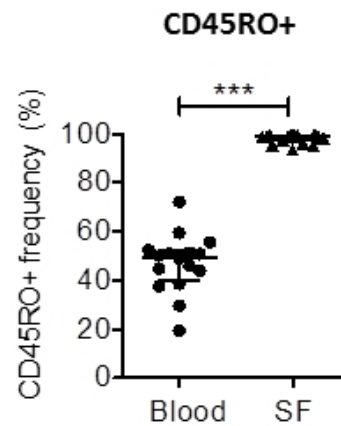
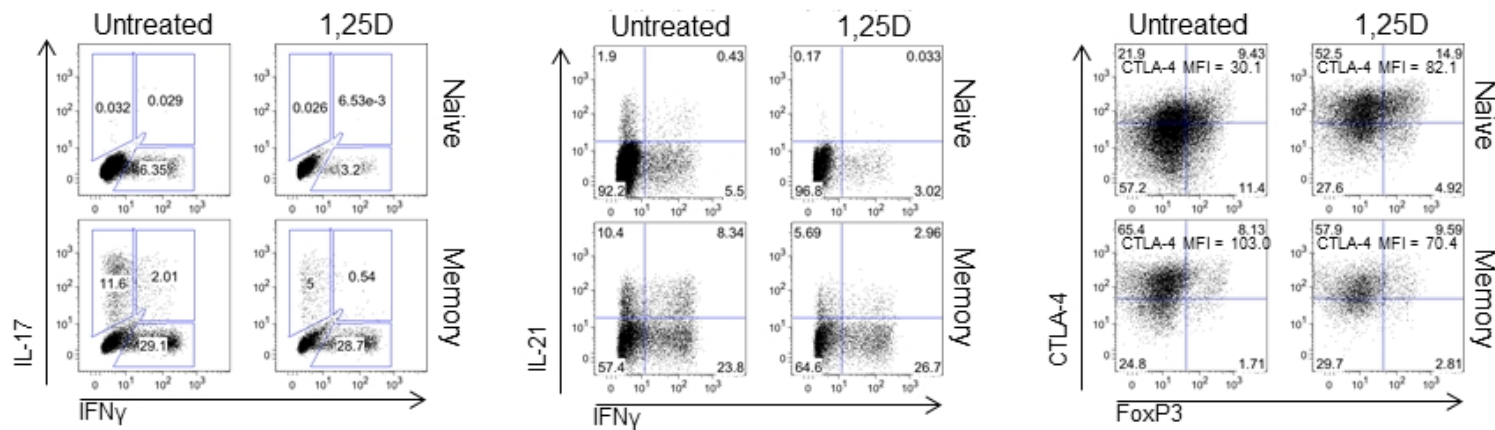


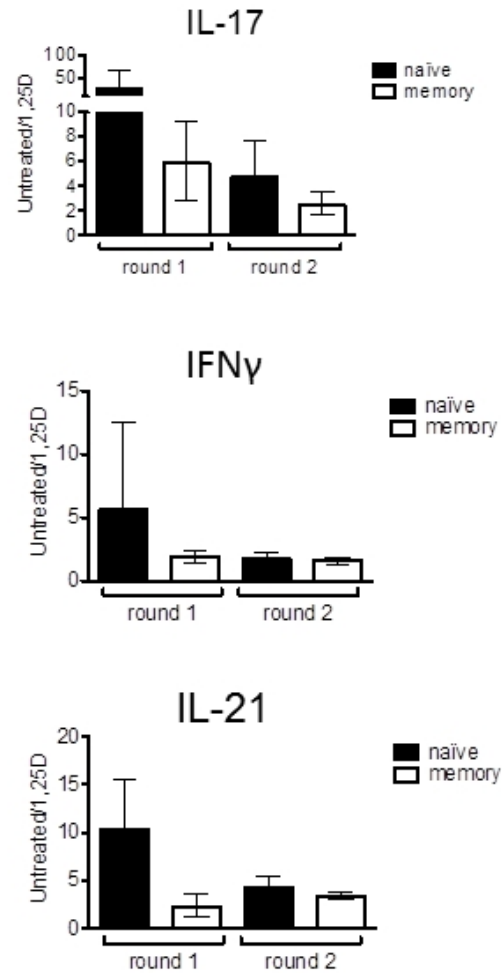
**S1. Anti-inflammatory effects of 1,25(OH)<sub>2</sub>D<sub>3</sub> are reduced in CD8+ T cells from RA patients. (A).** Representative bivariate plots of IL-17 versus IFN $\gamma$  expression by CD8+ T cells. **(B).** Significant effects of 1,25(OH)<sub>2</sub>D<sub>3</sub> were tested for HC (n=9), RA blood (n=12), RA SF (n= 11) by Wilcoxon matched pairs or Mann Whitney nonparametric tests as appropriate. ns= non-significant, \* = P<0.05, \*\*=P<0.01, \*\*\*=P<0.001.



**S2. Memory T cells are abundant in synovial fluid.** Frequency of CD45RO+ CD4+ T cells in the blood and synovial fluid (SF) of RA patients was assessed by flow cytometry. Significance was tested by Wilcoxon matched pairs analysis \*\*\* =  $P < 0.001$ .



**S3. Effects of 1,25(OH) $_2$ D $_3$  are greater on naive than memory T cells.** Naive and memory CD4 $^+$  T cells were purified from the peripheral blood of healthy controls and stimulated with autologous monocytes and anti-CD3 in the presence or absence of 1,25(OH) $_2$ D $_3$  (+1,25D). Expression of inflammatory cytokines IL-17, IFN $\gamma$  and IL-21 was quantified at seven days and expression of CTLA-4 and FoxP3 measured at four days. Bivariate FACS profiles for one donor, representative of six are shown.

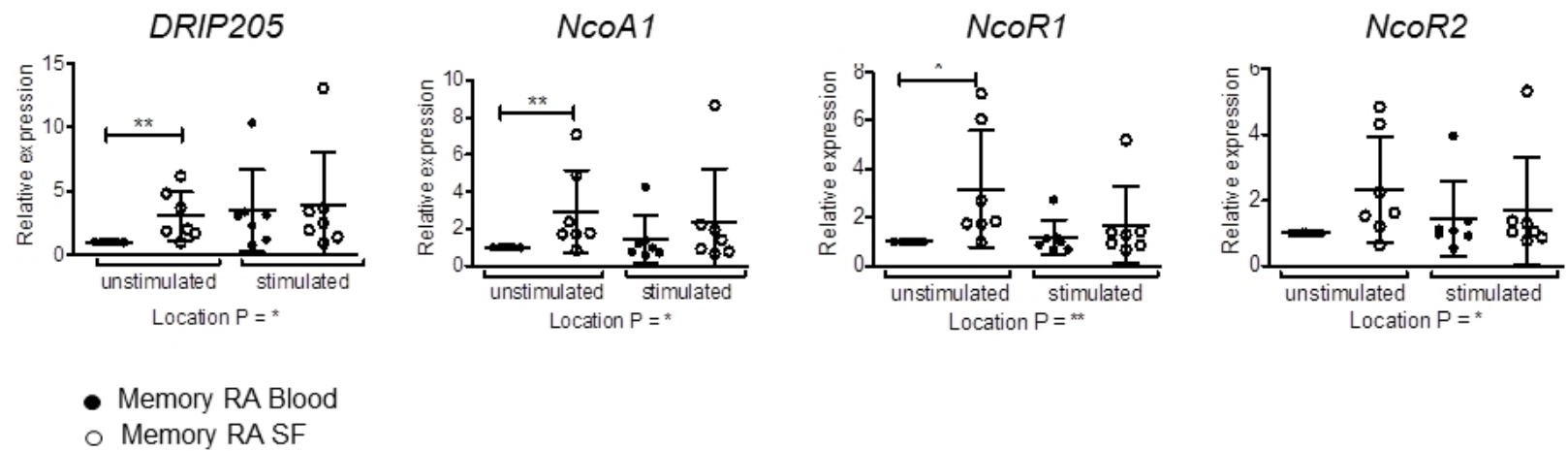


#### S4. Naïve T cell sensitivity to 1,25(OH) $_2$ D $_3$ decreases following stimulation

Naïve and memory CD4+ T cells were stimulated with monocytes and anti-CD3 for two sequential rounds of stimulation. The effect of 1,25(OH) $_2$ D $_3$  upon IL-17+, IFN $\gamma$ + and IL-21+ frequencies is given as the relative frequency of positive cells under untreated/1,25(OH) $_2$ D $_3$  conditions. Graphs show the mean and range of effect for n=3 donors.

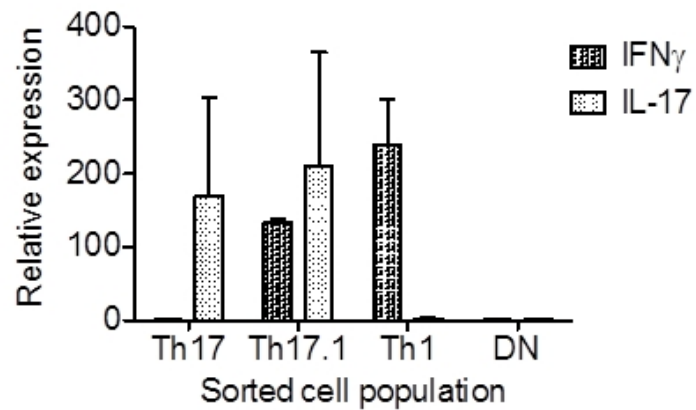
Co-enhancers

Co-repressors



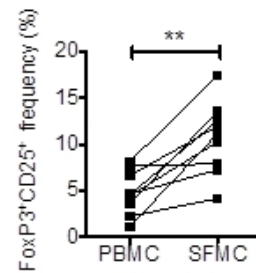
**S5. Expression of mRNA for VDR co-regulators in blood versus SF memory T cells**

In CD45RO+ memory T cells from RA patient blood and SF, qPCR was used to measure mRNA for the VDR co-activators DRIP205, NcoA1 and the VDR co-repressors NcoR1 and NcoR2. Data are shown for n=7 donors. Statistical significance was tested by repeated measures two-way ANOVA. \* = P<0.05, \*\*=P<0.01.

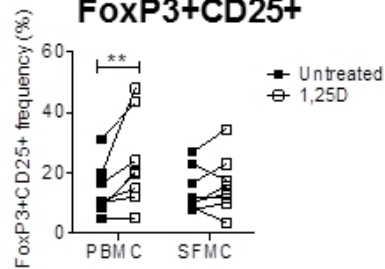


**S6. IL-17 and IFN $\gamma$  expression in purified Th17, Th17.1, Th1 and DN CD4+ T cells.** qPCR was used to measure IL-17 and IFN $\gamma$  mRNA expression in CD4+ T cells sorted into Th17, Th17.1, Th1 and DN subsets using cytokine secretion assays and flow sorting. Expression is given relative to the level in DN T cells.

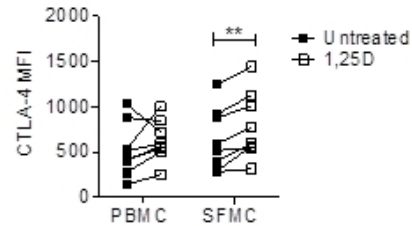
### A. FoxP3+CD25+



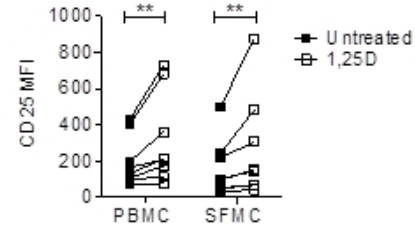
### B. FoxP3+CD25+



### CTLA-4



### CD25



**S7. 1,25(OH)<sub>2</sub>D<sub>3</sub> regulation of Treg markers in PBMC and SFMC from RA patients. A)** Ex-vivo frequencies of FoxP3+CD25+ CD4+ T cells. **B)** Frequencies of FoxP3+CD25+ CD4 T Cells and their median expression of CTLA-4 and CD25 in stimulated PBMC and SFMC cultures at three or four days. Significance was tested by Wilcoxon matched pairs analysis \*\* = P<0.01.