Editorial

Knowing the allograft's destiny

Vinayak S. Rohan, Kenneth D. Chavin

[1]Division of Transplant Surgery, Medical University of South Carolina, Charleston, SC, USA; [2]Transplant Institute, University Hospitals Cleveland Medical Center, Case Western Reserve University, Cleveland, Ohio, USA

Correspondence to: Kenneth D. Chavin, MD, PhD. Transplant Institute, University Hospitals Cleveland Medical Center, Case Western Reserve University, Cleveland, Ohio, USA. Email: Kenneth.Chavin@uhhospitals.org.

Provenance: This is a Guest Editorial commissioned by Editorial Board Member Dr. Xiongbing Zu, MD, PhD (Department of Urology, Xiangya Hospital, Central South University, Changsha, China).

Comment on: O'Connell PJ, Zhang W, Menon MC, *et al.* Biopsy transcriptome expression profiling to identify kidney transplants at risk of chronic injury: a multicentre, prospective study. Lancet 2016;388:983-93.

Submitted Jan 25, 2017. Accepted for publication Feb 05, 2017.
doi: 10.21037/tau.2017.03.27
View this article at: http://dx.doi.org/10.21037/tau.2017.03.27

Over the past 50 years the short term outcome of kidney transplantation has improved significantly but maintaining the graft long term has remained a challenge (1). Today, with the help of calcineurin inhibitors, we are able to keep the acute rejection rates low (less than 10%) (2). However, we have very few weapons in our armamentarium to identify and influence the chronic process like transplant glomerulopathy, interstitial fibrosis and tubular atrophy (1,3). Hence the importance of markers to identify grafts at risk for these chronic changes before they become permanent and irreversible.

The report by the GOCAR consortium published in 'The Lancet 'describes an externally validated 13 gene marker set that was expressed in biopsies 3 months after the transplantation and was independently predictive of fibrosis at 1 year (4). The investigators used biopsies at 3 months and 12 months identifying gene sets which correlated with CADI score at 3 and 12 months. From the 149 genes the investigators were able to identify 13 genes predictive of future fibrosis. This 13 gene panel consisted of genes involved in repair and regeneration pathways supporting the theory that subclinical inflammation and injury which lead to fibrosis, loss of function and ultimately organ failure.

Predicting the allografts fate with gene expression profiling is not new. Einecke *et al.* and Naesens *et al.* have previously shown the prognostic implication of gene expression profiling (5-7). The investigators in the present study have used a non-hypothesis driven approach to identify genes. Also the gene set is substantially smaller and able to predict the fibrosis at an early time post-transplant.

GOCAR scoring appears to be a very useful prognostic tool albeit with a few a limitation. All the patients in the study used calcineurin inhibitors based immunosuppression along with mycophenolate and azathioprine. The validity of the gene set for other immunosuppression has not been established. Besides the GOCAR score cannot capture the 'progressors' due to causes like delayed antibody mediated reaction and recurrent disease. Also 58 of the 159 patients in the study did not have a biopsy at 12 months which might have affected the gene profiling.

This study is an important step in identifying chronic graft failure with superior predictive value than the presently used clinical and histopathological parameters. With early identification of grafts at risk there is a potential to alter immunosuppression or identify medications which might slow, arrest and may be even reverse the chronic changes.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Meier-Kriesche HU, Schold JD, Srinivas TR, et al. Lack of improvement in renal allograft survival despite a marked decrease in acute rejection rates over the most recent era. Am J Transplant 2004;4:378-83.
2. Rohan VS, Taber DJ, Moussa O, et al. Transplanting Sensitized Kidney Transplant Patients With Equivalent Outcomes Utilizing Stringent HLA Crossmatching. Exp Clin Transplant 2017;15:47-55.
3. Nankivell BJ, Borrows RJ, Fung CL, et al. The natural history of chronic allograft nephropathy. N Engl J Med 2003;349:2326-33.
4. O'Connell PJ, Zhang W, Menon MC, et al. Biopsy transcriptome expression profiling to identify kidney transplants at risk of chronic injury: a multicentre, prospective study. Lancet 2016;388:983-93.
5. Einecke G, Reeve J, Sis B, Mengel M, et al. A molecular classifier for predicting future graft loss in late kidney transplant biopsies. J Clin Invest 2010;120:1862-72.
6. Naesens M, Khatri P, Li L, et al. Progressive histological damage in renal allografts is associated with expression of innate and adaptive immunity genes. Kidney Int 2011;80:1364-76.
7. Modena BD, Kurian SM, Gaber LW, et al. Gene Expression in Biopsies of Acute Rejection and Interstitial Fibrosis/Tubular Atrophy Reveals Highly Shared Mechanisms That Correlate With Worse Long-Term Outcomes. Am J Transplant 2016;16:1982-98.

Cite this article as: Rohan VS, Chavin KD. Knowing the allograft's destiny. Transl Androl Urol 2017;6(2):313-314. doi: 10.21037/tau.2017.03.27

