Longitudinal studies of a B cell-derived signature of tolerance in renal transplant recipients.


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Abstract

Biomarkers of transplant tolerance would enhance the safety and feasibility of clinical tolerance trials and potentially facilitate management of patients receiving immunosuppression. To this end, we examined blood from spontaneously tolerant renal transplant recipients and patients enrolled in two interventional tolerance trials using flow cytometry and gene expression profiling. Using a previously reported tolerant cohort as well as newly identified tolerant patients, we confirmed our previous finding that tolerance was associated with increased expression of B cell-associated genes relative to immunosuppressed patients. This was not accounted for merely by an increase in total B cell numbers, but was associated with the increased frequencies of transitional and naïve B cells. Moreover, serial measurements of gene expression demonstrated that this pattern persisted over several years, although patients receiving immunosuppression also displayed an increase in the two most dominant tolerance-related B cell genes, IGKV1D-13 and IGLL-1, over time. Importantly, patients rendered tolerant via induction of transient mixed chimerism, and those weaned to minimal immunosuppression, showed similar increases in IGKV1D-13 as did spontaneously tolerant individuals. Collectively, these findings support the notion that alterations in B cells may be a common theme for tolerant kidney transplant recipients, and that it is a useful monitoring tool in prospective trials.

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