Supplemental Digital Content 1

Summary of animal treatments, infection and immune status

group	animal ID	age#	polyICLC	SIV-specific IgG (plasma, week 6)
SIV-ART-	FG52	4.47	+	
	FJ20∗	4.26	+	
	FJ65	4.25	+	
	T377	13.5	+	
SIV-ART+	CR10∗	8.4	+	
	FJ68	4.25	+	
	GT56	5.89	+	
	M728	16.64	+	
SIV+ART-	AA47[1,2]	12.33	+	+
	DH85	7.41	+	+
	EB50	6.4	+	+
	EP43	5.41	+	+
	FH71	4.43	+	+
SIV+ART+	DF51	7.53	+	+
	EL42ϕ	5.49	+	+
	FH22	4.45	+	+
	FJ62	4.25	+	+
	P427ϕ	15.5	+	+

∗ animals were challenged with SIVmac239 but remained uninfected according to viral load determination on week 2 post-challenge and were SIV-Ab negative at week 6 and 16 post-challenge

age in years at the beginning of the study (average age of 7.5 years and weight of 9kg)

ϕ partially ART-responsive

[1]necropsy at week 33 post-challenge due to AIDS related pneumonia

[2] received only two polyICLC treatments

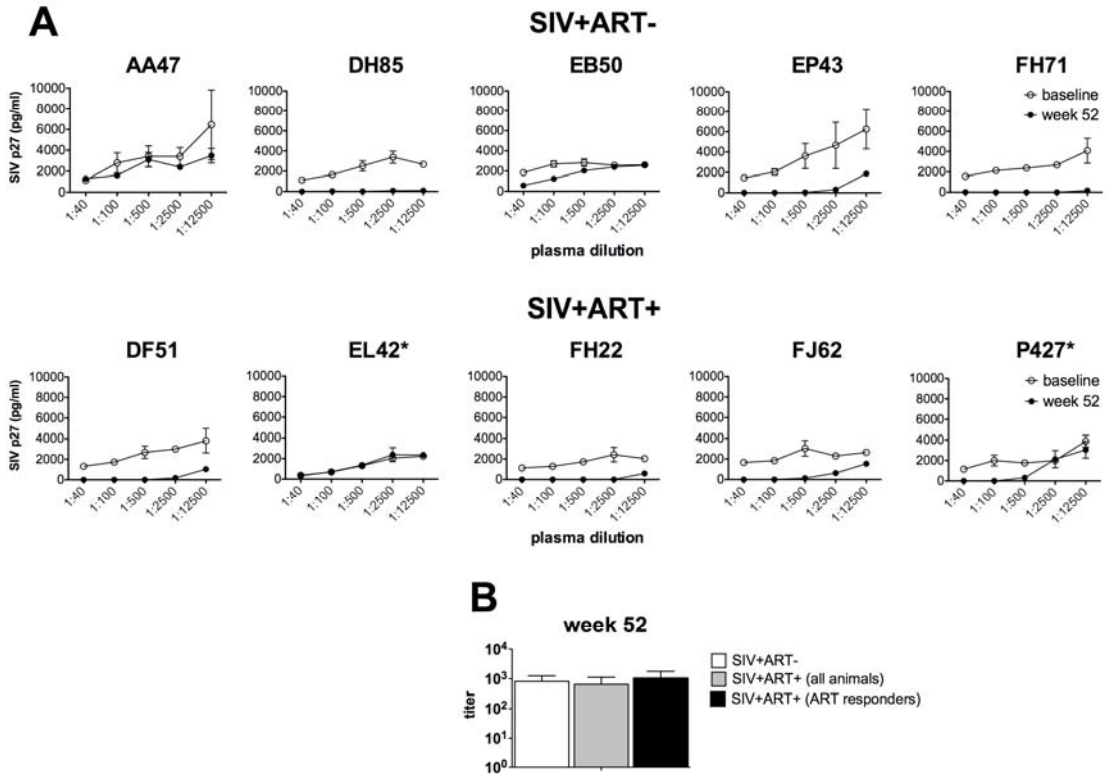
Supplemental Digital Content 2

ART treatment did not select for NRTI-resistant variants.

sample	K65R/N, M184V, T69 insertions, K70E
SIVmac239	0 (11)
EL42	0 (11)
P427	0 (8)

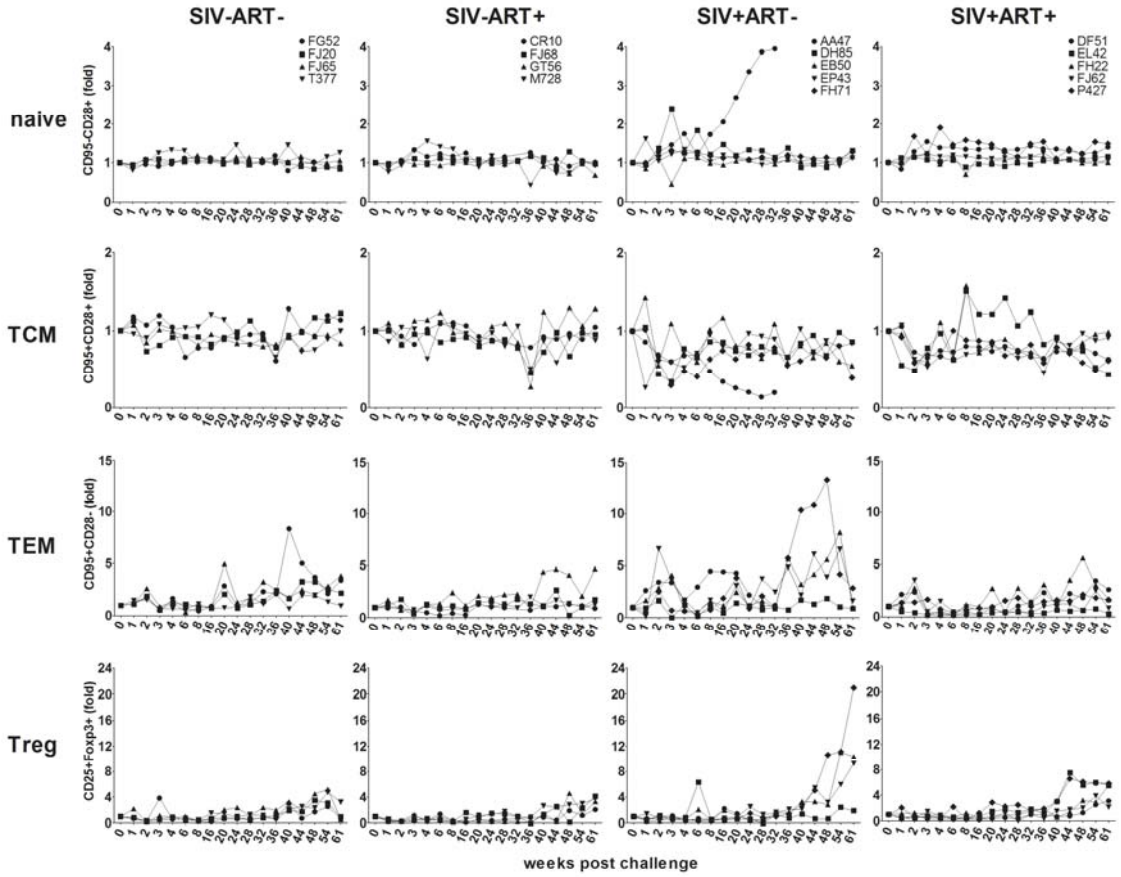
Analysis for NRTI-resistant variants was performed using the plasma collected at 35 weeks post infection. The table lists the number of clones in which amino acid mutations conferring NRTI resistance were detected. The challenge virus stock (SIVmac239) was sequenced in parallel to the plasma samples from the two poor ART responding animals. Parentheses indicate the total number of clones sequenced per sample.

Supplemental Digital Content 3



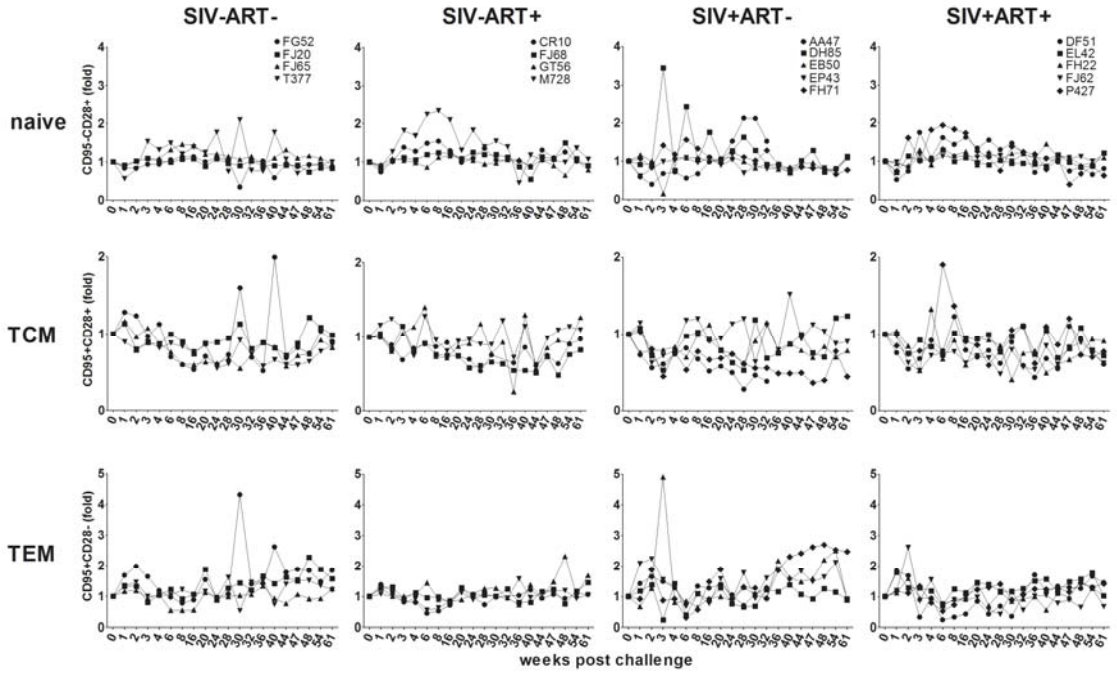
Supplemental Digital Content 3. Detection of neutralizing anti-SIV Ab activity in the plasma. Neutralizing Ab titers (against SIVmac251) in the plasma were detected at baseline and 52 w.p.i after four courses of polyICLC treatments. (A) The p27 concentrations detected in cell culture supernatants of 174xCEM cells incubated in the presence of heat inactivated diluted plasma are shown for each animal (the asterisks denote the animals that were transient ART responders). (B) The mean titer (±SEM) for each group is shown calculated based on the last dilution tested at which p27 concentration in cell culture supernatants was below the detection limit of the p27 ELISA (62.5 pg/ml).

Supplemental Digital Content 4



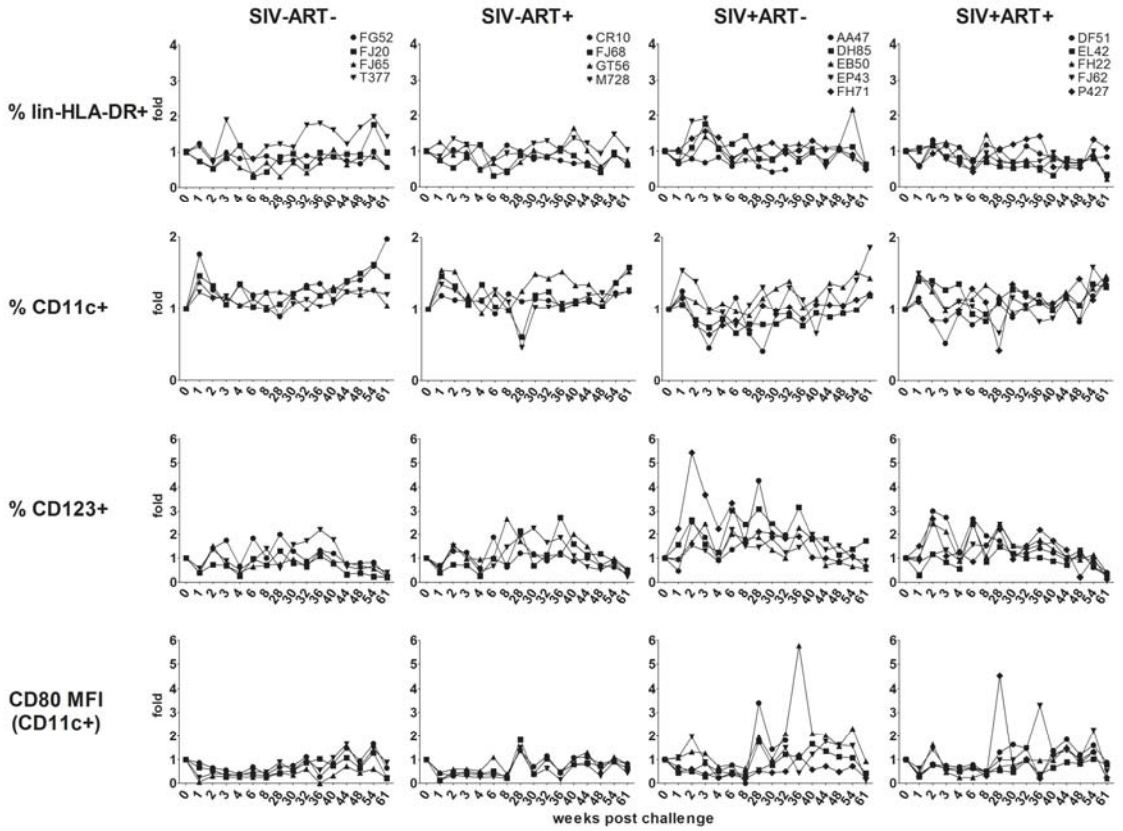
Supplemental Digital Content 4. Longitudinal assessment of the dynamics of CD4+ T cell subsets in the blood during and after ART. Polychromatic flow cytometric analysis was performed to identify naïve, central and effector memory and regulatory CD4+ T cells in PBMCs. T cell subsets were identified as described in Figure 3. The frequency of the indicated T cell subset is normalized on the baselines (three baseline time points were collected from each animal and the averaged was calculated and set as 1).

Supplemental Digital Content 5



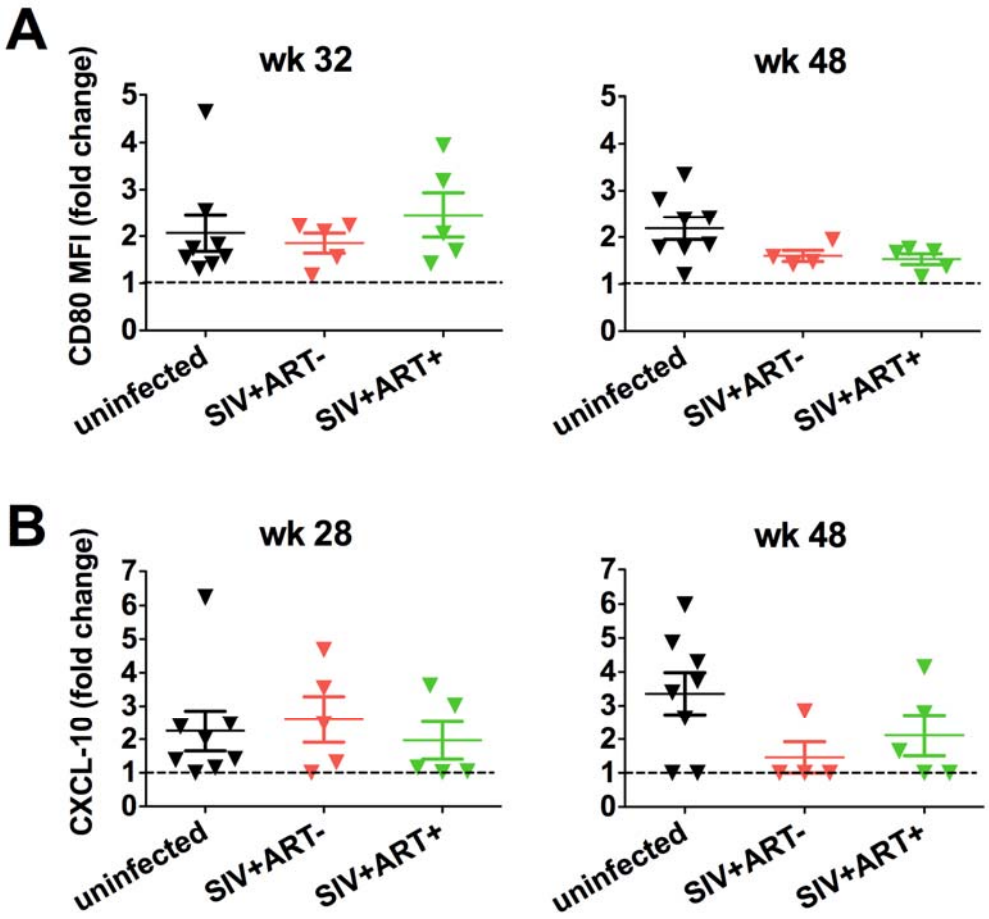
Supplemental Digital Content 5. Longitudinal analysis of the dynamics of CD8+ T cell subsets in the blood during and after ART. Naïve, central and effector memory CD8+ T cells in PBMCs were identified as described in Figure 3. The frequency of the indicated T cell subset is normalized on the baselines (three baseline time points were collected from each animal and the averaged was calculated and set as 1).

Supplemental Digital Content 6



Supplemental Digital Content 6. Longitudinal assessment of the dynamics of DC subsets in the blood during and after ART. DCs were identified as described in Figure 4. The frequency of the indicated DC subset is normalized on the baselines (two baseline time points were collected from each animal and the averaged was calculated and set as 1).

Supplemental Digital Content 7



Supplemental Digital Content 7. ART does not impede the responsiveness to an innate trigger. The expression of CD80 on mDCs was detected by polychromatic flow cytometry immediately before and 24h after polyICLC application. (A) Fold change in the expression of CD80 after the second and fourth PolyICLC treatment, (B) peak fold change of the CXCL10 production detected by ELISA in oral swabs after polyICLC application. Results are form 8 animals in the uninfected group (black symbols), 4 in the SIV+ART- group (except for week 28, n=5; red symbols) and 5 in the SIV+ART+ group (green symbols).

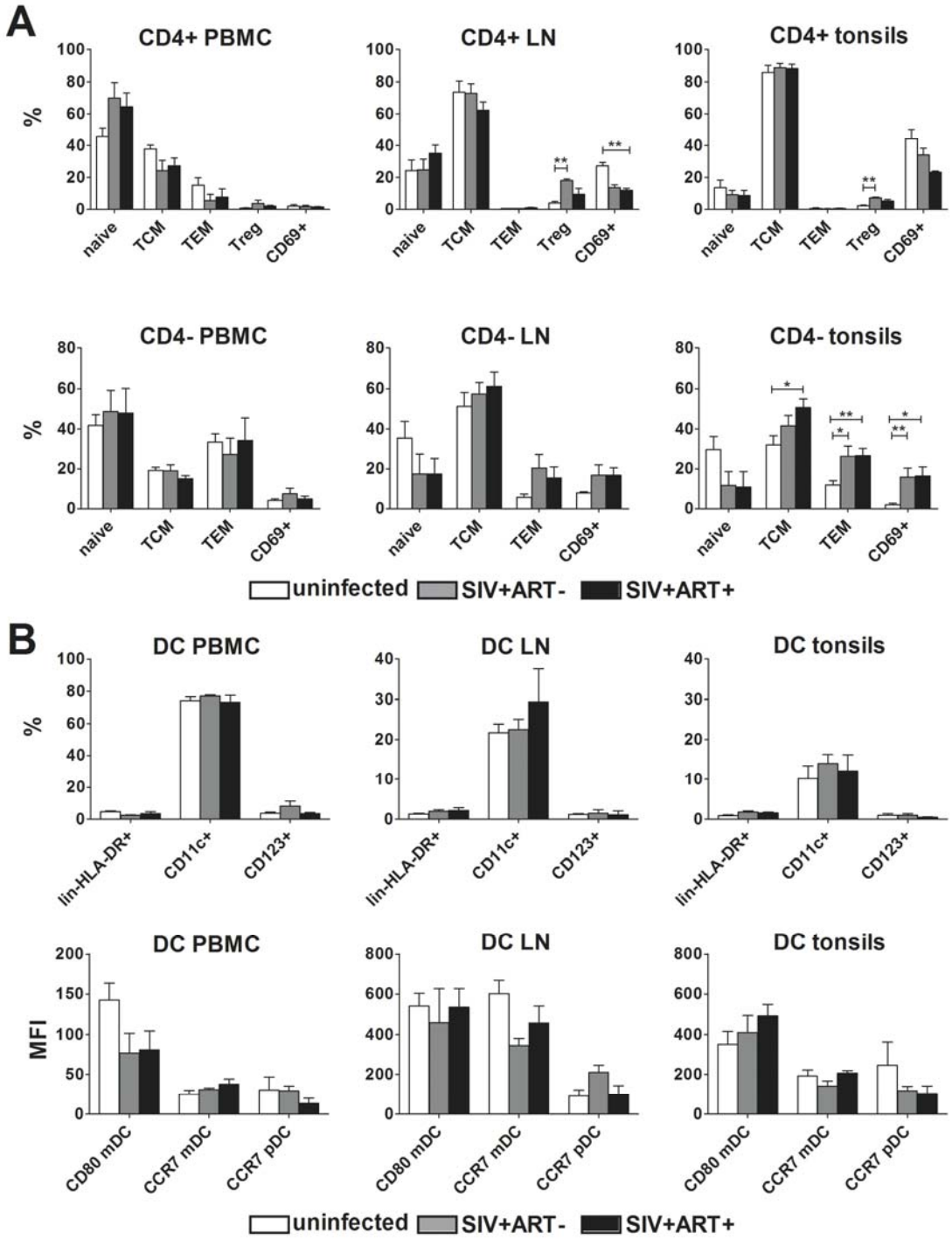
Supplemental Digital Content 8

Pathological alterations detected at necropsy

group	animal ID	necropsy (w.p.i.)	viral load (copies/ml)	clinical symptoms	pathology*
SIV-ART-	FG52	64	nd	nd	nd
	FJ20	64	nd	nd	nd
	FJ65	64	nd	nd	nd
	T377	65	nd	nd	nd
SIV-ART+	CR10	65	nd	nd	nd
	FJ68	65	nd	nd	nd
	GT56	66	nd	nd	nd
	M728	66	nd	nd	nd
SIV+ART-	AA47	33	$2x10^7$	*P. carinii* pneumonia	lung, inflammation (+++) thymus, atrophy (++) LN, hyperplasia (++) ileum, inflammation (+)
	DH85	61	$1.4x10^3$	-	spleen, hyperplasia (+) stomach, inflammation (+)
	EB50	61	$7.5x10^4$	-	spleen, hyperplasia (+)
	EP43	61	30	-	-
	FH71	62	$1.7x10^5$	-	spleen, hyperplasia (+) gallblader, inflammation (+) kidney, inflammation (+) pancreas, inflammation (+) LN, hyperplasia (++) stomach, inflammation (++) colon, inflammation (++)
SIV+ART+	DF51	62	30	-	kidney, inflammation (+) LN, hyperplasia (+) stomach, inflammation (+) lung, inflammation (+)
	EL42	62	$4.9x10^4$	-	lung, inflammation (+) LN, hyperplasia (+) stomach, inflammation (+)
	FH22	63	100	-	spleen, hyperplasia (++) LN, hyperplasia (+++) jejunum, atrophy (++) ileum, atrophy (++)
	FJ62	63	60	-	LN, hyperplasia (+++) jejunum, atrophy (++) colon, hyperplasia (++)
	P427	63	$6.7x10^5$	-	spleen, hyperplasia (+++) LN, hyperplasia (++) pancreas, amyloidosis (+++)

*grading: + mild, ++ moderate, +++ severe

Supplemental Digital Content 9



Supplemental Digital Content 9. Analysis of leukocyte subsets in PBMCs, lymph nodes and tonsils at necropsy. (A) T cell and (B) DC subsets were

identified as described in Figures 3 and 4. CD69+ T cells were also defined in the CD3+CD4+ and CD3+CD4- fractions (A). Average percentages (±SEM) for each group are shown. The MFIs of CD80 and CCR7 were also determined on the indicated DC subsets (lower panels in B). Results are from 8 animals in the uninfected group (white bars), 4 in the SIV+ART-naive group (grey bars) and 5 in the SIV+ART-receiving group (black bars). Asterisks indicate significant differences between the groups; * $p < 0.05$, ** $p < 0.01$.