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# A Test Identifying Biomarkers of Immunosuppression-Related Adverse Events in Kidney Transplant Recipients

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Modulating immunosuppression in kidney transplant recipients is still in its infancy. Decreasing immunosuppression to avoid infections, cardiovascular complications, and cancers is legitimate, but there is now compelling evidence that it leads to or may lead to under-immunosuppression, production of donor-specific antibodies, antibody-mediated rejection, and finally graft loss. In contrast, increasing immunosuppression to avoid or treat rejection will lead to various infections, cardiovascular complications, cancers, and potentially death of the patient while the kidney is working correctly. We just do not know how to precisely define the net state of immunosuppression.

There is, therefore, a real need to improve our immunosuppression modulation practices. Currently, in spite of intensive research, there is no such test available and widely used by the transplant community. There is a need to define biomarkers, well designed, well studied, compared with an adequate control group and confirmed with one or several validation cohorts.[1–3]

In this issue, Bouchard-Biotin *et al.*[4] report on a pilot study aiming at the validation of a test based on tumor necrosis factor-α production by monocytes stimulated with Epstein-Barr virus peptides as a marker of immunosuppression-related adverse events in kidney transplant recipients. The study involved 71 patients admitted for a kidney biopsy either for surveillance or for cause, and they were controls or cases at 1-year post-test. Cases were detected with 83% sensitivity and 68% specificity, whereas negative predictive value of the assay was 89%. In patients with a positive test, the hazard ratio for the occurrence of the endpoint was 6.8. It is possible the population was biased, because there is a difference between surveillance and a for-cause biopsy, post-transplant time of follow-up, and time to exposure to immunosuppression drugs was different between the 2 groups. In spite of the small number of patients included, this study is very interesting because each step of the study is precisely deciphered so that each factor is either taken into account or discussed to set the stage for a prospective trial to be performed in the months to come with an unbiased population of consecutive patients with a repeated test. It is also useful to read the article from Camargo *et al.*[5] on the use of biomarkers to predict patients at risk for rejection; they chose to study the population of transplant recipients with HIV to magnify this risk.

It is therefore not surprising that it is such a difficult task to conduct these studies because heterogeneity remains the rule in organ transplantation.

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## DISCLOSURE

The author declared no competing interests.

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