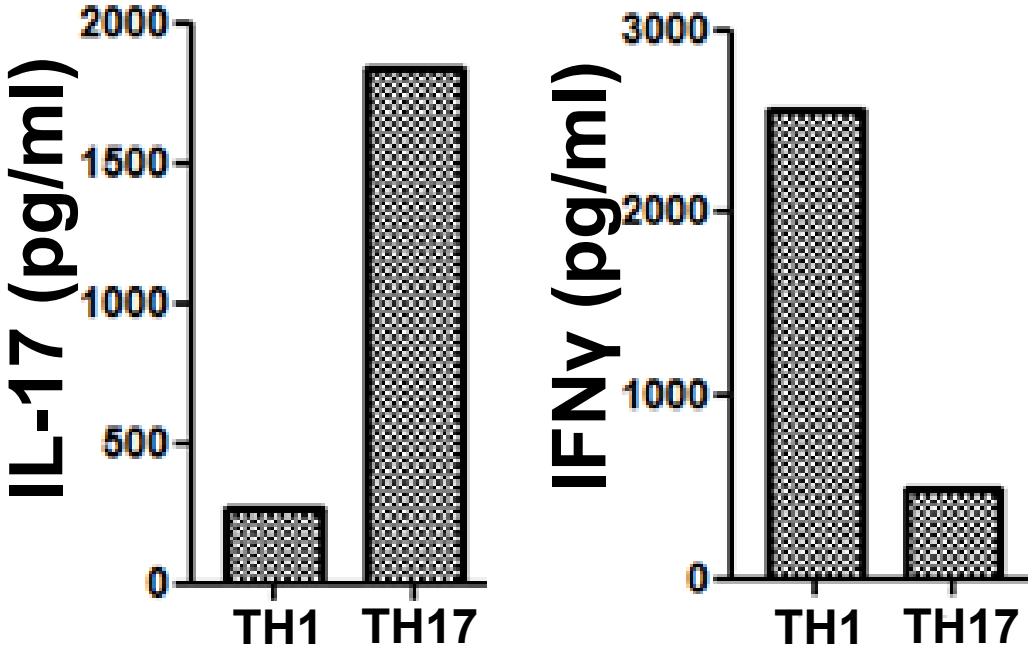
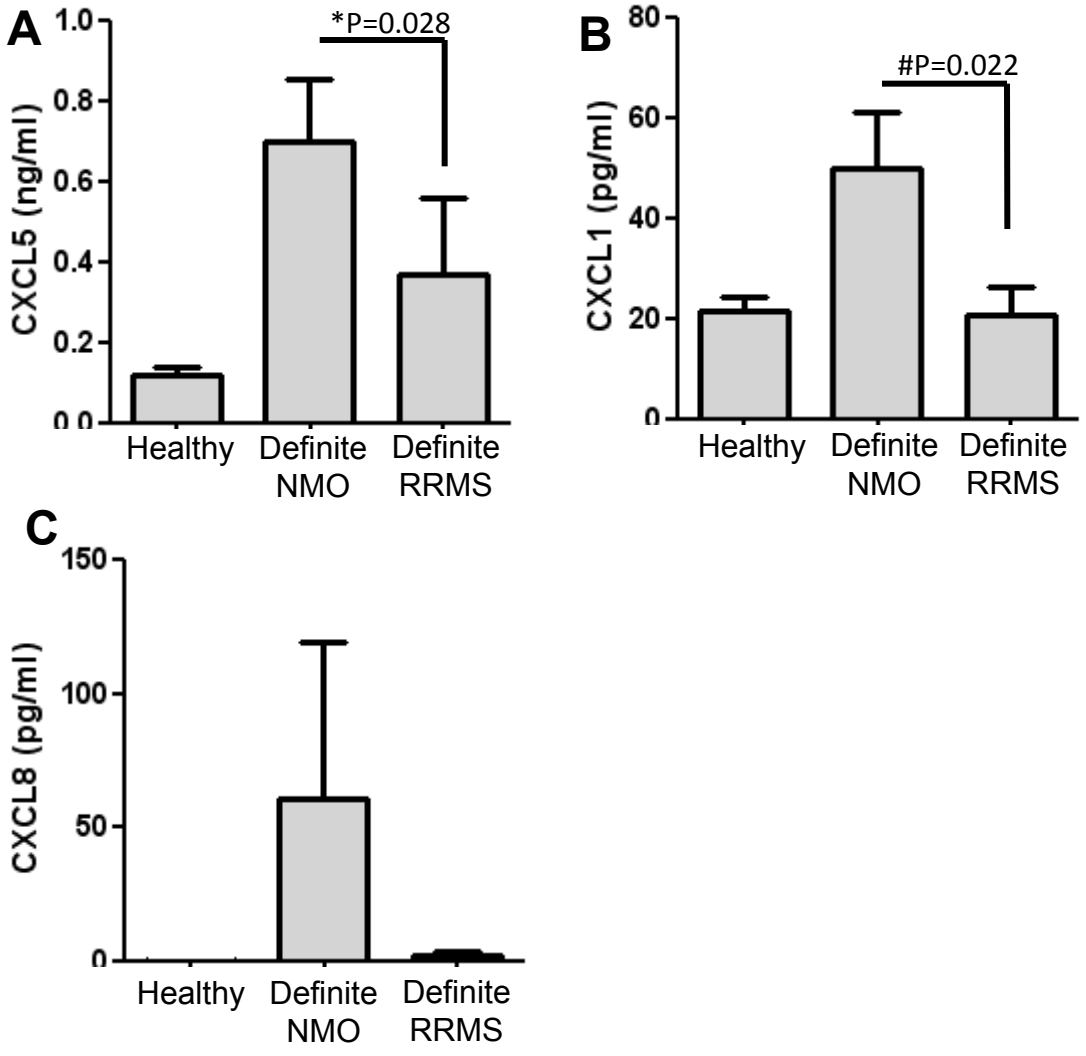


Supplementary Figure 1.
Characterization of TH1 and TH17 cultures prior to transfer. Spleens and Lymph nodes were harvested from mice 10 days after MOG_{35-55}peptide immunization and stimulated with MOG and IL-12 (TH1) or IL-23 (TH17) cells for 3 days. IL-17 and IFNγ production was measured by ELISA.

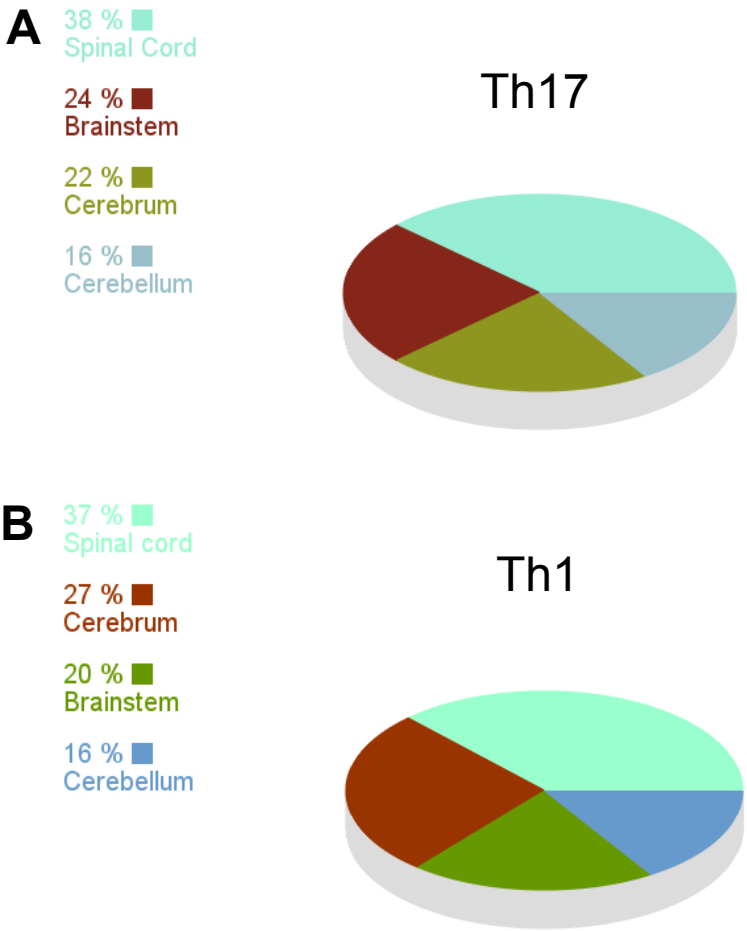
Supplementary Table. Clinical and demographic features of RRMS serum specimens.

Patient	Sex	Age at diagnosis [years]	Diagnosis	Disease duration [years]	Treatment*	# of relapses (2 years prior)	EDSS
1	F	36	RRMS	1.7	None	4	2
2	F	22	RRMS	4.7	Methylprednisolone	5	5.5
3	F	31	RRMS	5.2	Data unavailable	1	2
4	F	37	RRMS	5.3	Data unavailable	3	4
5	F	26	RRMS	3.3	Methylprednisolone	Data unavailable	2
6	F	27	RRMS	5.2	Data unavailable	2	3.5
7	M	23	RRMS	18.7	None	1	1
8	F	38	RRMS	1.6	None	Data unavailable	2
9	M	47	RRMS	2.8	Methylprednisolone	1	2.5
10	F	27	RRMS	2.9	None	2	1.5

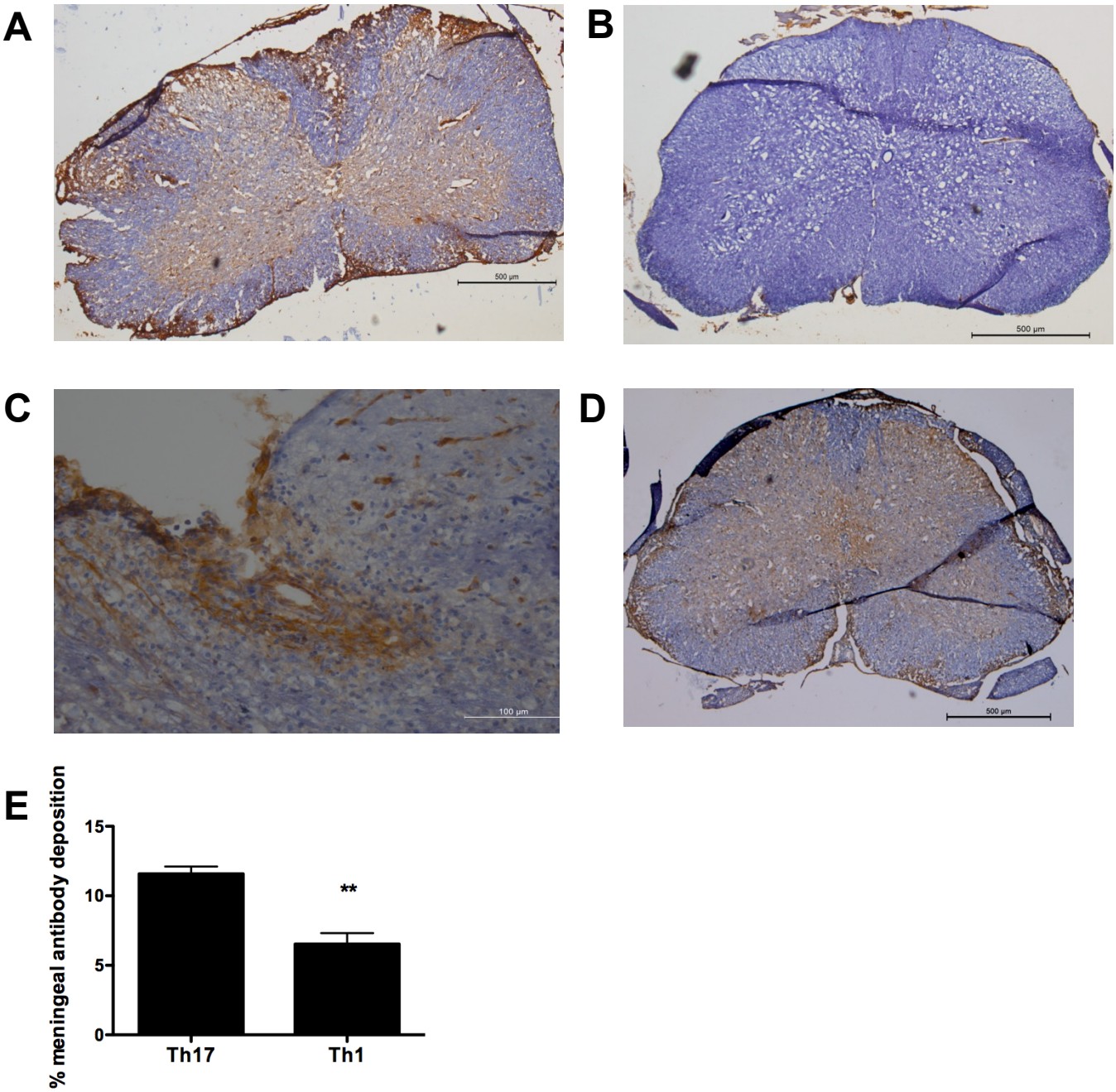
*All Samples were obtained from patients prior to the initiation of disease modifying therapy.



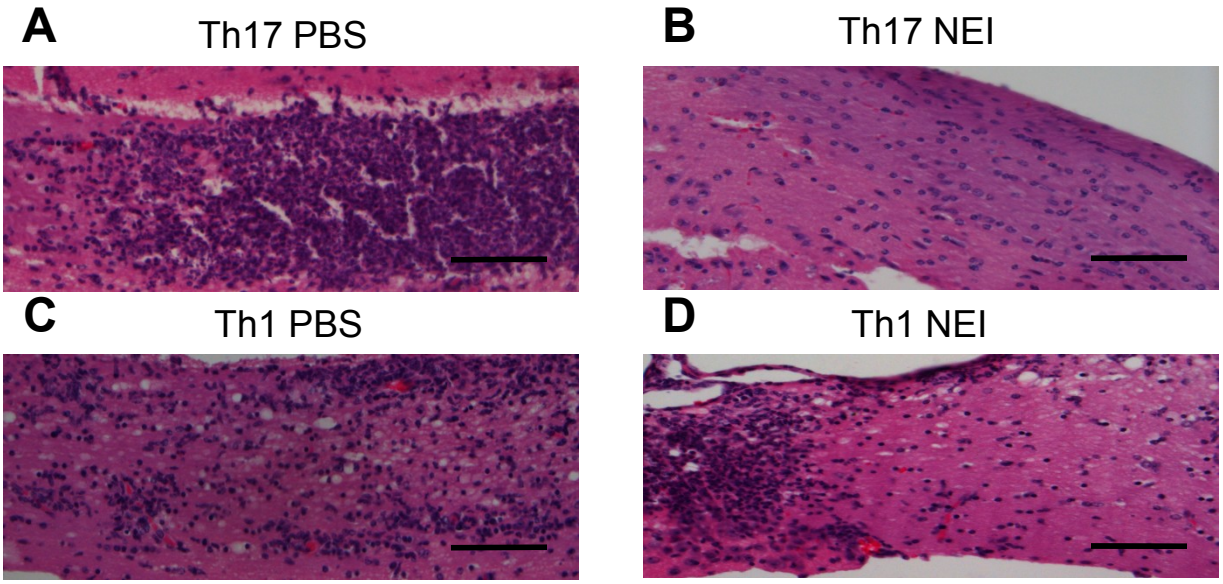
Supplementary Figure 2.
Definitive NMO serum has elevated levels of granulocyte chemokines compared to definitive RRMS. Serum Levels of A) CXCL5, B) CXCL1 and C) CXCL8 were measured by Luminex multiplex assay. Statistical significance was determined by using a paramentric T-test (#) or a non-parametric test (*).



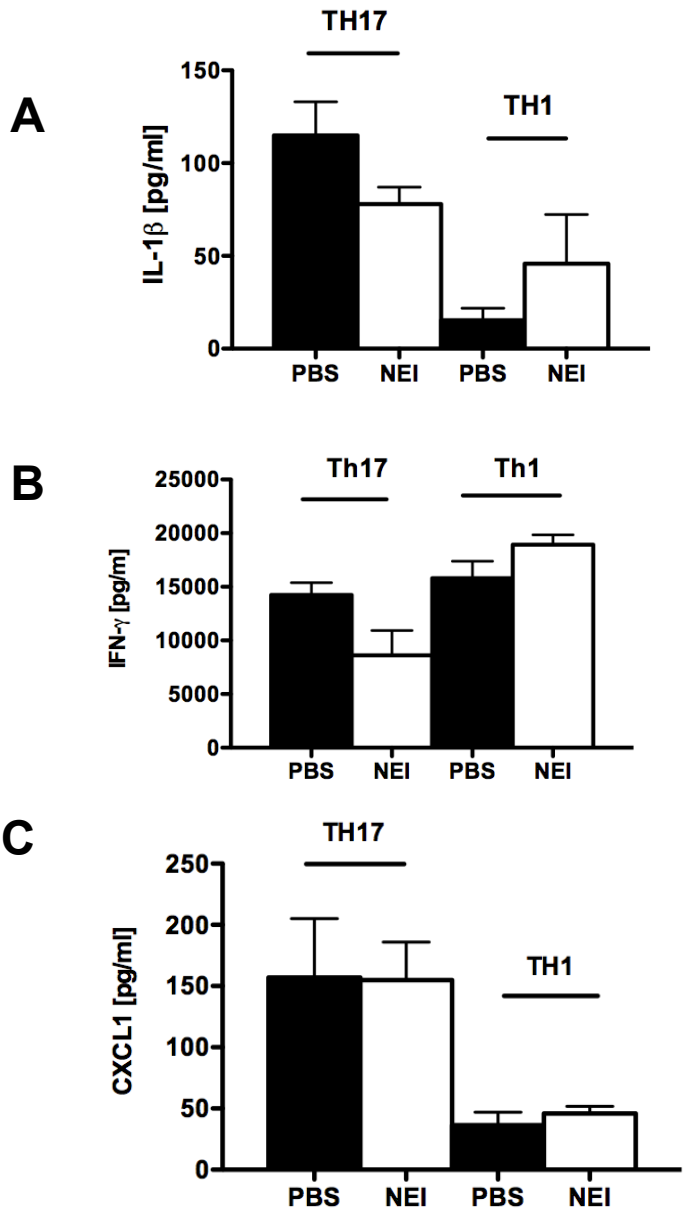
Supplementary Figure 3:
Lesions are equally distributed in CNS of animal with Th17 (**A**) and Th1 (**B**) EAE. Pie charts show percentage of lesions in spinal cord, brainstem, cerebrum and cerebellum compared to all lesions. n=3



Supplementary Figure 4:
IgG antibody staining of spinal cord and brain sections of Th17 and Th1 EAE shows meningeal and parenchymal deposition of antibodies. (A and B) Transverse spinal cord sections of Th17 mice with clinical score of 3 (A) and 0 (B). (C) Perivascular accumulation of antibodies in Th17 EAE . (D) Spinal cord section of Th1 EAE mouse with clinical score of 3. 500 micron (panels A,B, and D) 100 micron (panel C). (E) Quantification of meningeal IgG deposits in TH1 and TH17 EAE. ** $p<0.01$ determined by 2 tailed student's T-test.



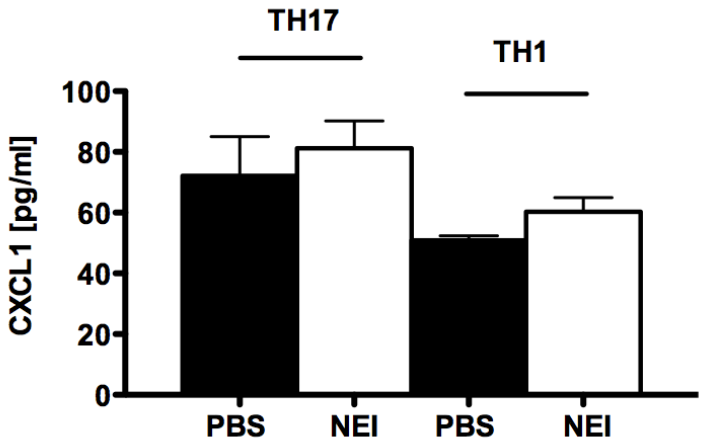
Supplementary Figure 5
Sivelestat reduces inflammation in the optic nerve in TH17 EAE. H&E staining of the optic nerve of TH17 (**A,B**) and TH1 (**C,D**) EAE treated with PBS (**A,C**) or Sivilestat (**B,D**). Scale bars: 100μm.



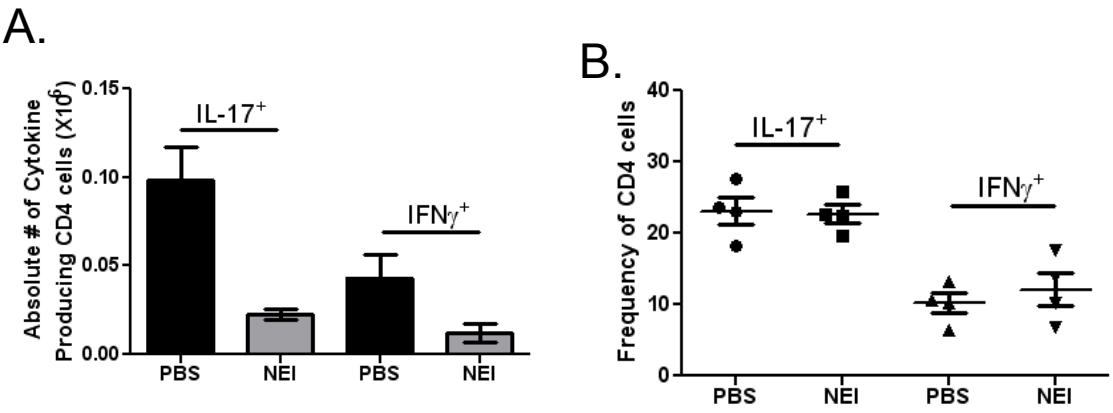
Supplementary Figure 6:

Treatment with Sivelestat does not influence the levels of IL-1β (**A**), IFN-γ (**B**) and CXCL1 (**C**) in spleen cell cultures.

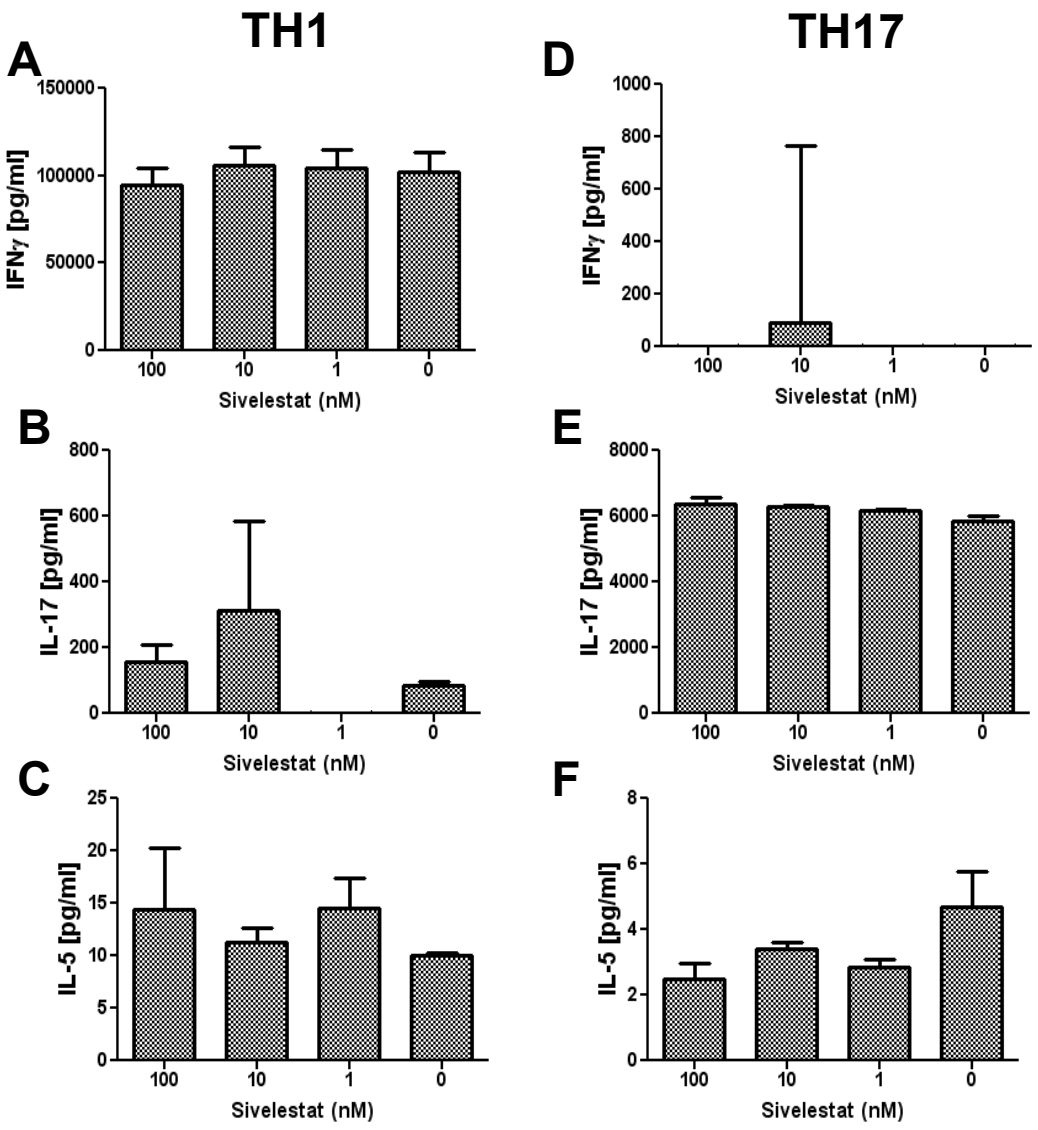
Spleen cell cultures of TH17 and TH1 EAE animals treated with Sivelestat or PBS were analyzed at peak of disease. Cells were restimulated with different concentrations of MOG_{35-55} for 3 days. Chemokines and cytokines were measured in supernatants of cell cultures by ELISA. Data is represented as mean ± s.e.m of three mice per group.



Supplementary Figure 7
Treatment with Sivelestat does not influence the level of CXCL1 in serum. Serum of TH17 and Th1 EAE animals treated with Sivelstat or PBS was collected at day 8 after adoptive transfer and was analyzed by ELISA. Data is represented as mean ± s.e.m of five mice per group.



Supplemental Figure 8.
Sivelestat does not change the frequency of IL-17+ or IFNγ+ CD4 T-cells that infiltrate the spinal cord in TH17 induce EAE. Mice induce with TH17 cells were treated with Sivelestat (NEI) or PBS from 6-10 days after transfer. 10 days after transfer, absolute number (**A**) and frequency (**B**) of cytokine producing T-cells in the spinal cord were assessed by intracellular flow cytometry.



Supplementary Figure 9:
In vitro treatment of Sivelestat does not directly effect TH1 or TH17 differentiation. Spleens cells from C57BL/6 mice depleted of CD8 T-cells were activated in TH1 (IL-12) and TH17 (IL-6 and TGFβ) in the presence of the indicated concentration of Sivelestat for 3 days. Cytokine secretion in supernatants were assayed by ELISA.