A: ST subjects

	plasma HIV RNA* (copies/mL)	duration of presumed HIV infection * (year)	Initiation of HAART after infection (month)	CD4+ cell count* (cells/mm³)	CD4 nadir (cells/mm³)	CD8+ cell count* (cells/mm³)	B- cell count* (cells/mm³)	Age* (year)	HAART*
1	<50	8	1	611	396	509	319	26	AZT ; 3TC ; NEV
2	<50	9	2	688	387	1273	209	48	AZT ; 3TC ; EFV
3	<50	14	19	434	112	583	121	53	3TC ; EFV ; ABA
4	<50	13	44	602	9	767	173	NA	3TC ; ABA ; SAQ
5	<50	8	6	544	181	699	363	55	IND ; 3TC ; AZT
6	<50	8	4	388	439	440	48	41	3TC ; D4T ; DEL
7	<50	8	1	702	NA	586	NA	29	AZT ; 3TC ; EFV
8	<50	12	NA	888	200	942	258	43	NA
9	<50	6	2	689	111	411	157	57	ATA ; TEN; RIT ; NEV
10	<50	12	NA	411	360	368	317	39	ATA ; ABA; 3TC
11	<50	21	57	657	255	1088	163	55	LAM ; RIT ; ABA ; LOP
12	<50	6	1	503	NA	911	193	39	RIT ; ATA
13	<50	6	2	841	NA	505	79	NA	AZT ; 3TC ; EFV
14	<50	6	6	NA	498	NA	24	NA	AZT ; 3TC ; EFV
15	<50	12	5	703	454	541	132	35	AZT ; 3TC ; IND
16	<50	7	6	921	253	309	NA	43	EFV ; IND
	Aviremic	9 (6-21)	14 (1-44)	599 (388-921)	282 (9-498)	662 (309-1273)	182 (24-363)	43 (26-57)	Yes

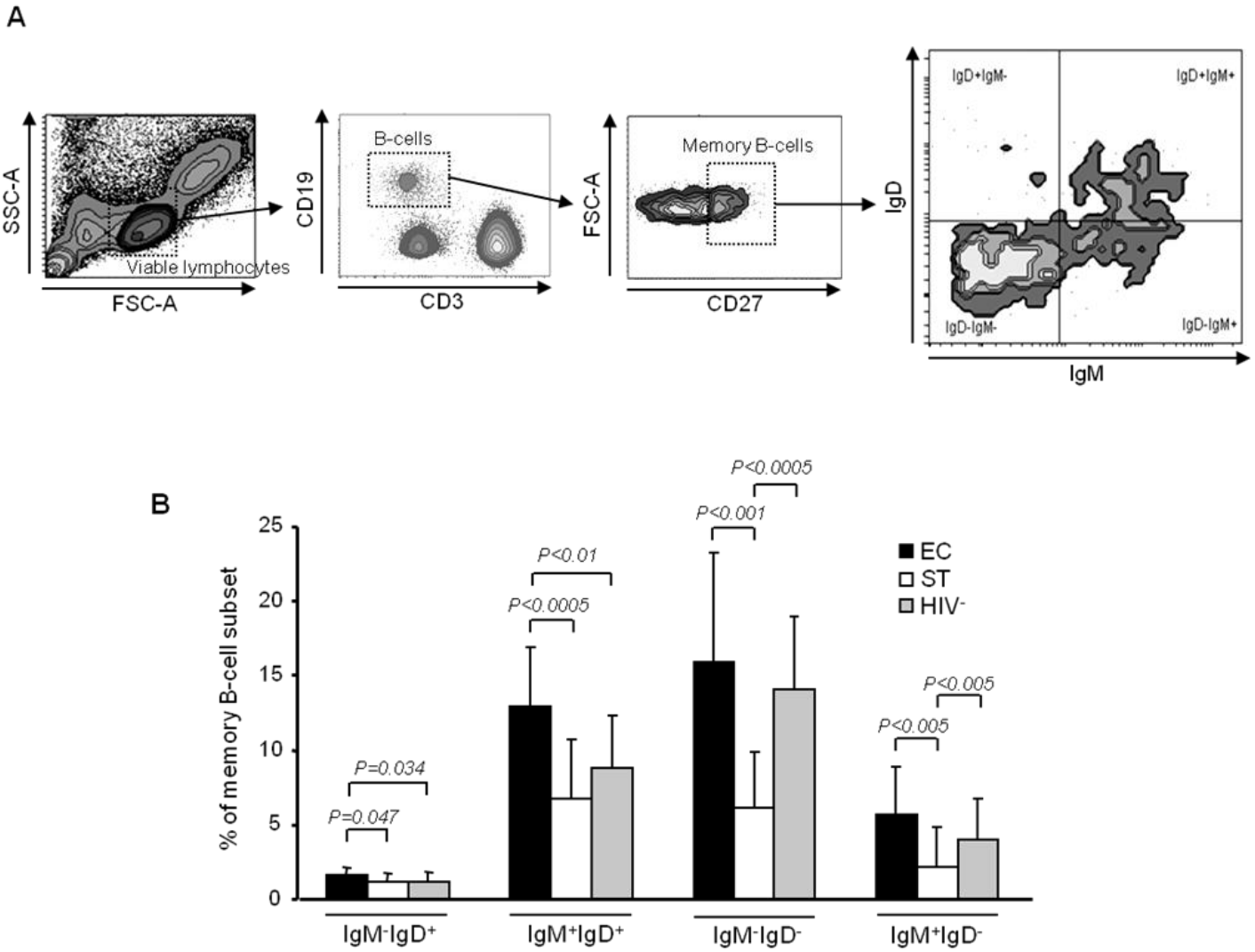
B: EC subjects

	plasma HIV RNA * (copies/mL)	duration of presumed HIV infection (year)*	CD4+ cell count* (cells/mm³)	CD8+ cell count* (cells/mm³)	B- cell count* (cells/mm³)	Age* (year)	CCR5 genotype	HAART
1	154	13	860	1148	52	37	WT/WT	none
2	52	9	760	539	188	33	WT/Δ32	none
3	< 50	13	711	574	178	54	WT/WT	none
4	121	11	641	1759	164	37	WT/WT	none
5	< 50	14	671	626	64	45	WT/Δ32	none
6	< 50	4	530	NA	50	NA	WT/WT	none
7	< 50	18	610	NA	110	NA	WT/Δ32	none
8	< 50	3	530	650	152	46	WT/WT	none
9	< 50	3	1040	1090	80	37	WT/WT	none
10	< 50	2	NA	NA	124	61	WT/Δ32	none
11	< 50	3	700	1250	128	69	WT/WT	none
12	70	3	NA	NA	60	47	WT/WT	none
13	< 50	4	NA	NA	327	42	WT/WT	none
14	< 50	4	779	860	NA	59	WT/WT	none
15	< 50	2	543	506	NA	31	WT/WT	none
	Aviremic (74%)	7 (2-18)	698 (530-1040)	900 (506-1759)	129 (52-327)	46 (31-69)	WT/WT (74%)	No

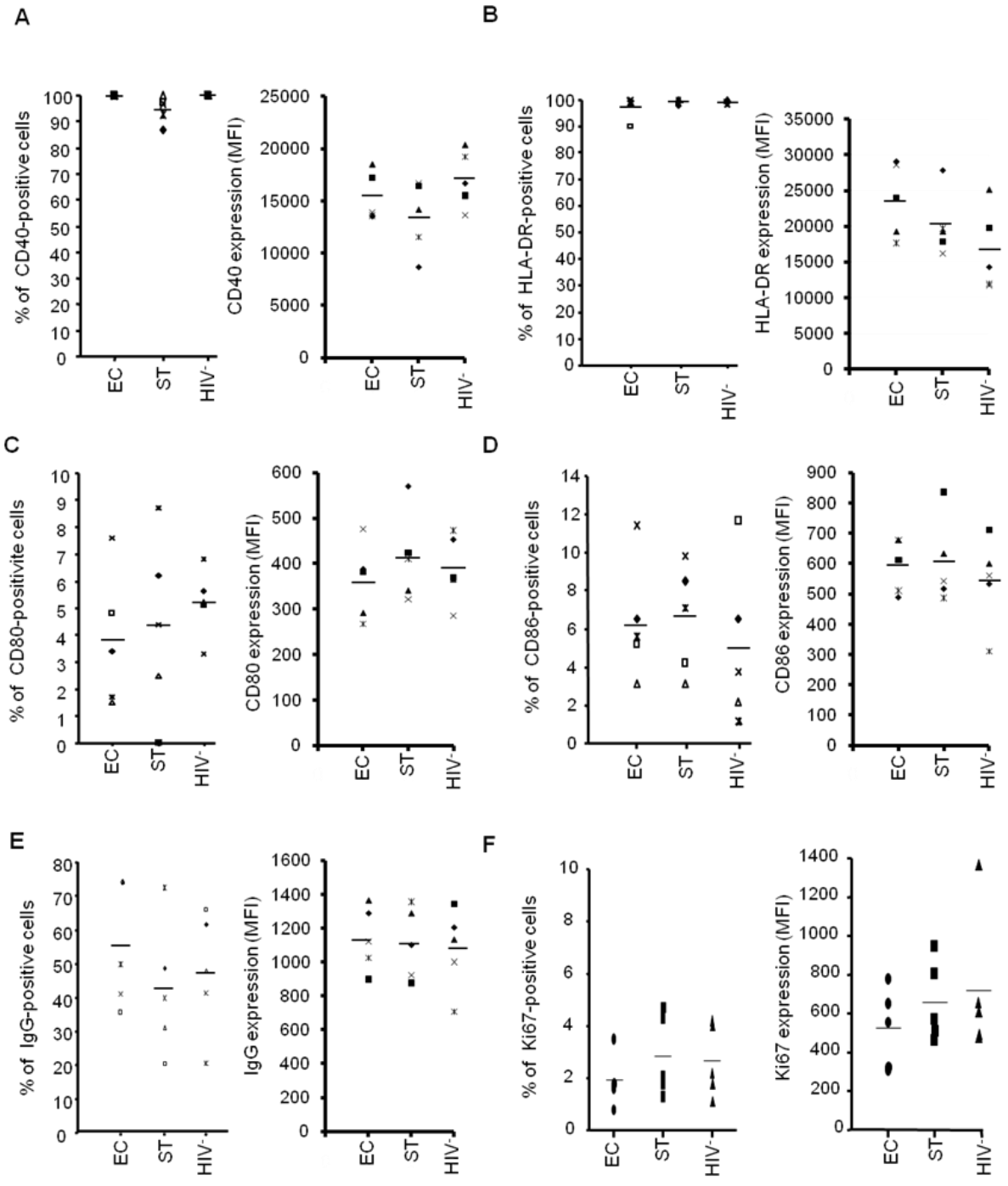
* clinical data collected at leukapheresis time

NA, Data not available

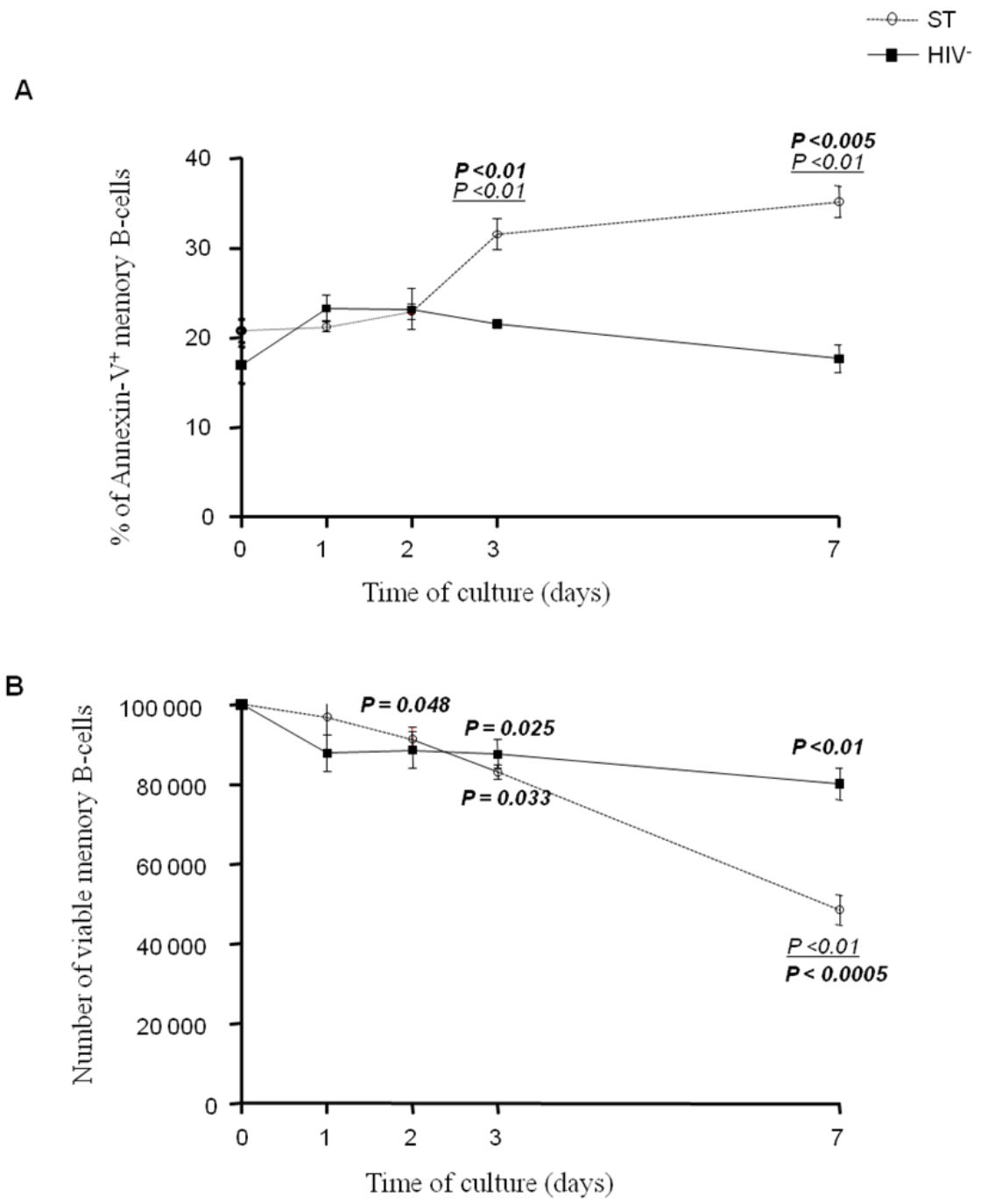
Supplemental Table 1. Clinical and immunological data of HIV+ subjects including absolute numbers of B-cells in blood. (A) Table includes 16 ST subjects chosen for their high CD4 counts and long-term treatment and (B) 15 EC subjects.



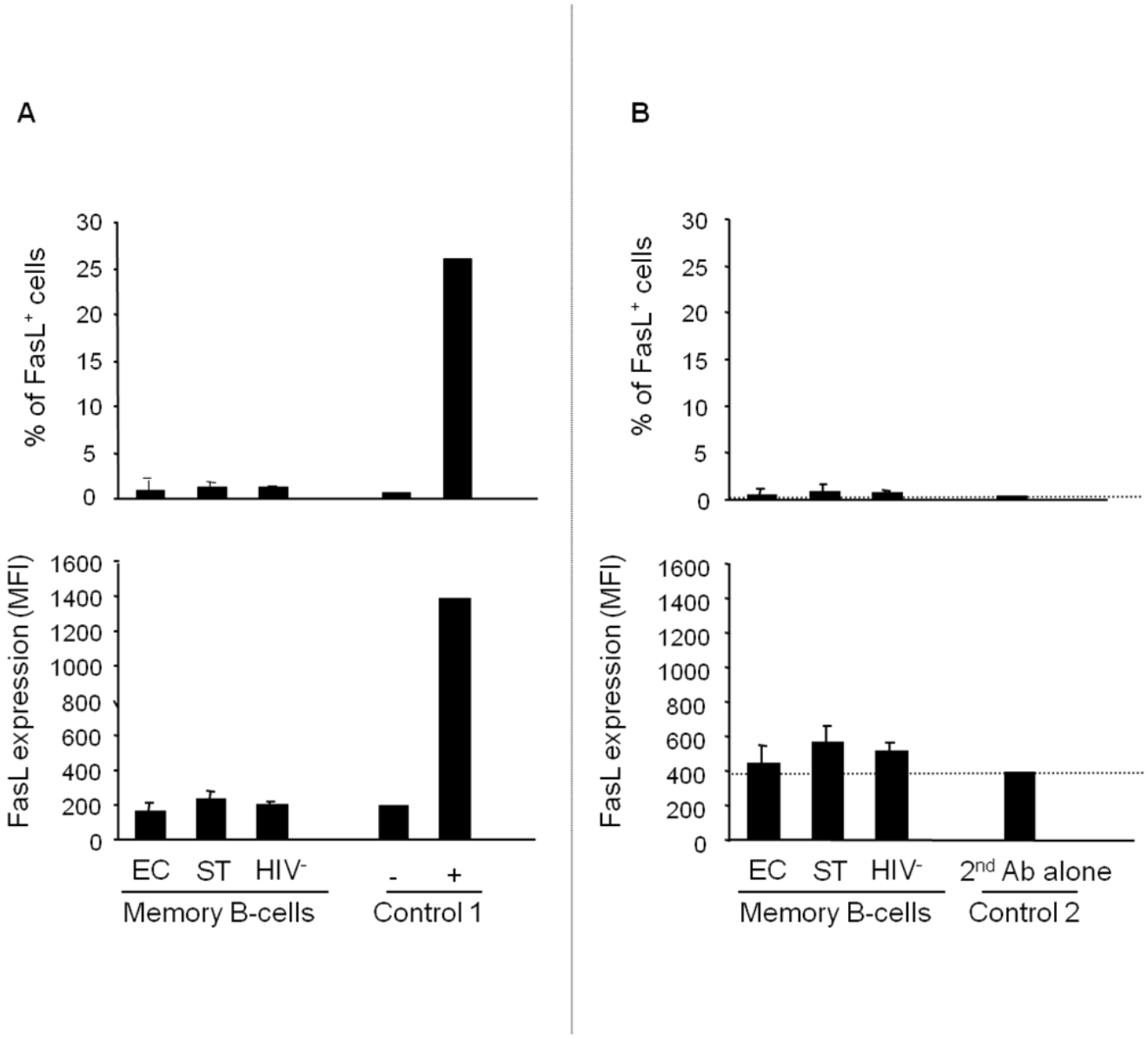
Supplemental Figure 1. Frequency of IgM and IgD memory B-cell subsets. (A) Gating strategy for the analysis of memory B-cell subsets on *ex vivo* PBMCs. (B) Frequency of four memory subsets defined by IgM and IgD surface expression in total B-cells from STs, ECs and HCs by using anti-IgM-PE Cy5 and anti-IgD-FITC antibodies. Results are expressed as the mean of apoptosis ± SD (n = 15).



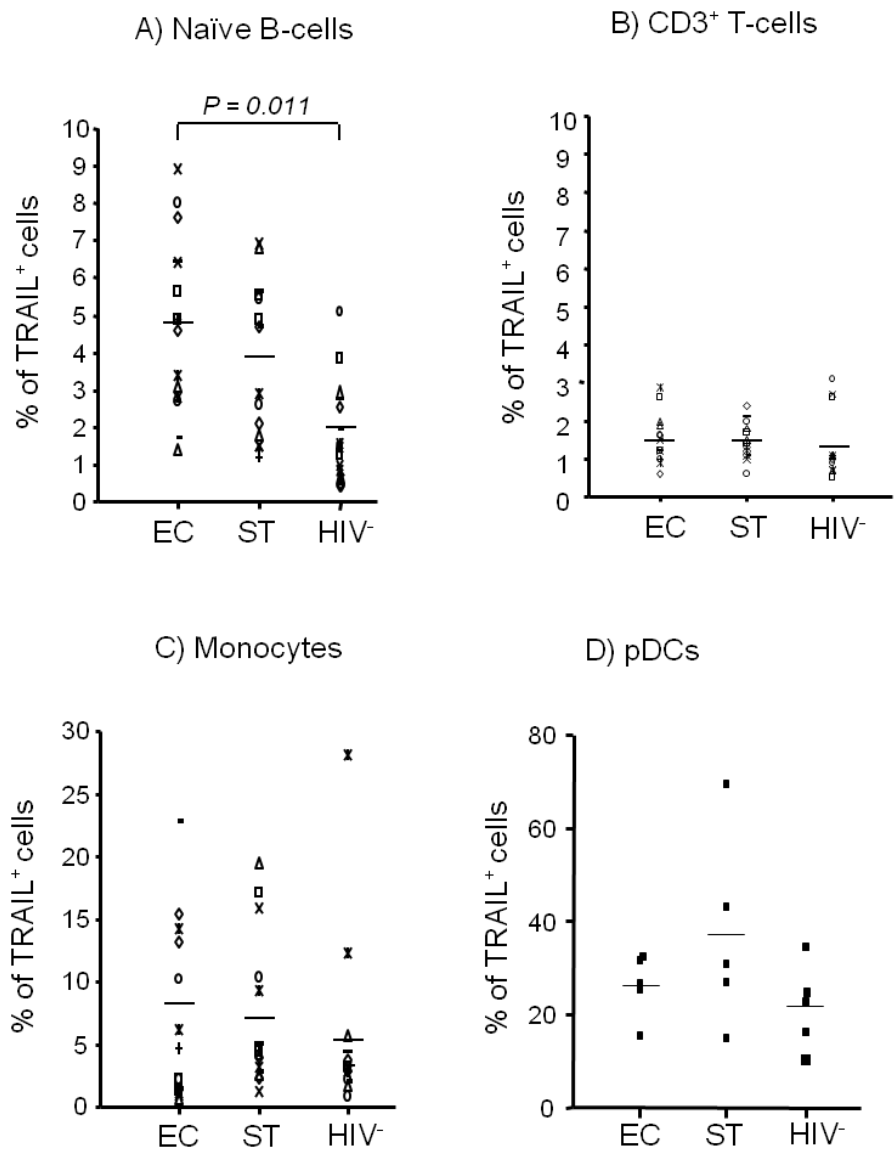
Supplemental Figure 2. Memory B-cells from ST, EC and HIV$^-$ subjects expressed similar levels of activation and proliferation markers at the onset of culture. PBMCs from STs and ECs were labelled with antibodies to 7AAD, CD3-PB, CD19-Alexa700, CD27-APC Cy7, and (A) CD40-FITC or (B) HLA-DR-PE Cy7 or (C) CD80-FITC or (D) CD86-PE or (E) IgG-PE. PBMCs were then fixed, permeabilized in 0.25 % of saponin and stained with (F) anti-Ki67-FITC antibodies. An average of 20,000 gated events were collected on a LSRII flow cytometer. Data was analyzed using the DIVA software. Results show the percentage of positive cells and MFI on gated viable memory B-cells (n = 5).



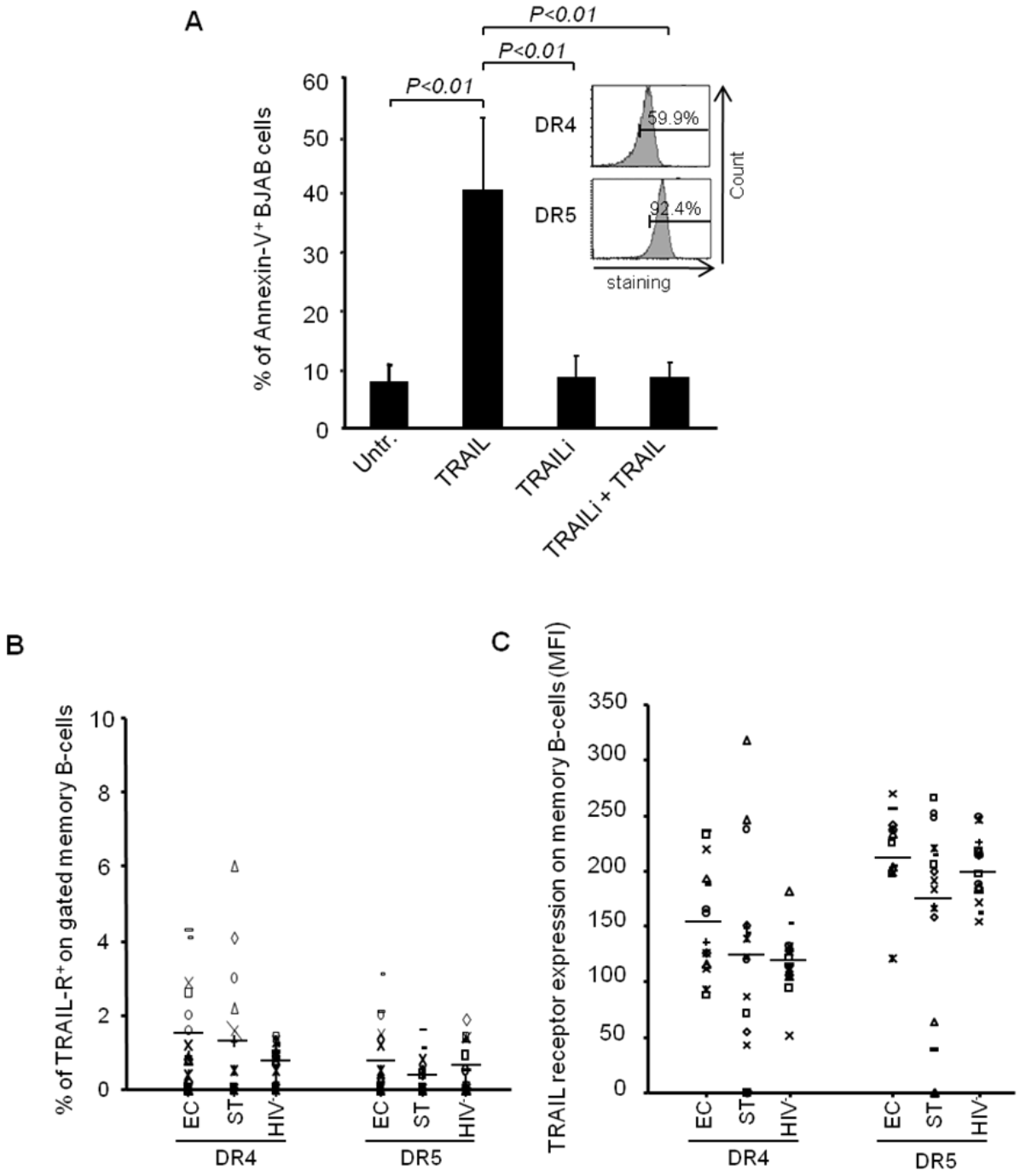
Supplemental Figure 3. Kinetic analysis showing that memory B-cells from STs displayed higher levels of apoptosis starting at day 3 of co-culture. (A-B) Memory B-cells from ST and HIV$^-$ subjects were co-cultured for 7 days with autologous CD19-depleted PBMCs (n = 5). Memory B-cells were assessed for (A) the level of apoptosis by Annexin-V staining and (B) the number of viable cells by trypan blue exclusion at days 0, 1, 2, 3 and day 7 of co-culture. Statistical *P* values (underlined) were determined at every time point of co-culture between ST and HIV$^-$ subjects (cross sectional analysis). In bold are the statistical *P* values, determined with the paired *t* test, for each corresponding time point when compared to day 0 (longitudinal analysis).



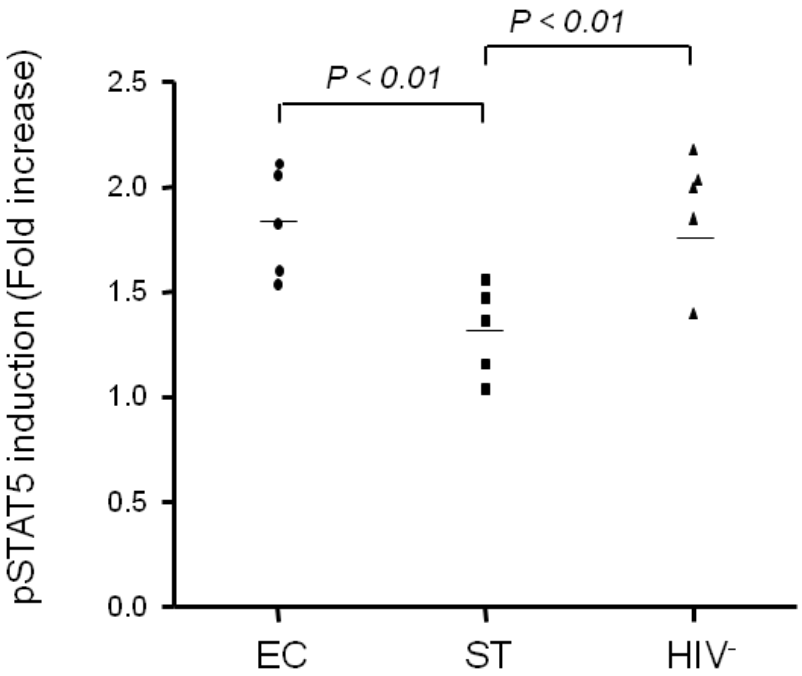
Supplemental Figure 4. Ex vivo memory B-cells from HIV$^+$ and HIV$^-$ subjects displayed similar intra-cellular and surface expression levels of FasL (n = 5). PBMCs from HIV$^+$ and HIV$^-$ subjects were stained with anti-CD3-PB, anti-CD19-Alexa700, anti-CD27-APC-Cy7 and anti-FasL-PE, washed twice, then fixed for 10 minutes at 37ºC using Cytofix buffer. Cells were permeabilized using PBS1X with 0.25% of saponin. To also measure intracellular FasL expression levels, cells were stained with a primary rabbit anti-FasL antibody for 30 minutes, washed twice and then labelled for 30 minutes with a secondary antibody anti-rabbit conjugated to Alexa647. Labelled PBMCs were subjected to flow cytometry analysis to determine (A) the surface expression of FasL-PE and (B) the intra-cellular levels of FasL-Alex647 in memory B-cells. In parallel, PBMCs from one HIV$^-$ donor was activated or not for 24 hours with 1 μg/mL of anti-CD3 + anti-CD28. Activated and gated CD3$^+$ T-cells (+) were used as a positive control for surface FasL expression when compared to their un-activated counterparts (-). Data represents mean ± SD.



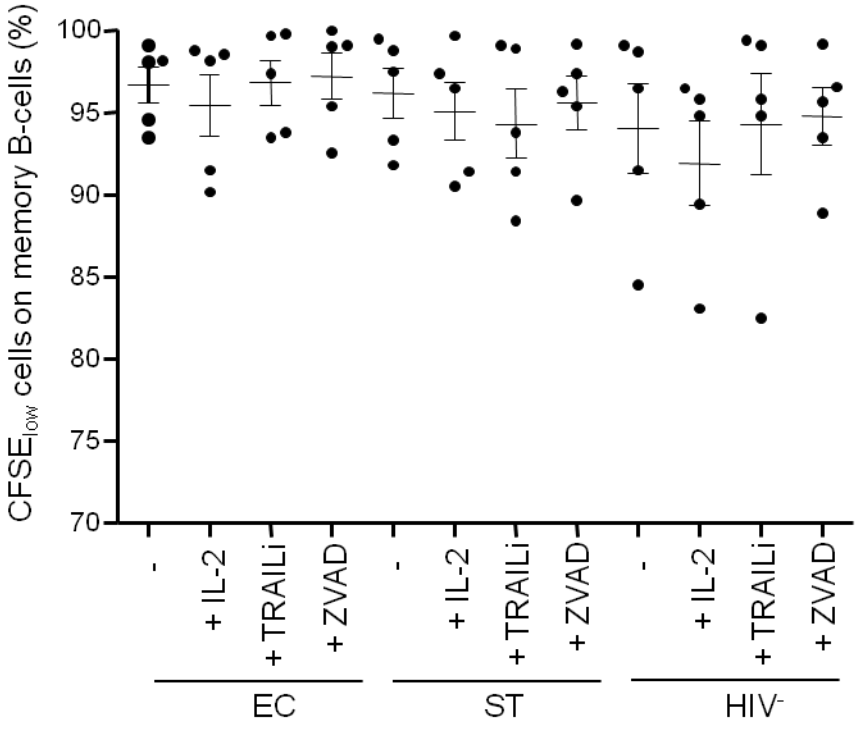
Supplemental Figure 5. Similar surface expression levels of TRAIL were found in immune cell subsets of ST, EC and HIV$^-$ subjects. (A-B) PBMCs from STs, ECs and HIV$^-$ were stained with anti-CD3-PB, anti-CD19-Alexa700, anti-CD27-APC-Cy7 and with primary rabbit anti-TRAIL antibodies for 10 minutes, labeled with Vivid for 10 extra minutes to monitor dead cells, washed twice in PBS, thereafter stained 25 minutes with secondary anti-rabbit antibodies conjugated with APC and finally subjected to flow cytometry analysis. Results shown represent the percentage of surface TRAIL expression on gated (A) naïve B-cells and (B) total CD3+ T-cells (n = 15). (C) To measure surface TRAIL on monocytes, PBMCs were first incubated 30 minutes at 4°C with PBS1X + 5% BSA to saturate non-specific sites, then stained with anti-CD3-PB and anti-CD14-Alexa700 antibodies and then subjected to flow cytometry analysis (n = 15). (D) surface expression were also determined on gated CD3$^-$CD14$^-$CD56$^-$CD19$^-$CD123$^+$CD11c$^+$HLADR$^+$ pDCs (n = 5). Of note, MFI gave similar information.



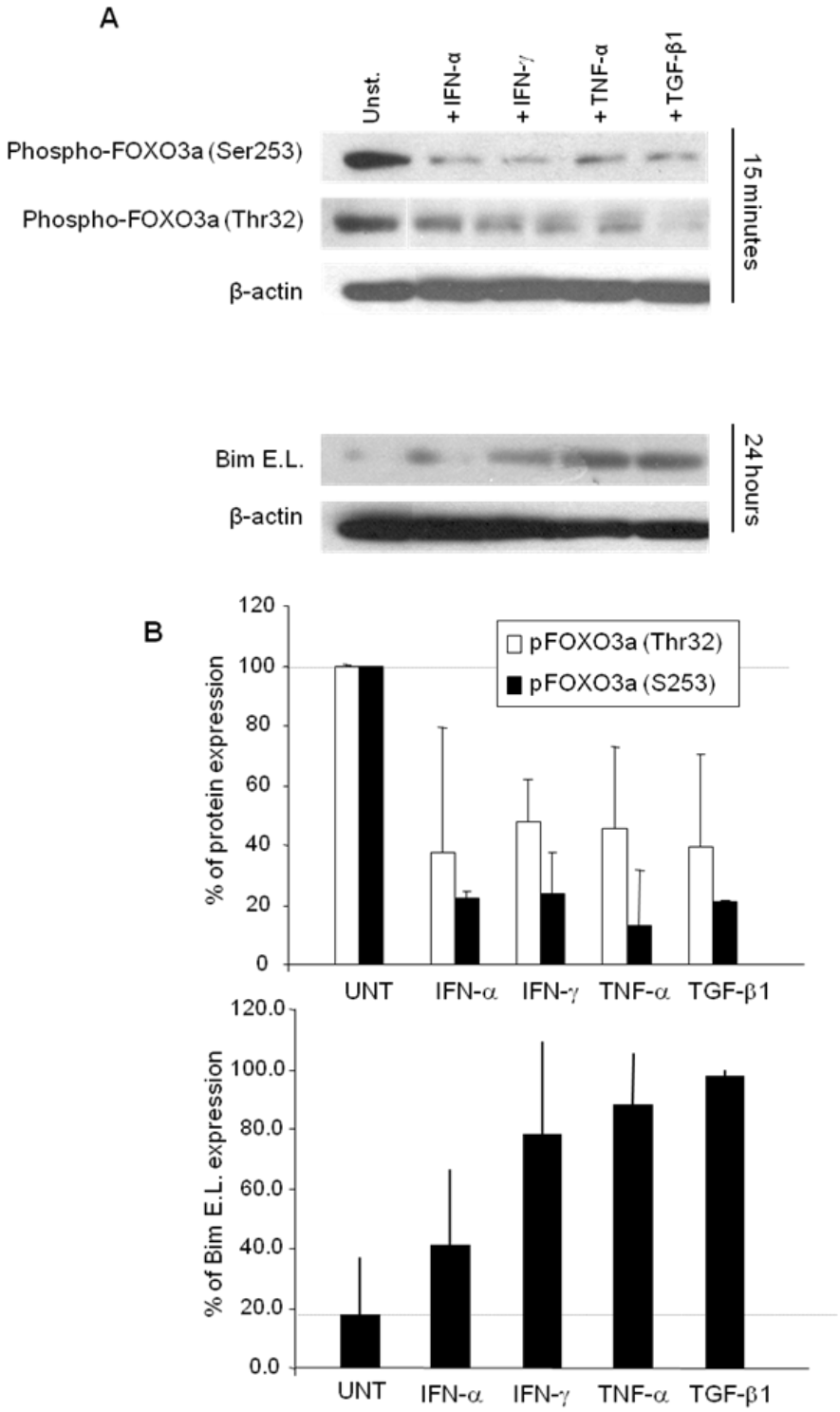
Supplemental Figure 6. (A) Inhibition of TRAIL-mediated apoptosis signaling using the DR4$^+$DR5$^+$ B-cell line BJAB. BJAB cells were stained with anti-DR4-PE and anti-DR5-FITC antibodies to measure the surface levels of TRAIL receptors. The histograms shown are representative of five independent experiments. BJAB cells were pre-treated (or not) for 2 hours with TRAILi and then cultured for 24 hours with or without 10 ng/mL of exogenous TRAIL. The flow cytometric results are depicted as percentages of apoptotic cells ± SD (n = 5). (B, C) *Ex vivo* memory B-cells from HIV$^+$ and HIV$^-$ subjects displayed similar levels of TRAIL receptors. PBMCs from HIV$^+$ and HIV$^-$ subjects were stained with 7AAD, anti-CD3-PB, anti-CD19-Alexa700, anti-CD27-APC Cy7, anti-DR4-PE and anti-DR5-FITC antibodies to measure the levels of TRAIL receptors on viable 7AAD$^-$ memory B-cells (n = 15). (B) Frequencies and (C) MFI of TRAIL receptors are shown on gated viable memory B-cells.



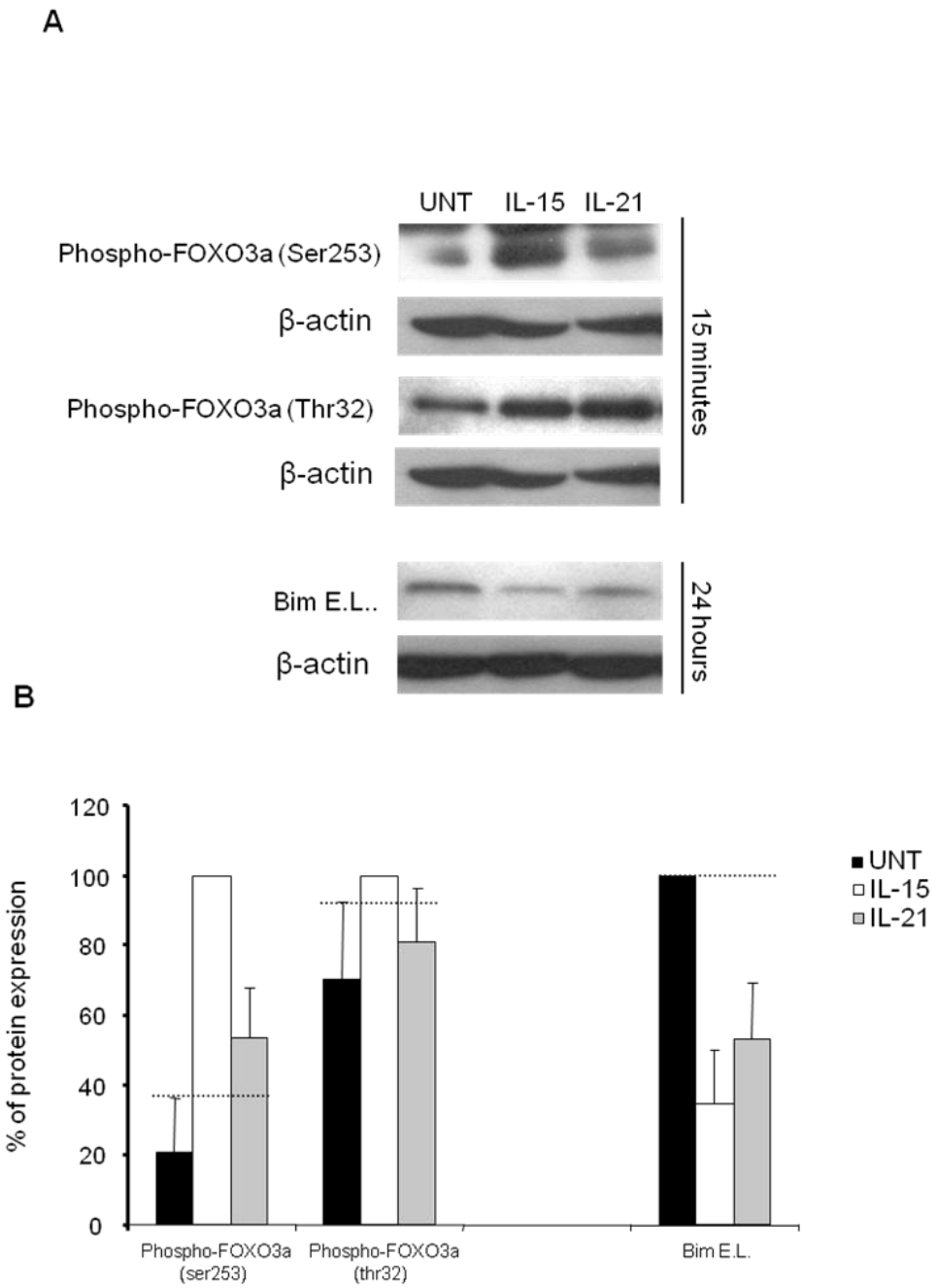
Supplementary Figure 7. Memory B-cells from STs were still responsive to exogenous IL-2 albeit at lower levels. PBMCs from ST, EC and HIV- subjects were treated for 15 minutes with or without 10 ng/mL IL-2. Cells were then labelled with 7AAD, anti-CD3-PB, anti-CD19-Alexa700 and anti-CD27-APC Cy7 antibodies and then subjected to PhosFlow staining with anti-phospho-STAT5 (pSTAT5-PE) antibody to measure pSTAT5 expression within viable memory B-cells. Results are expressed as the fold induction of pSTAT5 expression in memory B-cells from STs, ECs and HIV- after stimulation with IL-2. This induction was determined by the formula: Fold increase = pSTAT5 expression on IL-2-stimulated cells (MFI) / pSTAT5 expression on un-treated cells (MFI) for the same subjects (n = 5 per group).



Supplemental Figure 8. Activated memory B-cells from STs showed similar levels of proliferation to those from ECs and HIV$^-$. Purified CFSE-labeled memory B-cells were polyclonally activated for 3 days in co-culture assay as described in *Methods*. Proliferation levels were then determined in flow cytometry by CFSE dilution on memory B-cells at day 3. Results show percentages of CFSElow on gated viable Annexin-V- memory B-cells (n = 5).



Supplemental Figure 9. Up-stream signals increased pro-apoptotic FOXO3a transcriptional activity. Purified memory B-cells from HIV$^-$ subjects were stimulated for 15 minutes and 24 hours with or without IFN-α (1000 U /mL), IFN-γ (50 ng/mL), TNF-α (10 ng/mL) or TGF-β1 (10 ng/mL) to measure pFOXO3a and Bim E.L. expression levels respectively. (A) The blots shown were representative of two separate experiments. (B) Densitometric values were determined using ImageQuant software and expressed as relative expression of proteins between different conditions (mean ± SD).



Supplemental Figure 10. Stimulation with IL-15 and IL-21 increased FOXO3a phosphorylation and decreased Bim E.L. expression. Purified memory B-cells from HIV$^-$ subjects were stimulated for 15 minutes (to monitor FOXO3a phosphorylation) and 24 hours (to measure the expression of Bim E.L.) with or without 10 ng/mL of IL-15 or 10 ng/mL of IL-21. (A) Expression levels of phosphorylated forms of FOXO3a and Bim E.L. were determined on memory B-cells following treatment as indicated. Blots shown represented protein expression levels of one of three independent experiments. (B) Densitometric values were calculated and results were expressed as the mean of relative expression of proteins between different conditions ± SD (n = 3).