Table S1. Clinical score guide for the EAE mice.

Score	Signs	Comment
0	No clinical signs	Normal mouse
1	Partially loss of tail tonus	Normal gait. Half of the tail or more has lost tonus. Absence of curling at the tip of the tail when mouse is handled.
2	Paralyzed tail	Normal gait. Complete flaccidity of the tail.
3	Moderate hind limb paraparesis	Hind limb weakness: waddling gait; the posture of the hind legs when the mouse is placed at the edge of the hind legs when the mouse is placed at the edge of the cage is not adequate and it falls easily
4	Severe hind limb weakness: Marked difficulty to right	Severe hind limb paraparesis after placing on back
5	Inability to right within 5s after placing on back.	Partial hind limb paralysis, dragging one hind limb.
6	Hind limb paralysis	Dragging both hind limbs
7	Hind limb paralysis; one forelimb paralysis	It has some mobility in one of the forelimbs
8	Hind limbs paralyzed, both forelimbs paralyzed	Mouse cannot move; both forelimbs do not respond to toe pinch.
9	Moribund	No movement
10	Death	

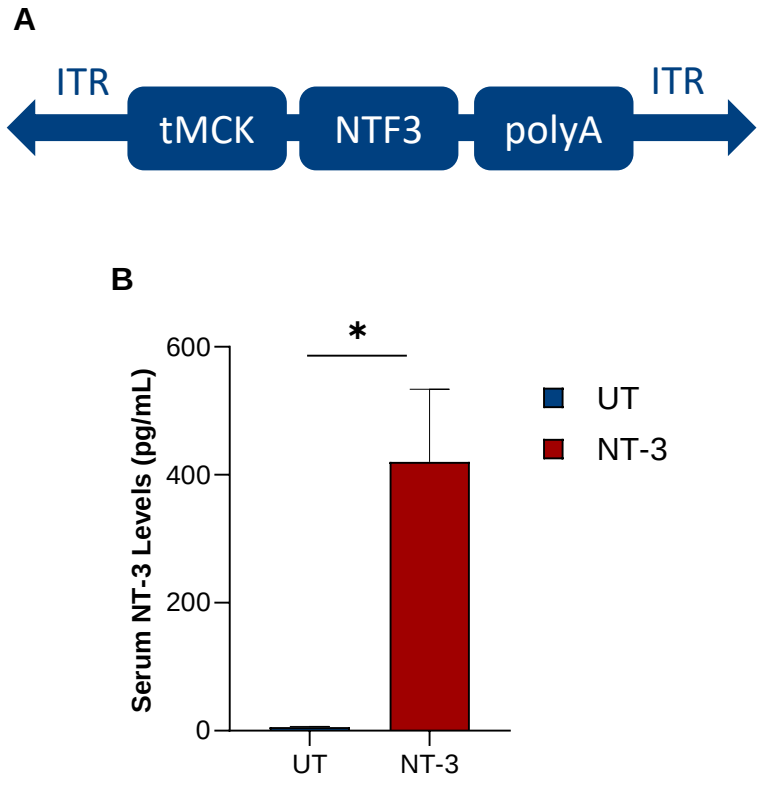

Figure S1. Schematic diagram of scAAV1.tMCK.NT-3 vector and NT-3 serum levels. A NT-3 is expressed under the control of a tMCK promoter in the scAAV vector backbone. The diagram of the cassette shows a tMCK enhancer/ promoter region (714 bp), the full-length cDNA of NTF3 (774 bp) and the SV40 polyA tail (211 bp). **B** AAV1.tMCK.NT-3 gene therapy induces detectable levels of NT-3 in serum. EAE mice were injected with a total of 1 x 10^{11} vg of AAV1.tMCK.NT-3 into right gastrocnemius muscle. Blood samples were obtained from mice at 7 weeks post-injection, and NT-3 serum levels were determined by enzyme-linked immunosorbent assay. Data presents Mean ± SEM (Female cohort: *n*=3 for untreated, and *n*=4 for NT-3 treated cohort; Male cohort: *n*=3 for both treated and untreated). *p<0.05

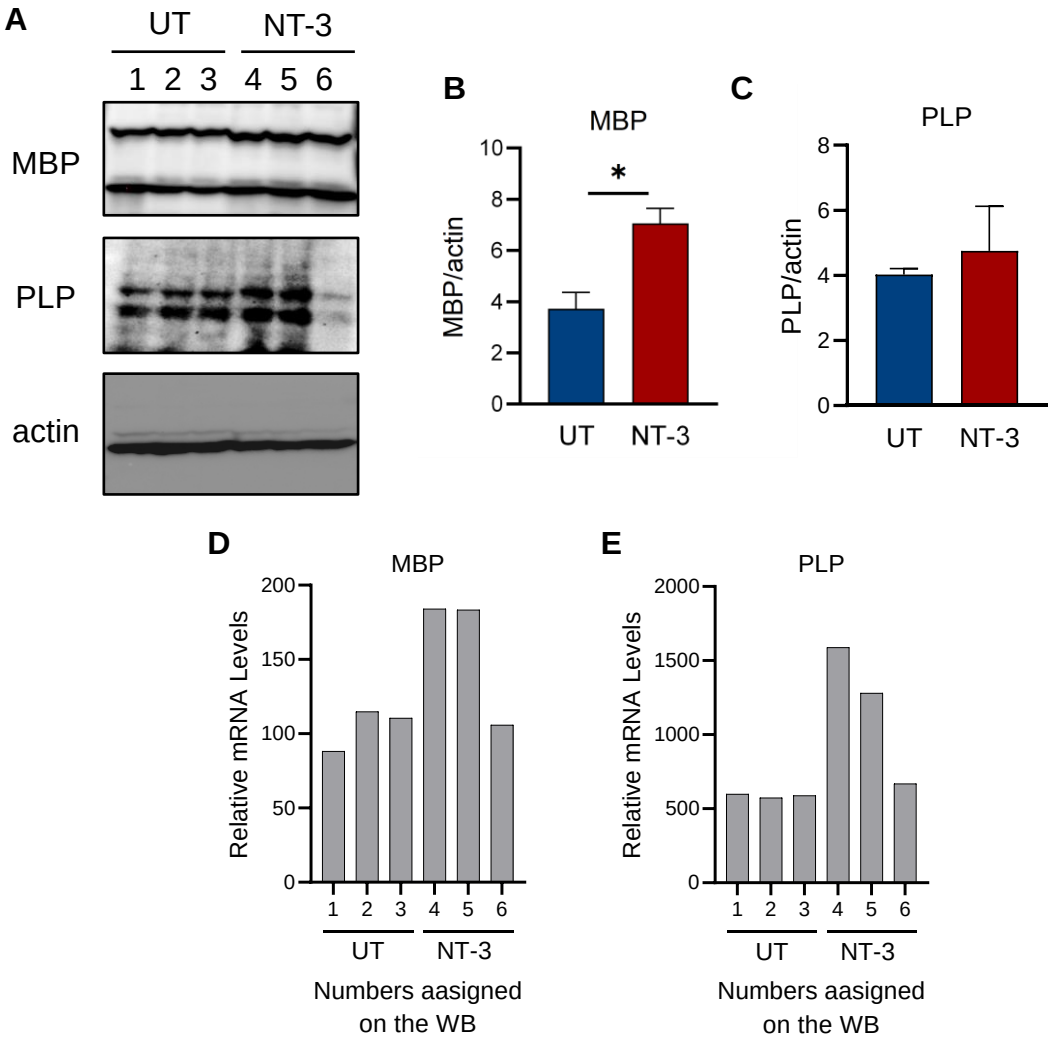

Figure S2. AAV1.NT-3 treatment increased the protein level of MBP and PLP in the EAE mouse. (A) WB shows the expression of MBP and PLP protein extracted from spinal cord of UT and AAV1.NT-3 treated EAE mouse (*n*=3; males) with **(B, C)** quantitative analysis of band intensity normalized to actin. Relative mRNA expression levels of the MBP **(D)** and PLP **(E)** genes were given individually for each mice, in the order shown in WB from panel A. Data are represented as ± SEM (**p*<0.05).

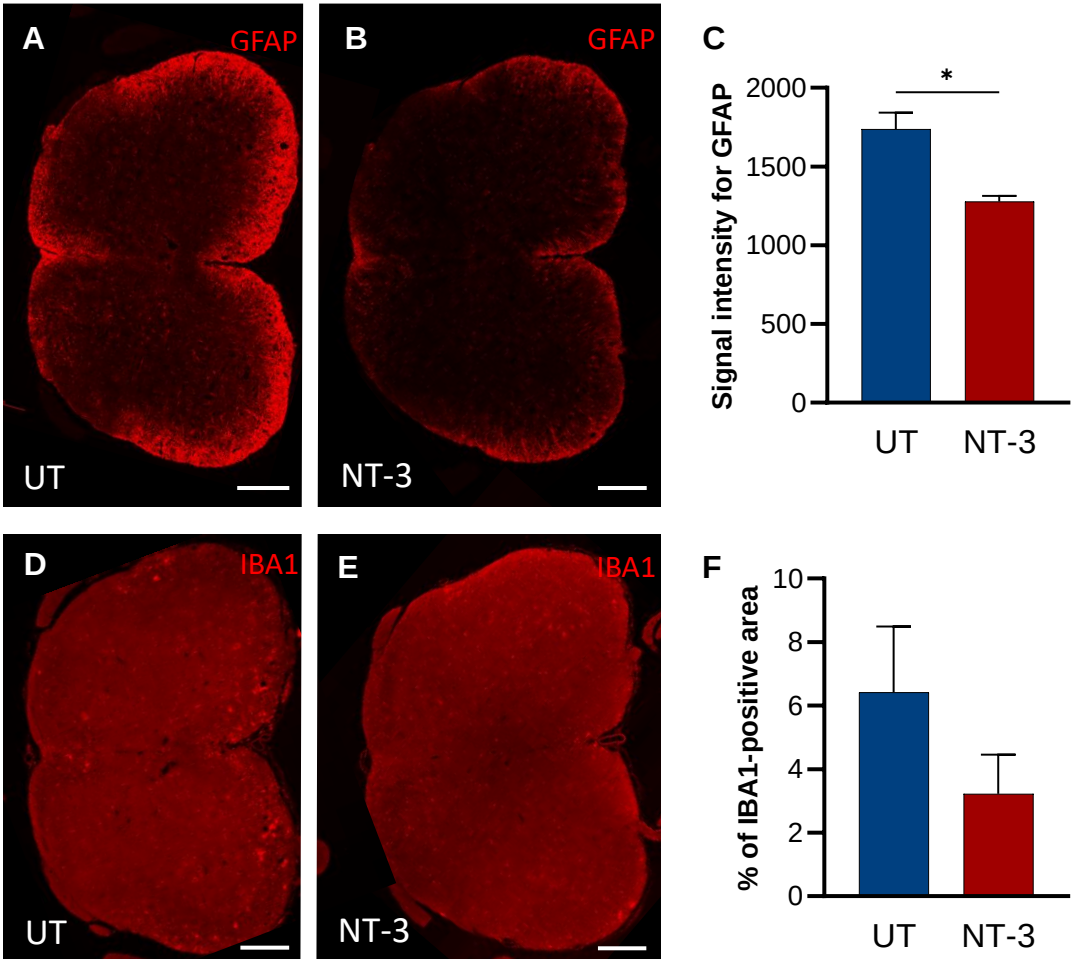

Figure S3. AAV1.NT-3 treatment in EAE mice reduced astrogliosis and microgliosis in the spinal cord. Representative GFAP immunofluorescent staining of lumbar spinal cord segments from UT (A) and NT-3 treated (B) showing decreased astrogliosis. Bar graph shows the signal intensity was significantly decreased (C, n=3 for each cohort, p=0.0203). IBA1 staining as microgliosis marker is shown from UT (D), and NT-3 treated spinal cord (E). Percentage of IBA1-positive areas in treated mice was decreased (F) without a change in staining intensity (not shown) . Scale bar=200 µm.

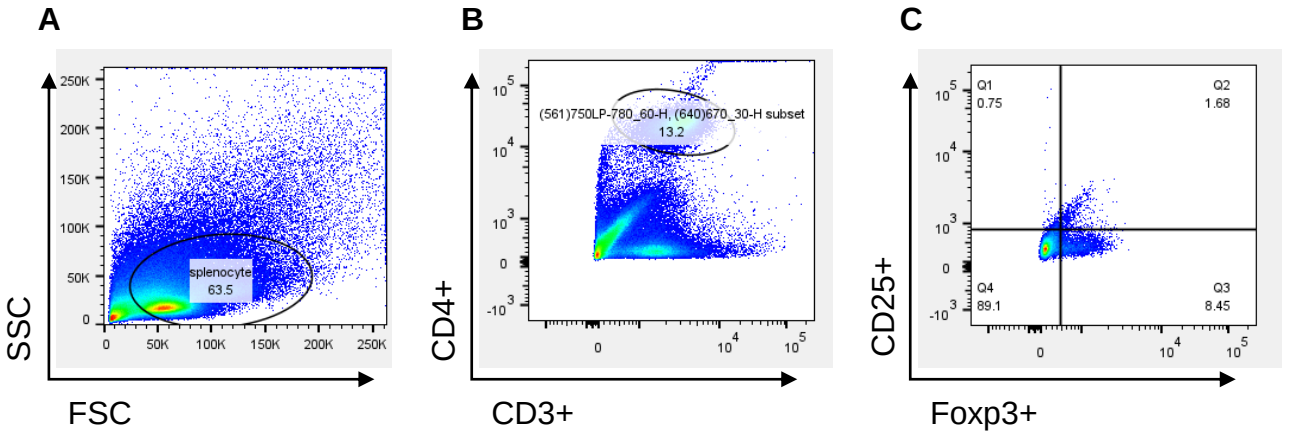

Figure S4. Example of flow cytometry analysis scheme is shown in this figure. 100,000 to 200,000 cells were analyzed in the samples. Live splenocyte/lymphocyte were gated using SSC and FSC scale. CD3 and CD4 positive cells were gated next. CD3+CD4+ cells were then analyzed for Foxp3 and CD25 signals.

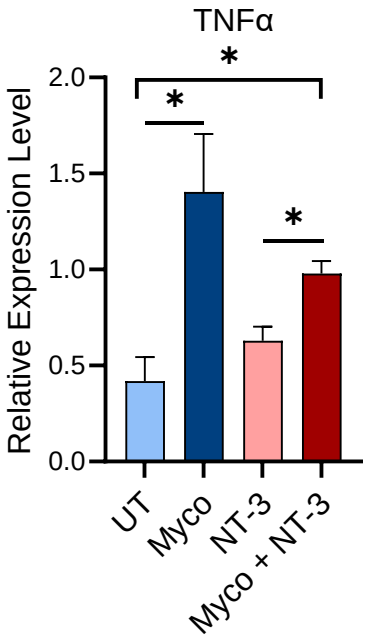

Figure S5. Immunol response of DCs from WT mouse. Dendritic cells were isolated from bone marrow of WT b/6 mice. DCs were challenged with mycobacterium with or without the treatment of recombinant NT-3 for 24 hours. The TNFα level was measured by qPCR. Data represents Mean ± SEM. *p<0.05