude that the "kSORT assay is a simple, robust, and clinically applicable blood test." They are using kSORT in a prospective observational trial as well as a second prospective, randomized, double-blinded clinical interventional trial, which will establish how "kSORT can be used serially post-transplant to complement current clinical practice guidelines for stratifying patient immune risk, medication load, and requirement for biopsy."

More information: Roedder S, Sigdel T, Salomonis N, Hsieh S, Dai H, et al. (2014) The kSORT Assay to Detect Renal Transplant Patients at High Risk for Acute Rejection: Results of the Multicenter AART Study. *PLoS Med* 11(11): e1001759. DOI: 10.1371/journal.pmed.1001759

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