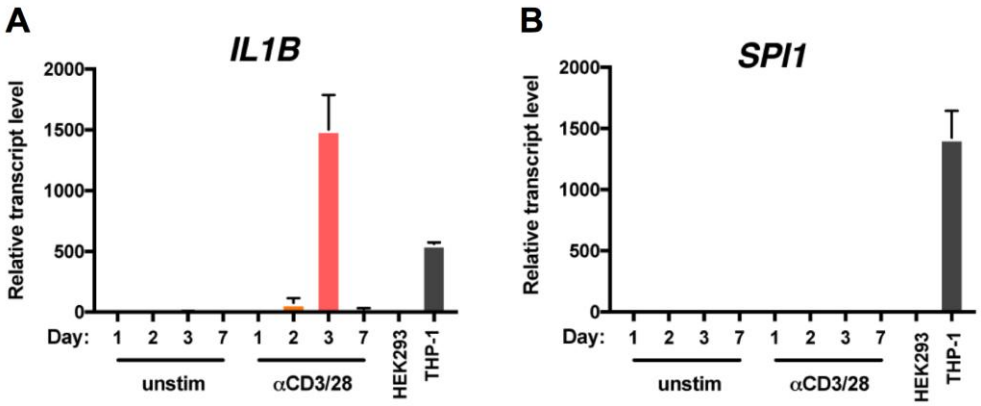
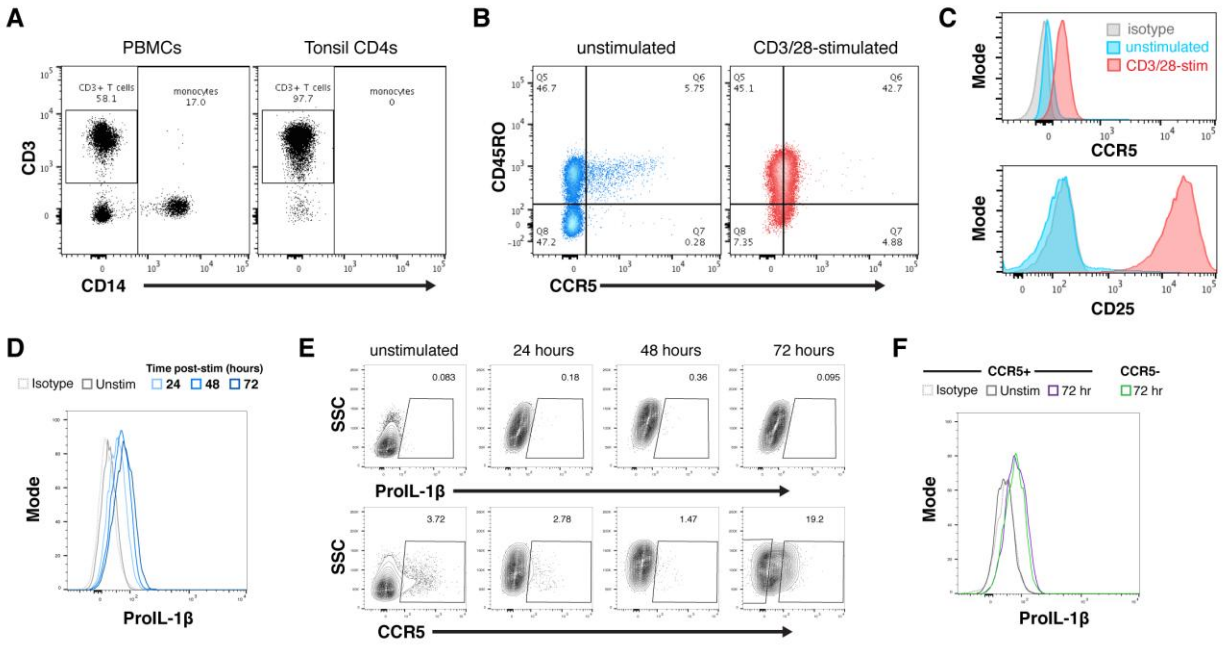
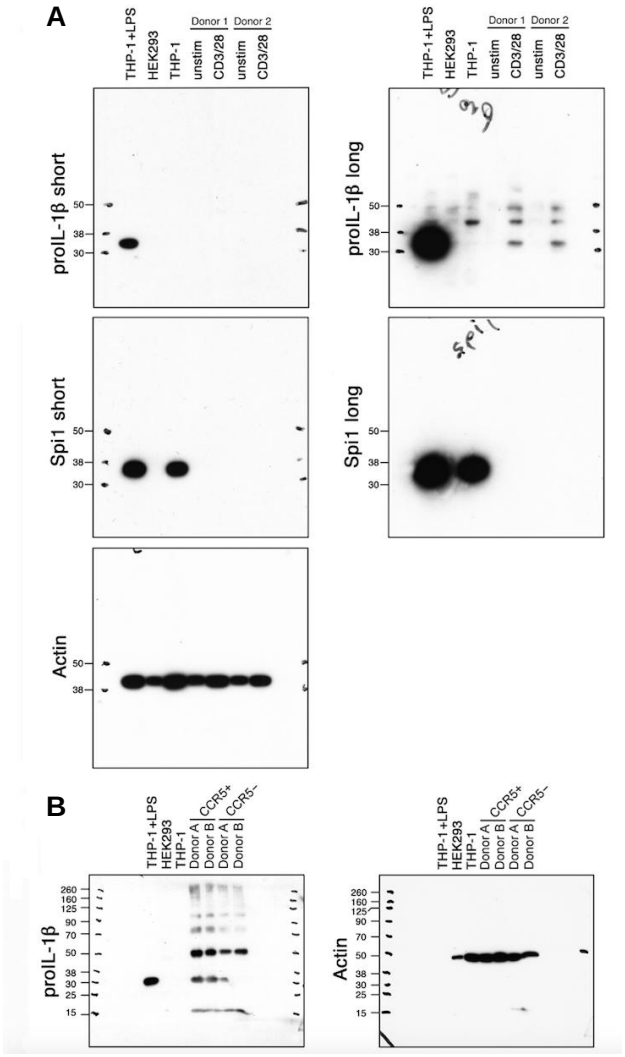
SUPPLEMENTARY INFORMATION



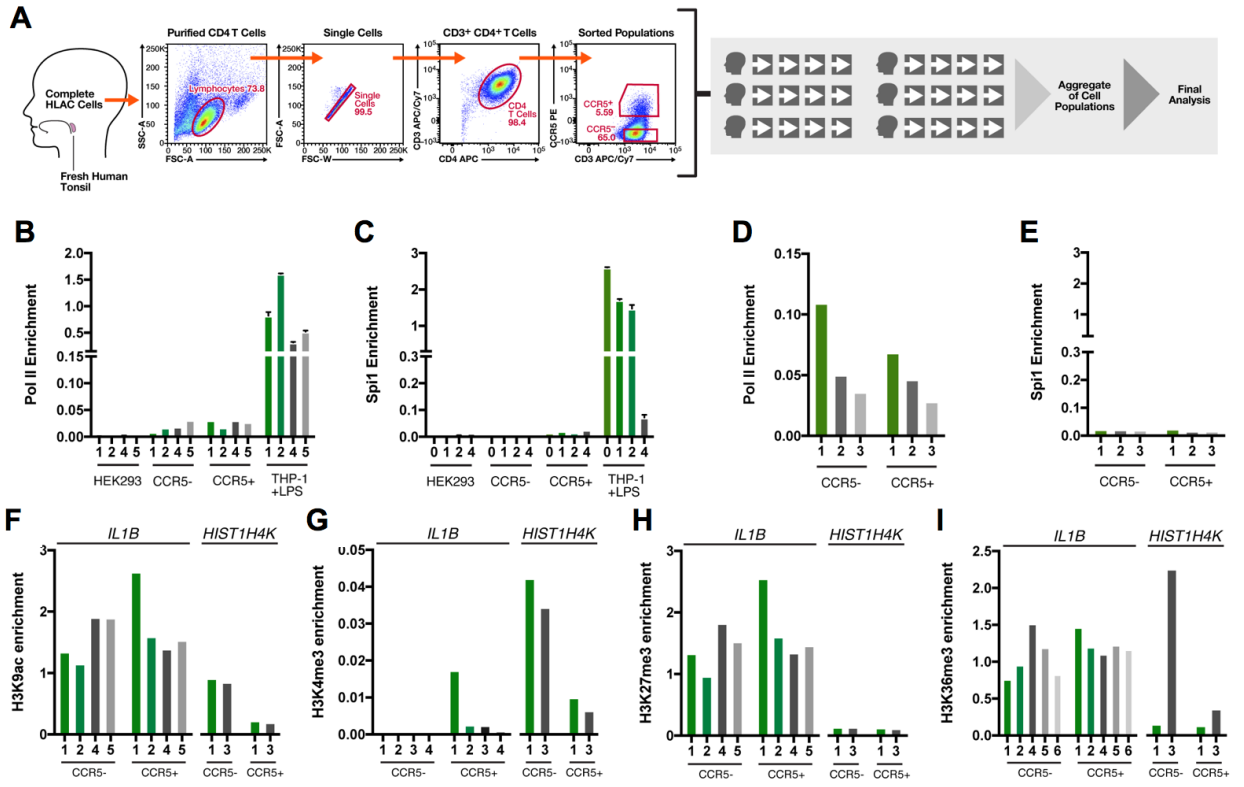
Supplementary Figure 1. CD4 T cells express maximal *IL1B* mRNA after 3 days of TCR activation. Kinetic mRNA profile for **(A)** *IL1B* and **(B)** *SPI1* in CD4 T cells following the TCR activation for indicated time. The values were normalized to HEK293 negative control cells. For comparison, unstimulated THP-1 cells are shown, which express low levels of *IL1B* mRNA and constitutive *SPI1*.



Supplementary Figure 2. Characterization of *ex vivo* differentiated CD4 T cells. (**A**) Fresh human PBMCs were isolated and analyzed by flow cytometry and compared to CD4 T cells, which were magnetically purified by negative selection from tonsil. Note the lack of monocytes in CD4 T cell preparations. (**B&C**) Purified CD4 T cells from tonsil, stimulated with anti-CD3/28 beads or resting for 3 days of culture were surface-stained for CD45RO (memory marker), CCR5, and CD25. TCR stimulation induces an activated memory phenotype, including upregulation of CD25 and CD45RO, and homogenous increase of CCR5. (**D**) Time course showing increasing proIL-1β following CD3/CD28 activation (blue traces). Cells were stimulated with anti-CD3/28 beads for time indicated, then treated with GolgiPlug (BD Biosciences) for two hours, surface stained as described in Methods, then fixed and permeabilized (eBiosciences Cytofix/Perm). Intracellular proIL-1β was stained using Alexa647 anti-IL-1β (BioLegend). Shown here are representative cytograms from one donor, representative of four individual donors. (**E**) Increase in proIL-1β production among the activated T cells is likely from almost all cells; not the result of a few high producers. (**F**) Among CD3/CD28 activated T cells, proIL-1β is produced by both CCR5+ and CCR5- cells (gated as in E).



Supplementary Figure 3. CD4 T cells express proIL-1β following TCR stimulation independent of Spi1. (A) Full-length blots of cropped images from Fig. 1C. The short and long exposures of proIL-1β and Spi1 blots illustrate the relative abundance of these proteins in *ex vivo* TCR-activated CD4 T cells in comparison with resting CD4 T cells, HEK293 cells, and THP-1 cells (unstimulated or LPS-treated for 1.5 h) for two individual patient donors. Membranes were stripped and re-probed for β-actin. Samples were normalized by cell equivalents, $1.5x10^5$ for all lanes. **(B)** Full-length blots of cropped images from Fig. 2D show expression of proIL-1β for *in vivo*-differentiated CCR5+ and naïve CCR5- CD4 T lymphocytes from two individual patient donors. HEK293, unstimulated and 1.5 h LPS-treated THP-1 cells were used as controls. Membranes were stripped and re-probed for β-actin. Samples were normalized by cell equivalents: $1.5x10^4$ cell equivalents for THP-1+LPS and $1.5x10^5$ in all other lanes.



Supplementary Figure 4. The Spi1 independent *IL1B* gene for *in vivo* differentiated CCR5+ CD4 T cells exhibit similar bivalent H3K4me3^{+}/H3K27me3^{+} epigenetic marks as *ex vivo* TCR-activated CD4 T cells. (A) Shown is a flow-sort from six individual donors pooled together to separate CCR5+ and CCR5- CD4 T cells for ChIP analyses. Cells were sorted from the CCR5+ and CCR5- gates as shown, after performing negative-selection magnetic enrichment of CD4 T cells from fresh human tonsil. **(B)** Pol II and **(C)** Spi1 ChIP on *IL1B* gene was performed in these CD4 T cell population. **(D&E)** Actively transcribing *HIST1H4K* gene from same chromatin was used as control. For sake of comparison, Pol II and Spi1 ChIP data for HEK 293 and LPS stimulated THP-1 cells are included. Histone modification ChIP on *IL1B* and *HIST1H4K* genes in CCR5+ and CCR5- CD4 T cell populations: (**F**) H3K9Ac; (**G**) H3K4me3; (**H**) H3K27me3; and (**I**) H3K36me3. Gene schematics for *IL1B* and *HIST1H4K* genes with exons labeled as Roman numerals are provided in Fig. 3A and 4A respectively. Promoter-proximal amplicons are shown as green bars, whereas downstream amplicons are shown as gray scale.

Supplementary Table 1

A. Primer sequences used for mRNA analysis

Gene	Forward Primer	Reverse Primer
h*IL1B*	TCCAGGGACAGGATATGGAG	TCTTTCAACACGCAGGACAG
h*Spi1*	CCAGCTCAGATGAGGAGGAG	AGGCGGATCTTCTTCTTGCT

B. Human IL1B and HIST1H4K ChIP primer sequences

IL1B

Position (Number)	Forward Primer	Reverse Primer
-279	TGTGTGTCTTCCACTTTGTCCCAC	CCTGACAATCGTTGTGCAGTTGATG
-223	TGTGGACATCAACTGCACAACG	TTCATGGAAGGGCAAGGAGTAGCA
-155	TTGCTACTCCTTGCCCTTCCATGA	GAGTATTGGTGGAAGCTTCTTAGGG
-91 (0)	CCCTAAGAAGCTTCCACCAATACTC	GCAGAAGTAGGAGGCTGAGAAA
-19 (1)	ACAACTAGGTGCTAAGGGAGTC	AGGAGAGGGAGAGACAGAGAAAGA
+36 (2)	AAACCTCTTCGAGGCACAAG	GAGCAATGAAGATTGGCTGA
+98	CAGCCAATCTTCATTGCTCA	GCATACACACAAAGAGGCAGAG
+160	CTCTGCCTCTTTGTGTGTATGC	GAGGGAAGGAGAGGGAGAGA
+223	TCTCCCTCTCCTTCCCTCTC	TTCCCAGAATATTTCCCGAGT
+271	GCCAGGTGTAATATAATGCTTATGACTCGG	GACACTAACCTTTAGGGTGTCAGC
+505 (3)	TGCACTGGATGCTGAGAGAAA	GGCTGCTTCAGACACCTGTG
+3325 (4)	AATCTCCGACCACCACTACAGCAA	AAGGGAAAGAAGGTGCTCAGGTCA
+5389 (5)	ACTGCTGTGTCCCTAACCACAAGA	TTCAACACGCAGGACAGGTACAGA
+6268 (6)	TCGCTGCAGAGTGTAGATCCCAAA	TGCTTGAGAGGTGCTGATGTACCA

HIST1H4K

Position (Number)	Forward	Reverse
+35 (7)	GACTCCTCTTGCTCGTCATGTCTG	CGCCTTTGCCAAGACCCT
+237 (8)	GGTGCTGAAGGTGTTCCTGG	CGCTTGGCGTGCTCTGTA
+382 (9)	GGTTGAGCGTCCCTTTCTATCAACA	TGGGCAAACAAGCATCACGG

Supplementary Table 1: Primer sequences used for mRNA and ChIP analysis (**A**) Primer Sequences used for mRNA expression analysis. (**B**) Human *IL1B* and *HIST1H4K* primer sequences used for ChIP. Numbers indicate the midpoint of amplicons in relation to the Transcription start site. Arabic numbers in red indicate the amplicons number in reference to gene schematic in Fig. 3A and Fig. 4E.