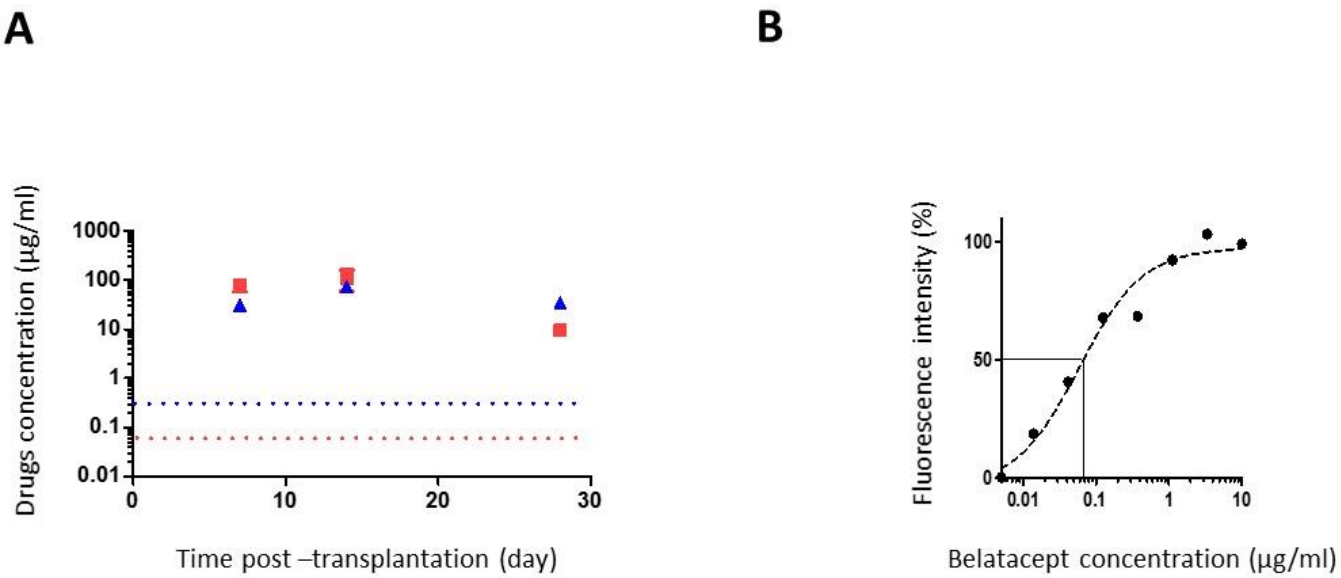
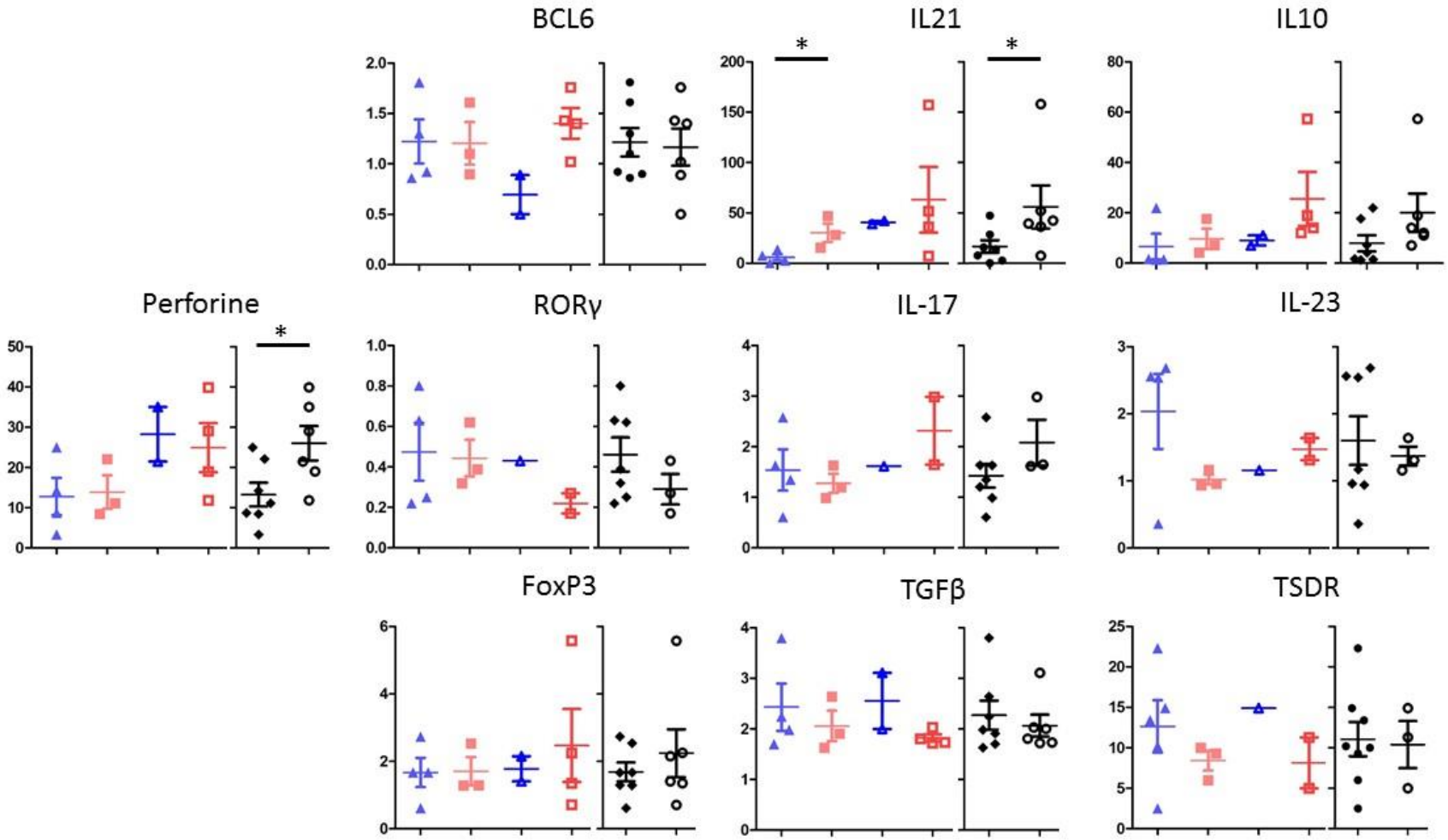
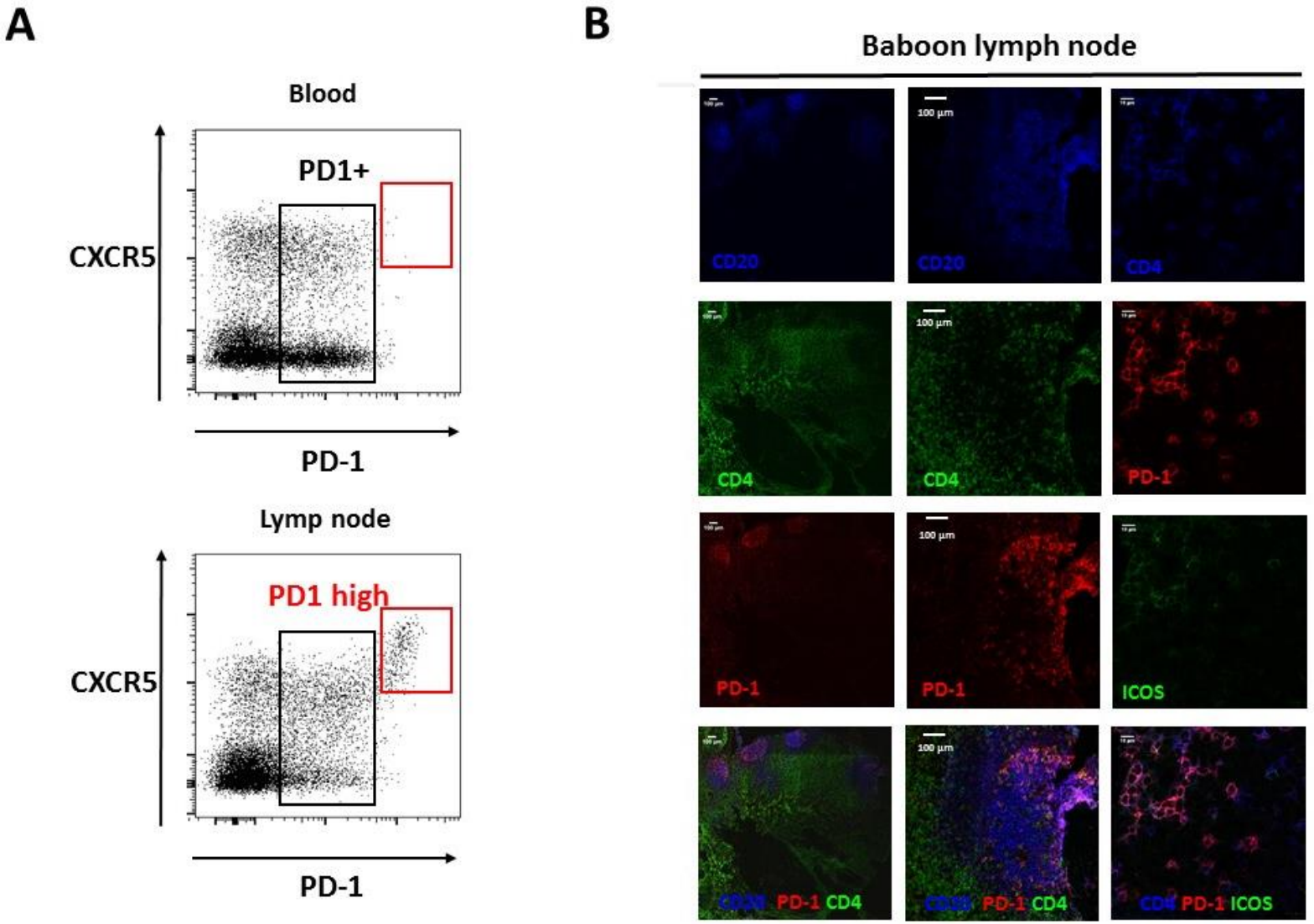


Supplementary Figure 1. (**A**) Trough concentrations of FR104 (blue triangle, n = 2) and Belatacept (red square, n = 2) in serum of kidney allograft recipients. For each drug, dotted lines represent the ED_{50} measured by flow cytometry. (**B**) Binding profile of Belatacept on baboon PBMC by flow cytometry.



Supplementary Figure 2. Quantitative real-time PCR measurement of mRNA expression on one month protocol biopsies from animals treated with FR104 (blue triangle) or Belatacept (red square), and on rejection biopsies from animals treated with FR104 (open blue triangle) and Belatacept (open red square). Black symbols represent all protocol biopsies and open circles represent all rejection biopsies. Target gene expression is relative to HPRT. Data are mean +/- SEM. A Mann-Whitney non-parametric test was used, p values less than 0.05 are considered as significant.



Supplementary figure 3. (**A**) Flow cytometry plot representative of baboon blood and lymph node cell suspension showing CXCR5 and PD1 staining on $CD4^+$ cells. $CD4^+$ $CXCR5^{hi}PD1^{hi}$ cells (red gate) correspond to follicular helper T cells (Tfh) and are present only in the lymph node. (**B**) Immunostaining of a baboon lymph node showing the B cell zone, marked with an anti-CD20 staining (blue), and the T cell zone around the B follicle identified by anti-CD4 staining (green). Only a few CD4+ T cells located into the B follicle (i.e Tfh) are detectably marked with anti-PD1 staining (red). These cells express also ICOS.

Supplementary methods

Drugs dosage (ELISA)

Recombinant human CD28-Fc (R&D Systems) or monoclonal mouse anti-human CTLA-4 (BNI3, BD Biosciences) was diluted to 2 mg/mL in carbonate buffer (pH 9.2) to coat 96-well microtiter plates (Maxisorp Nunc, Dutscher) overnight at 4°C. Reactive sites were blocked with 1% bovine serum albumin (Sigma–Aldrich) in 0.1% Tween-PBS for 2 h at 37°C. Serum samples were incubated for 2 h at 37°C FR104 was detected by monoclonal mouse anti-human kappa chain antibody (BioAtlantique) at 0.2 mg/mL (1 h, 37°C) and by HRP-conjugated donkey anti-mouse Ig antibody (0.4 g/mL, 1 h at 37°C; Jackson Immunoresearch). Belatacept was detected by HRP-conjugated donkey anti-human IgG Fc antibody (0.4g/mL, 1h at 37°C; Jackson Immunoresearch). Optical density was recorded at 450 nm after TMB revelation.

Binding assay

PBMC were isolated from whole baboon blood by density centrifugation over Ficoll-Paque (Eurobio). Freshly isolated PBMC were incubated for 30 min at room temperature with indicated Belatacept concentration. Belatacept staining was performed with a fluorescent goat anti-human IgG Fc antibody (Sigma-Aldrich). Saturation of baboon PBMC was determined by performing the ratio of median fluorescent intensity (MFI) of Belatacept staining between an unmodified blood sample and a blood sample incubated for 30 min at room temperature with a saturating concentration of Belatacept (1 mg/mL). Samples were acquired on a BD FACSCANTO^{TM} flow cytometer (BD Bioscience) and analyzed with FlowJo software.