Table S1. Combinations of fluorochrome-conjugated antibodies used in panels for this study

Fluorochrome	*T-cell differentiation/activation*	*T cell function*	*Apoptosis*
FITC	Ki-67	Ki-67	CD45RA
CY7 APC	CD3	CD3	CD3
Alexa 680	CD38	CCR7	CCR7
APC	BrdU	CD95	
Qdot 800	CD8	CD8	CD8
Qdot 655	CD45RA	CD45RA	
Qdot 605	CD28		
Qdot 585	CD4	CD4	CD4
Qdot 545	CD14		
ViViD Pacific Blue	ViViD	ViViD	ViViD
CY7 PE	CD25	TNF-α	CD25
Alexa 700-PE	HLA-DR	CD11a	HLA-DR
CY5 PE	CD95	CD28	CD95
Alexa 594	CCR7	IFN-γ	
PE	CCR5	IL-2	Annexin V

Figure S1. IL-15 combined with ART expands T_N cells. Fold change in $CD4^+$ and $CD8^+$ T_N absolute counts in the peripheral blood during treatment with IL-15, ART or ART+IL-15. The horizontal grey line indicates no change vs. baseline. Data were expressed as in Fig. 1b.

Figure S2. No effect of treatment on the turnover of memory T-cell subsets. Fold change in $BrdU^+$ T_{CM} and T_{TM} $CD4^+$ or T_{CM} and T_{EM} $CD8^+$ T cells in the peripheral blood after treatment initiation. Data were expressed as in Fig. 1b.

Figure S3. Baseline plasma IL-15 levels do not influence T-cell responsiveness to IL-15 therapy. a) Plasma IL-15 levels as measured by ELISA at d-7 and in SIV-uninfected macaques. The median of the distribution is indicated; b) correlation between plasma IL-15 levels at d-7 and SIV load; c) correlation between plasma IL-15 levels at d-7 and fold expansion of $CD4^+$ (left) and $CD8^+$ (right) T cells at d46 after treatment with ART+IL-15.

Figure S4. IL-15 promotes $CD8^+$ T-cell expansion in peripheral tissues. a) Percent of total $CD8^+$ T cells in the lymphocyte gate in the ILN, BAL and jejunum at pre-therapy (d-13) and at d28 after therapy initiation. Each line corresponds to a single animal.

Figure S5. ART or IL-15 treatments do not shape the quality of CMV-specific $CD4^+$ T-cell responses. a) Pie charts and bars representing the quality of the CMV-specific $CD4^+$ response at baseline and at d46 after ART treatment. Data were expressed as in Fig. 4b. c) As in b) but in the different treatment groups at d46 after treatment initiation. IL-15 group is not shown because only one animal had detectable CMV-specific $CD4^+$ T cell response.

Figure S6. Previous IL-15 administration does not shape the quality of the SIV-specific response upon treatment interruption. Bar graph representing the quality of the SIV-specific (Gag and Env averaged) $CD8^+$ response at d-7, 7 and 46 in the different treatment groups. Data were expressed as in Fig. 2b. #= $P<0.05$ vs. d46; Wilcoxon rank sum test. Colors of the # symbol refers to the group whose mean is statistically significant when compared to the reference group.

Figure S7. Dynamics in differentiation phenotype of SIV-specific $CD4^+$ T cells after treatment interruption. Percentage of SIV-specific (Gag and Env averaged) $CD4^+$ T cells with T_{CM}, T_{TM} or T_{EM} phenotype out of total memory cells before treatment interruption (d46) and at d59 and 70. Data were expressed as in Fig. 1b. #= $P<0.05$ vs. d46; Wilcoxon rank sum test.

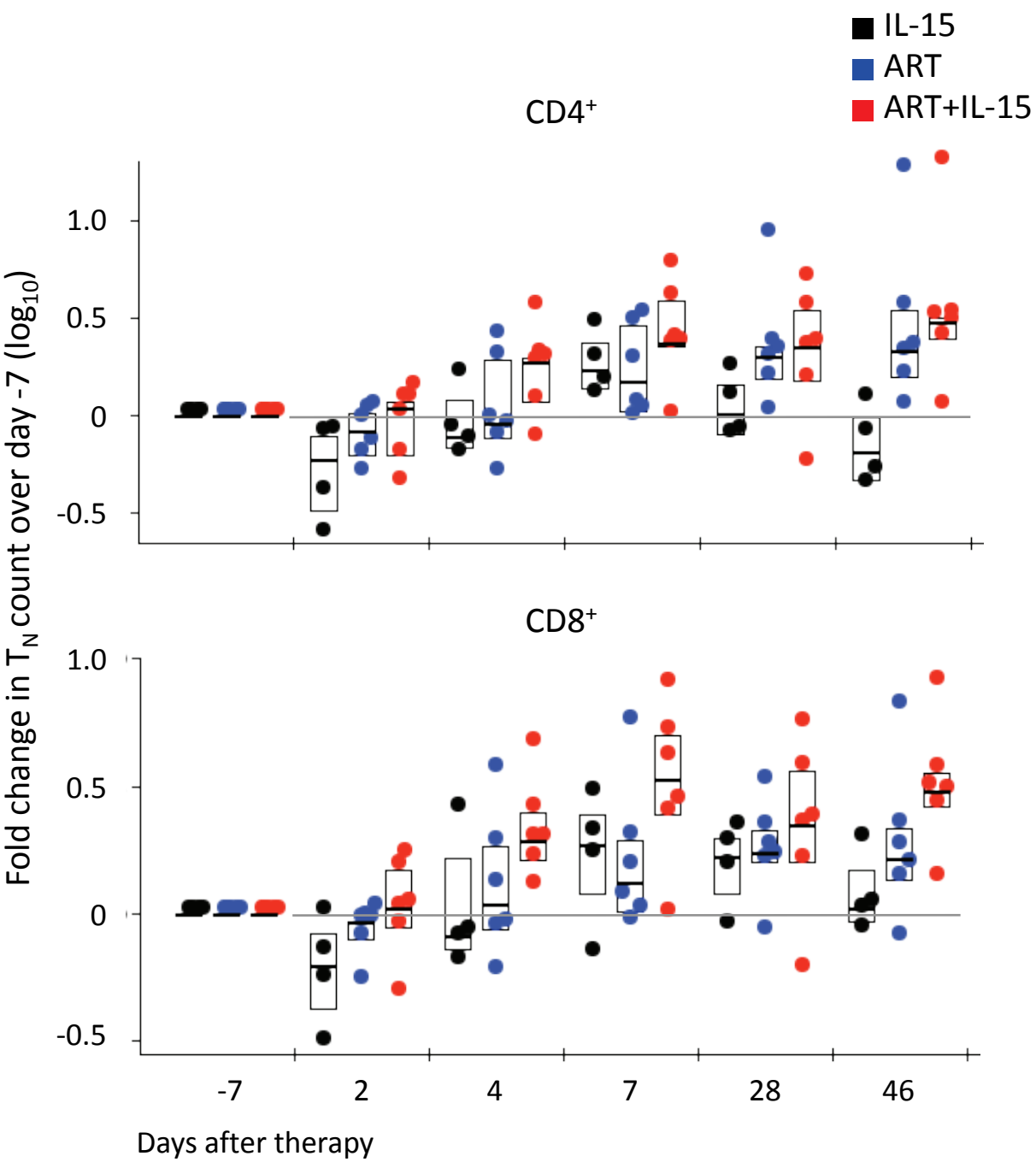
IL-15
ART
ART+IL-15
CD4+
CD8+
Fold change in TN count over day -7 (log10)
1.0
0.5
0
-0.5
-7
2
4
7
28
46
Days after therapy

Figure S1

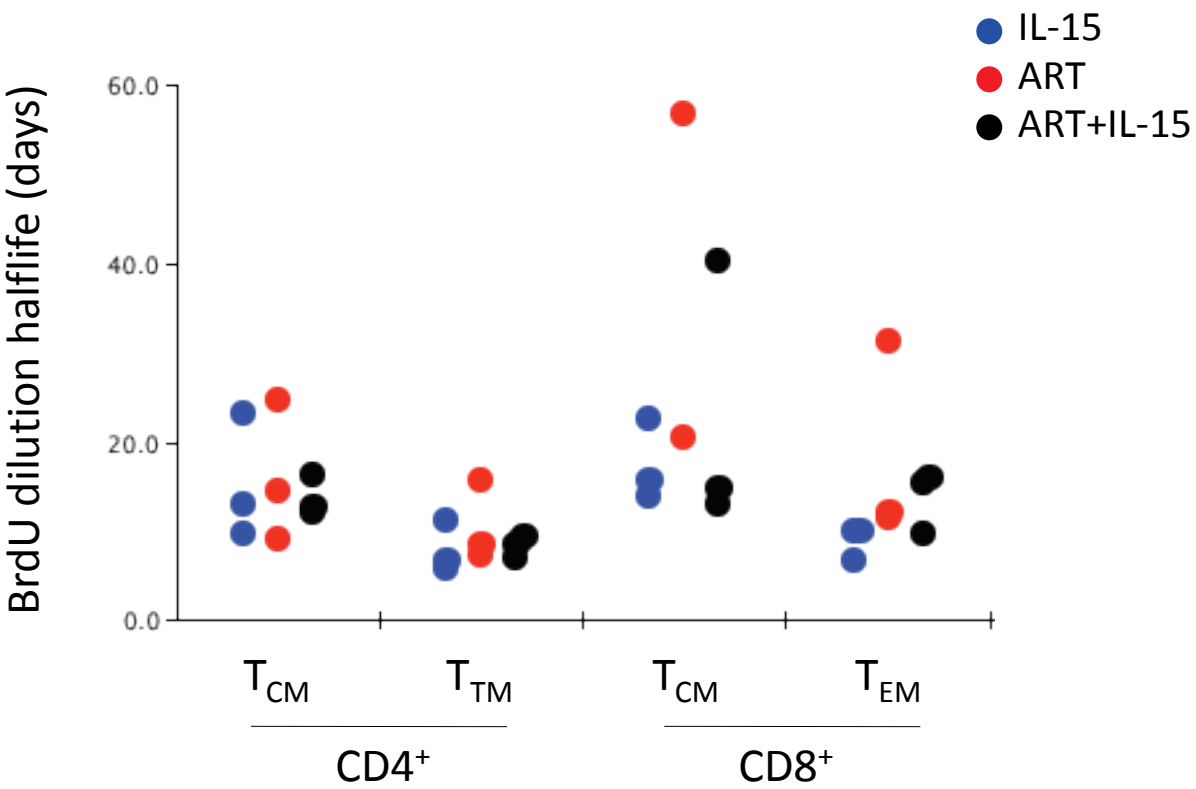
IL-15
ART
ART+IL-15
BrdU dilution halflife (days)
60.0
40.0
20.0
0.0
T_{CM}
T_{TM}
T_{CM}
T_{EM}
$CD4^+$
$CD8^+$

Figure S2

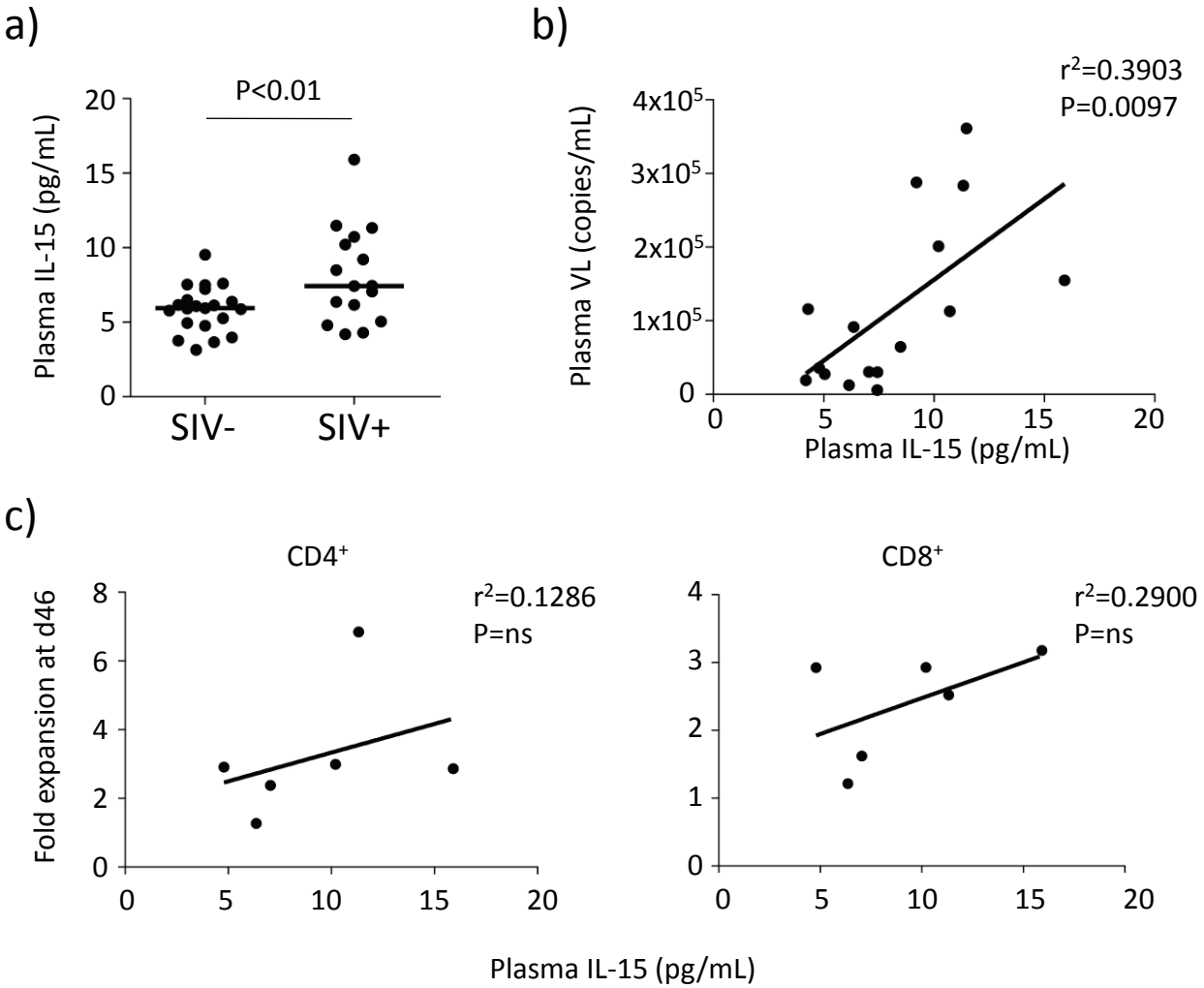
a)
P<0.01
Plasma IL-15 (pg/mL)
20
15
10
5
0
SIV-
SIV+
b)
r²=0.3903
P=0.0097
Plasma VL (copies/mL)
4x10⁵
3x10⁵
2x10⁵
1x10⁵
0
0
5
10
15
20
Plasma IL-15 (pg/mL)
c)
CD4⁺
r²=0.1286
P=ns
Fold expansion at d46
8
6
4
2
0
0
5
10
15
20
CD8⁺
r²=0.2900
P=ns
4
3
2
1
0
0
5
10
15
20
Plasma IL-15 (pg/mL)

Figure S3

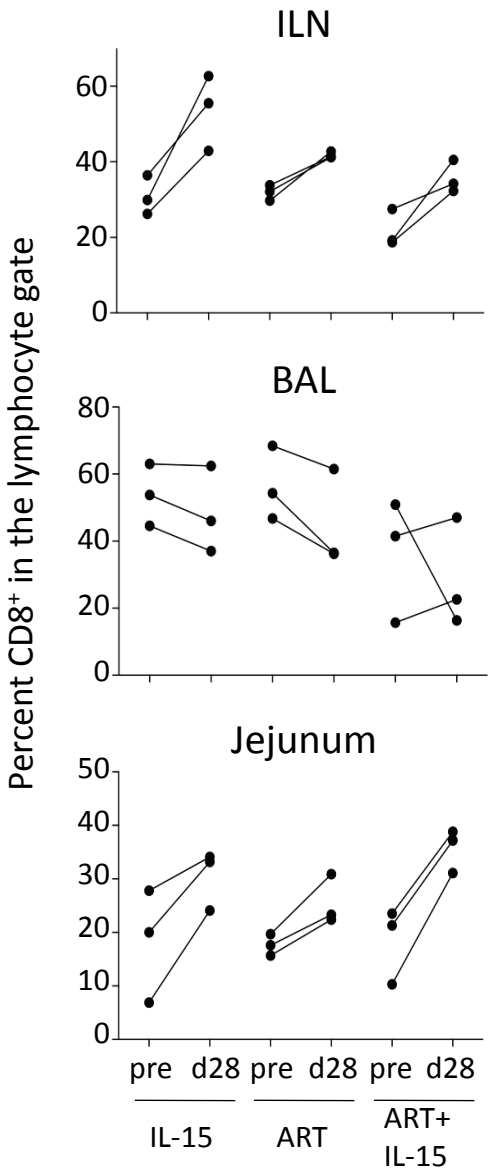
ILN
BAL
Jejunum
Percent CD8+ in the lymphocyte gate
0
20
40
60
80
10
30
50
pre
d28
IL-15
ART
ART+
IL-15

Figure S4

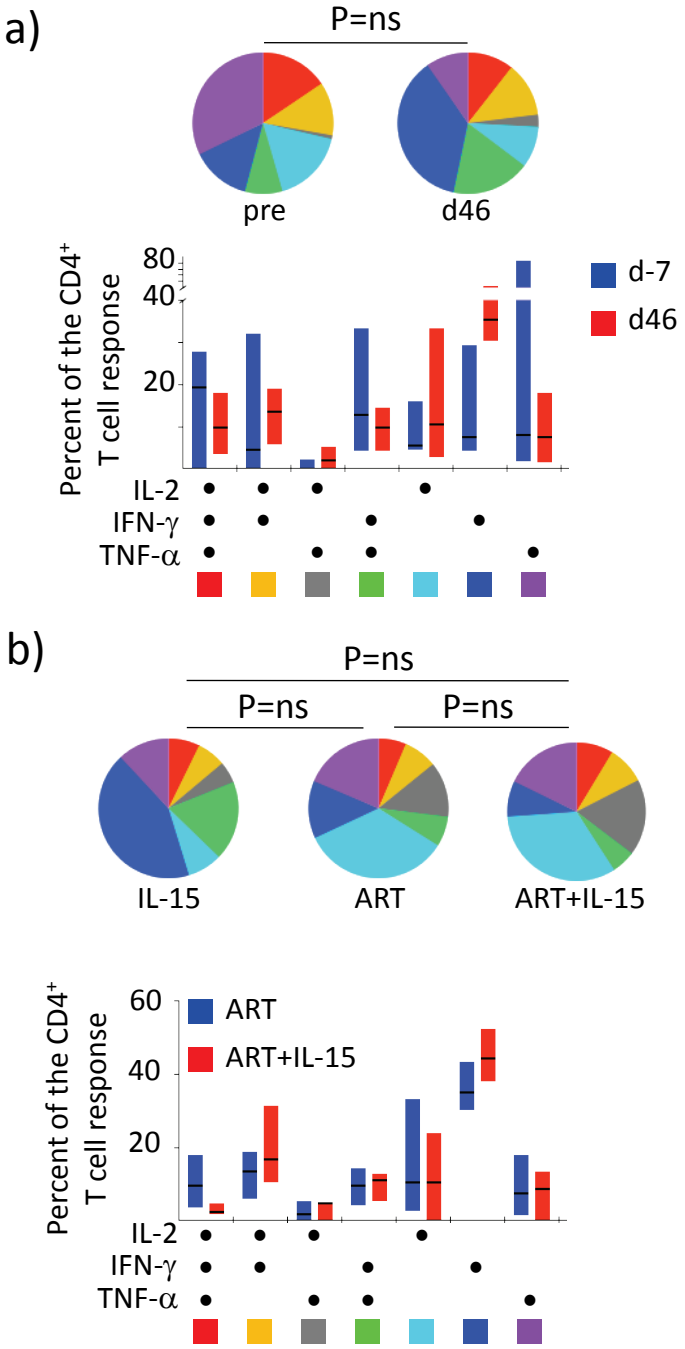
a)
P=ns
pre
d46
Percent of the CD4+ T cell response
80
40
20
d-7
d46
IL-2
IFN-γ
TNF-α
b)
P=ns
P=ns
P=ns
IL-15
ART
ART+IL-15
Percent of the CD4+ T cell response
60
40
20
ART
ART+IL-15
IL-2
IFN-γ
TNF-α

Figure S5

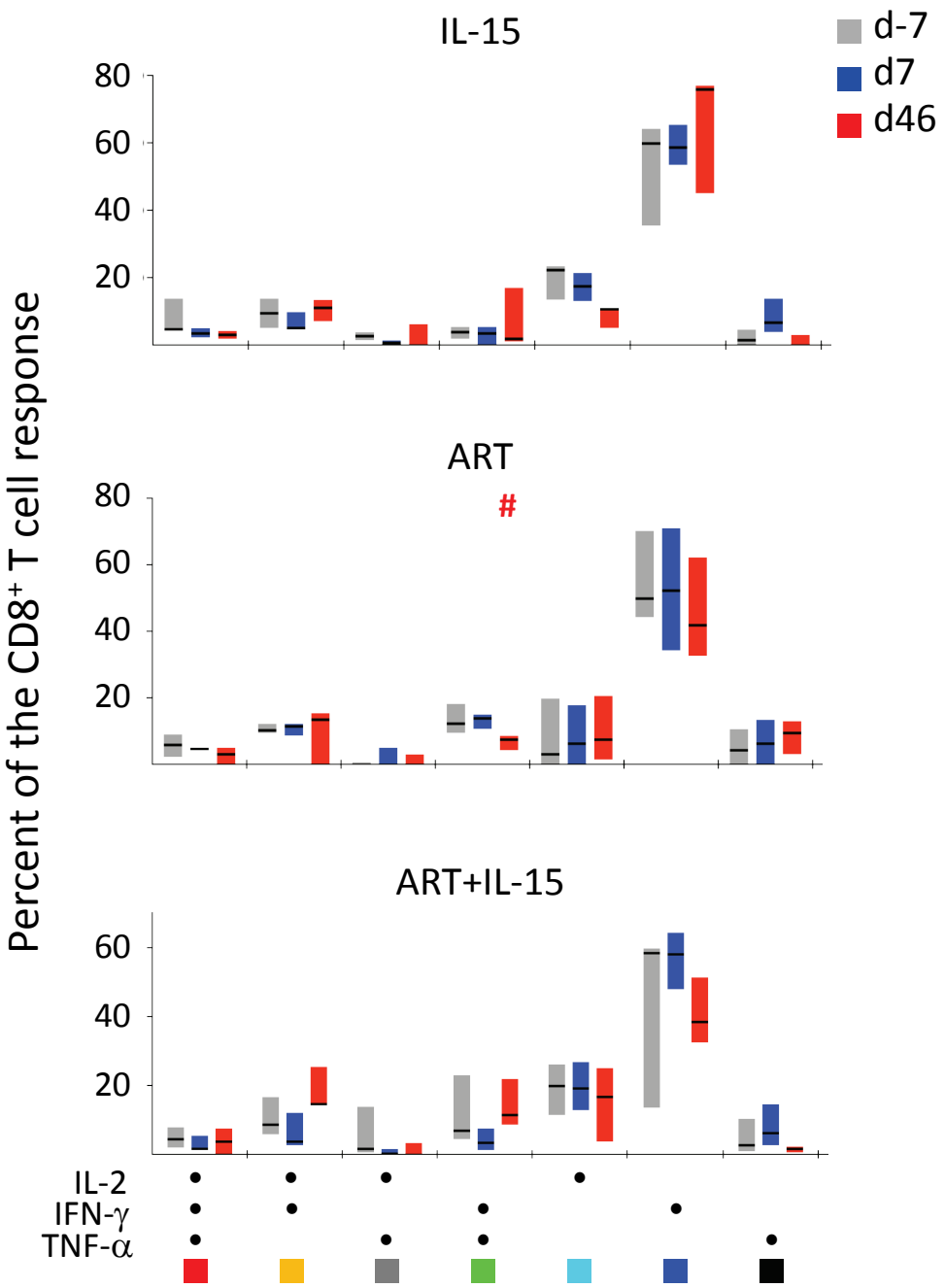
IL-15
ART
#
ART+IL-15
d-7
d7
d46
Percent of the CD8+ T cell response
80
60
40
20
IL-2
IFN-γ
TNF-α

Figure S6

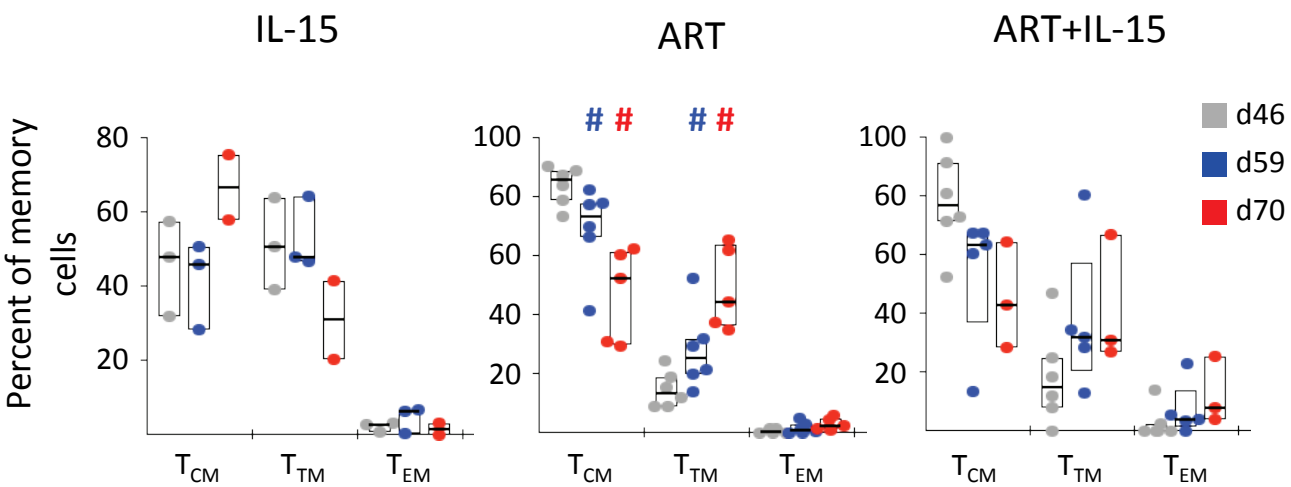
IL-15
ART
ART+IL-15
Percent of memory cells
80
60
40
20
100
60
60
40
20
100
60
60
40
20
# #
# #
d46
d59
d70
T_{CM}
T_{TM}
T_{EM}
T_{CM}
T_{TM}
T_{EM}
T_{CM}
T_{TM}
T_{EM}

Figure S7