Pre-transplant CD45RC expression on blood T cells differentiates patients with cancer and rejection after kidney transplantation

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Résumé en anglais	Background Biological biomarkers to stratify cancer risk before kidney transplantation are lacking. Several data support that tumor development and growth is associated with a tolerant immune profile. T cells expressing low levels of CD45RC preferentially secrete regulatory cytokines and contain regulatory T cell subset. In contrast, T cells expressing high levels of CD45RC have been shown to secrete proinflammatory cytokines, to drive alloreactivity and to predict acute rejection (AR) in kidney transplant patients. In the present work, we evaluated whether pre-transplant CD45RClow T cell subset was predictive of post-transplant cancer occurrence. Methods We performed an observational cohort study of 89 consecutive first time kidney transplant patients whose CD45RC T cell expression was determined by flow cytometry before transplantation. Post-transplant events including cancer, AR, and death were assessed retrospectively. Results After a mean follow-up of 11.1 ± 4.1 years, cancer occurred in 25 patients (28.1%) and was associated with a decreased pre-transplant proportion of CD4+CD45RChigh T cells, with a frequency below 51.9% conferring a 3.7-fold increased risk of post-transplant malignancy (HR 3.71 [1.24–11.1], p = 0.019). The sensibility, specificity, negative predictive and positive predictive values of CD4+CD45RChigh<51.9% were 84.0, 54.7, 89.8 and 42.0% respectively. Confirming our previous results, frequency of CD8+CD45RChigh T cells above 52.1% was associated with AR, conferring a 20-fold increased risk (HR 21.7 [2.67–176.2], p = 0.0004). The sensibility, specificity, negative predictive and positive predictive values of CD8+CD45RChigh>52.1% were 94.5, 68.0, 34.7 and 98.6% respectively. Frequency of CD4+CD45RChigh T cells was positively correlated with those of CD8+CD45RChigh (p<0.0001), suggesting that recipients with high AR risk display a low cancer risk. Conclusion High frequency of CD45RChigh T cells was associated with AR, while low frequency was associated with cancer. Thus, CD45RC expression on T cells appears as a double-edged sword biomarker of promising interest to assess both cancer and AR risk before kidney transplantation.
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