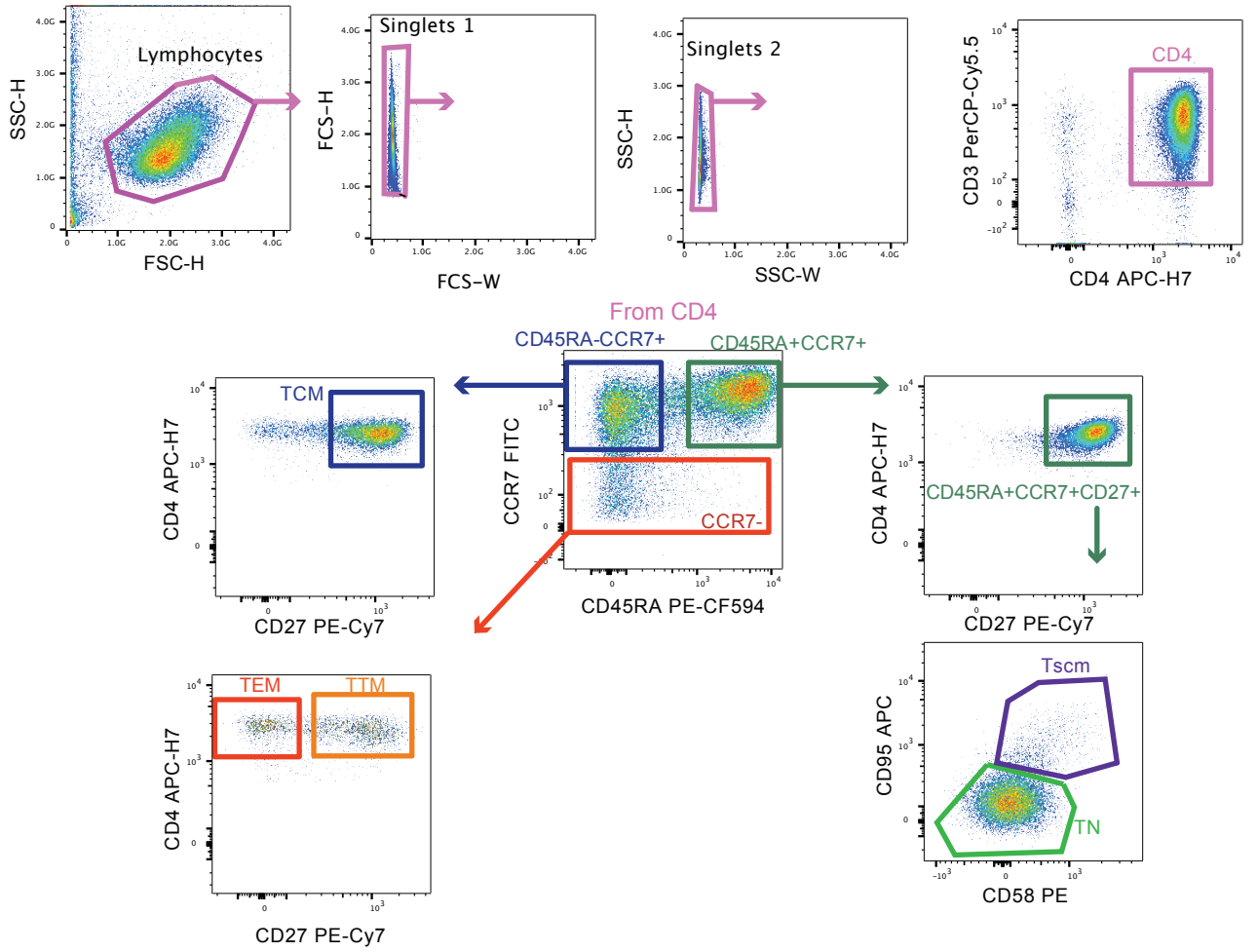
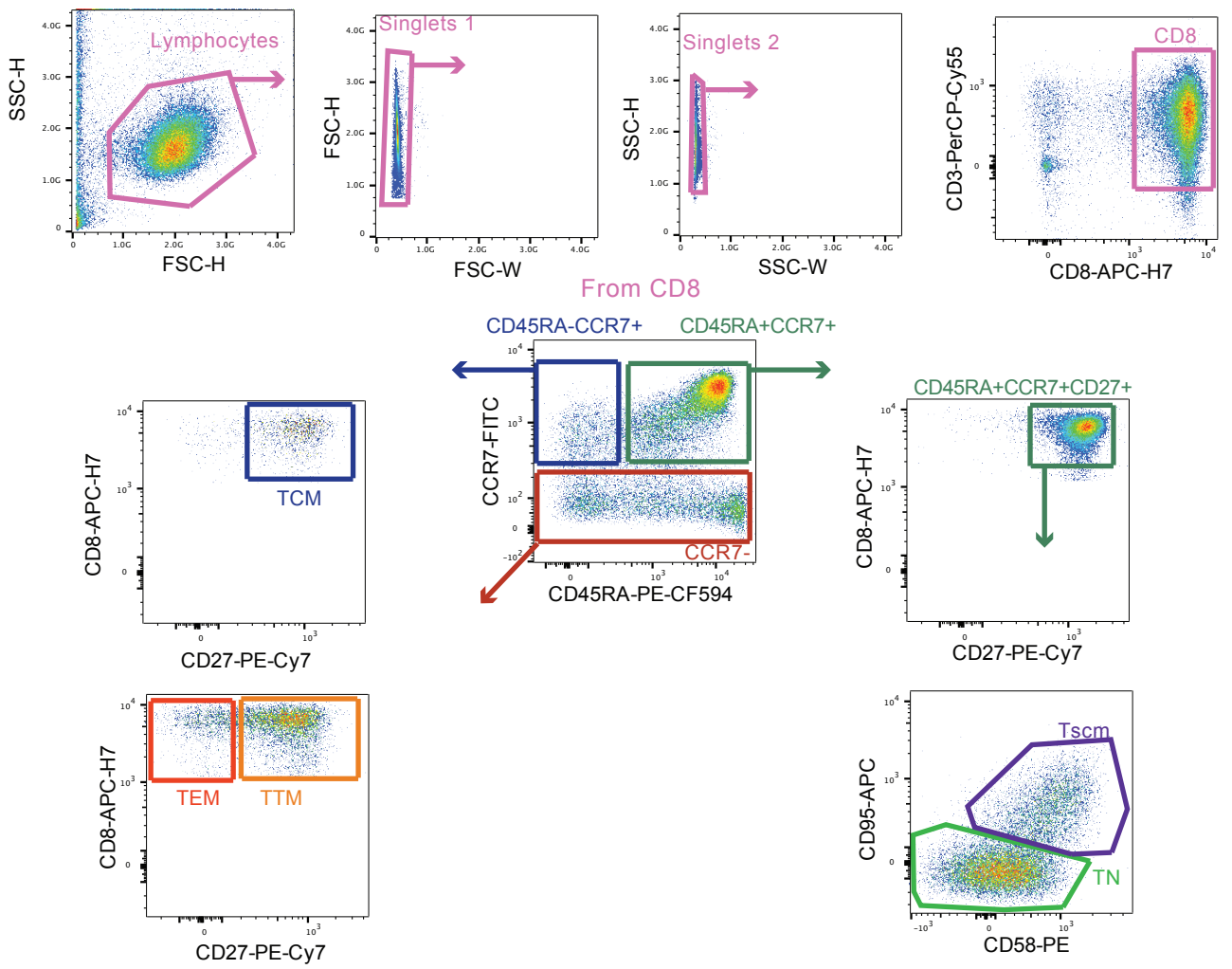
Supplemental Figure 1. Gating Strategy. Gating strategy used to identify T-cell subsets from peripheral blood mononuclear cells within the $CD4^+$ (Panel A) and $CD8^+$ (Panel B) lymphocyte populations.

Supplemental Figure 1. Gating strategy

A. Enriched CD4 T cells



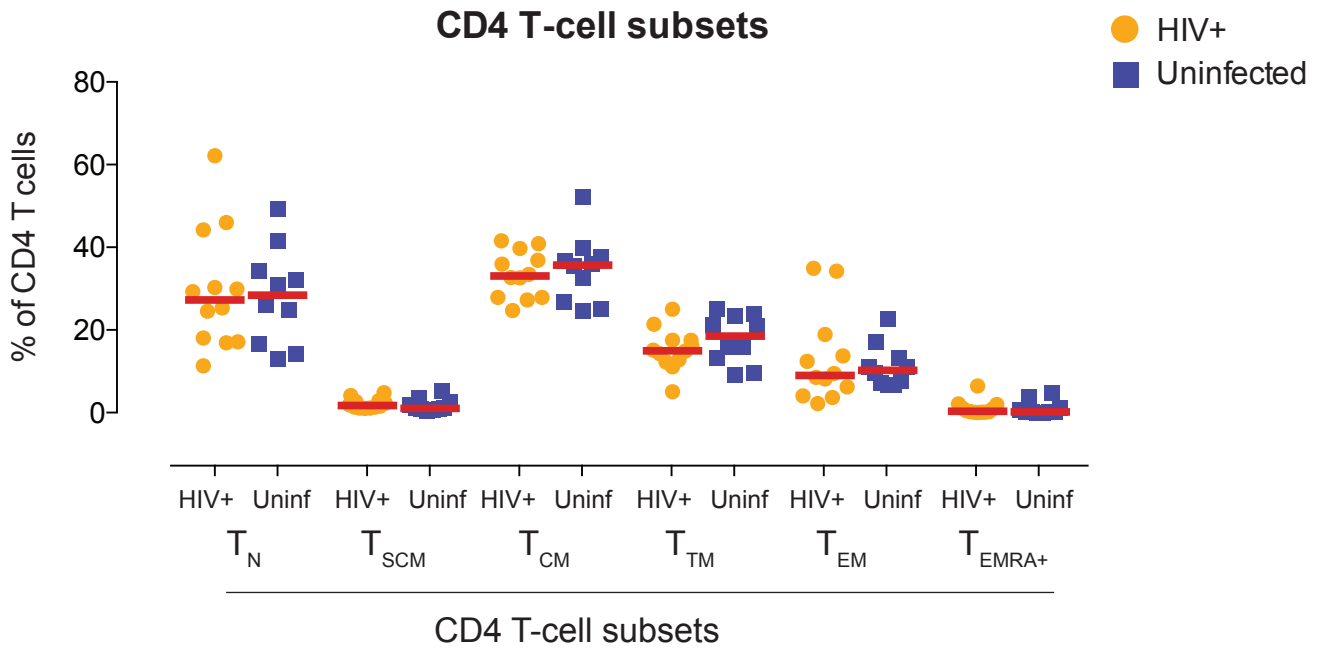
B. Enriched CD8 T cells



Supplemental Figure 2. T-cell subsets. Percentages of T-cells in each $CD4^+$ (Panel A) and $CD8^+$ (Panel B) T-cell subset in both HIV-infected and uninfected subjects. No difference was found between the two groups for any T-cell subset.

Supplemental Figure 2. T cell subsets.

A



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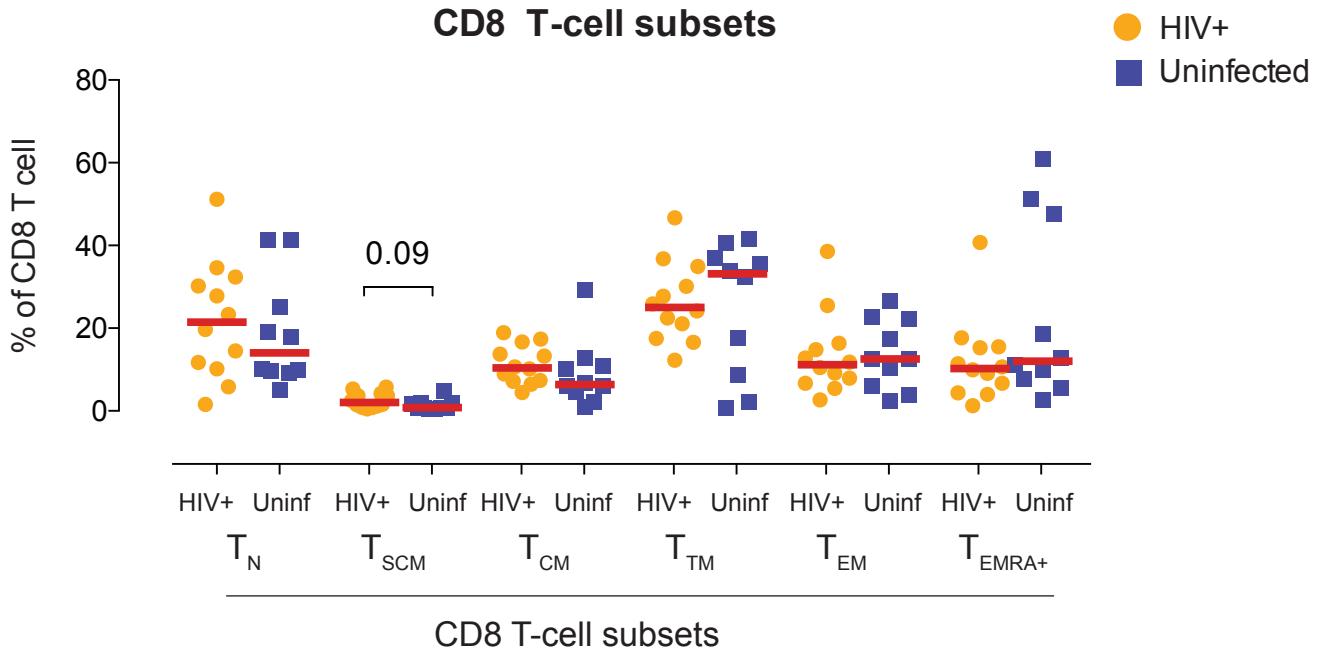
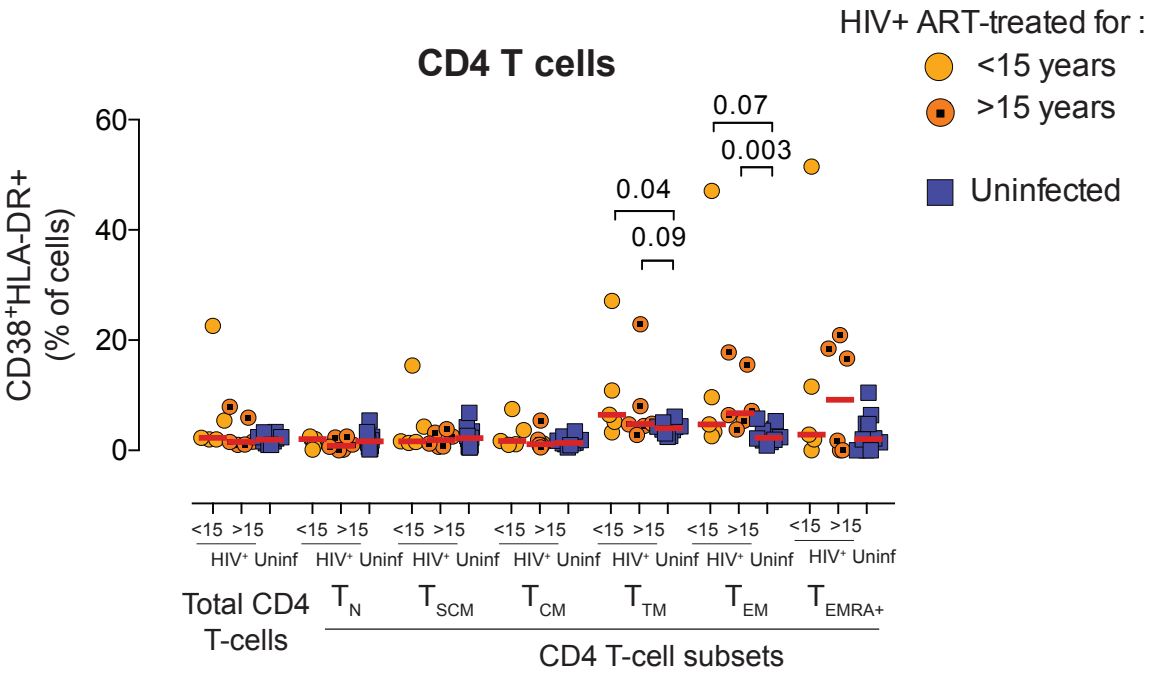


S**upplemental Figure 3. Immune Activation.** Immune activation measured by $CD38^+HLADR^+$ expression in $CD4^+$ (Panel A) and $CD8^+$ (Panel B) T-cell subsets in uninfected individuals, and those infected with HIV for >15 years and <15 year. P-values between age matched infected and uninfected individuals are indicated.

Supplemental Figure 3. Immune activation

A



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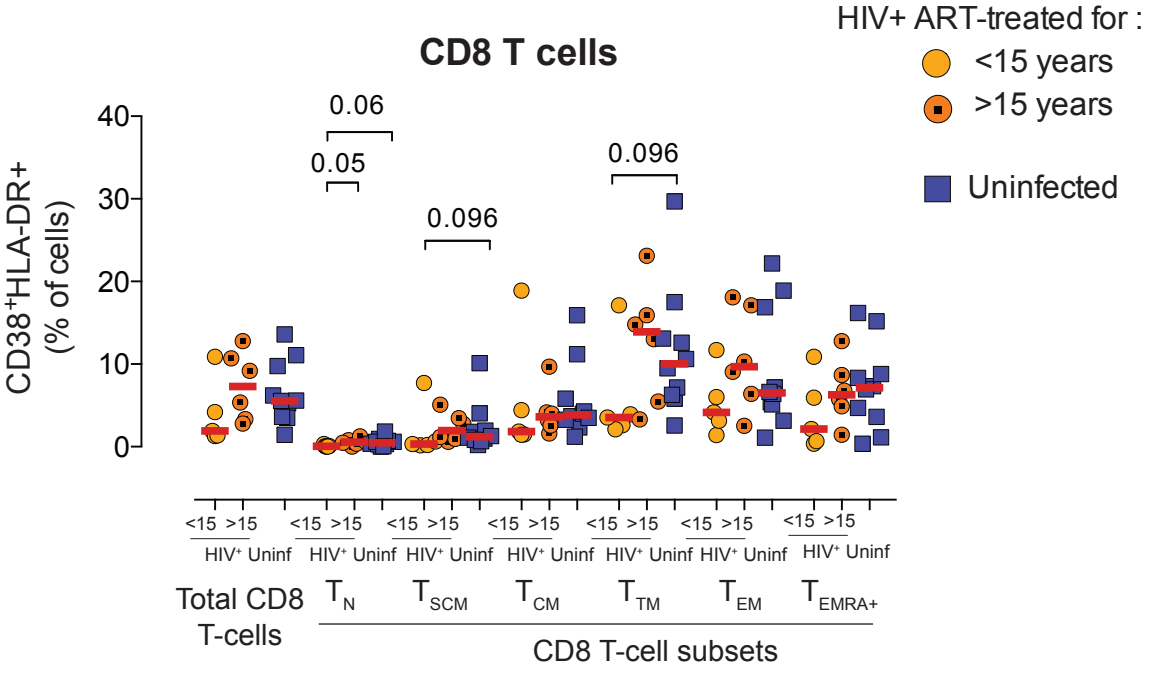
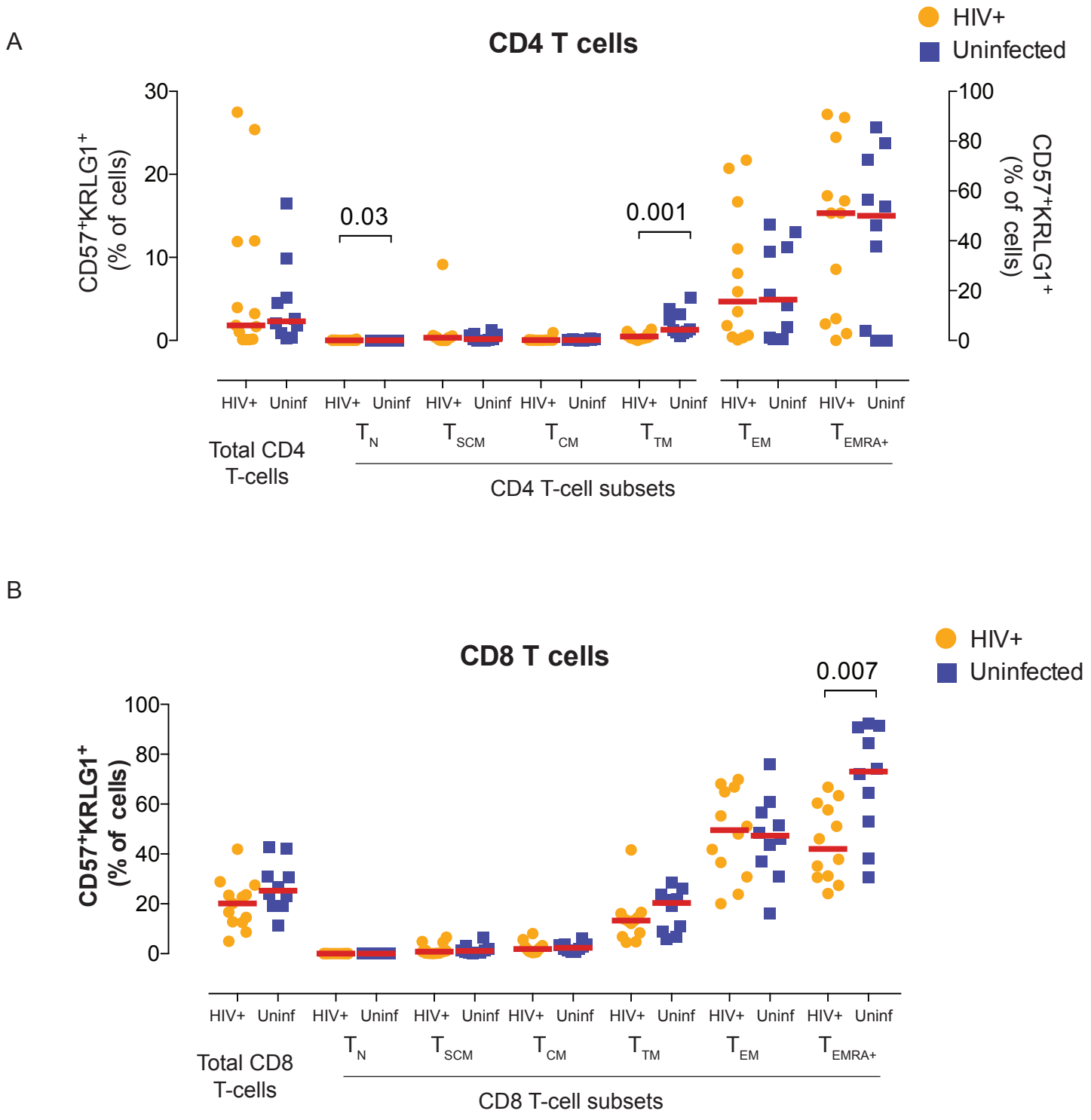


Supplemental Figure 4. Senescence. Senescence measured by $KRLG1^{+}CD57^{+}$ dual expression in $CD4^{+}$ (Panel A) and $CD8^{+}$ (Panel B) T-cell subsets. P-values between age matched infected and uninfected individuals are indicated.

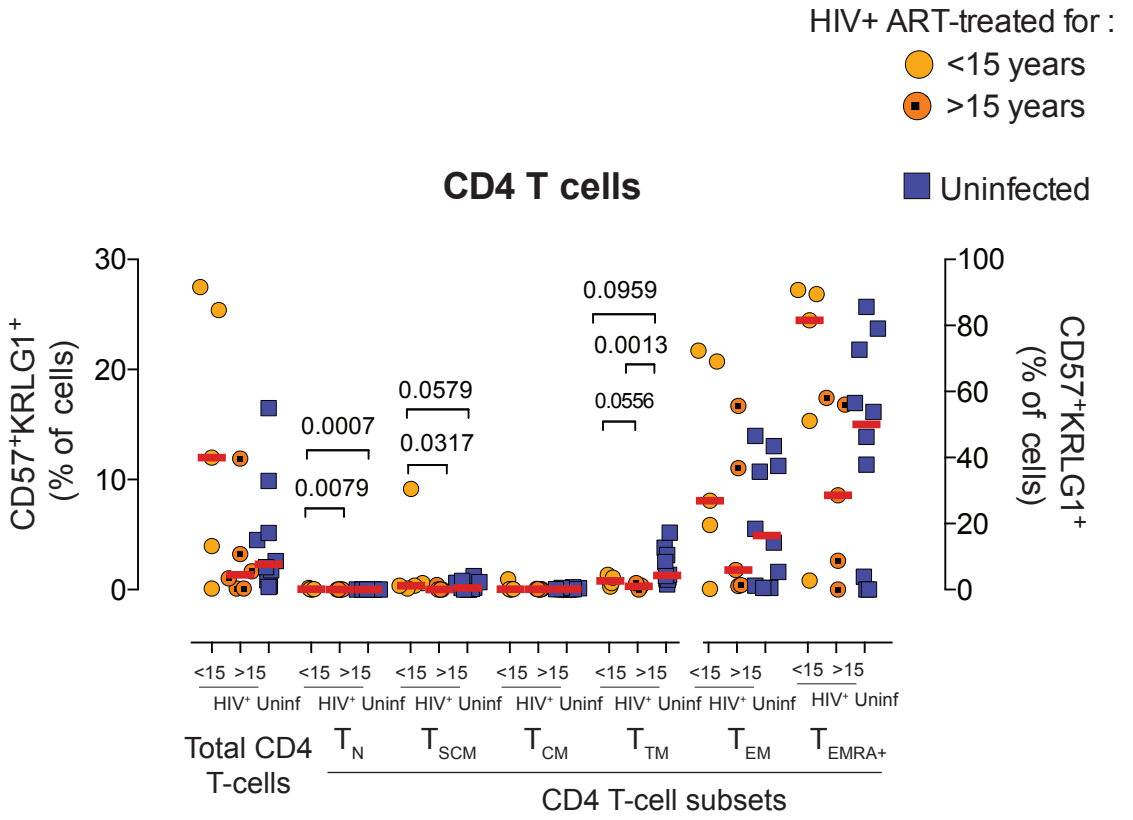
Supplemental Figure 4. Senescence.



Supplemental Figure 5. Senescence. Senescence measured by KRLG1^{+} expression in CD4^{+} (Panel A) and CD8^{+} (Panel B) T-cell subsets by time on HIV therapy (<15 years, >15 years or uninfected). P-values between age matched infected and uninfected individuals are indicated.

Supplemental Figure 5. Senescence.

A



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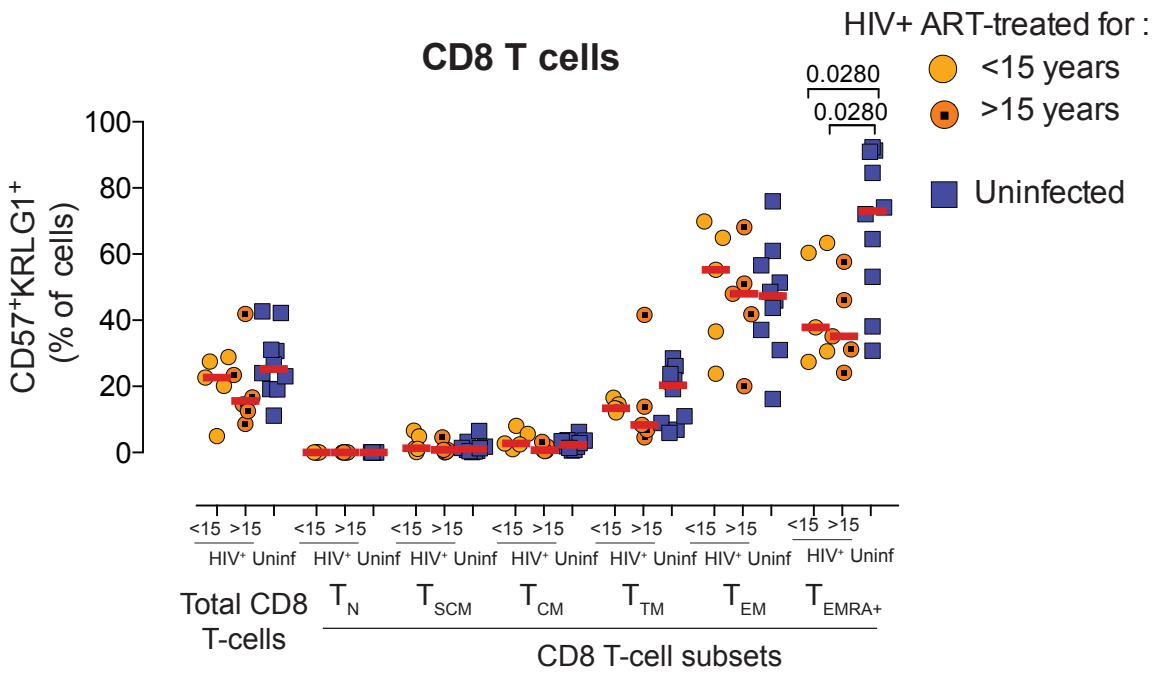
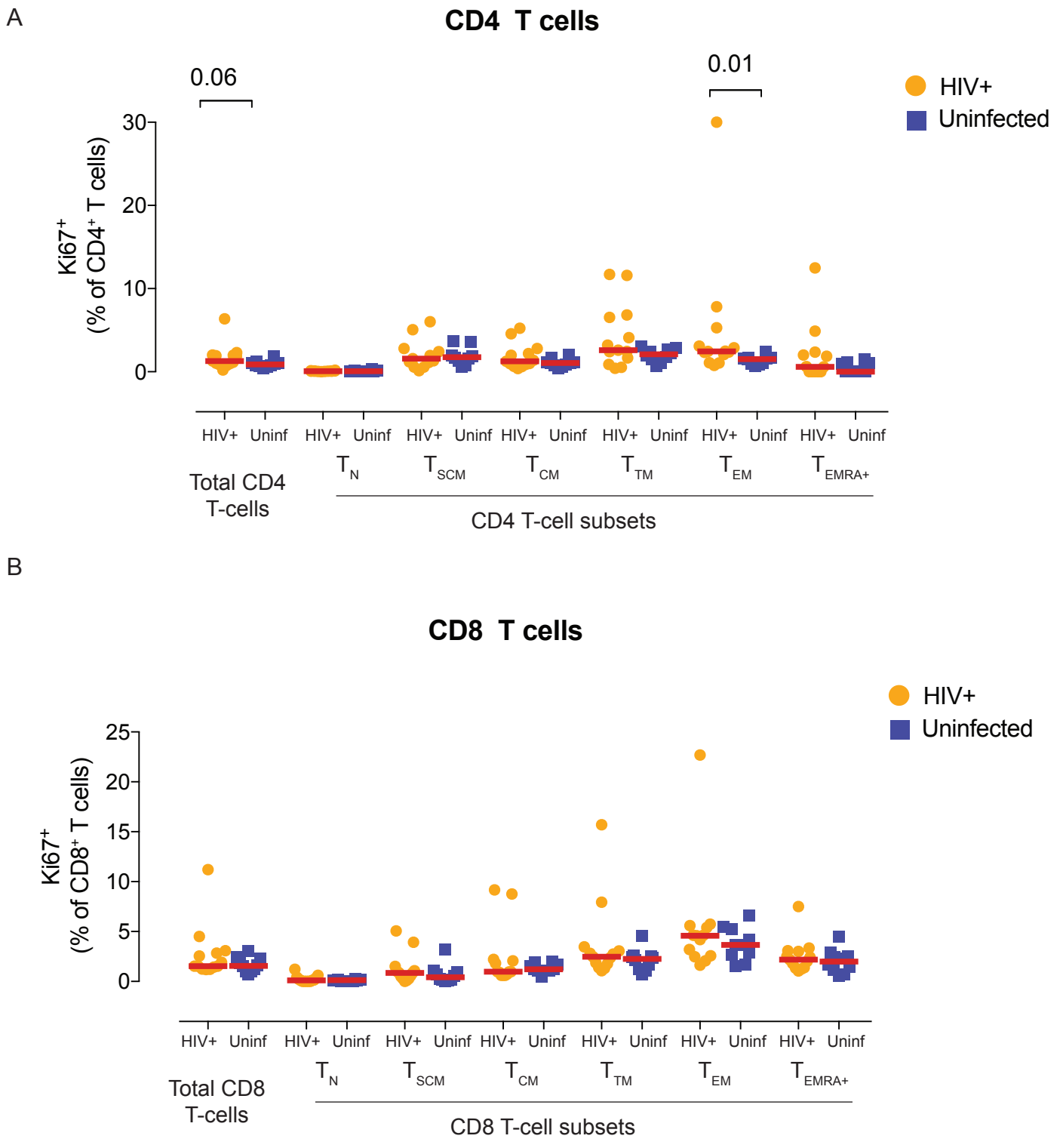


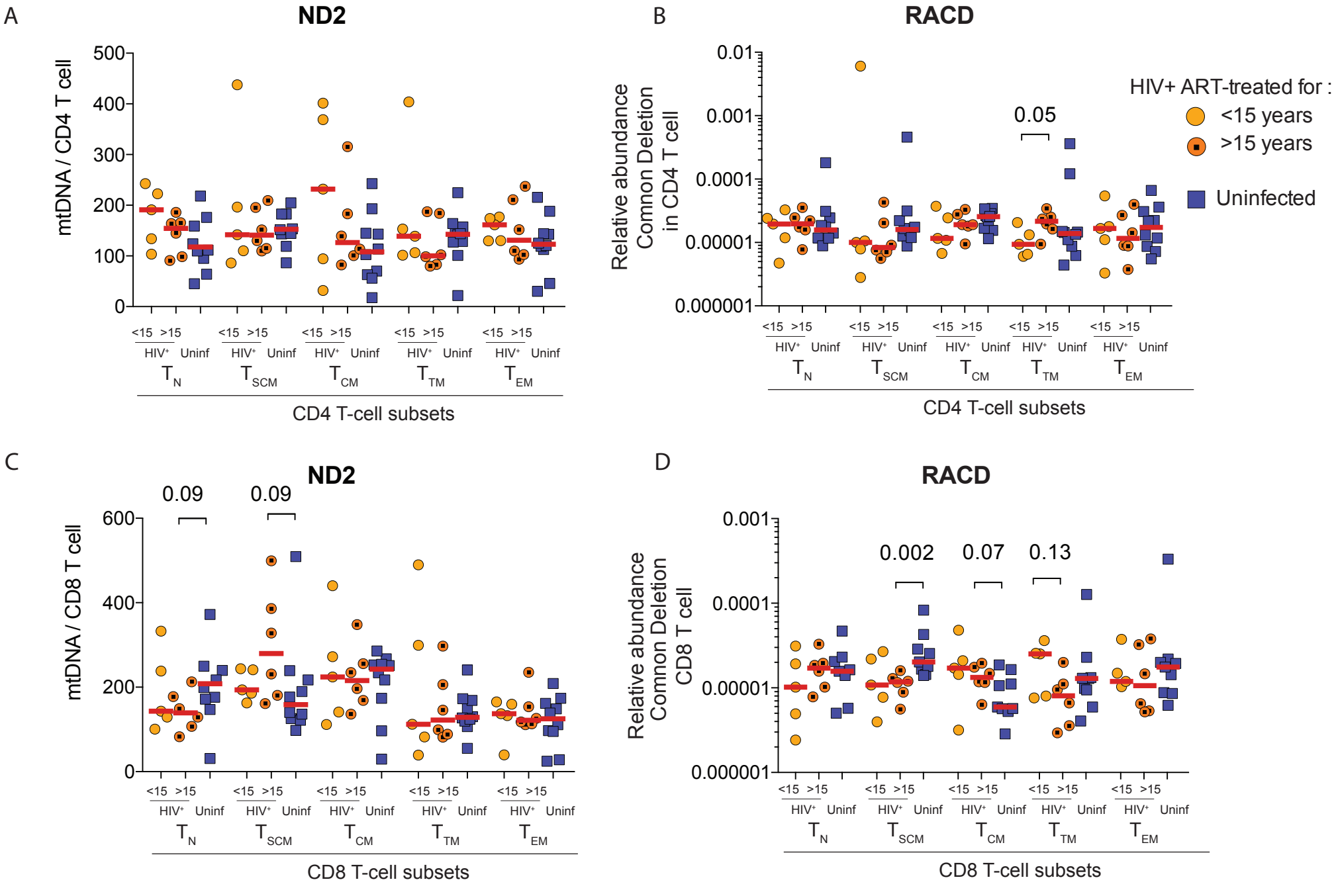
Supplemental Figure 6. Proliferation. Proliferation measured by Ki67$^+$ expression in CD4$^+$ (Panel A) and CD8$^+$ (Panel B) T-cell subsets by HIV infected or uninfected. P-values between age matched infected and uninfected individuals are indicated.

Supplementary Figure 6



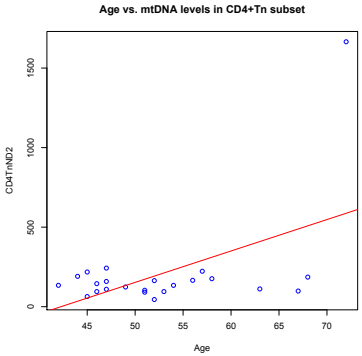
Supplemental Figure 7. Mitochondrial DNA Measurements. Mitochondrial DNA copy number (ND2) and the relative proportion of mitochondrial DNA carrying the common deletion (RACD) in CD4 (Panel A and C) and CD8 (Panel B and D) T-cells separated by time on HIV therapy (<15 years, >15 years, or uninfected**.** P-values between age matched infected and uninfected individuals are indicated.

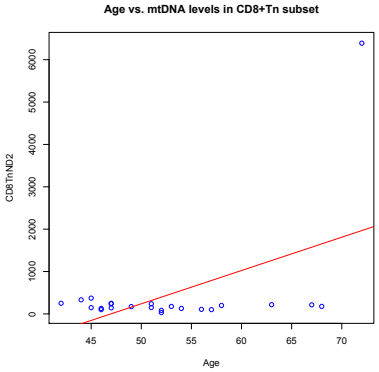
Supplementary Figure 7.

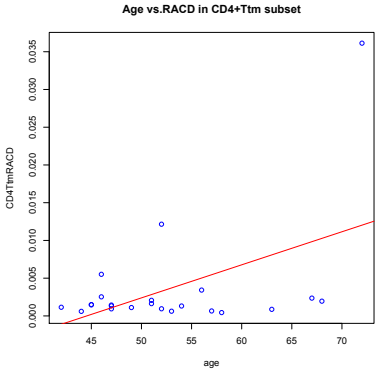


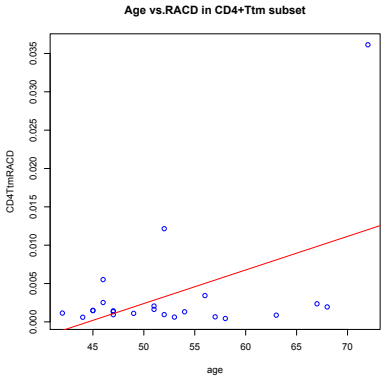
Supplemental Figure 8. Temporal Correlations with mtDNA Measurements. Panels A and B demonstrate a positive correlation between age and mtDNA in $CD4^+T_N$ (r^2=0.25, p=0.014) and $CD8^+T_N$: r^2=0.245, p=0.015. Panels C, D, and E demonstrate a positive correlation between age and RACD for $CD4^+T_{TM}$(r^2=0.23, p=0.02) $CD8^+T_{TM}$(r^2=0.22, p=0.025), nad $CD8^+T_{EM}$: r^2=0.28, p=0.009). Panel F demonstrates a negative correlation with length of HIV infection and mtDNA in $CD4^+T_N$ (r^2=0.29, p=0.09). Panel G demonstrates a positive correlation of length of infection with RACD in the $CD4^+T_{TM}$ subset (r^2=0.41, p=0.03). Finally, panel H demonstrates that time on ART also postively correlated with RACD in the $CD4^+T_{TM}$ subset (r^2=0.51, p=0.014).

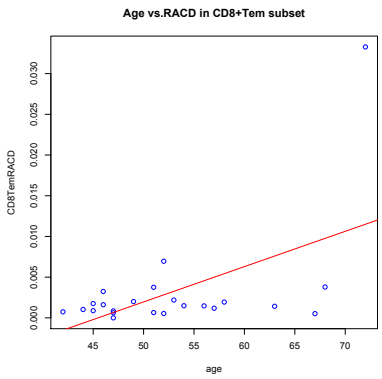
Supplementary Figure 8.

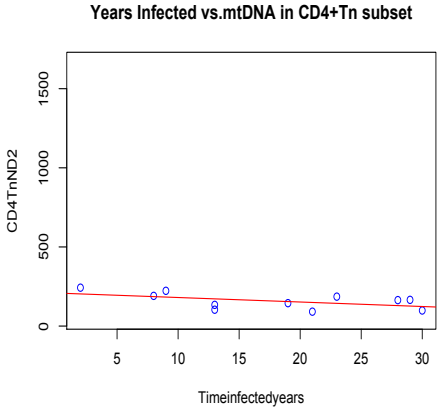


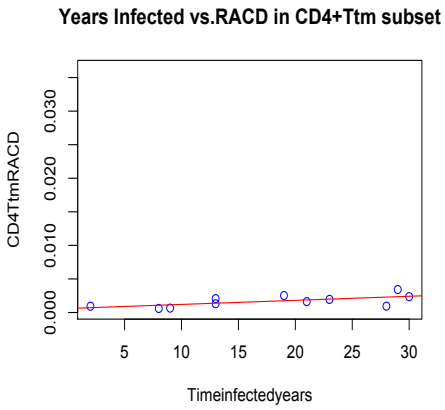


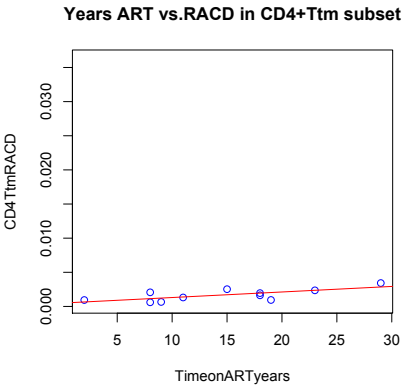












Supplemental Tables

Supplemental Table 1. Correlation between RACD and Proliferation in CD4$^+$ T-cell subsets

		CD4TnRACD	CD4TscmRACD	CD4TcmRACD	CD4TtmRACD	CD4TemRACD
ProlifKi67 CD4naive	Pearson Correlation	-0.007	-0.050	-0.309	0.038	0.375
	Sig. (2-tailed)	0.974	0.827	0.162	0.866	0.085
	N	22	22	22	22	22
ProlifKi67 CD4Tscm	Pearson Correlation	**.728****	-0.079	-0.012	**.691****	**.473***
	Sig. (2-tailed)	**0.000**	0.727	0.958	**0.000**	**0.026**
	N	22	22	22	22	22
ProlifKi67 CD4Tcm	Pearson Correlation	-0.133	-0.201	-0.221	-0.185	-0.319
	Sig. (2-tailed)	0.556	0.370	0.322	0.409	0.148
	N	22	22	22	22	22
ProlifKi67 CD4Ttm	Pearson Correlation	-0.127	-0.202	-0.239	-0.173	-0.374
	Sig. (2-tailed)	0.574	0.367	0.284	0.442	0.087
	N	22	22	22	22	22
ProlifKi67 CD4Tem	Pearson Correlation	-0.147	-0.092	-0.157	-0.091	-0.195
	Sig. (2-tailed)	0.515	0.685	0.485	0.687	0.386
	N	22	22	22	22	22

**Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).

Supplemental Table 2. Correlation between RACD and Proliferation in CD8$^+$ T-cell subsets

		CD8TnRACD	CD8TscmRACD	CD8TcmRACD	CD8TtmRACD	CD8TemRACD
ProlifKi67 CD8Naive	Pearson Correlation	-0.067	-0.351	-0.047	0.409	0.311
	Sig. (2-tailed)	0.768	0.109	0.835	0.059	0.159
	N	22	22	22	22	22
ProlifKi67 CD8Tscm	Pearson Correlation	-0.134	-0.124	-0.151	-0.230	0.024
	Sig. (2-tailed)	0.554	0.582	0.502	0.304	0.916
	N	22	22	22	22	22
ProlifKi67 CD8Tcm	Pearson Correlation	-0.134	-0.072	-0.155	-0.235	0.005
	Sig. (2-tailed)	0.553	0.751	0.492	0.293	0.981
	N	22	22	22	22	22
ProlifKi67 CD8Ttm	Pearson Correlation	-0.163	-0.158	-0.183	-0.116	0.058
	Sig. (2-tailed)	0.469	0.482	0.416	0.607	0.798
	N	22	22	22	22	22
ProlifKi67 CD8Tem	Pearson Correlation	-0.150	-0.222	-0.178	-0.129	0.087
	Sig. (2-tailed)	0.505	0.321	0.427	0.568	0.702
	N	22	22	22	22	22

**Correlation is significant at the 0.01 level (2-tailed).
*Correlation is significant at the 0.05 level (2-tailed).