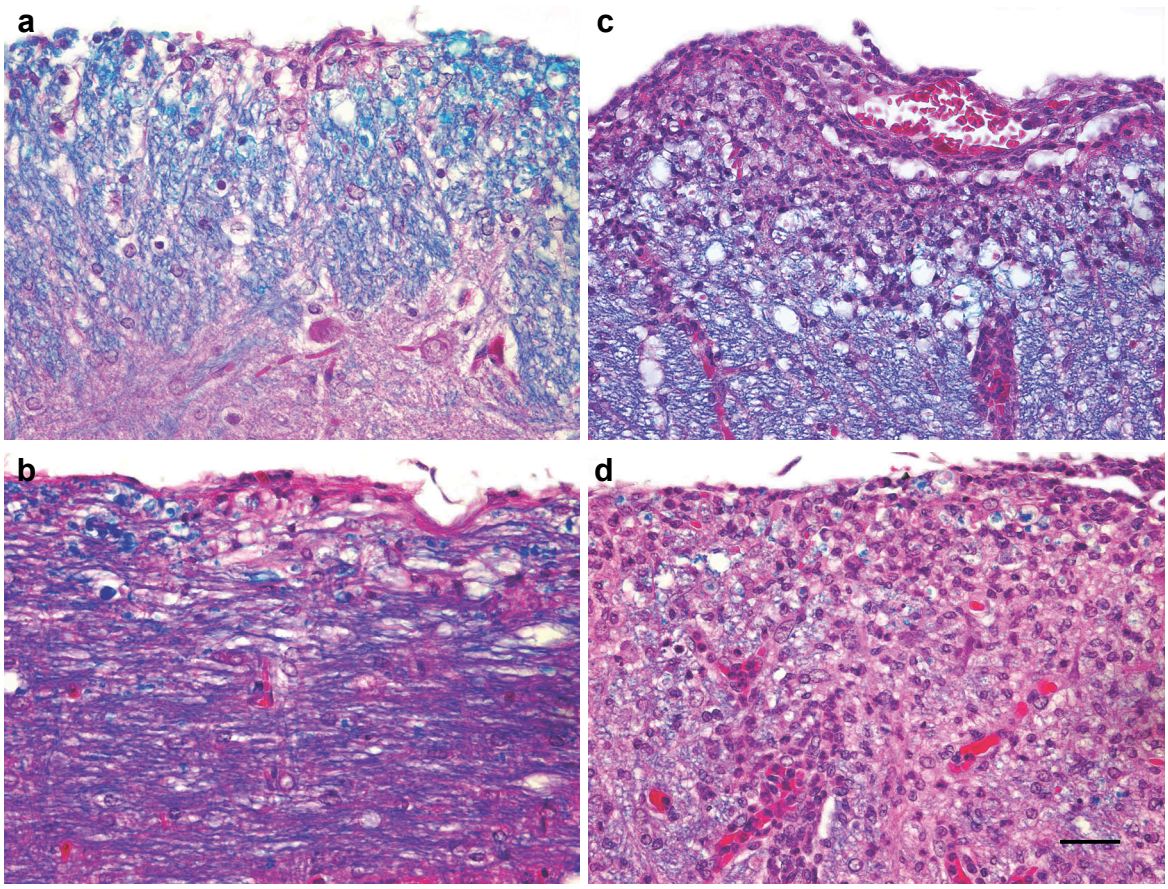
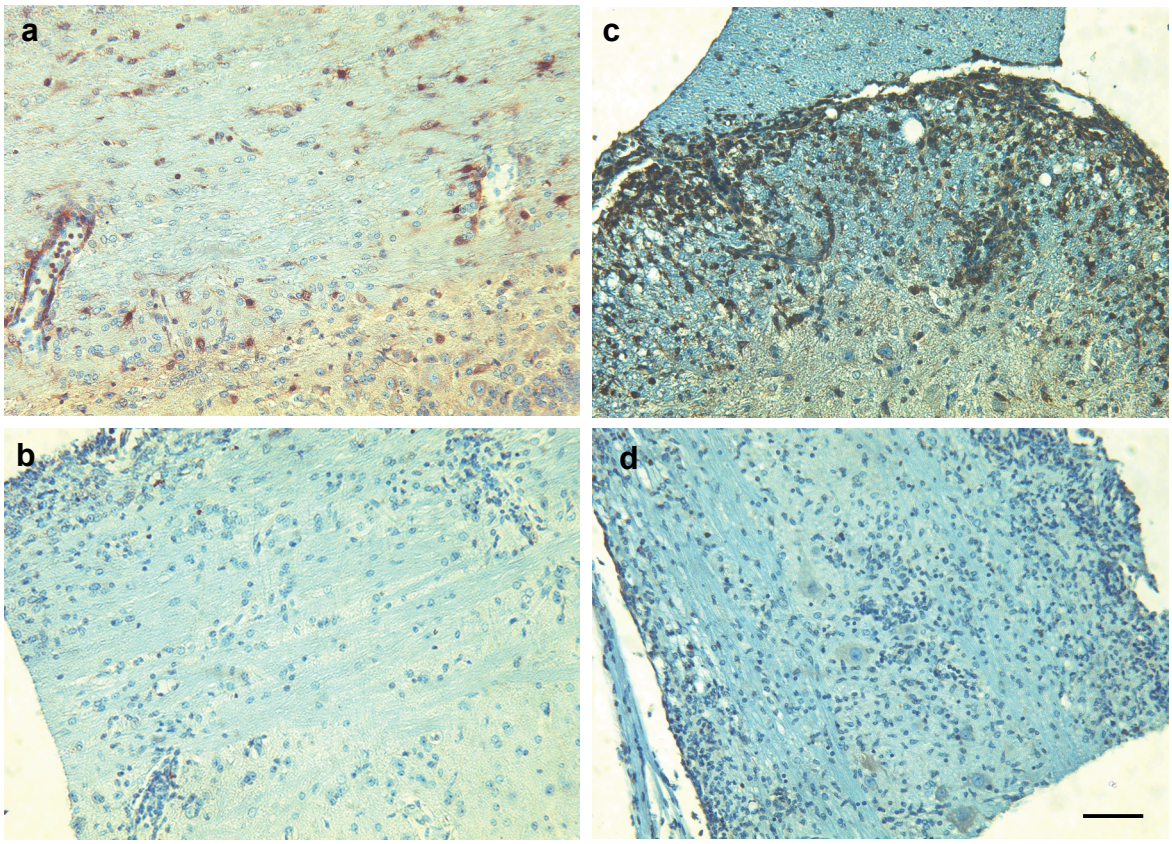
Supplementary Table S1: Cumulative analysis of four experiments comparing WT vs αBC$^{-/-}$ mice with EAE.

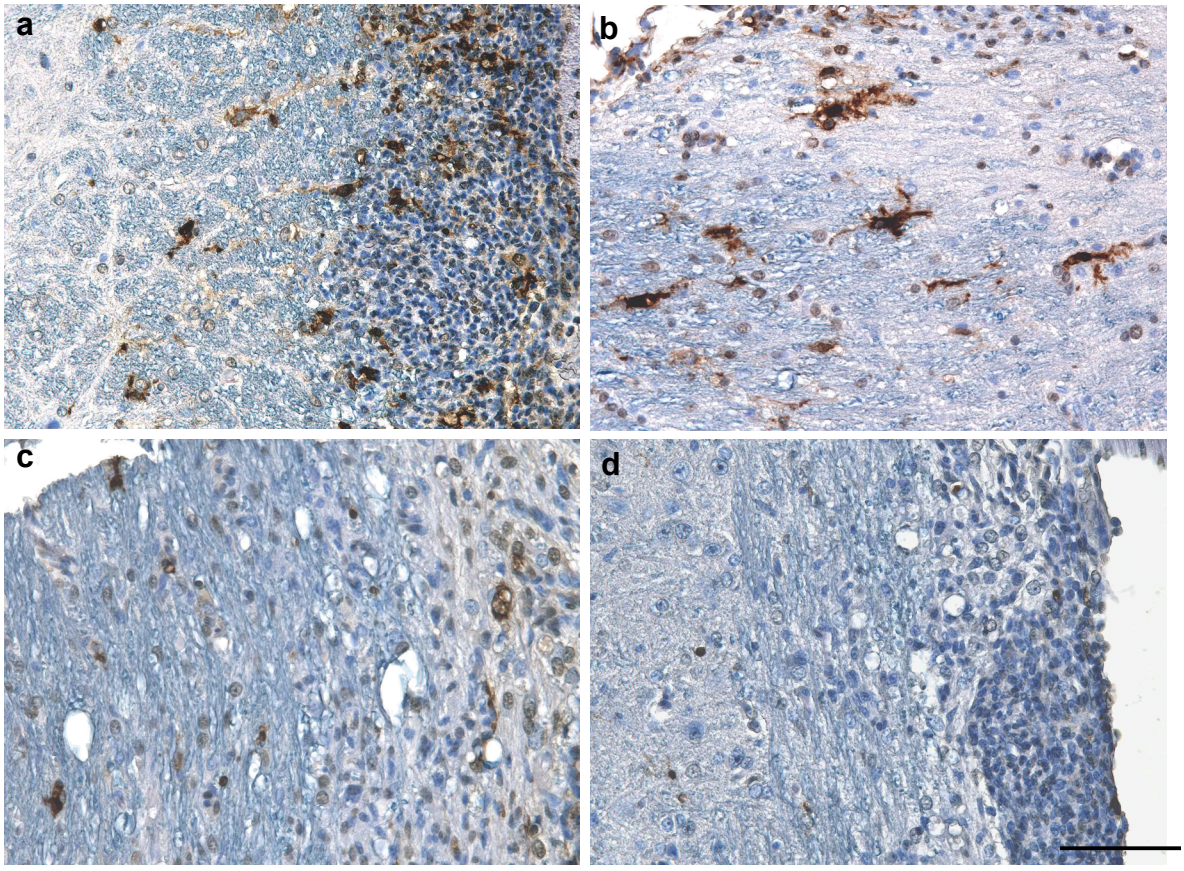
Days	# WT EAE mice	# αBC$^{-/-}$ EAE mice	p value Mann Whitney
12	27	27	0.044
13	27	27	0.105
14	27	27	0.230
15	27	27	0.058
16	27	27	0.103
17	27	27	0.0051
18	27	27	0.0045
19	27	27	0.0012
20	27	27	0.0018
21	27	27	0.0039
22	27	27	0.0367
23	26	26	0.0367
24	25	25	0.1492
25	25	25	0.156
26	25	25	0.0968
27	25	25	0.0465
28	25	25	0.0475
29	25	25	0.0174
30	20	20	0.0055
31	20	20	0.005
32	20	20	0.0041
33	20	19	0.0045
34	20	19	0.0003
35	20	19	0.0037
36	20	19	0.0069
37	20	19	0.0014
38	20	19	0.0007
39	20	19	0.0078
40	20	19	0.009
41	15	15	0.0351



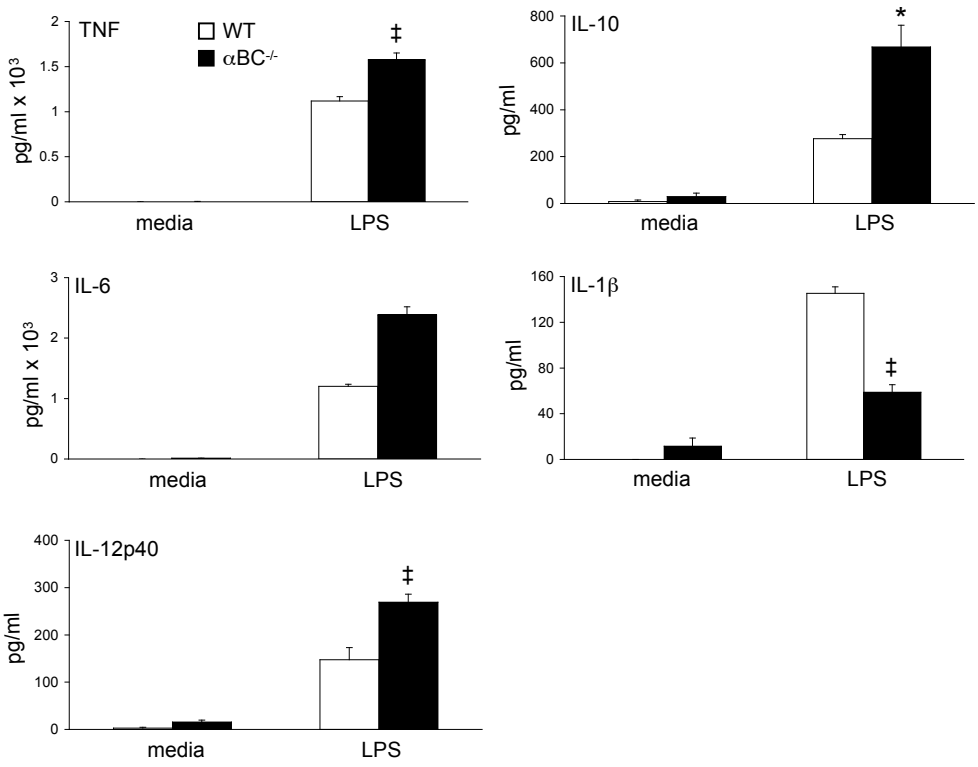
Supplementary Figure S1: αBC$^{-/-}$ mice have more severe inflammatory/ demyelinating lesions in acute and progressive EAE. Paraffin-embedded spinal cord sections taken at day 14 (a, c) and day 42 (b, d) from WT (a, b) and αBC$^{-/-}$ (c, d) animals with EAE and stained with luxol fast blue and hematoxylin-eosin. Scale bar=200 μm.



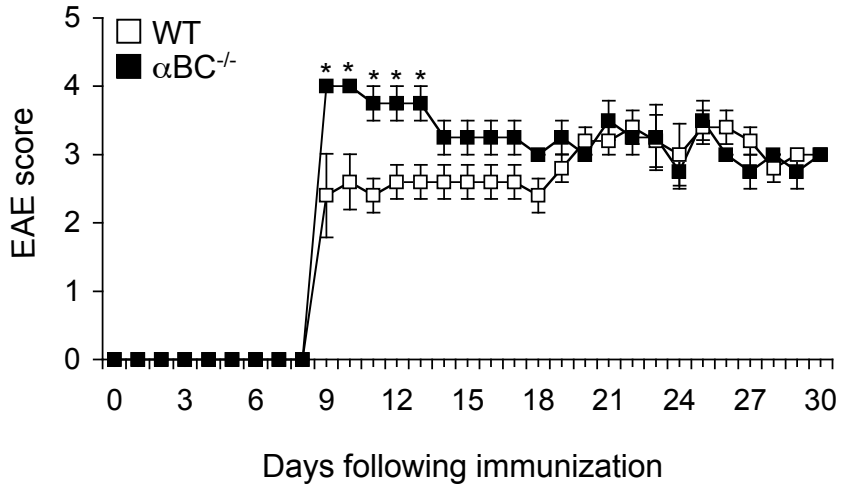
Supplementary Figure S2: αBC$^{-/-}$ mice have higher expression of uncleaved caspase-3 in acute EAE. Paraffin-embedded spinal cord sections taken at day 14 from WT (a, b) and αBC$^{-/-}$ (c, d) animals with EAE and immuno-stained for cleaved (b, d) and uncleaved caspase-3 (a, c). Scale bar=400 μm.



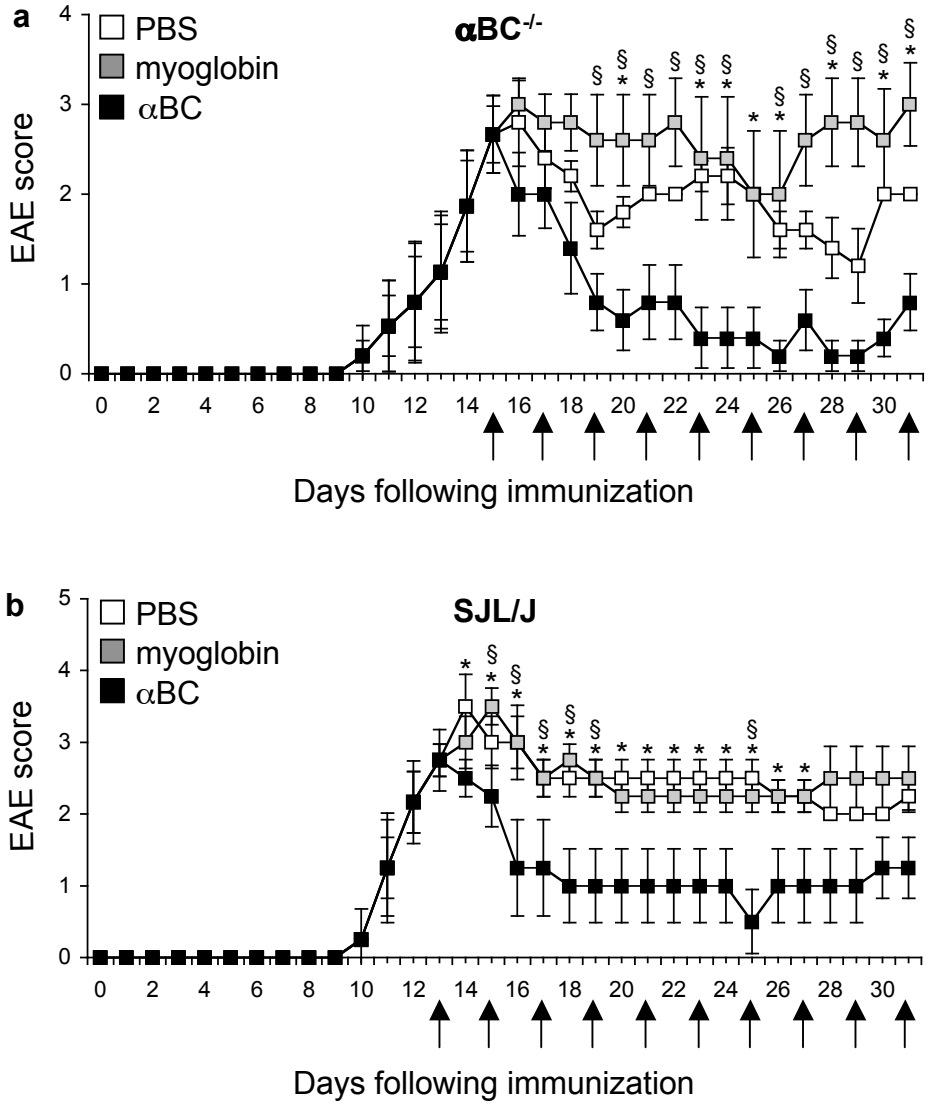
Supplementary Figure S3: **EAE mice treated with αBC have fewer TUNEL positive cells in their spinal cord.** Paraffin-embedded spinal cord sections taken at day 32 from WT mice with EAE and treated with PBS (a, b) and recombinant αBC (c, d) and processed for TUNEL staining. Scale bar=100 μm.



Supplementary Figure S4: αBC$^{-/-}$ dendritic cells are hyper-responsive. Representative graphs from two experiments showing production of cytokines (IL-1β, TNF, IL-6, IL-12p40, IL-10) (pg/ml) by WT (□) and αBC$^{-/-}$ (■) dendritic cells stimulated *in vitro* with LPS for 48h or 72h, mean ± s.e.m.; *p<0.02, ‡p<0.005, Student's t-test.



Supplementary Figure S5: Rag2$^{-/-}$ mice adoptively transferred with αBC$^{-/-}$ splenoctes developed worse clinical EAE at theacute phase. (a) Mean ± s.e.m. clinical scores of Rag2$^{-/-}$ mice adoptively transferred with MOG-reactive WT (□) or αBC$^{-/-}$ (■) splenocytes; *p<0.05, Student's t-test, n=5 animals/group.



Supplementary Figure S6: Recombinant αBC suppresses Clinical disease in αBC$^{-/-}$ and SJL/J mice with EAE. Mean ± s.e.m.clinical scores of αBC$^{-/-}$ and SJL/J (b) EAE mice treatedwith recombinant αBC (■), PBS (□) or recombinant myoglobin (▒) following immunization with MOG 35-55 (αBC$^{-/-}$) or PLP 139-151 (SJL/J); *§p<0.05 Mann-Whitney, αBC$^{-/-}$ n=2 experiments, SJL/J n=1 experiment (*αBC vs PBS) (§αBC vs myoglobin). Linear regression: days 13-22: αBC vs PBS, p=0.0156; αBC vs myoglobin, p=0.038 b) days 15-25: αBC vs PBS, p=0.014; αBC vs myoglobin, p=0.0093.

Supplementary Table S2: Densitometric quantification of protein level, following normalization to actin, in WT and αBC$^{-/-}$ CD3+ T cells stimulated with media or MOG and irradiated syngeneic splenocytes.

T cell	*Experiment*	*WT media*	*αBC$^{-/-}$ media*	*WT MOG*	*αBC$^{-/-}$ MOG*
p-p38	1	1.16	1.21	1.44	1.64
	2	0.81	1.05	1.33	1.99
	mean ± s.d.	**0.99 ± 0.25^**	**1.13 ± 0.11#**	**1.39 ± 0.08*^**	**1.82 ± 0.25*#**
p38	1	1.23	1.56	1.81	2.01
	2	0.67	0.72	0.88	1.26
	mean ± s.d.	**0.95 ± 0.40**	**1.14 ± 0.59**	**1.35 ± 0.66**	**1.64 ± 0.53**

*p=0.072 (p-p38: WT MOG vs αBC$^{-/-}$ MOG)
#p=0.035 (p-p38: αBC$^{-/-}$ media vs αBC$^{-/-}$ MOG)
^p=0.08 (p-p38 WT media vs WT MOG)
Student's t-test

Supplementary Table S3: Densitometric quantification of protein level, following normalization to actin, in WT and αBC$^{-/-}$ macrophages stimulated with media or LPS.

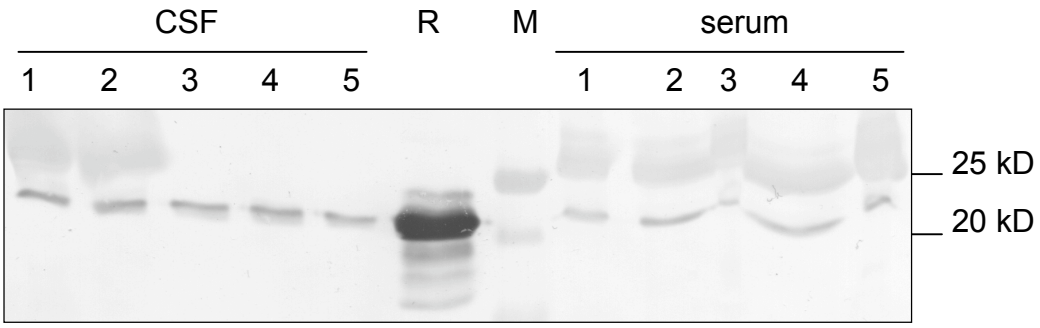
Macrophage	*Experiment*	*WT media*	*αBC$^{-/-}$ media*	*WT LPS*	*αBC$^{-/-}$ LPS*
p-p38	1	1.54	1.55	2.01	2.21
	2	1.25	1.45	1.34	1.89
	mean ± s.d.	**1.40 ± 0.21**	**1.50 ± 0.07***	**1.68 ± 0.47**	**2.05 ± 0.23***
p38	1	1.29	1.42	1.57	1.81
	2	1.89	2.00	2.01	2.28
	mean ± s.d.	**1.59 ± 0.42**	**1.71 ± 0.41**	**1.79 ± 0.26**	**2.05 ± 0.33**

*p=0.041 (p-p38: αBC$^{-/-}$ media vs αBC$^{-/-}$ LPS)
Student's t-test

Supplementary Table S4: Densitometric quantification of protein level, following normalization to actin, in WT and αBC$^{-/-}$ astrocytes stimulated with media or TNF.

Astrocytes	*Experiment*	*WT media*	*αBC$^{-/-}$ media*	*WT TNF*	*αBC$^{-/-}$ TNF*
p-ERK	1	1.04	0.91	1.00	1.07
	2	0.72	0.45	0.84	1.23
	mean ± s.d.	**0.88 ± 0.23**	**0.68 ± 0.33**	**0.92 ± 0.11**	**1.15 ± 0.11**
ERK	1	2.32	2.20	1.95	2.44
	2	1.25	1.32	1.35	2.21
	mean ± s.d.	**1.79 ± 0.78**	**1.76 ± 0.62**	**1.65 ± 0.42**	**2.33 ± 0.16**
p38	1	2.97	2.23	1.78	2.61
	2	1.84	2.05	1.74	3.60
	mean ± s.d.	**2.41 ± 0.80**	**2.14 ± 0.13**	**1.76 ± 0.03^**	**3.11 ± 0.70^**
NFκBp50	1	0.46	2.91	0.44	2.74
	2	0.52	2.44	0.51	3.63
	mean ± s.d.	**0.49 ± 0.05#**	**2.67 ± 0.33#**	**0.48 ± 0.05***	**3.19 ± 0.63***
NFκBp65	1	2.11	1.43	1.31	1.78
	2	3.19	1.58	2.64	2.56
	mean ± s.d.	**2.65 ± 0.76**	**1.51 ± 0.11**	**1.98 ± 0.94**	**2.17 ± 0.55**
IκBα	1	1.31	1.85	1.50	1.03
	2	1.04	1.16	1.50	0.64
	mean ± s.d.	**1.18 ± 0.19**	**1.51 ± 0.49**	**1.5 ± 0‡**	**0.84 ± 0.28‡**
cleaved caspase 3	1	0.77	0.86	0.71	1.68
	2	1.11	1.29	0.98	1.73
	mean ± s.d.	**0.94 ± 0.24**	**1.08 ± 0.30**	**0.85 ± 0.19***	**1.71 ± 0.04***
αBC	1	1.30	0	1.76	0
	2	2.22	0	3.13	0
	mean ± s.d.	**1.76 ± 0.65**	**0**	**2.45 ± 0.97**	**0**

#p=0.006 (NFκBp50: WT media vs αBC$^{-/-}$ media)
*p=0.012 (NFκBp50, cleaved caspase-3: WT TNF vs αBC$^{-/-}$ TNF)
‡p=0.038 (IκBα: WT TNF vs αBC$^{-/-}$ TNF)
^p=0.056 (p38: WT TNF vs αBC$^{-/-}$ TNF)
Student's t-test



Supplementary Figure S7: αBC is present in sera and CSF of MS patients. Western blot analysis of free αBC in sera and CSF of MS patients. Human recombinant αBC (0.4 mg) was used as a reference(R). Molecular markers (M) indicate 20 and 25 kDa positions.