Supplementary Materials (SM)

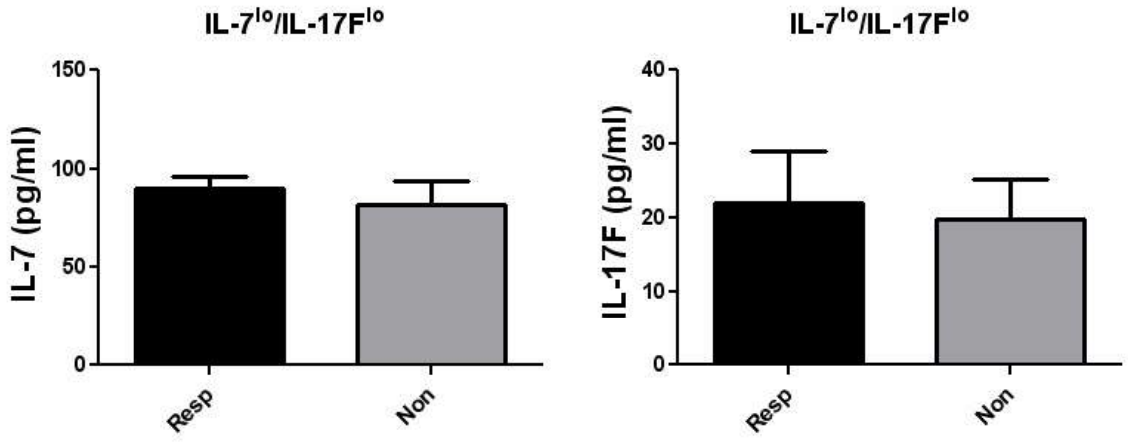
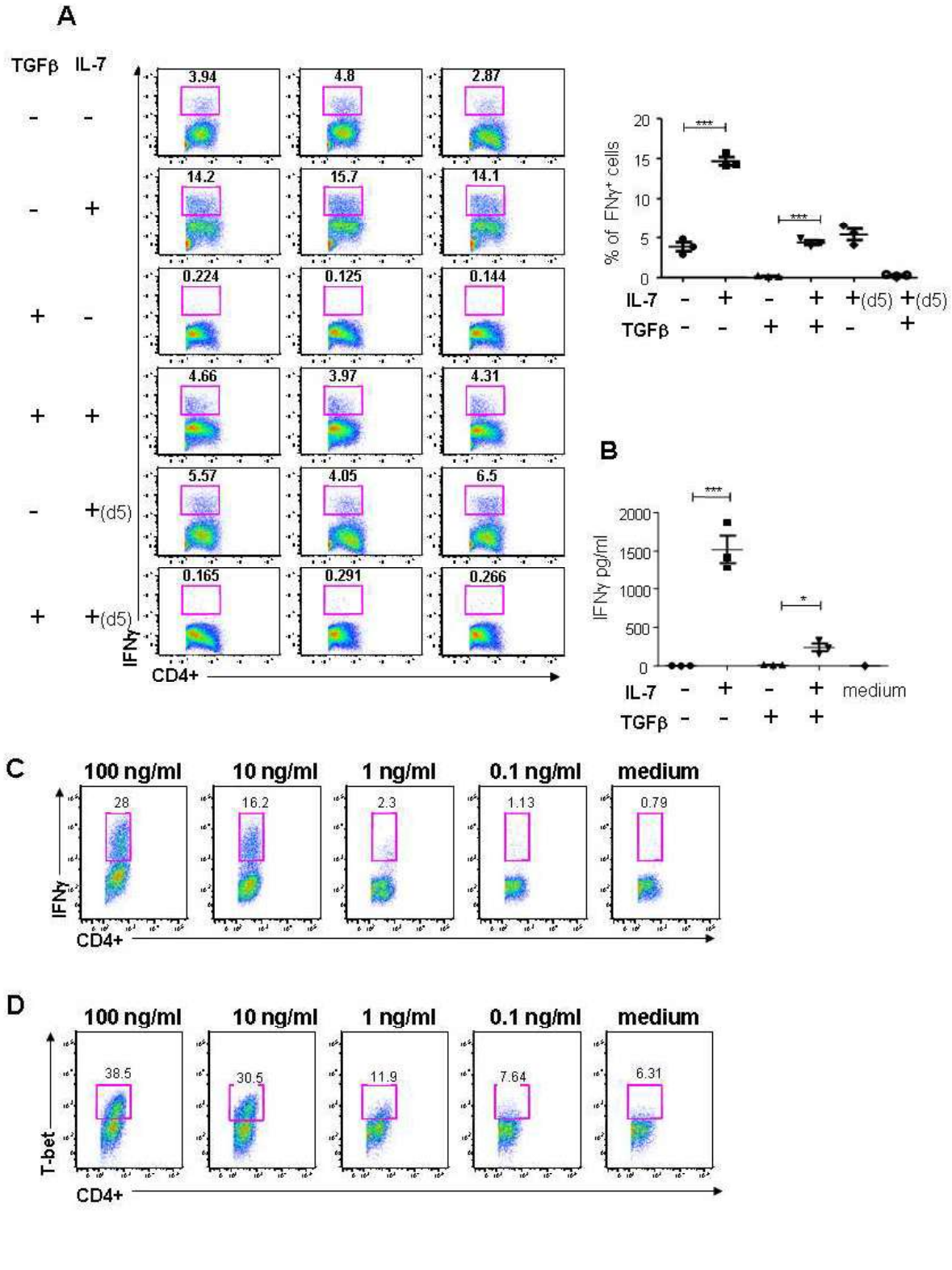


Figure S1. Levels of IL-7 or IL-17F do not differentiate responsiveness in the IL-17F^{lo}/IL-7^{lo} group.


A
TGFβ
IL-7
3.94
4.8
2.87
14.2
15.7
14.1
0.224
0.125
0.144
4.66
3.97
4.31
5.57
4.05
6.5
0.165
0.291
0.266
IFNγ
CD4+
% of FNγ+ cells
IL-7
TGFβ
+(d5)
B
IFNγ pg/ml
medium
C
100 ng/ml
10 ng/ml
1 ng/ml
0.1 ng/ml
medium
28
16.2
2.3
1.13
0.79
D
T-bet
38.5
30.5
11.9
7.64
6.31

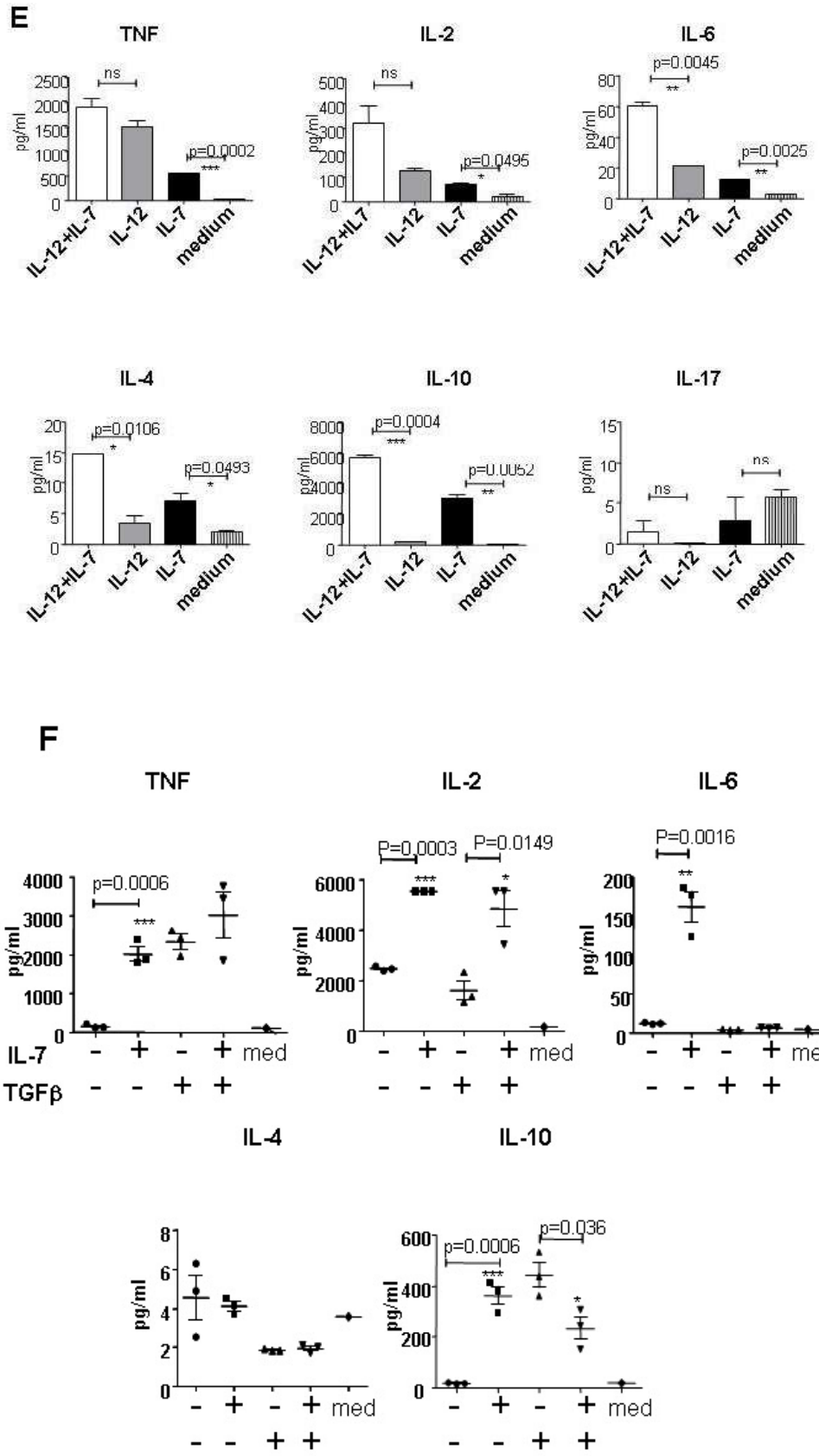

E
TNF
IL-2
IL-6
IL-4
IL-10
IL-17
pg/ml
ns
p=0.0002
p=0.0495
p=0.0045
p=0.0025
p=0.0106
p=0.0493
p=0.0004
p=0.0052
IL-12+IL-7
IL-12
IL-7
medium
F
TNF
IL-2
IL-6
IL-4
IL-10
p=0.0006
P=0.0003
P=0.0149
P=0.0016
p=0.036
IL-7
TGFβ
med

Figure S2. **IL-7 promotes T_H1 cell differentiation from human naïve $CD4^+$ T cells**. (A) Intracellular staining of IFNγ in naive cord blood $CD4^+$ T cells activated with antibodies to CD3 and CD28 and a combination of IL-1β, IL-23 and with or without TGF-β and with or without IL-7, analyzed on day 6. (B) IFNγ production from the cultures as described above by Cytometric bead assay (CBA). Data are representative of at least three independent donors. (C) Dose-dependent effect of IL-7 on (C) IFNγ and (D) T-bet producing cells in $CD4^+$ T cells. Intracellular staining of (C) IFNγ and (D) T-bet in cord blood sorted naive $CD4^+$ T cells activated with 0.1, 1, 10 or 100 ng/ml of hIL-7 in the absence of hIL-12. (E) Cytometric bead assay (CBA) of Th1/Th2/Th17 cytokine production by naive cord blood $CD4^+$ T cells activated with antibodies to CD3 and CD28 and IL-12 in the absence of presence of IL-7 or IL-7 alone. (F). CBA of Th1/Th2 cytokine production by naive cord blood $CD4^+$ T cells activated with antibodies to CD3 and CD28 and a combination of IL-1β, IL-23 and with or without TGF-β and with or without IL-7 as indicated, analyzed on day **5.** The mean percentage ± SEM (n=3 experiments) of cytokine is given and statistics were performed using a student's t test

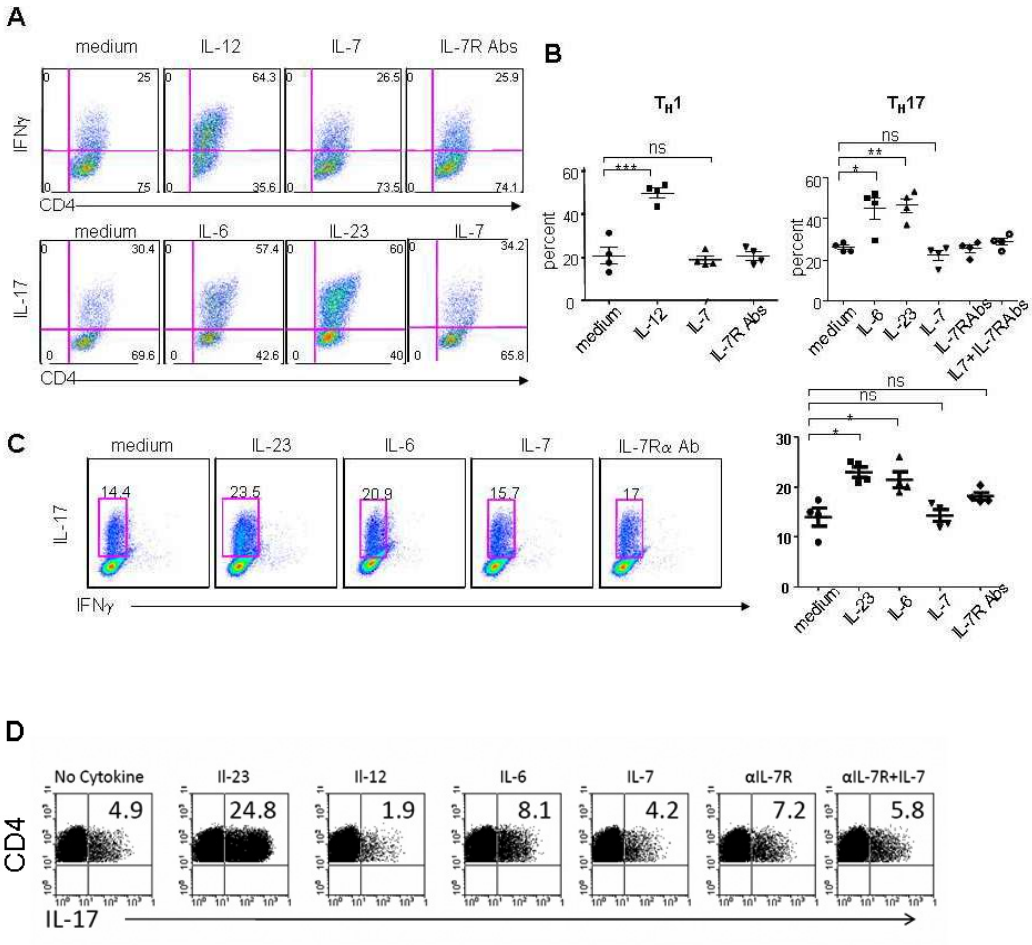
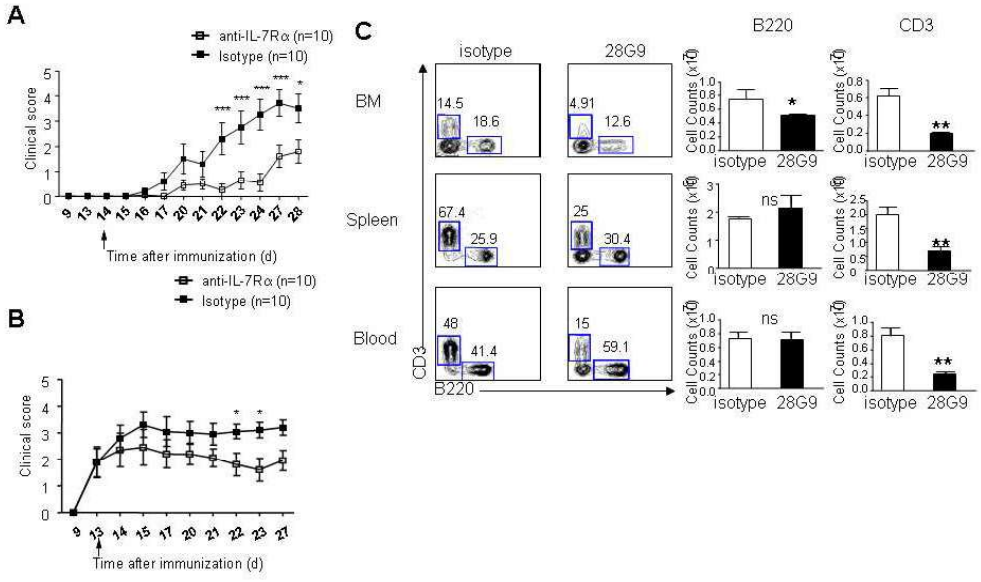


Figure S3. IL-7 is not required for T_H1 or T_H17 cell expansion from immunized 2D2 $CD4^+$ T cells. (**A,B**) Frequency of $CD4^+$ lymphocytes expressing IFNγ and IL-17. $CD4^+$ splenic T cells from immunized 2D2 mice were activated in the presence of MOG35-55 plus the respective T_H1 (upper) or T_H17 (bottom) polarizing conditions. After T_H1 or T_H17 differentiation, cells were rested for 48 hrs followed by re-stimulation with MOG35-55 in the presence or absence of IL-12, IL-7, IL-6, IL-23 or IL-7Rα-specific antibody as indicated during expansion period. (**B**) Quantification of IFNγ and IL-17 produced $CD4^+$ T cells from immunized 2D2 mice in the presence or absence of IL-7 during expansion. (C) Purified $CD4^+$ T cells from MOG-immunized 2D2 mice were cultured with the

indicated cytokines for 72 hr and analyzed for the percentage of IL-17 producing cells (right). Quantification of IL-17 produced $CD4^+$ T cells in the presence or absence of IL-7 during expansion (left). (D) Frequency of $CD4^+$ lymphocytes expressing IL-17. $CD4^+$ splenic T cells from immunized 2D2 mice were activated in the presence of MOG35-55 plus T_H17 polarizing conditions. After T_H17 differentiation, cells were rested for two days followed by re-stimulation with MOG35-55 in the presence or absence of IL-12, IL-7, IL-6, IL-23 or IL-7Rα-specific antibody as indicated during expansion period. Data are representative of three experiments. The mean percentage ± SEM of cytokine-positive cells is given. Each experiment is comprised of four to five mice per group. *p<0.05, **p<0.01, **p<0.001.



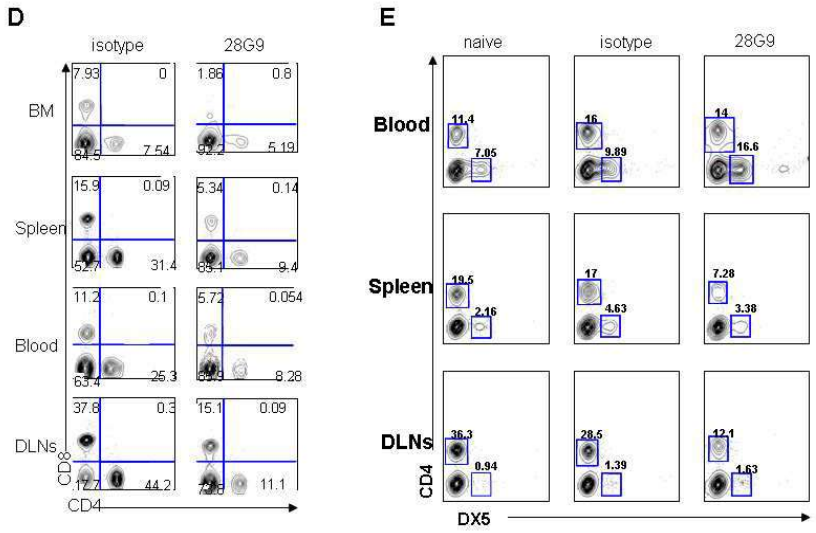


Figure S4. Antibody specific to IL-7Rα is efficacious in EAE either before or after symptom onset. (**A**) Clinical scores of MOG-induced EAE mice treated with IL-7Rα-specific antibody (3 mg/kg, anti-I IL-7Rα) or isotype control once weekly started from day 14 before symptom onset as indicated by arrow. (**B**) Clinical score of PLP-induced EAE in SJL mice treated with 10 mg/kg of anti-IL7Rα from day 13 after symptom onset in PLP-induced twice weekly after immunization as indicated by arrow. *P<0.05, ***P<0.001. Error bars represented mean ± SEM. Statistics were performed using one way ANOVA. (C-E) IL-7Rα-specific antibody reduced $CD4^+$ and $CD8^+$ T cells but preserved B and NK cells. (**C-D**) T and B cells from mice treated with IL-7R antibody by FACS staining and total cell counts. Cells were isolated from bone marrow (BM), spleen, blood or draining lymph nodes (DLN) of EAE mice treated with isotype control or 28G9 at day 21 after immunization. FACS analysis was performed in total cells using (C) CD3 and B220 antibodies or (D) CD4 and CD8 antibodies. **(C)** Total cell counts of T and B cells from 3 independent experiments with n =3 mice for each experiment. *P<0.01.

(D) Percentages of $CD4^+$ and $CD8^+$ in bone marrow (BM), spleen, blood and draining lymph nodes (DLNs). **(E)** NK cells from mice treated with IL-7R antibody by FACS staining Cells were isolated from spleen, blood or draining lymph nodes (DLN) of EAE mice treated with isotype control or 28G9 at day 21 after immunization. FACS analysis was performed in total cells using CD4 and DX5 antibodies.

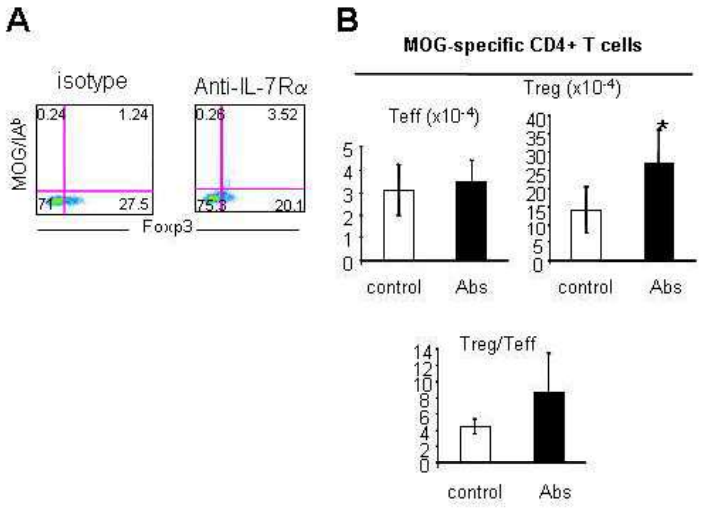


Figure S5. IL-7Rα **antibody treatment does not affect T_{reg} numbers from lymph nodes.** (**A**) Representative FACS showing MOG-specific T cells following antibody or control antibody treatments at day 7 post-treatment as determined by FACS. $CD4^+$ T cells were staining with MOG/IAb or control tetramers and Foxp3. Representative MOG-specific T^{eff} (MOG/IAb-tetramer$^+$CD4$^+$FoxP3$^-$) and T_{reg} (MOG/IAb-tetramer$^+$CD4$^+$FoxP3$^+$) frequencies are shown within the indicated $CD4^+$ T cell quadrants. Numbers indicate percentages of $CD4^+$ T cells within each quadrant. (**B**) Bar graphs indicate numbers (mean ± SEM, $n \geq 3$ experiments) of T_{eff} and T_{regs}, and the ratio of T_{eff}/T_{regs} following antibody (black bars) or control antibody (white bars) treatments; $^*P < 0.05$.

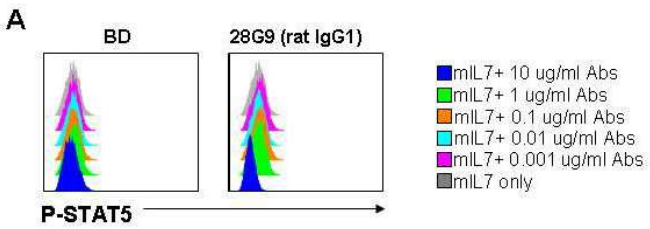


Figure S6. Dose response of p-STAT5 by 28G9 or SB/14. Different concentration of antibody was added as indicated in the presence of IL-7 (1ng/ml). Splenocyte from wild type mice were subjected to the stimulation of 1 ng of mouse IL-7 protein in the presence or absence of different anti-IL7Rα antibodies. Cells were simultaneously stained with CD11b-FITC, TCRβ-PE, B220-Cy5.5PerCP, and pStat5 (Y694).

Analyte	p-value t-test
PDGFBB	0.015
IL-7	0.028
TGFβ	0.063
IFNβ	0.080
IL-13	0.084
IL-7F	0.086
EOTAXIN	0.086
IL-1α	0.089
MCP-3	0.098
LIF	0.146

Table S1. *P* values for the top 10 analytes for prediction of outcome and responder versus nonresponder to IFN-β. Measured in a sample of 26 patients with relapsing remitting MS. These p-values are from a two-tailed Student's t-test. Samples were analyzed as described in methods with the Luminex cytometer on the ProCarta50 plexmulti-analyte array.

Analyte	*P* value t-test
PDGFBB	0.015
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IL-1α	0.089
MCP-3	0.098
LIF	0.146

Table S2. The effect of different cytokines on mouse T_H1 and T_H17 cell expansion under T_H17-polarizing conditions.

Primary Stim ↓ TH17

	media	IL-23	IL-12	IL-6	IL-7	αIL-7R	αIL-7R +IL-7
%IL-17$^+$	24.8	55.6	6.6	37.6	20.5	29.5	24.5
%IFNγ$^+$	2.7	1.3	36.6	1.7	3.0	3.2	3.2

Table S3. The binding interaction between mouse FcγR and 28G9 or SB/14 was evaluated with a Biacore biosensor (GE).

	FcγRI	FcγRIIb	FcγRIII
SB/14 rIgG2a	-	-	-
28G9 rIgG1	++	++	+

+ = binding

- = no binding