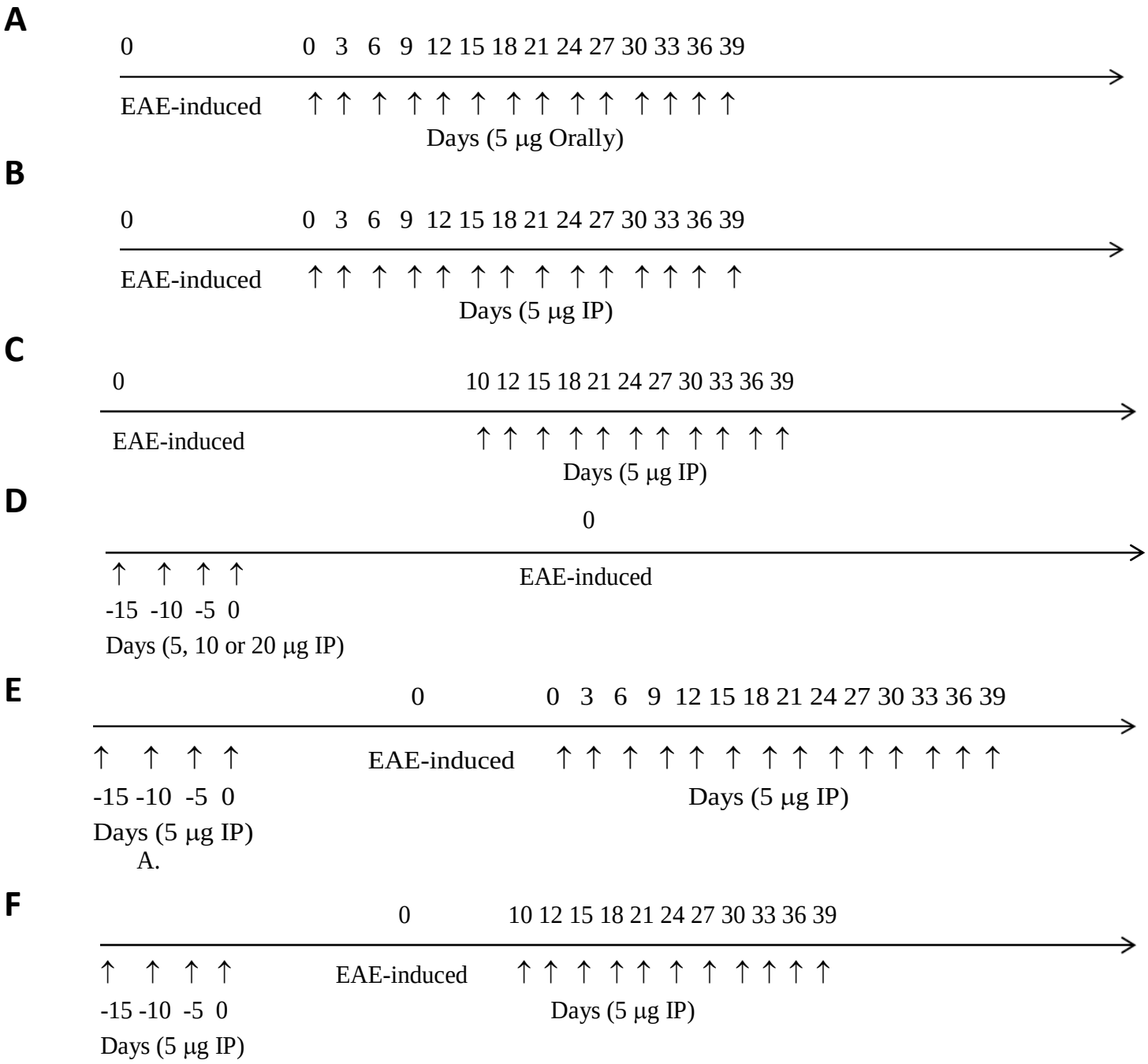
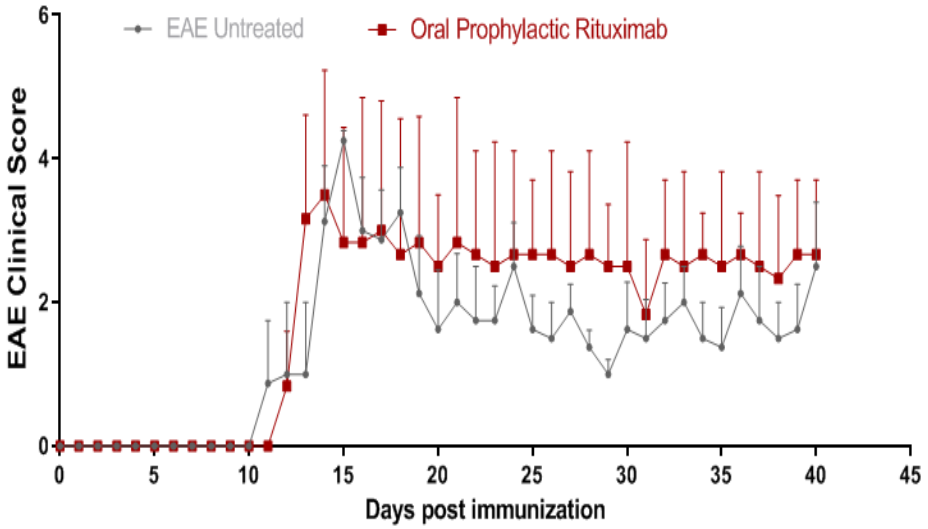
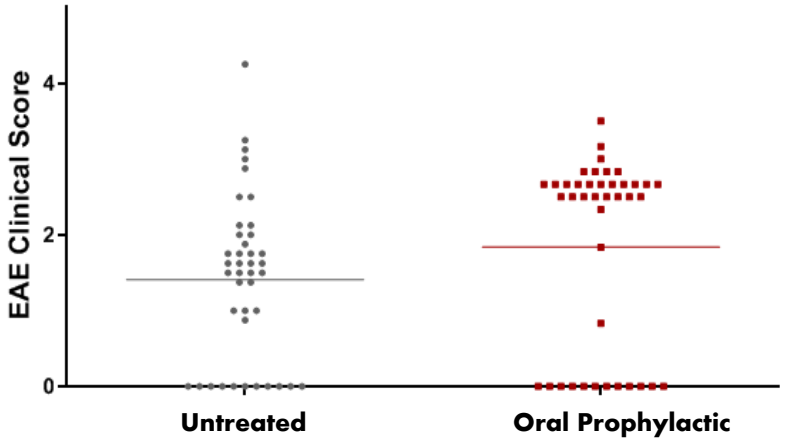

A
0
0 3 6 9 12 15 18 21 24 27 30 33 36 39
EAE-induced
Days (5 μg Orally)
B
0
0 3 6 9 12 15 18 21 24 27 30 33 36 39
EAE-induced
Days (5 μg IP)
C
0
10 12 15 18 21 24 27 30 33 36 39
EAE-induced
Days (5 μg IP)
D
0
EAE-induced
-15 -10 -5 0
Days (5, 10 or 20 μg IP)
E
0
0 3 6 9 12 15 18 21 24 27 30 33 36 39
EAE-induced
-15 -10 -5 0
Days (5 μg IP)
Days (5 μg IP)
A.
F
0
10 12 15 18 21 24 27 30 33 36 39
EAE-induced
-15 -10 -5 0
Days (5 μg IP)
Days (5 μg IP)

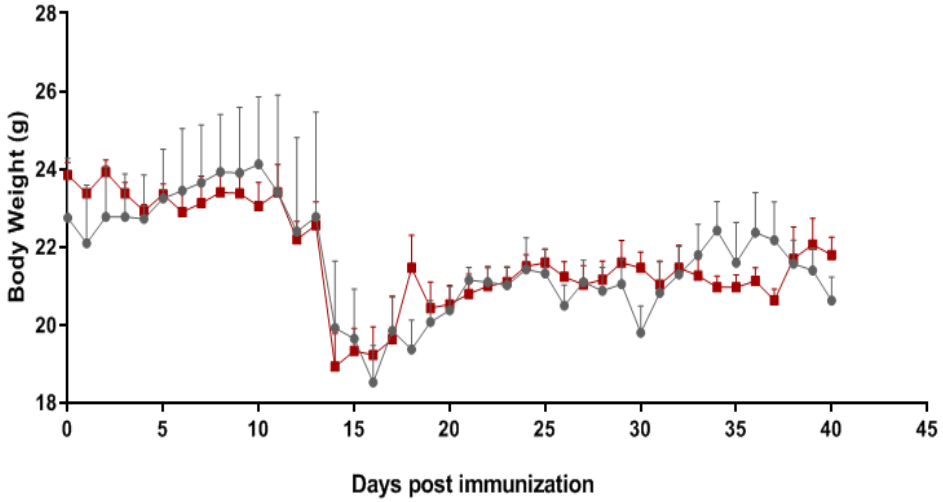
Supplementary Figure 1. Various treatment regiments of EAE mice. (A) oral prophylactic treatment. (B) Intraperitoneal (IP) prophylactic treatment. (C) IP therapeutic treatment. (D) Prevention treatment. (E) Prevention plus prophylactic treatment. (F) Prevention plus therapeutic treatment. 0 indicates the time of inducing the disease. Arrows indicate injection time of RTX

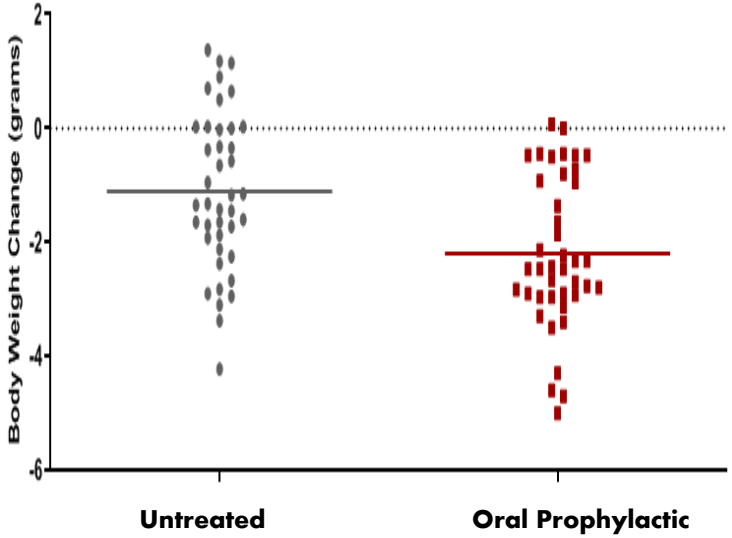
A


EAE Untreated
Oral Prophylactic Rituximab
EAE Clinical Score
Days post immunization

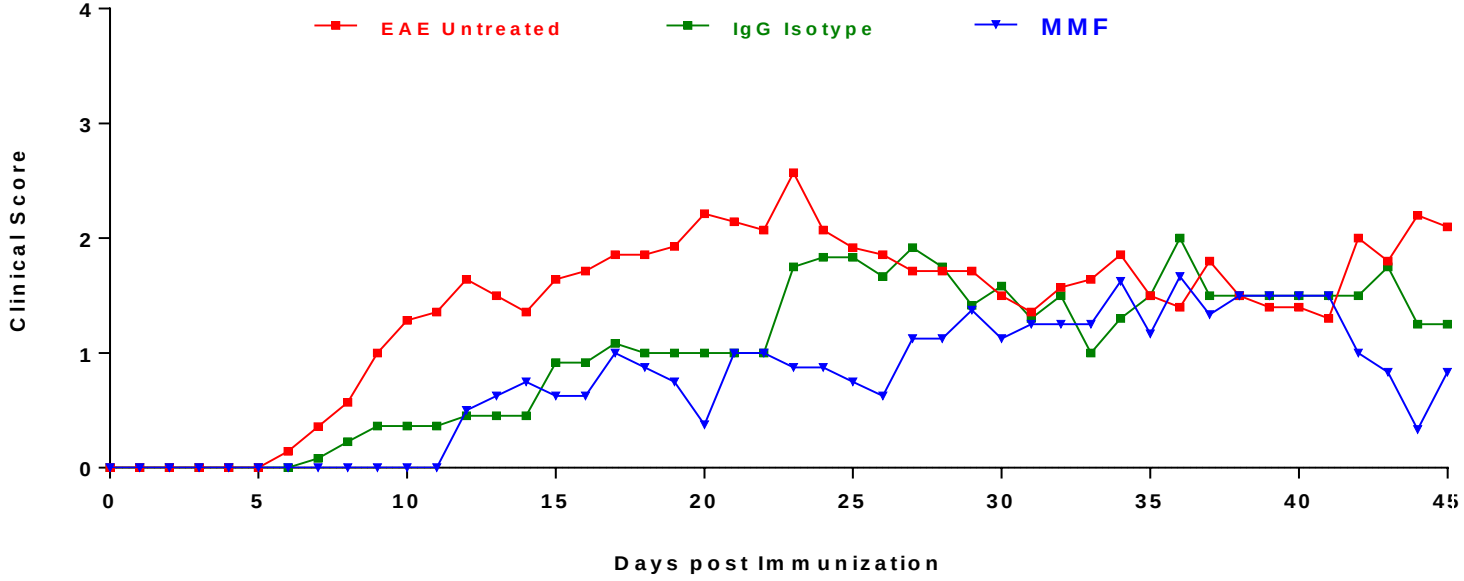

EAE Clinical Score
Untreated
Oral Prophylactic

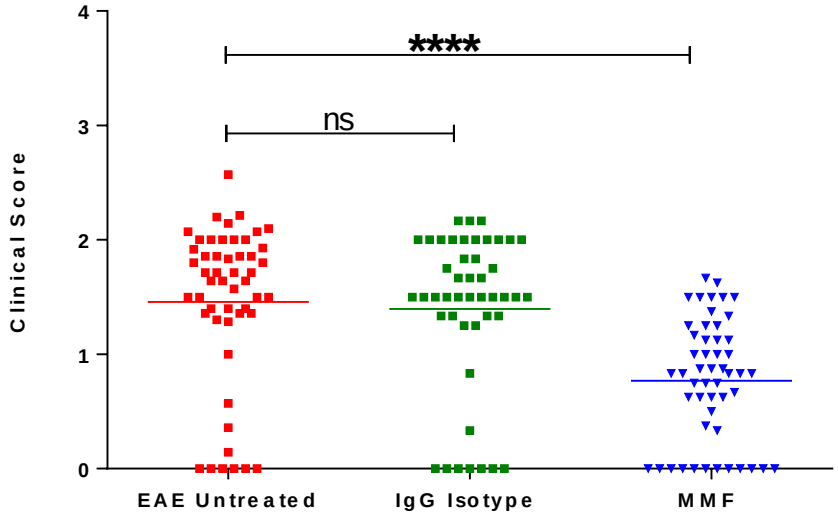
B


Body Weight (g)
Days post immunization

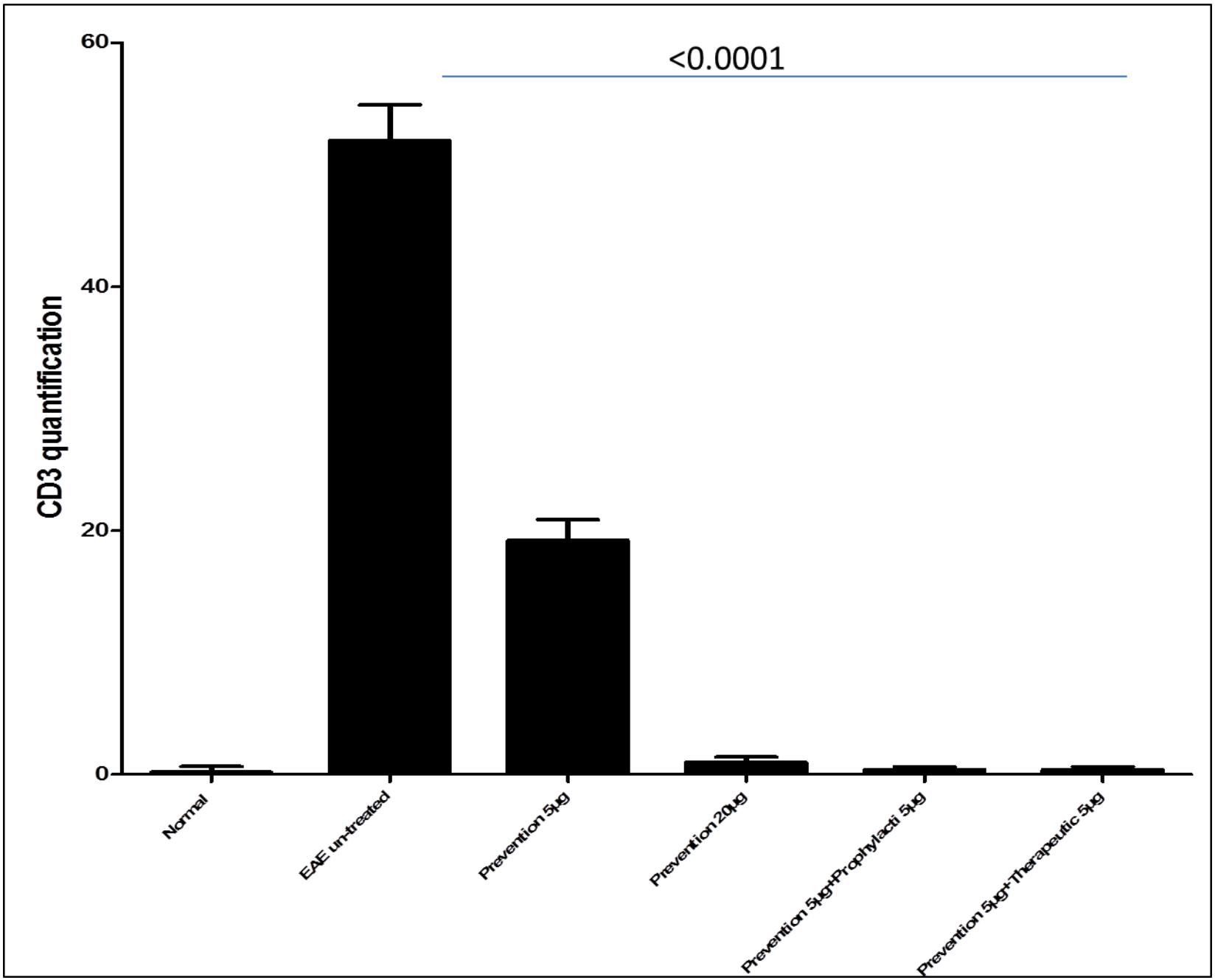

Body Weight Change (grams)
Untreated
Oral Prophylactic

Supplementary Figure 2. Oral prophylactic treatment with RTX does not affect the EAE clinical score. (A) Female SJL mice were induced to develop EAE (grey line). These mice were dosed orally with 5 g/mouse RTX at the start of disease induction (day 0) and continued every three days until the termination of the experiment (red line). (B) Body weight of animals measured every day since the induction of the disease.


EAE Untreated
IgG Isotype
MMF
Clinical Score
Days post Immunization
0
1
2
3
4
0
5
10
15
20
25
30
35
40
45


****
ns
Clinical Score
0
1
2
3
4
EAE Untreated
IgG Isotype
MMF

Supplementary Figure 3. Monomethyl fumarate (MMF) but not IgG ameliorates EAE clinical score. Comparison of the EAE clinical score among untreated mice (red line), mice treated with IgG (green line) or those fed with MMF (blue lines) for 40 days (upper panel). Results were evaluated by area under curve analysis (lower panel). The significant values were calculated using one way ANOVA followed by Sidak's multiple comparison test during the entire period of the experiments. $P<0.0001$. ns=not significant.


60
40
20
0
CD3 quantification
<0.0001
Normal
EAE un-treated
Prevention 5µg
Prevention 20µg
Prevention 5µg+Prophylacti 5µg
Prevention 5µg+Therapeutic 5µg

Supplementary Figure 4. Quantitation of T cells infiltrating the PVS of normal mice, EAE untreated mice or EAE mice treated with 5 g or 20 g RTX. Combination of 5 g/mouse RTX administered preventively with prevention or therapeutic protocols showed ablation of T cells.