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Letter to the Editor

Gene expression biomarkers for kidney transplant rejection – The entire landscape

John Friedewald [a,*], Michael Abecassis [a], Sunil Kurian [b]

[a] Northwestern University Feinberg School of Medicine, Chicago, IL, USA
[b] Scripps Health, La Jolla, CA, USA

We read with interest the article and editorial in your most recent issue on non-invasive testing to detect rejection in kidney transplant recipients [1,2]. The prospective, serial presentation of gene expression data is a strength of the study. We were surprised, however, to read the claims that there were no other studies evaluating biomarkers for subclinical rejection. Our recently published, prospective CTOT-08 clinical trial (NCT01289717) [3] was designed to detect and study subclinical kidney transplant rejection and led to the development and validation of a blood-based gene expression profile for subclinical rejection. Importantly, the clinical phenotype of subclinical rejection was tightly-defined and always proven with contemporaneous biopsy in our trial, allowing for an accurate assessment of the rate of true positives and true negatives. We did find that subclinical rejection as detected by biopsy or blood gene expression profile test was associated with progression to future episodes of clinical acute rejection, but not in all cases. And our study and others demonstrate that outcomes were worse even in patients with subclinical rejection that did not progress to clinical acute rejection [4].

We agree with the editorial statement regarding *a priori* bias in biomarker gene selection. For that reason, we chose an unbiased, whole transcriptome "microarray-based approach" to discover and validate our 57-gene biomarker panel (GEO Accession #GSE107509). Subsequent studies using our biomarker have further validated its utility in clinical practice [5]. So, we believe that the answer to "Are we ready to implement non-invasive tests to detect allograft rejection in a daily praxis" is definitely, yes.

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* Corresponding author.
E-mail address: john.friedewald@nm.org (J. Friedewald).

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