Supplemental Methods

**Isolation of naïve and memory CD8⁺ T cell populations.** CD8⁺ T cells were negatively isolated and divided into CD45RA and CD45RO fractions by positive selection with magnetically labelled antibodies (EasySep, Stemcell technologies).

**CD4⁺ Treg Suppression assay.** PBMC were plated out with 1 µg/ml OKT3, washed and rested over 5 d, as described in the suppression assay methods. The sample was split into two, and CD4⁺ and CD8⁺ T cells were then isolated by negative selection and subsequently split into CD8⁺CD25⁺, CD4⁺CD25⁺ or CD4⁺CD25⁻ T cells by positive selection with magnetic beads (purities for FOXP3 > 80%) (Miltenyi Biotec). Autologous frozen cells were then thawed and their CD8⁺ T cells were isolated. The PBMC depleted of CD8⁺ T cells were stained with 1µM CFSE then cultured at 1×10⁵ cells with 1 CD8⁺CD25⁺, CD4⁺CD25⁺ or CD4⁺CD25⁻ T cell to 5 CD4⁺ T cells. Cultures were then stimulated with 1 µg/ml SEB for 3 d and CD4⁺ T cell proliferation was analyzed. Supernatants were stored for cytokine analysis.

**Phosphoflow of p38.** RA PBMCs were isolated and rested at 37°C for 2 hours. PBMC were then stimulated with 1 µg/ml OKT3 for 0, 3, 5 or 15 mins, then fixed with Cytofix™ Buffer (BD Pharmingen) at 37°C for 10 minutes. Cells were permeabilized with 90% ice-cold Phosflow Perm Buffer III (BD Pharmingen) for 15 min, then stained directly with conjugated antibodies against CD4-PB (BD Pharmingen), CD8-FITC (BD Pharmingen), CD45RA-PE
(eBioscience), CD45RO-APC (eBioscience) and phospho-p38-PEcy7 (BD™ Phosflow) or PECy7 isotype (BD Pharmingen).