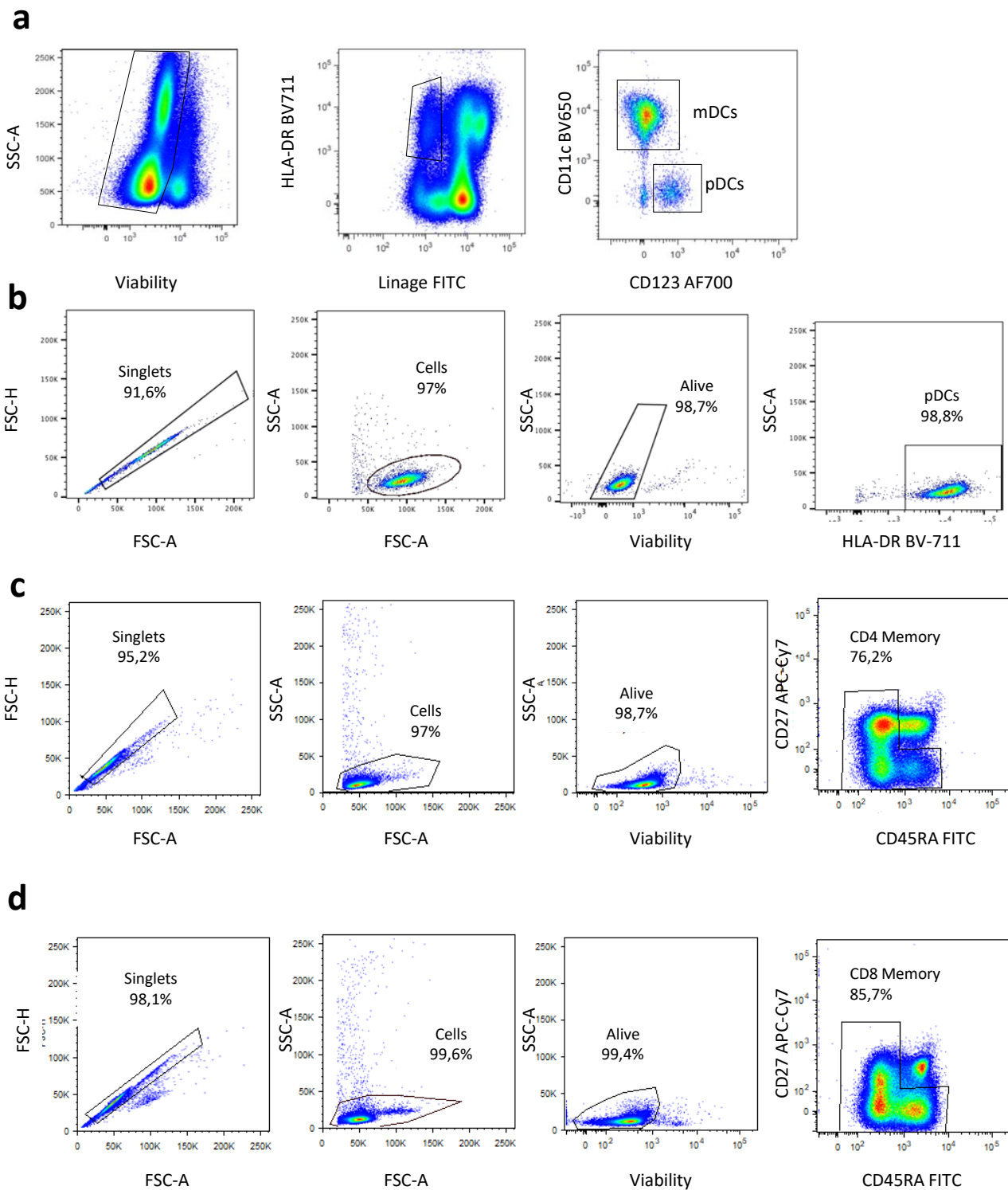


Supplementary table 1. Specific primers for qPCR in isolated pDCs

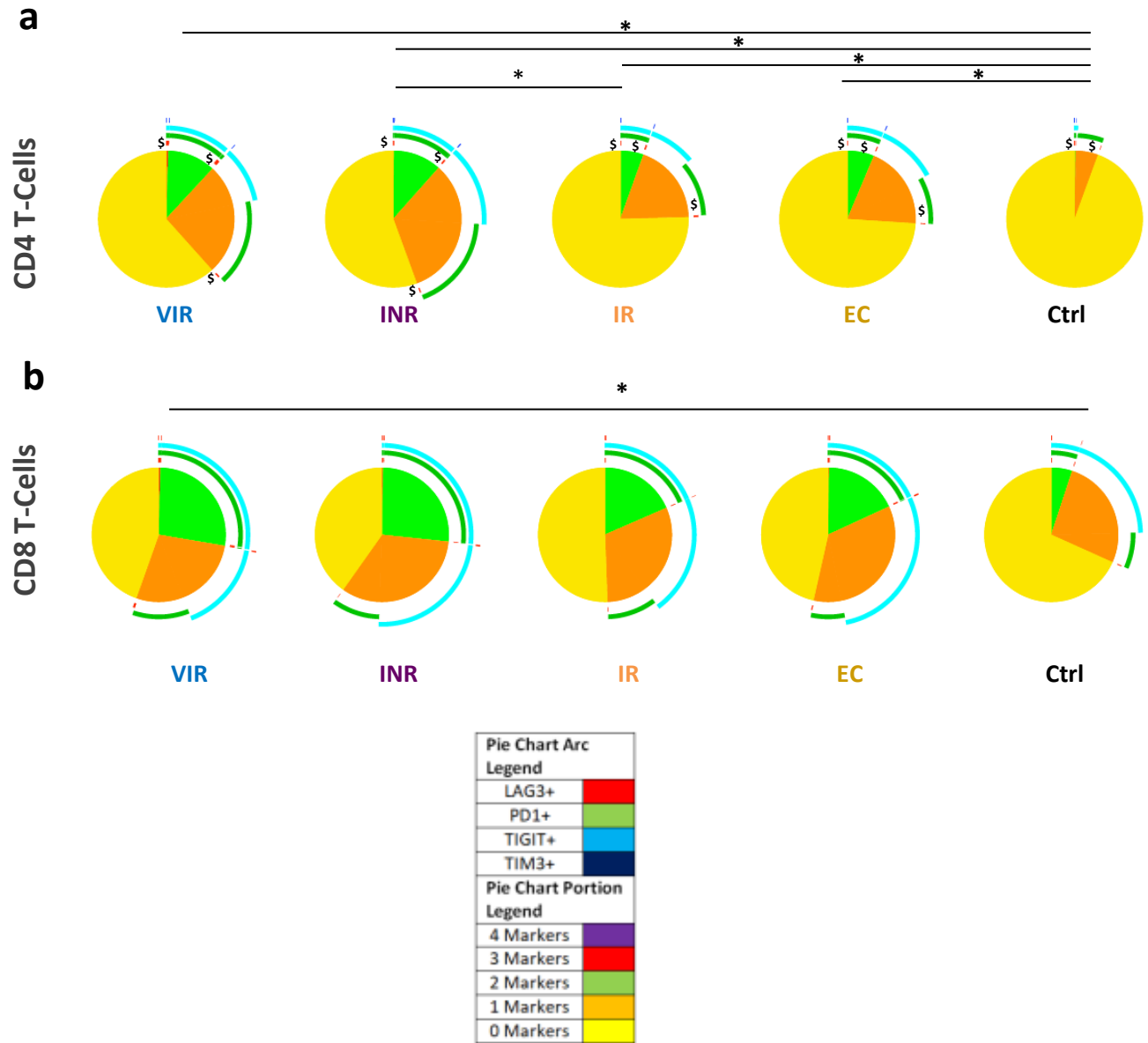
IRF3	5'-GAGGTGACAGCCTTCTACCG-3'
	5'-TGCCTCACGTAGCTCATCAC-3'
	FAM-TCTTCCAGCAGACCATCTCC-BBQ
IRF7	5'-AGGTGAGACCAGAGCCTCAA-3'
	5'-CTAGGTGCACTCGGCACAG-3'
	Cy5-TACACCGGGTCACTGACAGA-BBQ
IFNL3	5'-CTGCTGAAGGACTGCAAGTG-3'
	5'-GAGGATATGGTGCAGGGTGT-3'
	Cy5-ACGCTGAAGGTTCTGGAGG-BBQ
IFNα	5'-GGGATGAGACCCTCCTAGACAAATT-3'
	5'-ACACAGGCTTCCAGGTCA TTCAG-3'
	FAM-CTGCACCGAACTCTAC-BBQ
TNFα	5'-TCCTTCAGACACCCTCAACC-3'
	5'-AGGCCCCAGTTTGAATTCTT-3'
	FAM-GATTCAGGAATGTGTGGCCT-BBQ
TLR7	5'-CCTTGAGGCCAACAACATCT-3'
	5'-GTAGGGACGGCTGTGACATT-3'
	FAM-CTCTACCTGGGCCAAAAGTGG-BBQ
TLR9	5'-GCTAGACCTGTCCCACAATAA-3'
	5'-CAAGTCCAGCCAGATCAAAA-3'
	FAM-ACAACAACATCCACAGCCAA-BBQ
Trim5α	5'-GAGAGACATCCTGGACTGGG-3'
	5'-TGAAGCAGCTCCATCACTGA-3'
	Cy5-AACTGAGATGGTGCAGCAGA-BBQ
BST2	5'-TGCTGGGGATAGGAATTCTG-3'
	5'-TCAGCTCTTGTGTCAGGAGA-3'
	FAM-GGGGTGCCCTTGATTATCTT-BBQ
HDAC6	5'-AAGTAGGCAGAACCCCAAGT-3'
	5'-GTGCTTCAGCCTCAAGGTTC-3'
	Cy5-CAGTGTCACCTTCGAAGCGAA-BBQ
SAMHD1	5'-AGCGATTGGTTCAAATCCAC-3'
	5'-TCGATTGTGTGAAGCTCCTG-3'
	FAM-AATGATCCTATCCATGGCCA-BBQ
APOBEC3G	5'-GAGCGGCCTGTCTTTATCAG-3'
	5'-TGCTCCAAGCTTCTGGTTTT-3'
	Cy5-GGAGGTCACCTTAGGGAGGG-BBQ
TRAIL	5'-GGAACCCAAGGTGGGTAGAT-3'
	5'-TCTCACCACTGCAACCTC-3'
	Cy5-AATTAGCTGGGTGTGTTGGC-BBQ

Supplementary Table 2

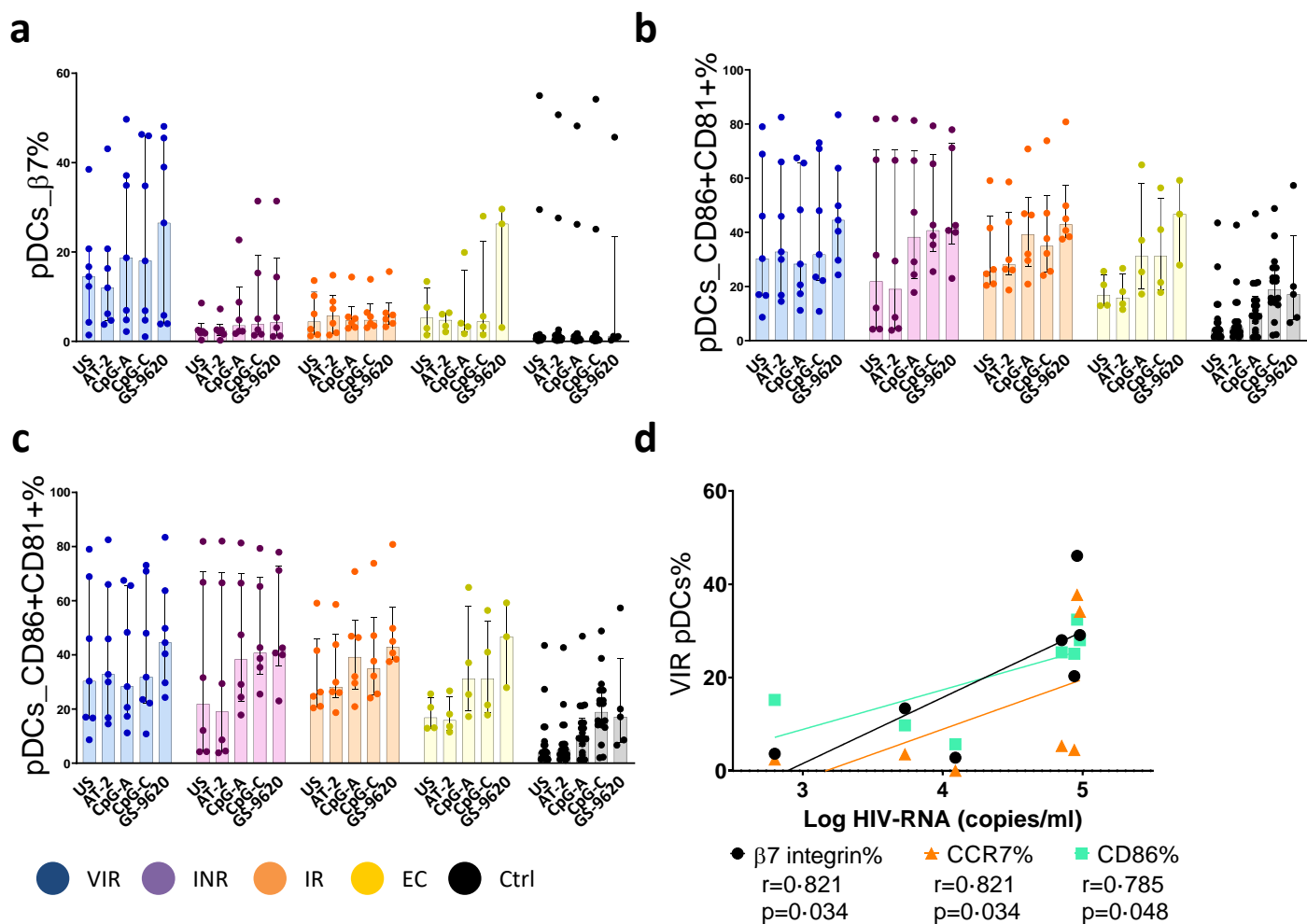
Antibodies	SOURCE	IDENTIFIER
Purified anti-human CD49d, clone 9F10	BD Biosciences	Cat# 555501
Purified anti-human CD28, clone CD28.2	BD Biosciences	Cat# 555725
BV650 anti-human CD107a, clone H4A3	BioLegend	Cat# 328638
FITC anti-human CD45RA, clone L48	BD Biosciences	Cat# 335039
APCH7 anti-human CD27, clone M-T271	BD Biosciences	Cat# 560222
FITC Lin-2 (anti-human CD3, CD14, CD19, CD20, CD56), CD3 21 clone SK7, CD19 clone SJ25C1, CD20 clone L27, CD14 clone M ϕ P9 and CD56 clone 22 NCAM16.2	BD Biosciences	Cat# 643397
BV421 anti-human CD86, clone 2331 (FUN-1)	BD Biosciences	Cat# 562432
BV786 anti-human PD-1 (CD279), clone EH12-1	BD Biosciences	Cat# 563789
BV605 anti-human LAG3, clone 11C3C65	Biolegend	Cat# 369324
PerCPCy5,5 anti-human TIGIT, clone A15153G	Biolegend	Cat# 372718
BV421 anti-human IL-2, clone MQ1-17H12	BD Biosciences	Cat# 564164
PeCy7 anti-human IFN γ , clone B27	BD Biosciences	Cat# 557643
AF700 anti-human TNF α , clone MAb11	BD Biosciences	Cat# 557996
Pe anti-human Perforin, clone B-D48	BioLegend	Cat# 353304
BV786 anti-human CCR7 (CD197), clone 3D12	BD Biosciences	Cat# 563710
Pe anti-human IDO, clone eyedio	eBioscience, San Diego, CA, USA	Cat#12-9477-42
BV711 anti-human HLA-DR, clone G46-6	BD Biosciences	Cat# 563696
PeCF594 anti-human PDL1 (CD274), clone MIH1	BD Biosciences	Cat# 563742
APC anti-human Integrin- β 7, clone FIB504	BD Biosciences	Cat# 551082
PerCPCy5,5 anti-human CD4, clone OKT4	BioLegend	Cat# 317428
AF700 anti-human CD123 (anti-hIL-3), clone 32703	N R&D, San Diego, CA	Cat# FAB301
APC-Cy7 anti-human CD1c, clone L161	BioLegend	Cat# 331520
PeCy7 anti-human CD141, clone M80	BioLegend	Cat# 344110
BV650 anti-human CD11c, clone B-ly6	BD Biosciences	Cat# 563404
BV605 anti-human CD16, clone 3G8	BD Biosciences	Cat# 563172
FITC anti-human CD81, clone JS-81	BD Biosciences	Cat# 551108
BV605 anti-human CD4, clone RPA-T4	BD Biosciences	Cat# 562658
BV650 anti-human CD86, clone 2331(FUN-1)	BD Biosciences	Cat# 563412
APC-Cy7 anti-human CD5, clone UCHT2	BD Biosciences	Cat# 563516
PeCy5.5 anti-human CD2, clone S5.5	ThermoFisher	Cat# CD0218
PE/Dazzle 594 Anti-human TIM3, F38-2E2	Biolegend	Cat# 345033
AF700, anti-human TNF- α , clone Mab11	BD Biosciences	Cat# 557996
AF700, anti-human TLR-7	R&D SYSTEM	Cat# IC5875N
BV421, anti-human TLR-9	Novus Biologicals	Cat# 26C593.2
BV711, anti-humna integrin β 7, clone FIB504	BD Biosciences	Cat# 744012
BV510, anti-human CD123, clone 7G8	BD Biosciences	Cat# 563072
PE, anti-human IL-17A, Clone eBio64DEC16	ThermoFisher	Cat# 12-7179-40
BV421, anti-human IL2, clone MQ1-17H12	BD Biosciences	Cat#566273



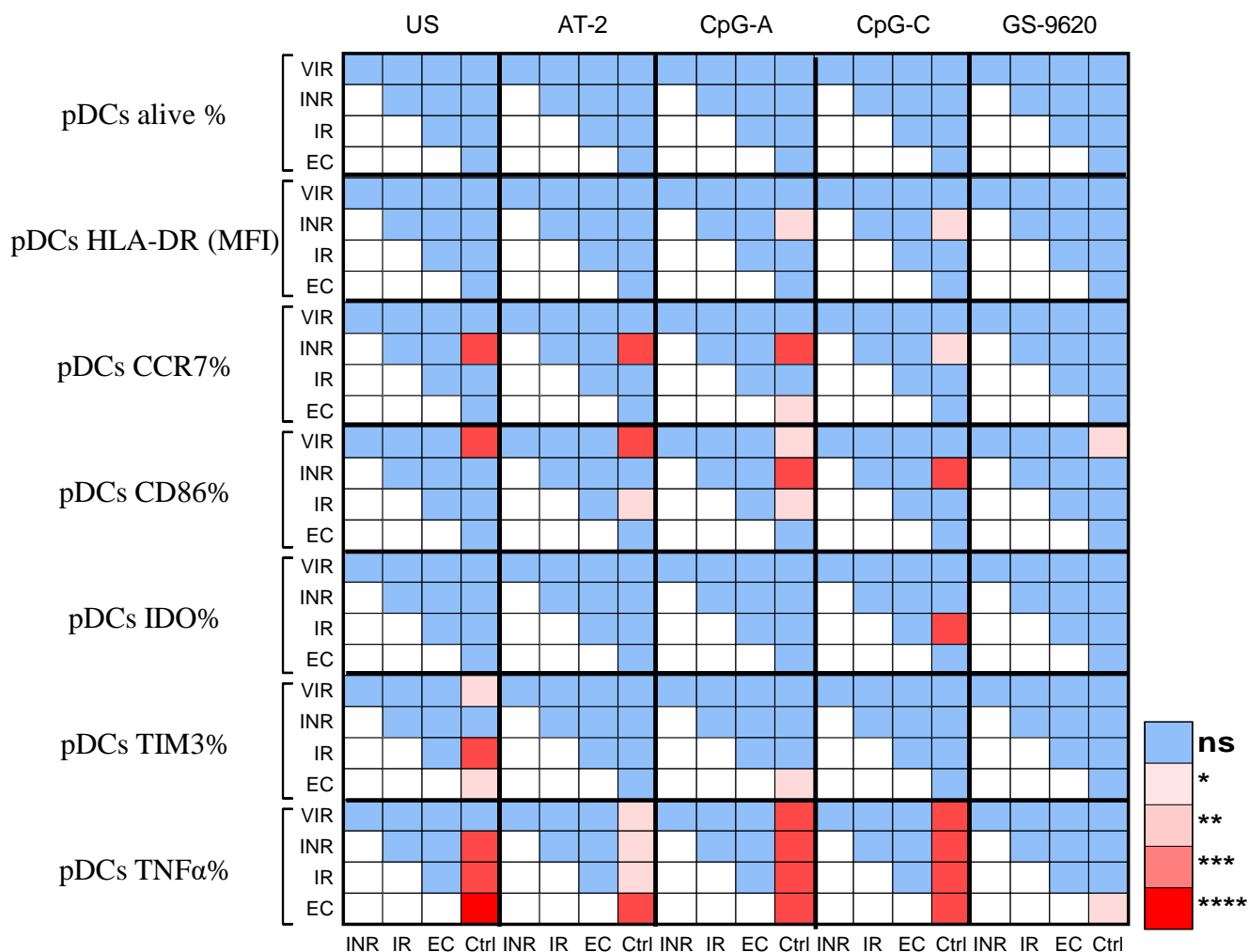
Supplementary Figure 1. Gating strategies. Schematic diagram of the PBMCs gating strategy to identify mDCs and pDCs (a), isolated pDCs (b), isolated CD4 (c) and isolated CD8 T-cell (d).



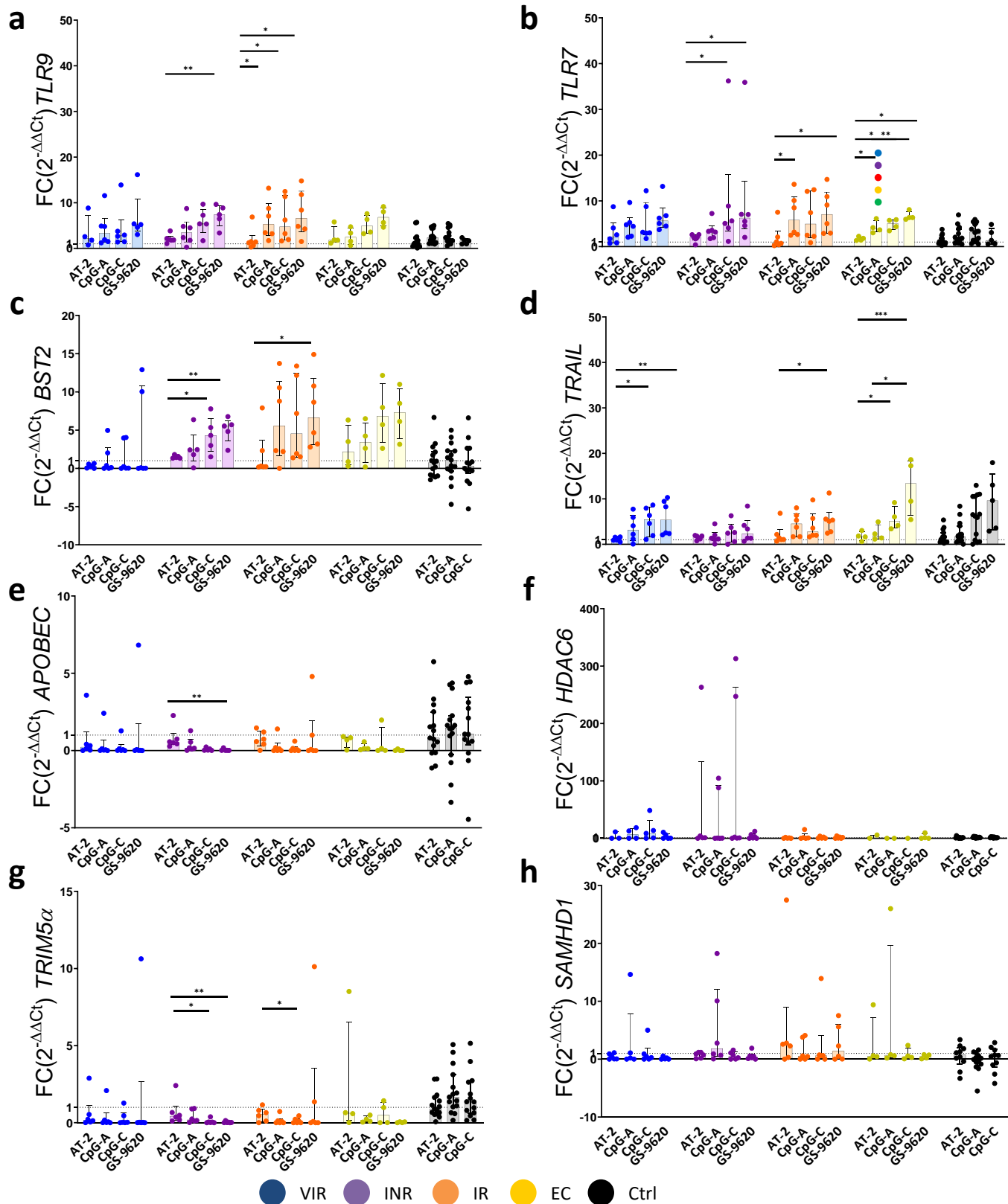
Supplementary Figure 2. Exhaustion markers are increased in PLWH. *Ex vivo* multiple exhaustion phenotype of memory CD4 (a) and CD8 T-cells (b) represented as pie charts. Permutation test, following the Spice version 6 software was used to assess the differences between pie charts. Statistical significant values are shown as: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Abbreviations: VIR, Viremic; INR, Immune Non Responders; IR, Immune Responders; EC, HIV Elite Controllers and Ctrl, Control group. \$: Arc representing Lag3+ cells in CD4+ T-cells in CD8+ T-cell there is not Tim3 expression.



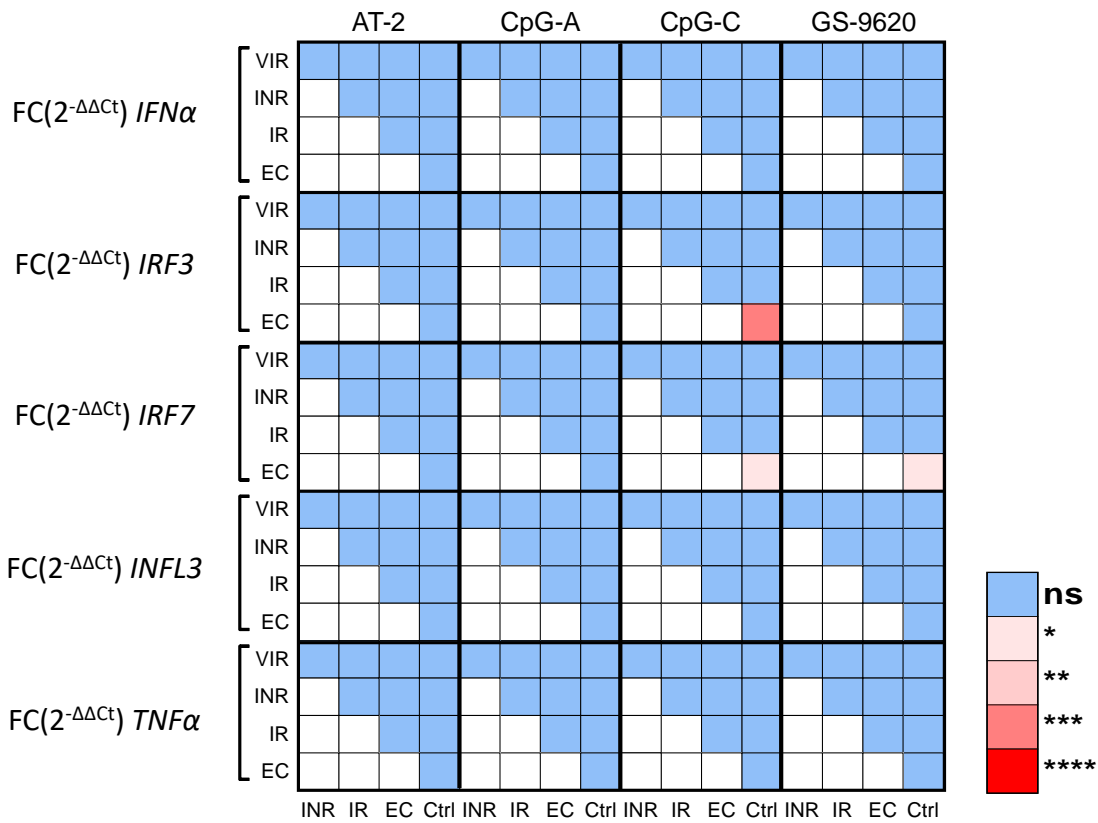
Supplementary Figure 3. pDCs phenotype and correlation with HIV viremia. pDCs markers expression after AT-2, CpG-A, CpG-C and GS-9620 stimulation (a-c). Correlation between HIV viral load pDCs phenotype before stimulation in participants with detectable viremia (VIR) (b). Spearman p correlation coefficient test and Friedman test including Dunn's multiple comparisons test correction were applied. Statistical significant values are shown as: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Abbreviations: VIR, Viremic; INR, Immune Non Responders; IR, Immune Responders; EC, HIV Elite Controllers and Ctrl, Control group.



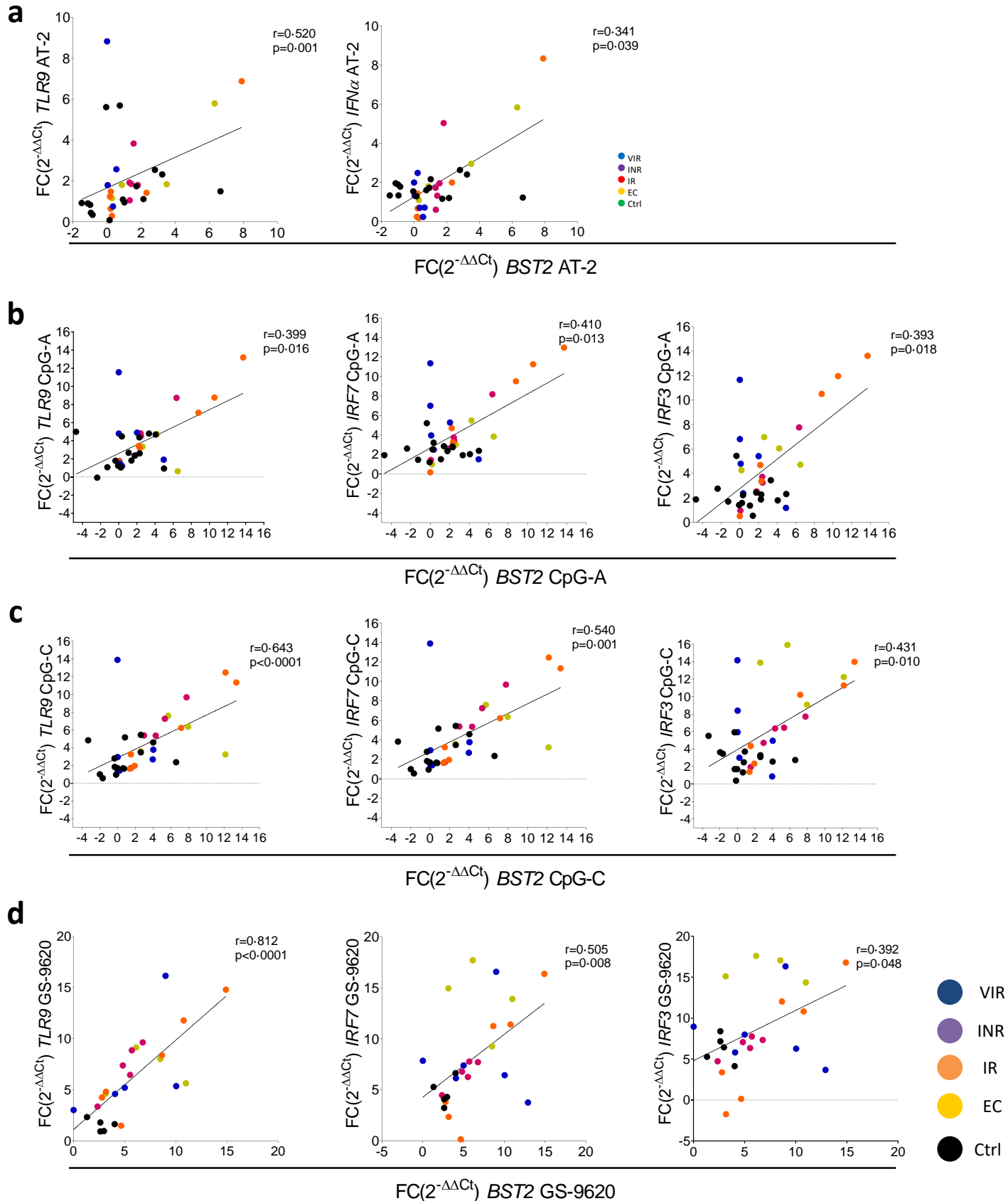
Supplementary Figure 4. Association matrix of pDCs activated phenotype after TLR agonist stimulation. Association matrix representing non significance (blue square) and statistical significance (red square) between the study groups (VIR, INR, IR, EC and Ctrl) after TLR agonist stimulations (US, AT-2, CpG-A, CpG-C and GS-9620). Kruskal-Wallis test including Dunn's multiple comparisons test correction was applied. Statistical significant values are shown as: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$. Abbreviations: VIR, Viremic; INR, Immune Non Responders; IR, Immune Responders; EC, HIV Elite Controllers and Ctrl, Control group.



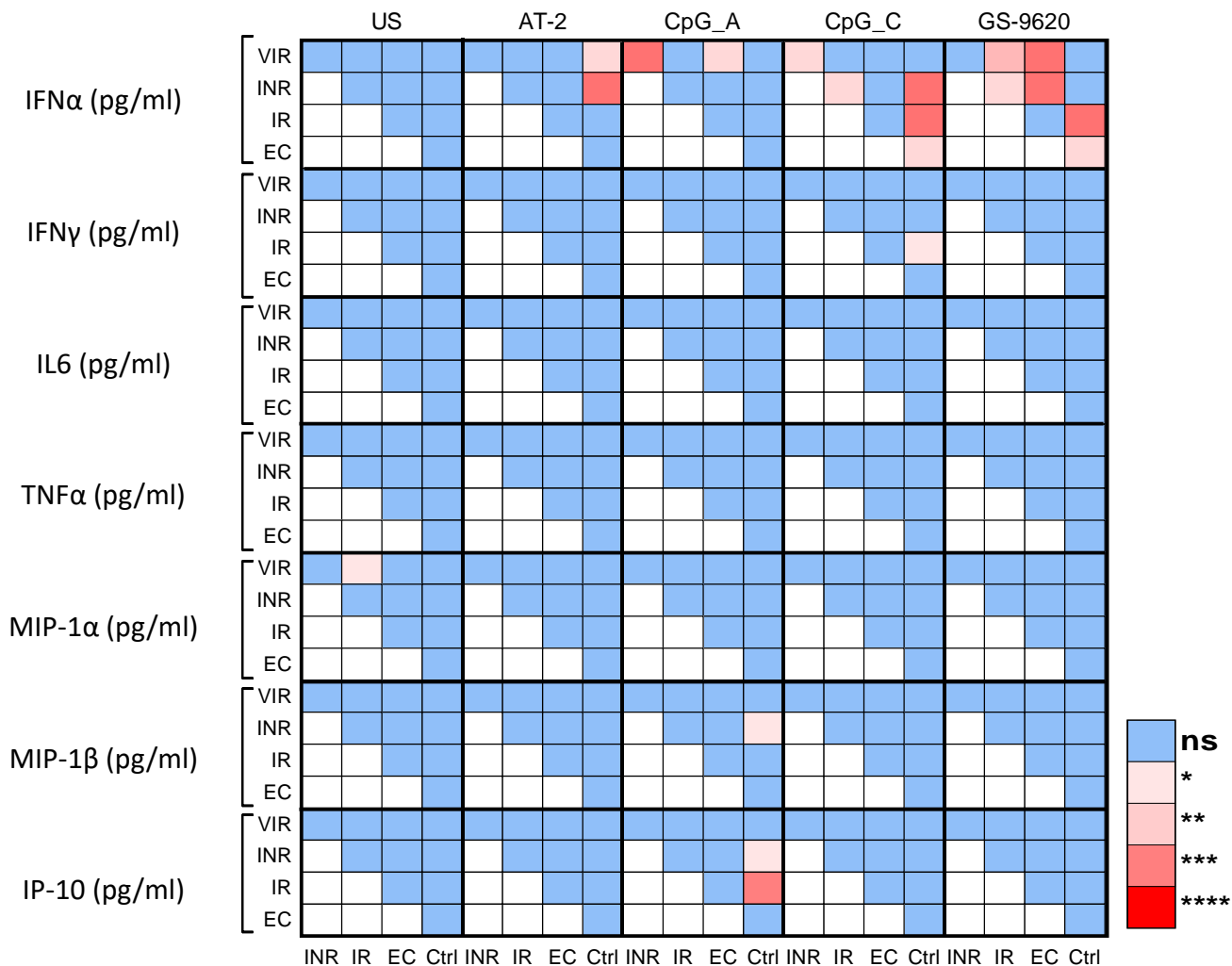
Supplementary Figure 5. pDCs gene expression profile after TLR stimulations. Fold change expression of TLR-9 (a), TLR-7 (b), BST2 (c), TRAIL (d), APOBEC (e), HDAC6 (f), TRIM5 α (g) and SAMHD1 (h) of the different stimuli related to the unstimulated condition. The Friedman test including Dunn's multiple comparisons correction test were used to assess differences between stimuli. Statistical values are shown as: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Abbreviations: VIR, Viremic; INR, Immune Non Responders; IR, Immune Responders; EC, HIV Elite Controllers and Ctrl, Control group.



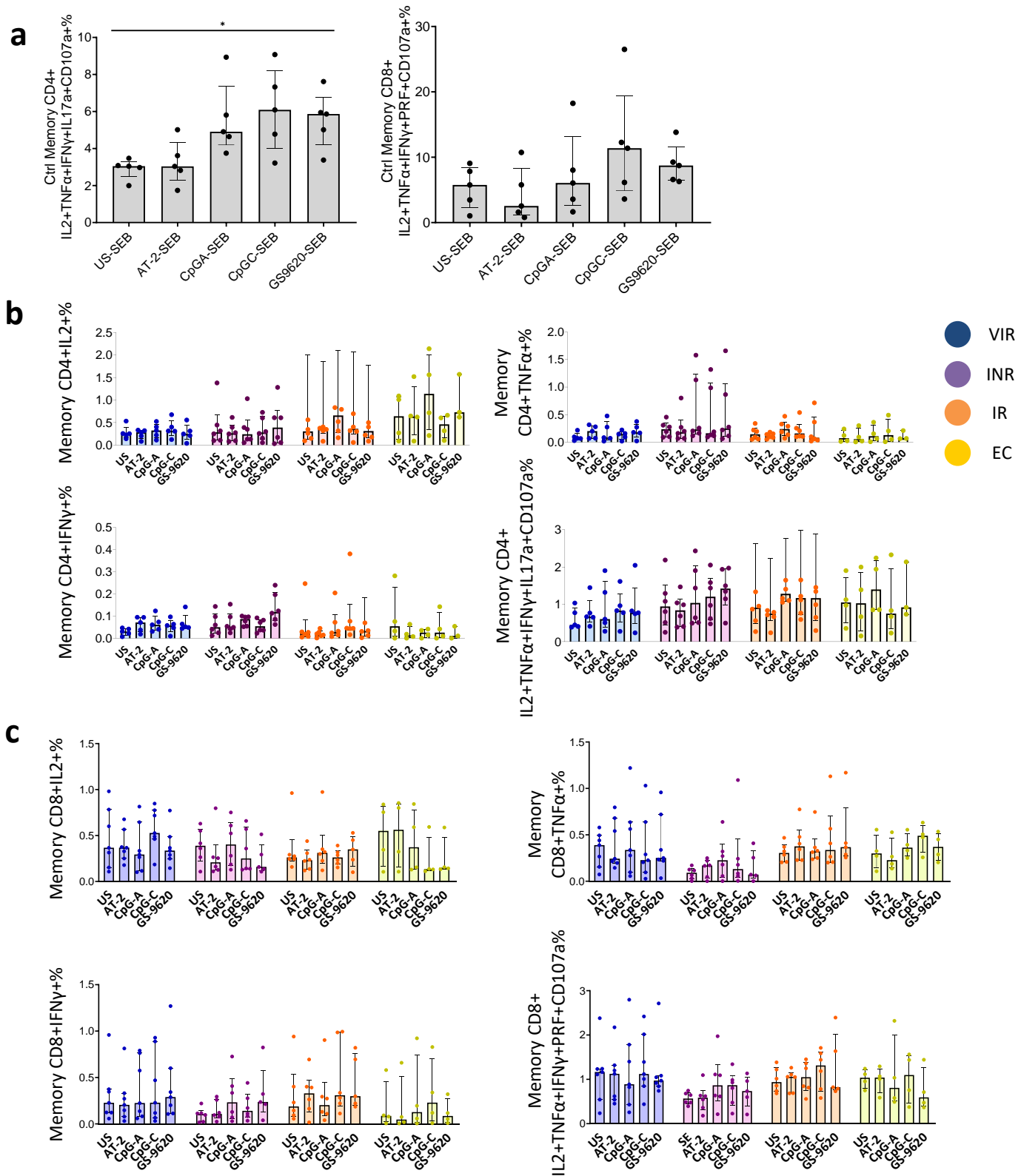
Supplementary Figure 6. Association matrix of pDCs gene expression profile after TLR stimulations. Association matrix representing non significance (blue square) and statistical significance (red square) between the study groups (VIR, INR, IR, EC and Ctrl) after TLR agonist stimulations (US, AT-2, CpG-A, CpG-C and GS-9620). Kruskal-Wallis test including Dunn's multiple comparisons test correction was applied. Statistical significant values are shown as: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$. Abbreviations: VIR, Viremic; INR, Immune Non Responders; IR, Immune Responders; EC, HIV Elite Controllers and Ctrl, Control group.



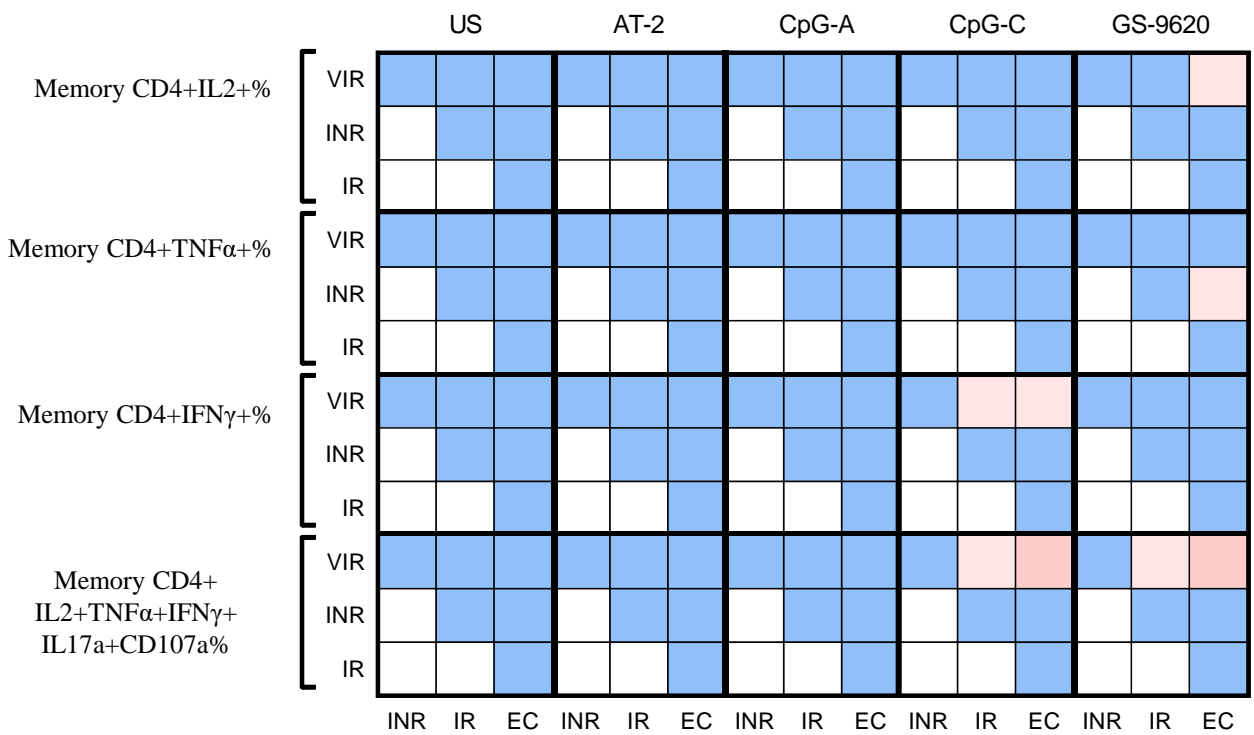
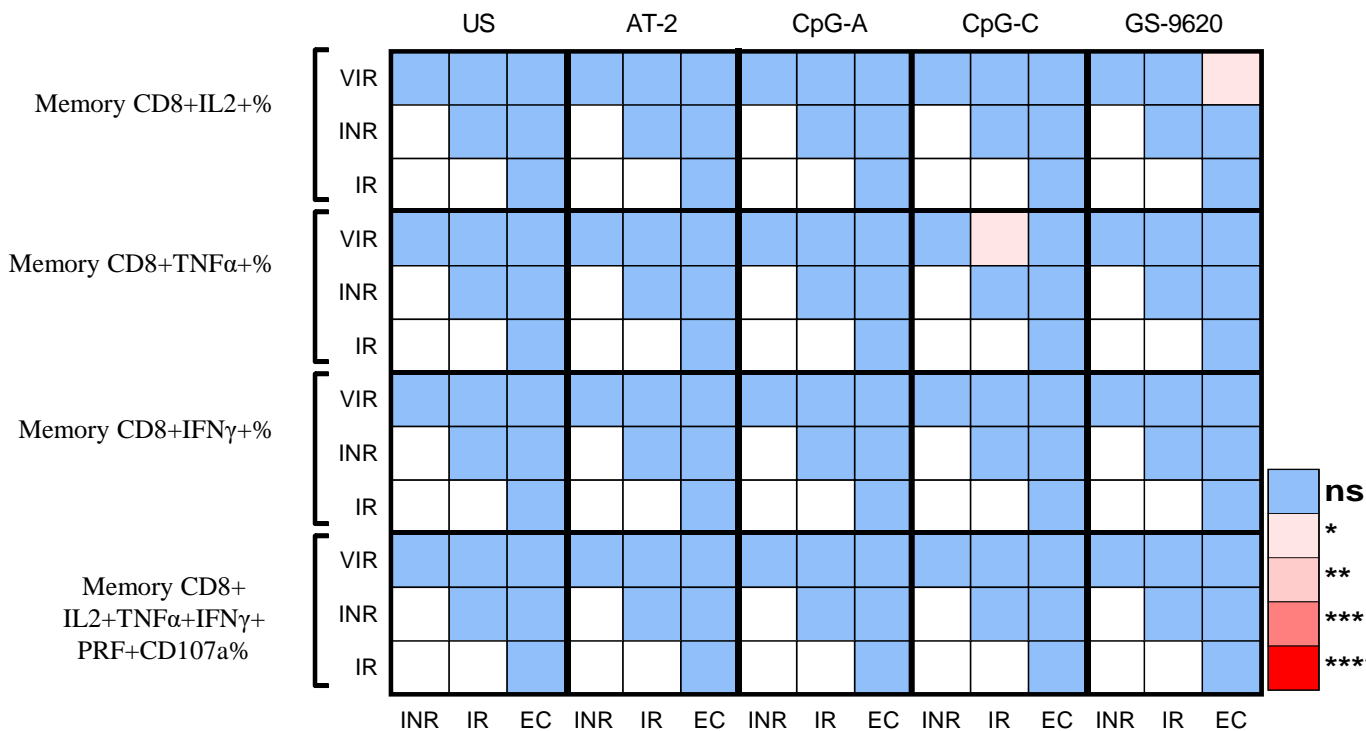
Supplementary Figure 7. Expression levels of *BST2* are directly associated with *TLR9* and *IRFs* gene expression levels in pDC. Spearman correlation between pDCs fold change expression of the restriction factor *BST2* and the fold change expression of *TLR9*, *IFN α* , *IRF7* and *IRF3* among AT-2 (a), CpG-A (b), CpG-C (c) and GS-9620 (d). Abbreviations: VIR, Viremic; INR, Immune Non Responders; IR, Immune Responders; EC, HIV Elite Controllers and Ctrl, Control group.



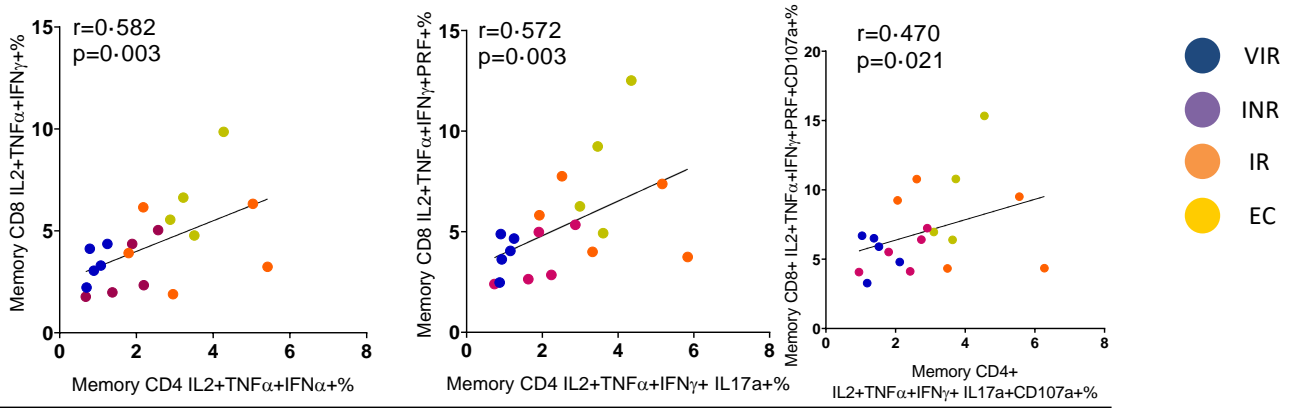
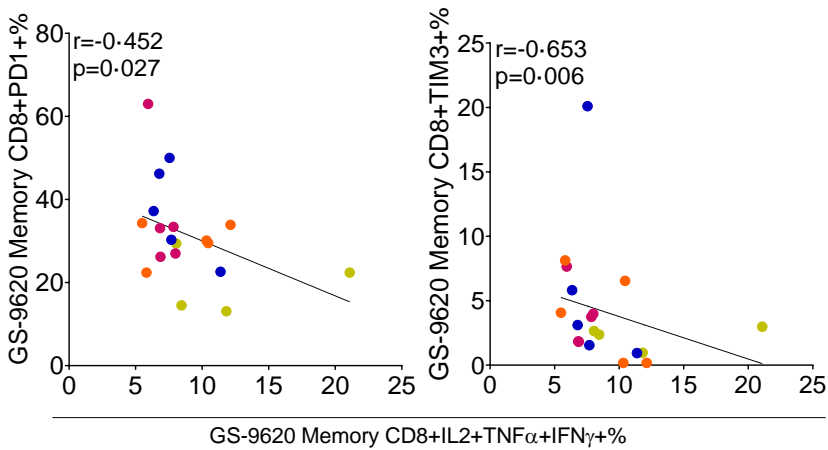
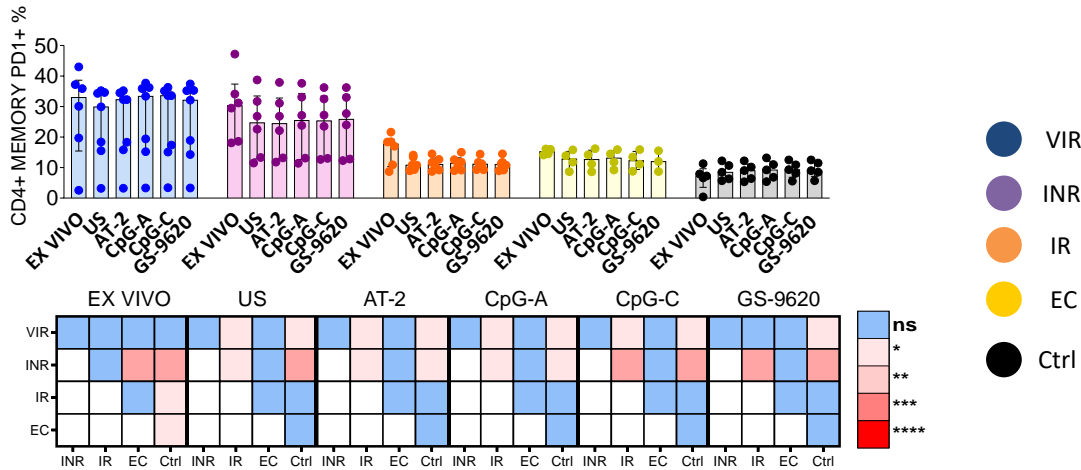
Supplementary Figure 8. Association matrix of pDCs cytokine expression profile after TLR stimulations. Association matrix representing non significance (blue square) and statistical significance (red square) between the study groups (VIR, INR, IR, EC and Ctrl). Kruskal-Wallis test including Dunn's multiple comparisons test correction was applied. Statistical significant values are shown as: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$. Abbreviations: VIR, Viremic; INR, Immune Non Responders; IR, Immune Responders; EC, HIV Elite Controllers and Ctrl, Control group.



Supplementary Figure 9. T-cell response mediated by pDCs in controls and in PLWH without HIV-specific stimulation. Increased in Ctrl memory CD4+ and CD8+ T-cell response mediated by pDCs (a). Single cytokine and the sum of IL2, TNF α , IFN γ , IL17a and CD107a intracellular memory CD4+ T-cell production after the coculture with previously stimulated pDCs without HIV (Gag)-specific peptide pool (b). Single cytokine and the sum of IL2, TNF α , IFN γ , PRF and CD107a intracellular memory CD8+ T-cell production after the coculture with previously stimulated pDCs without HIV (Gag)-specific peptide pool (c). The Friedman test including Dunn's multiple comparisons correction test were used to assess differences between stimuli. Statistical values are shown as: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. Abbreviations: VIR, Viremic; INR, Immune Non Responders; IR, Immune Responders; EC, HIV Elite Controllers and Ctrl, Control group.

a**b**

Supplementary Figure 10. Association matrix of HIV-specific memory T-cell response. Association matrix of HIV-specific memory CD4+ (a) and memory CD8+ (b) T-cell response. Association matrix representing non significance (blue square) and statistical significance (red square) between the study groups (VIR, INR, IR, EC and Ctrl). Kruskal-Wallis test including Dunn's multiple comparisons test correction was applied. Statistical significant values are shown as: *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001. Abbreviations: VIR, Viremic; INR, Immune Non Responders; IR, Immune Responders and EC, HIV Elite Controllers.

a**b****c**

Supplementary Figure 11. Increased in HIV-specific memory CD8+ T-cell response mediated by pDCs is inversely associated with CD8+ T-cell exhaustion. Spearman positive correlation between HIV (Gag)-specific CD4 and CD8 T-cell response (a). Spearman negative correlation between HIV (Gag)-specific CD8 T-cell response and PD1 and TIM3 CD8 memory T-cell levels (b). PD1 CD4 memory T-cell levels after coculture with pDCs previously stimulated with TLR agonist. Association matrix representing non significance (blue square) and significance (red square) between the study groups (c). Friedman and Kruskal-Wallis test including Dunn's correction was applied. Spearman p correlation coefficient test was used. Statistically significant values are shown as: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$. Abbreviations: VIR, Viremic; INR, Immune Non Responders; IR, Immune Responders; EC, HIV Elite Controllers and Ctrl, Control group.