

## SUPPLEMENTARY INFORMATION

Supplementary Table 1:

<b>Treatment</b>	<b>Incidence</b>	<b>Mean day of onset (mean <math>\pm</math> SD)</b>	<b>Mean maximum score (mean <math>\pm</math> SD)</b>
<b>Control</b>	42 of 49 (87 %)	13.6 $\pm$ 2.8	2.4 $\pm$ 1.4
<b>TCDD 1 <math>\mu</math>g</b>	4 of 40 (10 %)*	21.8 $\pm$ 1.5*	0.2 $\pm$ 0.6*
<b>TCDD 0.1 <math>\mu</math>g</b>	5 of 5 (100 %)	17.0 $\pm$ 1.2	3.1 $\pm$ 0.5
<b>TCDD 0.01 <math>\mu</math>g</b>	7 of 7 (100 %)	14.1 $\pm$ 2.9	2.7 $\pm$ 0.6

Mice treated with corn oil (Control) or TCDD (1, 0.1 or 0.01  $\mu$ g/mouse) were immunized with MOG<sub>35-55</sub> peptide in CFA and monitored for EAE development. Statistical analysis was performed by comparing groups using one-way analysis of variance.

\*  $P < 0.0001$  vs group control, TCDD 0.01, TCDD 0.1  $\mu$ g and TCDD 0.01  $\mu$ g.

Supplementary Table 2:

<b>Treatment</b>	<b>Incidence</b>	<b>Mean day of onset (mean <math>\pm</math> SD)</b>	<b>Mean maximum score (mean <math>\pm</math> SD)</b>
<b>WT Control</b>	12 of 14 (86 %)	13.9 $\pm$ 1.9	2.4 $\pm$ 1.4
<b>AHR-d TCDD</b>	9 of 11 (82 %)	17.3 $\pm$ 3.0 <sup>†</sup>	2.2 $\pm$ 1.4
<b>WT TCDD</b>	1 of 10 (10 %) <sup>#</sup>	21	0.2 $\pm$ 0.6*

C57BL/6 (WT) and AHR-d mice treated with corn oil (control) or TCDD (1  $\mu$ g/mouse), immunized with MOG<sub>35-55</sub> peptide in CFA and monitored for EAE development. Statistical analysis was performed by comparing groups using one-way analysis of variance.

\*  $P < 0.001$  vs WT Control group and  $P < 0.01$  vs AHR-d TCDD group.

<sup>†</sup>  $P = 0.0046$  vs WT Control group.

<sup>#</sup>  $P = 0.0005$  vs WT Control group  $P = 0.0019$  vs AHR-d TCDD group.



	70 kDa Heat Shock Protein peptide aa 376–395	Biopolymers Facility / Harvard Medical School
	70 kDa Heat Shock Protein peptide aa 391–410	Biopolymers Facility / Harvard Medical School
	70 kDa Heat Shock Protein peptide aa 406–425	Biopolymers Facility / Harvard Medical School
	70 kDa Heat Shock Protein peptide aa 421–440	Biopolymers Facility / Harvard Medical School
	70 kDa Heat Shock Protein peptide aa 436–455	Biopolymers Facility / Harvard Medical School
	70 kDa Heat Shock Protein peptide aa 451–470	Biopolymers Facility / Harvard Medical School
	70 kDa Heat Shock Protein peptide aa 466–485	Biopolymers Facility / Harvard Medical School
	70 kDa Heat Shock Protein peptide aa 46–65	Biopolymers Facility / Harvard Medical School
	70 kDa Heat Shock Protein peptide aa 481–500	Biopolymers Facility / Harvard Medical School
	70 kDa Heat Shock Protein peptide aa 496–515	Biopolymers Facility / Harvard Medical School
	70 kDa Heat Shock Protein peptide aa 511–530	Biopolymers Facility / Harvard Medical School
	70 kDa Heat Shock Protein peptide aa 526–545	Biopolymers Facility / Harvard Medical School
	70 kDa Heat Shock Protein peptide aa 541–560	Biopolymers Facility / Harvard Medical School
	70 kDa Heat Shock Protein peptide aa 556–575	Biopolymers Facility / Harvard Medical School
	70 kDa Heat Shock Protein peptide aa 571–590	Biopolymers Facility / Harvard Medical School
	70 kDa Heat Shock Protein peptide aa 586–605	Biopolymers Facility / Harvard Medical School
	70 kDa Heat Shock Protein peptide aa 601–620	Biopolymers Facility / Harvard Medical School
	70 kDa Heat Shock Protein peptide aa 616–635	Biopolymers Facility / Harvard Medical School
	70 kDa Heat Shock Protein peptide aa 61–80	Biopolymers Facility / Harvard Medical School
	70 kDa Heat Shock Protein peptide aa 631–640	Biopolymers Facility / Harvard Medical School
	70 kDa Heat Shock Protein peptide aa 76–95	Biopolymers Facility / Harvard Medical School
	70 kDa Heat Shock Protein peptide aa 91–110	Biopolymers Facility / Harvard Medical School
	71 kDa Heat Shock Protein M. tuberculosis	Biopolymers Facility / Harvard Medical School
	90 kDa Heat Shock Protein	Stressgen
	GroEL	Stressgen
CNS	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa106-125	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa1-20	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa121-140	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa136-155	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa151-170	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa16-35	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa166-185	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa181-200	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa196-215	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa211-230	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa226-245	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa241-260	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa256-275	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa271-290	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa286-305	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa301-320	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa31-50	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa316-335	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa331-350	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa346-365	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa361-380	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa376-395	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa391-410	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa406-421	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa46-65	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa61-80	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa76-95	Biopolymers Facility / Harvard Medical School
	2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa91-110	Biopolymers Facility / Harvard Medical School
	Acetyl Cholinesterase	Sigma Aldrich
	ADAM-10	Sigma Aldrich
	alpha-Cristallin	Stressgen
	beta-Cristallin	Sigma Aldrich
	bovine Myelin Basic Protein	Sigma Aldrich
	Brain Extract I	Sigma Aldrich
	Brain Extract II	Sigma Aldrich
	Brain Extract III	Sigma Aldrich
	Glial Filament Acidic Protein	Research Diagnostic
	guinea pig Myelin Basic Protein	Sigma Aldrich
	human Myelin Basic Protein	Sigma Aldrich
	Myelin-Associated Oligodendrocytic Basic Protein peptide aa 106-125	Biopolymers Facility / Harvard Medical School
Myelin-Associated Oligodendrocytic Basic Protein peptide aa 1-20	Biopolymers Facility / Harvard Medical School	
Myelin-Associated Oligodendrocytic Basic Protein peptide aa 121-140	Biopolymers Facility / Harvard Medical School	
Myelin-Associated Oligodendrocytic Basic Protein peptide aa 136-155	Biopolymers Facility / Harvard Medical School	
Myelin-Associated Oligodendrocytic Basic Protein peptide aa 151-170	Biopolymers Facility / Harvard Medical School	

Myelin-Associated Oligodendrocytic Basic Protein peptide aa 16-35	Biopolymers Facility / Harvard Medical School
Myelin-Associated Oligodendrocytic Basic Protein peptide aa 166-185	Biopolymers Facility / Harvard Medical School
Myelin-Associated Oligodendrocytic Basic Protein peptide aa 181-200	Biopolymers Facility / Harvard Medical School
Myelin-Associated Oligodendrocytic Basic Protein peptide aa 31-50	Biopolymers Facility / Harvard Medical School
Myelin-Associated Oligodendrocytic Basic Protein peptide aa 46-65	Biopolymers Facility / Harvard Medical School
Myelin-Associated Oligodendrocytic Basic Protein peptide aa 61-80	Biopolymers Facility / Harvard Medical School
Myelin-Associated Oligodendrocytic Basic Protein peptide aa 76-95	Biopolymers Facility / Harvard Medical School
Myelin-Associated Oligodendrocytic Basic Protein peptide aa 91-110	Biopolymers Facility / Harvard Medical School
Myelin/oligodendrocyte glycoprotein peptide aa 106-125	Biopolymers Facility / Harvard Medical School
Myelin/oligodendrocyte glycoprotein peptide aa 1-20	Biopolymers Facility / Harvard Medical School
Myelin/oligodendrocyte glycoprotein peptide aa 121-140	Biopolymers Facility / Harvard Medical School
Myelin/oligodendrocyte glycoprotein peptide aa 136-155	Biopolymers Facility / Harvard Medical School
Myelin/oligodendrocyte glycoprotein peptide aa 151-170	Biopolymers Facility / Harvard Medical School
Myelin/oligodendrocyte glycoprotein peptide aa 16-35	Biopolymers Facility / Harvard Medical School
Myelin/oligodendrocyte glycoprotein peptide aa 166-185	Biopolymers Facility / Harvard Medical School
Myelin/oligodendrocyte glycoprotein peptide aa 181-200	Biopolymers Facility / Harvard Medical School
Myelin/oligodendrocyte glycoprotein peptide aa 196-215	Biopolymers Facility / Harvard Medical School
Myelin/oligodendrocyte glycoprotein peptide aa 211-230	Biopolymers Facility / Harvard Medical School
Myelin/oligodendrocyte glycoprotein peptide aa 226-247	Biopolymers Facility / Harvard Medical School
Myelin/oligodendrocyte glycoprotein peptide aa 31-50	Biopolymers Facility / Harvard Medical School
Myelin/oligodendrocyte glycoprotein peptide aa 35-55	Biopolymers Facility / Harvard Medical School
Myelin/oligodendrocyte glycoprotein peptide aa 46-65	Biopolymers Facility / Harvard Medical School
Myelin/oligodendrocyte glycoprotein peptide aa 61-80	Biopolymers Facility / Harvard Medical School
Myelin/oligodendrocyte glycoprotein peptide aa 76-95	Biopolymers Facility / Harvard Medical School
Myelin/oligodendrocyte glycoprotein peptide aa 91-110	Biopolymers Facility / Harvard Medical School
murine Myelin Basic Protein	Sigma Aldrich
Myelin Associated Glycoprotein	Sigma Aldrich
Myelin Basic Protein peptide aa 104-123	Biopolymers Facility / Harvard Medical School
Myelin Basic Protein peptide aa 11-30	Biopolymers Facility / Harvard Medical School
Myelin Basic Protein peptide aa 113-132	Biopolymers Facility / Harvard Medical School
Myelin Basic Protein peptide aa 1-20	Biopolymers Facility / Harvard Medical School
Myelin Basic Protein peptide aa 121-138	Biopolymers Facility / Harvard Medical School
Myelin Basic Protein peptide aa 124-142	Biopolymers Facility / Harvard Medical School
Myelin Basic Protein peptide aa 138-147	Biopolymers Facility / Harvard Medical School
Myelin Basic Protein peptide aa 141-161	Biopolymers Facility / Harvard Medical School
Myelin Basic Protein peptide aa 143-168	Biopolymers Facility / Harvard Medical School
Myelin Basic Protein peptide aa 155-178	Biopolymers Facility / Harvard Medical School
Myelin Basic Protein peptide aa 26-35	Biopolymers Facility / Harvard Medical School
Myelin Basic Protein peptide aa 31-50	Biopolymers Facility / Harvard Medical School
Myelin Basic Protein peptide aa 41-60	Biopolymers Facility / Harvard Medical School
Myelin Basic Protein peptide aa 51-70	Biopolymers Facility / Harvard Medical School
Myelin Basic Protein peptide aa 61-80	Biopolymers Facility / Harvard Medical School
Myelin Basic Protein peptide aa 71-92	Biopolymers Facility / Harvard Medical School
Myelin Basic Protein peptide aa 84-94	Biopolymers Facility / Harvard Medical School
Myelin Basic Protein peptide aa 89-101	Biopolymers Facility / Harvard Medical School
Myelin Basic Protein peptide aa 173-186	Biopolymers Facility / Harvard Medical School
Myelin Basic Protein peptide aa 93-112	Biopolymers Facility / Harvard Medical School
Myelin Protein 2 peptide aa 106-125	Biopolymers Facility / Harvard Medical School
Myelin Protein 2 peptide aa 1-20	Biopolymers Facility / Harvard Medical School
Myelin Protein 2 peptide aa 121-132	Biopolymers Facility / Harvard Medical School
Myelin Protein 2 peptide aa 16-35	Biopolymers Facility / Harvard Medical School
Myelin Protein 2 peptide aa 31-50	Biopolymers Facility / Harvard Medical School
Myelin Protein 2 peptide aa 46-65	Biopolymers Facility / Harvard Medical School
Myelin Protein 2 peptide aa 61-80	Biopolymers Facility / Harvard Medical School
Myelin Protein 2 peptide aa 76-95	Biopolymers Facility / Harvard Medical School
Myelin Protein 2 peptide aa 91-110	Biopolymers Facility / Harvard Medical School
Neurofilament 160kd	Chemicon
Neurofilament 200kd	Chemicon
Neurofilament 68kd	Chemicon
Neuronal Enolase	Calbiochem
Nicastrin	GeneTex
NMDA receptor	Novus Biologicals
NOGO	Sigma Aldrich
Olygodendrocyte-Specific Protein peptide aa 106-125	Biopolymers Facility / Harvard Medical School
Olygodendrocyte-Specific Protein peptide aa 1-20	Biopolymers Facility / Harvard Medical School
Olygodendrocyte-Specific Protein peptide aa 121-140	Biopolymers Facility / Harvard Medical School
Olygodendrocyte-Specific Protein peptide aa 136-155	Biopolymers Facility / Harvard Medical School
Olygodendrocyte-Specific Protein peptide aa 151-170	Biopolymers Facility / Harvard Medical School
Olygodendrocyte-Specific Protein peptide aa 16-35	Biopolymers Facility / Harvard Medical School

Olygodendrocyte-Specific Protein peptide aa 166-185	Biopolymers Facility / Harvard Medical School
Olygodendrocyte-Specific Protein peptide aa 181-199	Biopolymers Facility / Harvard Medical School
Olygodendrocyte-Specific Protein peptide aa 195-217	Biopolymers Facility / Harvard Medical School
Olygodendrocyte-Specific Protein peptide aa 31-50	Biopolymers Facility / Harvard Medical School
Olygodendrocyte-Specific Protein peptide aa 46-65	Biopolymers Facility / Harvard Medical School
Olygodendrocyte-Specific Protein peptide aa 61-80	Biopolymers Facility / Harvard Medical School
Olygodendrocyte-Specific Protein peptide aa 76-95	Biopolymers Facility / Harvard Medical School
Olygodendrocyte-Specific Protein peptide aa 91-110	Biopolymers Facility / Harvard Medical School
Proteolipid Protein	Abnova
Proteolipid Protein peptide aa 100-119	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 10-29	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 110-129	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 1-19	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 125-141	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 137-150	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 137-154	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 150-163	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 151-173	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 158-166	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 161-180	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 178-191	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 180-199	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 190-209	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 20-39	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 205-220	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 215-232	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 220-239	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 220-249	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 248-259	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 250-269	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 265-277	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 35-50	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 40-59	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 50-69	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 65-84	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 80-99	Biopolymers Facility / Harvard Medical School
Proteolipid Protein peptide aa 91-110	Biopolymers Facility / Harvard Medical School
Retinol Binding Protein	Sigma Aldrich
S100beta protein	Assay Designs
Super Oxide Dismutase	Sigma Aldrich
Synuclein, beta	Sigma Aldrich
Synuclein, gamma	Sigma Aldrich
<b>Tissue</b>	
Amygdala	ProSci Inc.
Amygdala AD	ProSci Inc.
Brain lysate	ProSci Inc.
Brain Tissue Membrane	ProSci Inc.
Cerebellar pedunculus	ProSci Inc.
Cerebral meninges	ProSci Inc.
Corpus Callosum	ProSci Inc.
Corpus Callosum AD	ProSci Inc.
Diencephalon	ProSci Inc.
Fetal brain	ProSci Inc.
Frontal lobe	ProSci Inc.
Frontal lobe AD	ProSci Inc.
Hippocampus	ProSci Inc.
Hippocampus AD	ProSci Inc.
Insula	ProSci Inc.
Occipital lobe	ProSci Inc.
Occipital lobe AD	ProSci Inc.
Olfactory region	ProSci Inc.
Optic Nerve	ProSci Inc.
Parietal lobe	ProSci Inc.
Parietal lobe AD	ProSci Inc.
Pons	ProSci Inc.
Pons AD	ProSci Inc.
Postcentral gyrus	ProSci Inc.
Postcentral gyrus AD	ProSci Inc.
Precentral gyrus	ProSci Inc.
Precentral gyrus AD	ProSci Inc.

	Spinal cord	ProSci Inc.
	Temporal lobe	ProSci Inc.
	Temporal lobe AD	ProSci Inc.
	Thalamus	ProSci Inc.
	Thalamus AD	ProSci Inc.
<b>AD related</b>	Amyloid beta	Sigma Aldrich
	Amyloid beta 10-20	Sigma Aldrich
	Amyloid beta 1-12	Sigma Aldrich
	Amyloid beta 12-28	Sigma Aldrich
	Amyloid beta 1-23	Sigma Aldrich
	Amyloid beta 1-38	Sigma Aldrich
	Amyloid beta 17-40	Sigma Aldrich
	Amyloid beta 25-35	Sigma Aldrich
	Amyloid beta 34-42	Sigma Aldrich
	Amyloid bri protein precursor 227	Sigma Aldrich
	Amyloid DAN Protein Fragment 1-34	Sigma Aldrich
	Amyloid Precursor Protein	Sigma Aldrich
	Amyloid protein no AB component	Sigma Aldrich
	Secreted amyloid precursor protein (SAP) beta	Sigma Aldrich
	Tau isoform variant 0N3R	Sigma Aldrich
	Tau isoform variant 1N3R	Sigma Aldrich
	Tau isoform variant 0N4R	Sigma Aldrich
	Tau isoform variant 2N3R	Sigma Aldrich
	Tau phospho Ser412	Sigma Aldrich
	Tau phospho Ser441	Sigma Aldrich
Tau phospho Thr181	Sigma Aldrich	
Tau Protein human	EMD Biosciences	
<b>Lipids</b>	(±)9-HODE	Cayman Chemical
	1 Palmitoyl-2-(5'oxo-Valeroyl)-sn-Glycero-3-Phosphocholine	Avanti Polar Lipids
	15a-hydroxycholestene	Avanti Polar Lipids
	15-ketocholestane	Avanti Polar Lipids
	15-ketocholestene	Avanti Polar Lipids
	1-Palmitoil-2-(9'oxo-Nonanoyl)-sn-Glycero-3-Phosphocholine	Avanti Polar Lipids
	1-Palmitoil-2-Azelaoyl-sn-Glycero-3-Phosphocholine	Avanti Polar Lipids
	1-Palmitoil-2-Glutaroyl-sn-Glycero-3-Phosphocholine	Avanti Polar Lipids
	5 α-cholestane-3 β,15 α-diol	Avanti Polar Lipids
	9(S)-HODE	Cayman Chemical
	Asialoganglioside-GM1	Sigma Aldrich
	Asialoganglioside-GM2	Sigma Aldrich
	Brain ceramides	Avanti Polar Lipids
	Brain D-erythrospingosine	Avanti Polar Lipids
	Brain lysophosphatidylethanolamine	Avanti Polar Lipids
	Brain L-α-lysophosphatidylserine	Avanti Polar Lipids
	Brain L-α-phosphatidylcholine	Avanti Polar Lipids
	Brain L-α-phosphatidyl-ethanolamine	Avanti Polar Lipids
	Brain L-α-phosphatidylserine	Avanti Polar Lipids
	Brain polar lipid extract	Avanti Polar Lipids
	Brain sphingomyelin	Avanti Polar Lipids
	Brain sulfatide	Avanti Polar Lipids
	Brain total lipid extract	Avanti Polar Lipids
	Cardiolipin	Sigma Aldrich
	Ceramide	Sigma Aldrich
	Ceramide 1-phosphate	Sigma Aldrich
	Cholesterol	Sigma Aldrich
	Disialoganglioside-GD1B	Sigma Aldrich
	Disialoganglioside-GD2	Sigma Aldrich
	Disialoganglioside GD1a	Sigma Aldrich
	Disialoganglioside GD3	HyTest
	Fucosyl-GM1	Calbiochem
	Galactocerebrosides	Sigma Aldrich
	Ganglioside Mixture	Sigma Aldrich
	Ganglioside-GM4	Calbiochem
	Gangliotetraosylceramide asialo-GM1	Avanti Polar Lipids
	HDL	Sigma Aldrich
	Hexacosanoic acid (26)	Sigma Aldrich
	Hydroxy fatty acid ceramide	Sigma Aldrich
	Isoprostone F2 I	Cayman Chemical
	Lactocerebrosides	Sigma Aldrich
	Lactosylceramide	Calbiochem

LDL	Sigma Aldrich
Lipid A, diphosphoryl from Salmonella enterica	Sigma Aldrich
Lipopolysaccharides from Escherichia coli	Sigma Aldrich
Lipopolysaccharides from Pseudomona aeruginosa	Sigma Aldrich
Lipopolysaccharides from Salmonella enterica	Sigma Aldrich
Lyso-GM1	Calbiochem
Monosialoganglioside GM1	Sigma Aldrich
Monosialoganglioside GM2	Sigma Aldrich
Monosialoganglioside GM3	Meridian
N-Hexanoyl-D-sphingosin	Sigma Aldrich
Non-hydroxy fatty acid ceramide	Sigma Aldrich
Phosphatidylinositol-4 phosphate	Sigma Aldrich
Squalene	Sigma Aldrich
Sulfatides	Sigma Aldrich
Tetracosanoic acid (24)	Sigma Aldrich
Tetrasialoganglioside-GQ1B	Calbiochem
TNPAL Galactocerebroside	Sigma Aldrich
Total brain gangliosides	Avanti Polar Lipids
Total cerebroside	Avanti Polar Lipids
Trisialoganglioside GT1a	HyTest
Trisialoganglioside-GT1B	Sigma Aldrich



Supplementary Table 4: Specificity of the IgG antibodies showing a significant (FDR &lt; 0.05) downregulation in TCDD-treated mice

Antigen	FDR
70 kDa. Heat Shock Protein peptide aa 331-350	1.78E-05
60 kDa. Heat Shock Protein peptide aa 255-275	0.00547
60 kDa. Heat Shock Protein peptide aa 13-35	0.00547
32 kDa. Heat Shock protein	0.00547
Myelin Basic Protein peptide aa 138-147	0.00547
Proteolipid Protein peptide aa 1-19	0.00547
Proteolipid Protein peptide aa 161-180	0.00547
Proteolipid Protein peptide aa 10-29	0.00547
60 kDa. Heat Shock Protein peptide aa 1-20	0.0055
70 kDa. Heat Shock Protein peptide aa 61-80	0.0055
Ceramide	0.0055
Myelin-Associated Oligodendrocytic Basic Protein peptide aa 91-110	0.0055
Proteolipid Protein peptide aa 137-150	0.0055
NOGO	0.00557
Oligodendrocyte-Specific Protein peptide aa 76-95	0.00557
b-Cristallin	0.0058
Myelin-Associated Oligodendrocytic Basic Protein peptide aa 121-140	0.00703
60 kDa. Heat Shock Protein peptide aa 225-244	0.00708
Myelin Basic Protein peptide aa 113-132	0.00925
Oligodendrocyte-Specific Protein peptide aa 46-65	0.00925
Myelin Protein 2 peptide aa 91-110	0.00925
Myelin-Associated Oligodendrocytic Basic Protein peptide aa 151-170	0.0093
Myelin/oligodendrocyte glycoprotein peptide aa 31-50	0.0093
NT-3	0.0093
Proteolipid Protein peptide aa 40-59	0.0116
70 kDa. Heat Shock Protein peptide aa 421-440	0.0118
Myelin Basic Protein peptide aa 173-186	0.0125
70 kDa. Heat Shock Protein peptide aa 121-140	0.0132
2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa 391-410	0.0132
Oligodendrocyte-Specific Protein peptide aa 136-155	0.0132
Oligodendrocyte-Specific Protein peptide aa 106-125	0.0134
70 kDa. Heat Shock Protein peptide aa 136-155	0.0141
2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa 406-421	0.0141
Myelin-Associated Oligodendrocytic Basic Protein peptide aa 166-185	0.0143
Myelin Protein 2 peptide aa 1-20	0.0143
Myelin Protein 2 peptide aa 76-95	0.0144
Proteolipid Protein peptide aa 125-141	0.0144
Proteolipid Protein peptide aa 178-191	0.0144
40 kDa. Heat Shock Protein	0.0145
2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa 106-125	0.0158
Oligodendrocyte-Specific Protein peptide aa 195-217	0.0174
2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa 240-259	0.0187
70 kDa. Heat Shock Protein peptide aa 76-95	0.0194
Proteolipid Protein peptide aa 265-277	0.0194
Myelin Basic Protein peptide aa 89-101	0.0199
Myelin Basic Protein peptide aa 71-92	0.0199
Myelin-Associated Oligodendrocytic Basic Protein peptide aa 16-35	0.0199
Proteolipid Protein peptide aa 265-277	0.0199
60 kDa. Heat Shock Protein peptide aa 46-65	0.0241
70 kDa. Heat Shock Protein peptide aa 166-185	0.0241
2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa 151-170	0.0241
2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa 376-395	0.0241
Myelin Basic Protein peptide aa 11-30	0.0241
Myelin/oligodendrocyte glycoprotein peptide aa 211-230	0.0241
Proteolipid Protein peptide aa 265-277	0.0241
70 kDa. Heat Shock Protein peptide aa 181-199	0.0242
Oligodendrocyte-Specific Protein peptide aa 31-50	0.0242
Proteolipid Protein peptide aa 265-277	0.0242
Myelin/oligodendrocyte glycoprotein peptide aa 91-110	0.0249
Optic Nerve lysate	0.0249
2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa 361-380	0.0258
Lactosylceramide	0.0258
Myelin Protein 2 peptide aa 31-50	0.0258
Myelin Basic Protein peptide aa 1-20	0.028

NMDA receptor	0.0285
CNF	0.0289
2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa 136-155	0.0292
Myelin Basic Protein peptide aa 141-161	0.0298
70 kDa. Heat Shock Protein peptide aa 406-425	0.0307
2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa 210-229	0.0307
Galactocerebrosides	0.0307
Myelin/oligodendrocyte glycoprotein peptide aa 46-65	0.0307
Proteolipid Protein peptide aa 150-163	0.0307
Proteolipid Protein peptide aa 265-277	0.0307
Proteolipid Protein peptide aa 80-99	0.0307
60 kDa. Heat Shock Protein peptide aa 210-229	0.0323
Proteolipid Protein peptide aa 137-154	0.0324
2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa 1-20	0.0337
2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa 225-244	0.0337
Myelin-Associated Oligodendrocytic Basic Protein peptide aa 61-80	0.0337
Proteolipid Protein peptide aa 158-166	0.0337
Ceramide 1 phosphate	0.0346
Myelin-Associated Oligodendrocytic Basic Protein peptide aa 136-155	0.0369
Myelin Basic Protein peptide aa 155-178	0.0379
Myelin/oligodendrocyte glycoprotein peptide aa 106-125	0.0392
Proteolipid Protein peptide aa 180-199	0.0408
Myelin Protein 2 peptide aa 121-132	0.0413
Myelin Basic Protein peptide aa 104-123	0.0419
70 kDa. Heat Shock Protein	0.0421
Non h fatty acid ceramide	0.0421
Myelin-Associated Glycoprotein	0.0452
Myelin Basic Protein peptide aa 143-168	0.0452
2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa 91-110	0.047
2',3'-cyclic nucleotide 3'-phosphodiesterase peptide aa 181-199	0.0476
70 kDa. Heat Shock Protein peptide aa 255-275	0.0486
Brain ceramides	0.0486
Myelin Protein 2 peptide aa 46-65	0.0496

Supplementary Table 5:

<b>Treatment</b>	<b>Incidence</b>	<b>Mean day of onset (mean <math>\pm</math> SD)</b>	<b>Mean maximum score (mean <math>\pm</math> SD)</b>
<b>CD4<sup>+</sup> Control</b>	7 of 7 (100 %)	12.3 $\pm$ 1.9	2.7 $\pm$ 1.0
<b>CD4<sup>+</sup> TCDD</b>	3 of 6 (57 %)	13.3 $\pm$ 0.6	0.7 $\pm$ 0.8*
<b>CD4<sup>+</sup>CD25<sup>-</sup> TCDD</b>	3 of 4 (75 %)	11.0 $\pm$ 0.0	2.6 $\pm$ 1.8

Naïve C57BL/6 mice received CD4<sup>+</sup> or CD4<sup>+</sup>CD25<sup>-</sup> T cells ( $5 \times 10^6$ ) purified from TCDD or control treated mice 10 days after immunization with MOG<sub>35-55</sub>/CFA. 24 h later EAE was induced in the recipient mice with MOG<sub>35-55</sub>/CFA, and the mice were monitored for EAE development. Statistical analysis was performed by comparing groups using one-way analysis of variance.

\*  $P < 0.05$  vs CD4<sup>+</sup> control group.

Supplementary Table 6:

<b>Treatment</b>	<b>Incidence</b>	<b>Mean day of onset (mean <math>\pm</math> SD)</b>	<b>Mean maximum score (mean <math>\pm</math> SD)</b>
<b>WT CD4<sup>+</sup> Control</b>	4 of 4 (100 %)	13.3 $\pm$ 2.1	2.1 $\pm$ 1.0
<b>WT CD4<sup>+</sup> TCDD</b>	2 of 4 (50 %)	13.0 $\pm$ 0.0	0.8 $\pm$ 1.0*
<b>DNTGFbRII CD4<sup>+</sup> TCDD</b>	4 of 4 (100 %)	14.0 $\pm$ 1.0	2.6 $\pm$ 1.8

WT or DNTGFbRII mice received CD4<sup>+</sup> T cells ( $5 \times 10^6$ ) purified from TCDD or control treated mice 10 days after immunization with MOG<sub>35-55</sub>/CFA. 24 h later EAE was induced in the recipient mice with MOG<sub>35-55</sub>/CFA, and the mice were monitored for EAE development. Statistical analysis was performed by comparing groups using one-way analysis of variance.

\*  $P < 0.05$  vs CD4<sup>+</sup> control group.

Supplementary Table 7:

<b>Treatment</b>	<b>Incidence</b>	<b>Mean day of onset (mean <math>\pm</math> SD)</b>	<b>Mean maximum score (mean <math>\pm</math> SD)</b>
<b>WT</b>	9 of 9 (100 %)	15.7 $\pm$ 1.9	2.2 $\pm$ 0.9
<b>AHR-d</b>	9 of 9 (100 %)	13.3 $\pm$ 1.1	3.3 $\pm$ 0.8*

EAE was induced in C57BL/6 (WT) or AHR-d mice with MOG<sub>35-55</sub>/CFA and the mice were monitored for EAE development. Statistical analysis was performed by comparing groups using Student's *t*-test.

\*  $P < 0.0295$  vs WT group.

Supplementary Table 8:

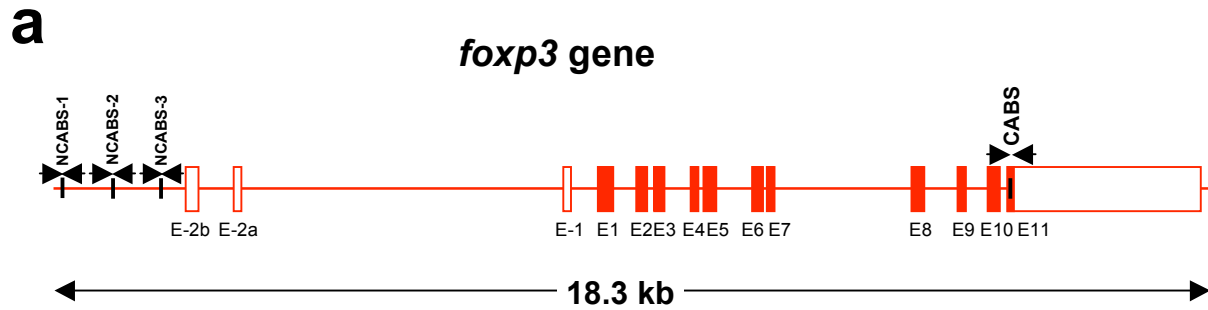
<b>Treatment</b>	<b>Incidence</b>	<b>Mean day of onset (mean <math>\pm</math> SD)</b>	<b>Mean maximum score (mean <math>\pm</math> SD)</b>
<b>Control</b>	9 of 9 (100 %)	15.6 $\pm$ 4.7	2.61 $\pm$ 1.5
<b>ITE</b>	8 of 9 (89 %)	16.25 $\pm$ 3.8	2.11 $\pm$ 1.6

C57BL/6 mice were treated with PBS (Control) or ITE, immunized with MOG<sub>35-55</sub> peptide in CFA and monitored for EAE development.

Supplementary Table 9:

<b>Treatment</b>	<b>Incidence</b>	<b>Mean day of onset (mean <math>\pm</math> SD)</b>	<b>Mean maximum score (mean <math>\pm</math> SD)</b>
<b>Control</b>	11 of 14 (79 %)	13.7 $\pm$ 1.9	2 $\pm$ 1.4
<b>FICZ</b>	12 of 15 (80 %)	13.3 $\pm$ 1.5	2.7 $\pm$ 1.8

Mice were treated with PBS (Control) or ITE, immunized with MOG<sub>35-55</sub> peptide in CFA and monitored for EAE development.



**b**

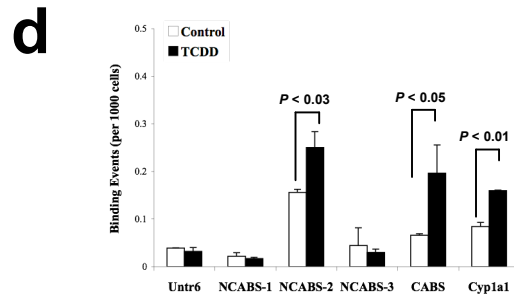
**CABS**

Zebrafish	AGAATGCGGTTTCGACATAACCTCAGCCTTCATAAGTGCTT <b>TTGTGCGTGT</b> GAAGGAAGGA
Human	AGAACGCCATCCGCCACAACCTGAGTCTGCACAAGTGCTT <b>TTGTGCGGGT</b> GGAGAGCGAGA
Mouse	13205 AGAATGCCATCCGCCACAACCTGAGCCTGCACAAGTGCTT <b>TTGTGCGAGT</b> GGAGAGCGAGA 13264
	**** * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
Zebrafish	AAGGTTCAAGTTGGACTGTGGATGAAGAGGAATTTCTTAGAAGAAAAGGTCAA
Human	AGGGGGCTGTGTGGACCGTGGATGAGCTGGAGTTCGCAAGAAACGGAGCCAG
Mouse	13265 AGGGAGCAGTGTGGACCGTAGATGAATTTGAGTTTCGCAAGAAGAGGAGCCAA 14317
	* * * * * * * * * * * * * * * * * * * * * * * * * * * * * *

**c**

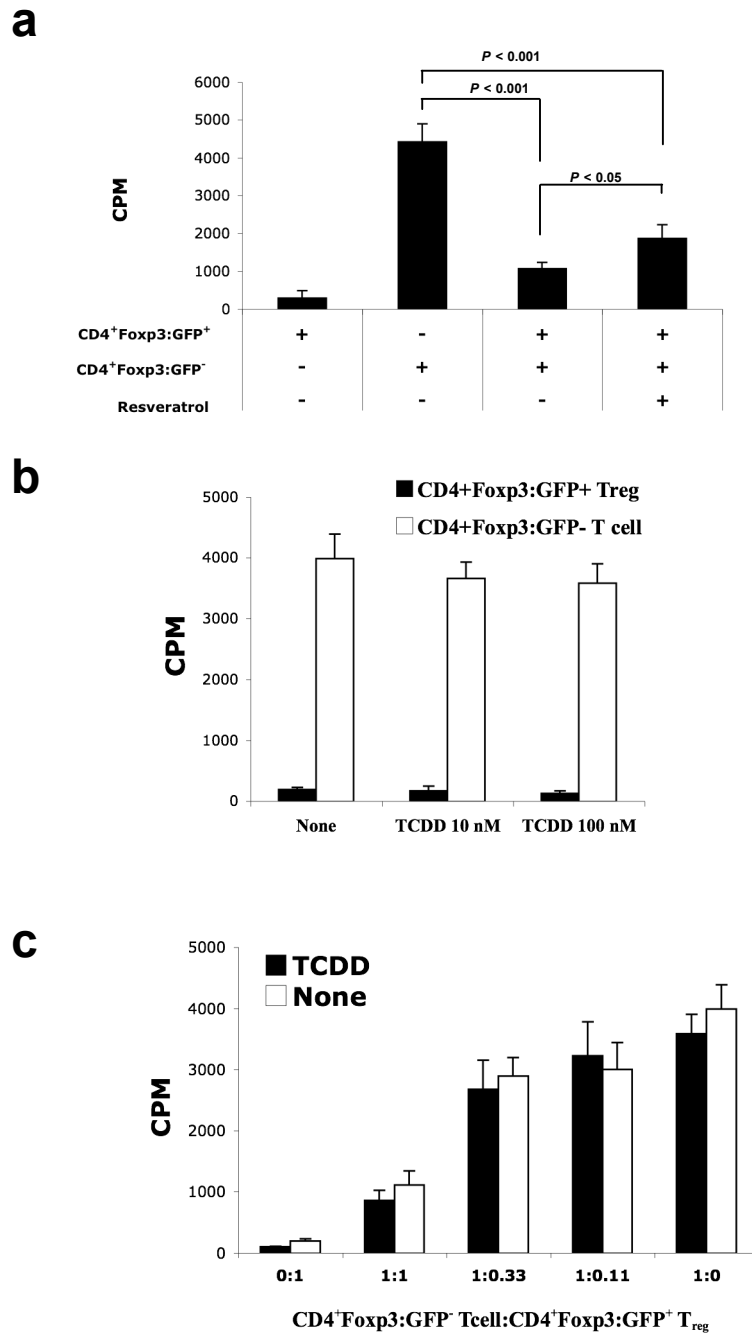
**NCABS**

NCABS-1 -2269	TCCTCTCAACTCAGGAC
NCABS-2 -1596	GGACACGCAGC
NCABS-3 -800	TGTGCGTGTTA

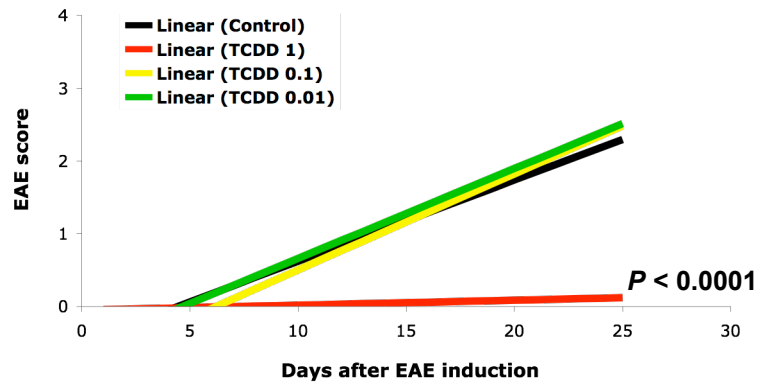


Supplementary Figure 1

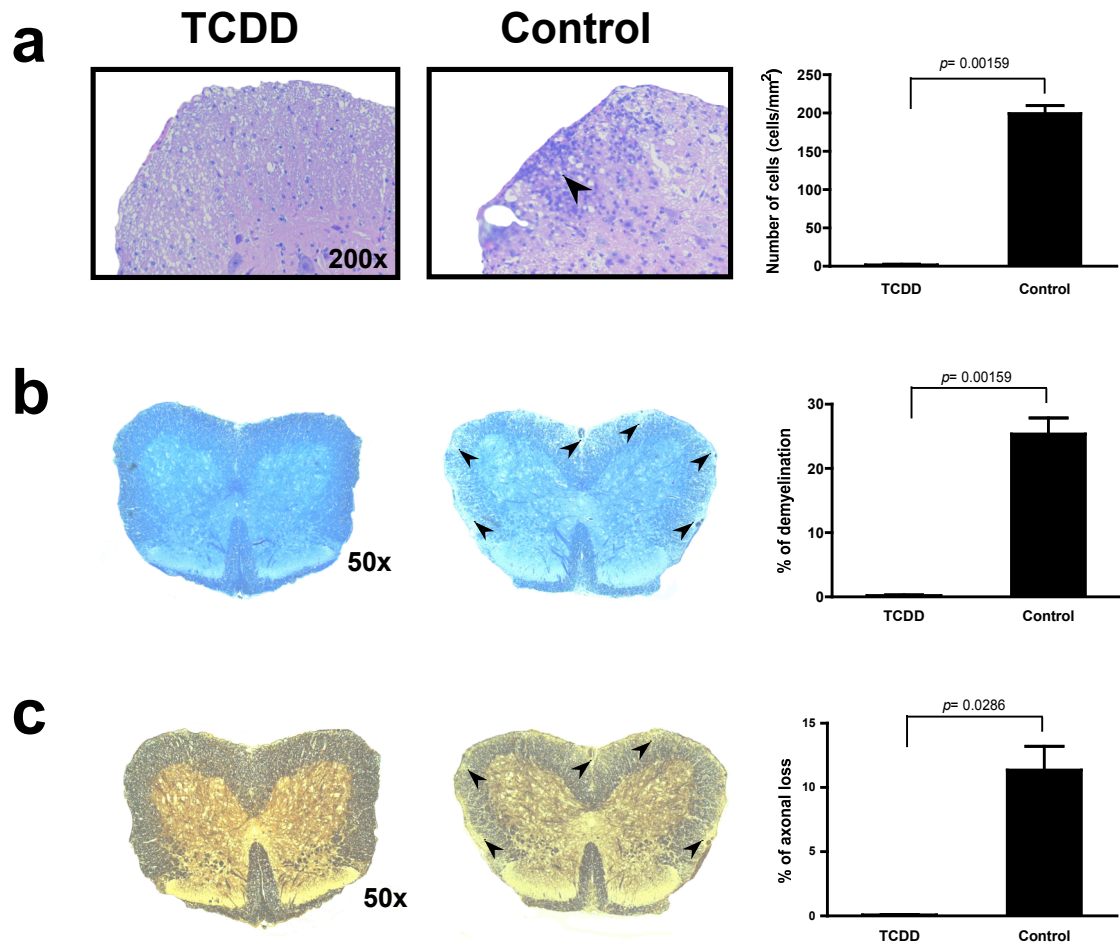




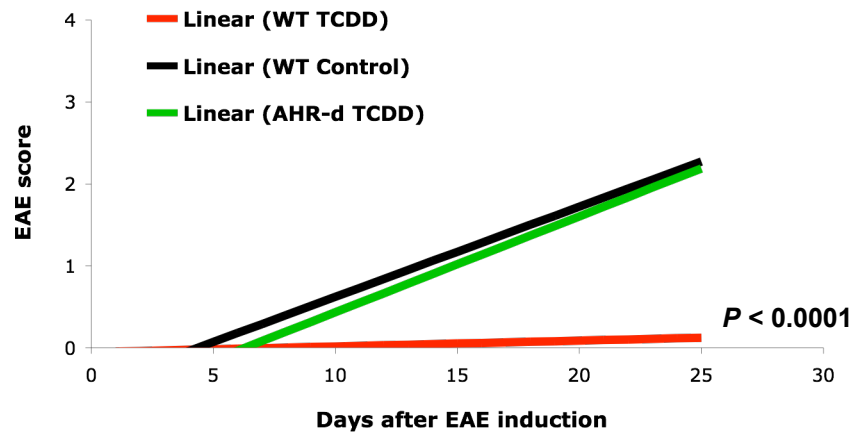
Supplementary Figure 2



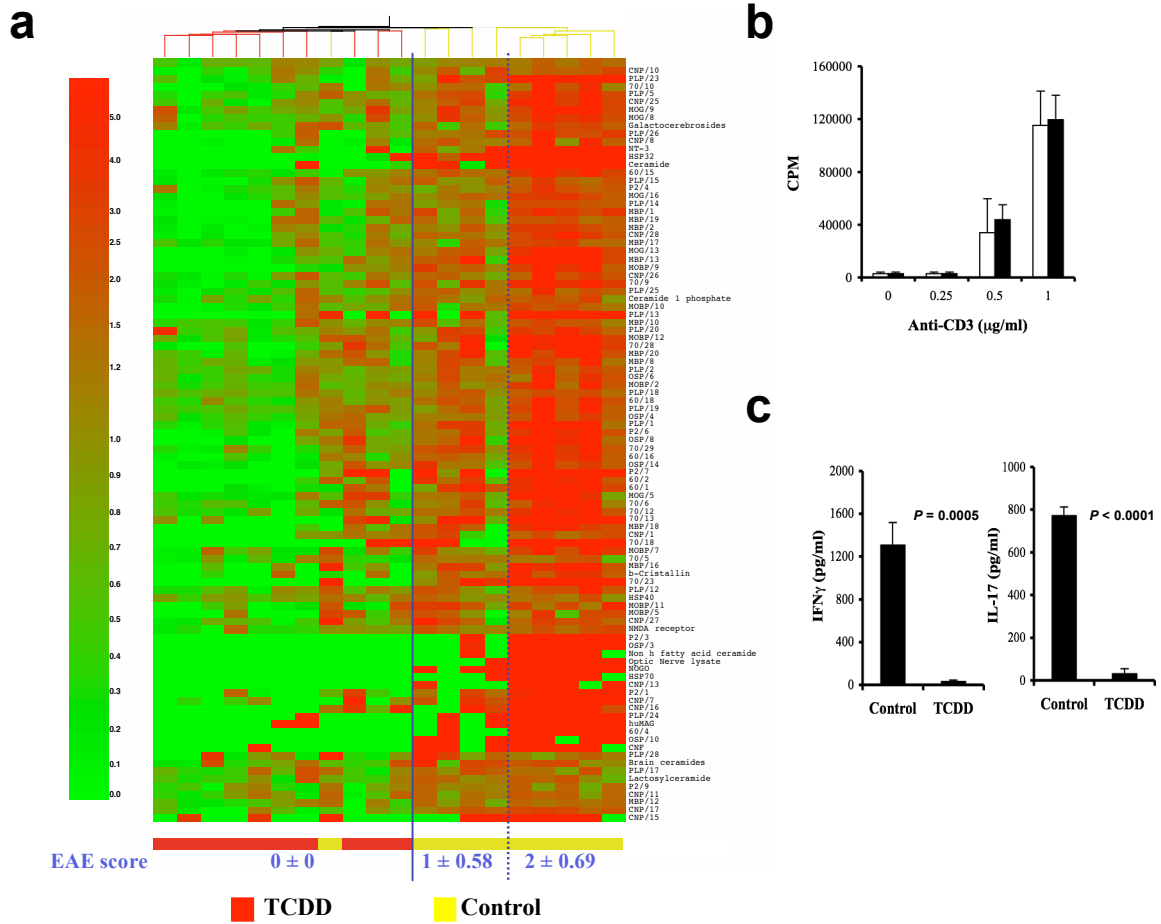
Supplementary Figure 3



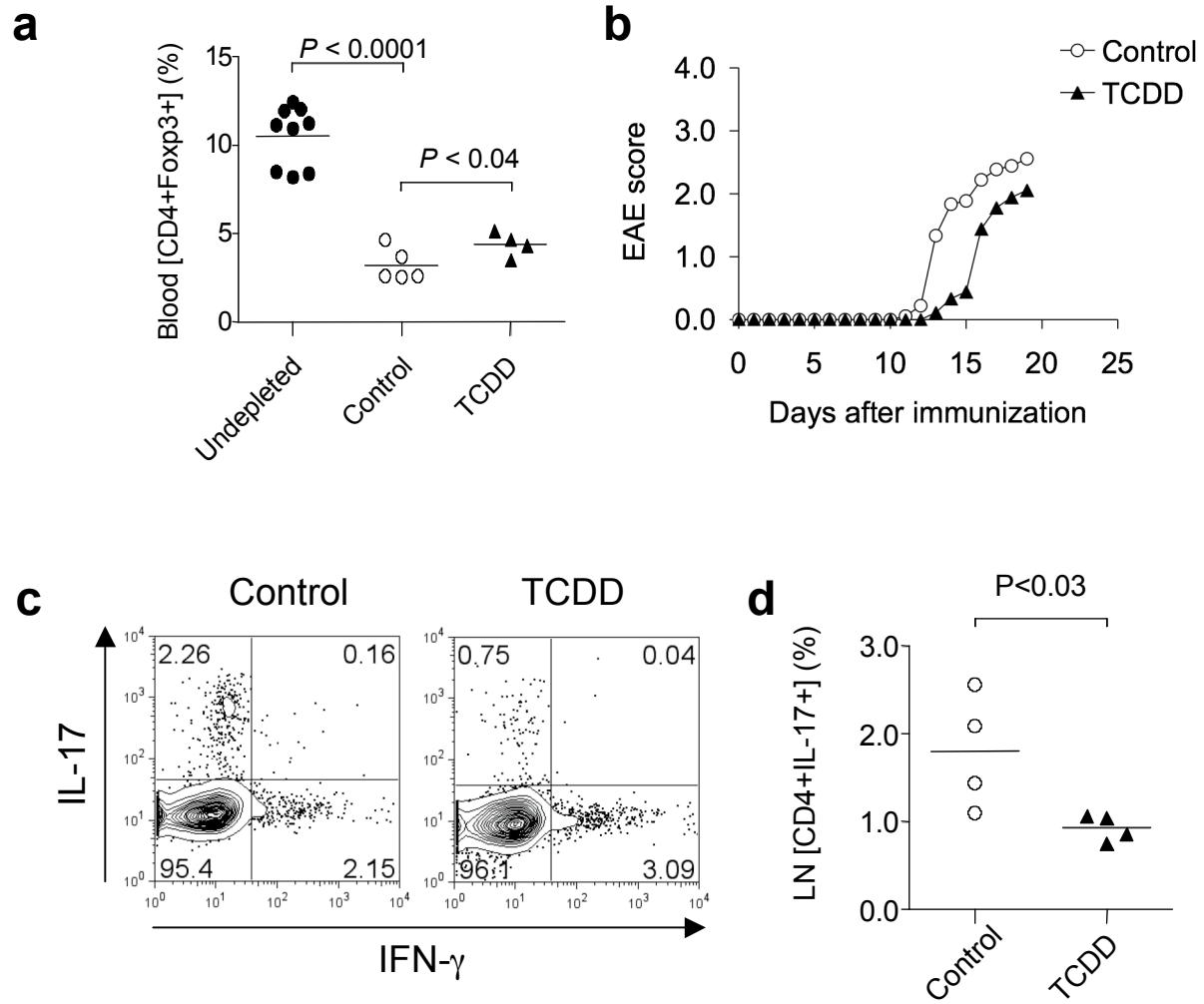
Supplementary Figure 4



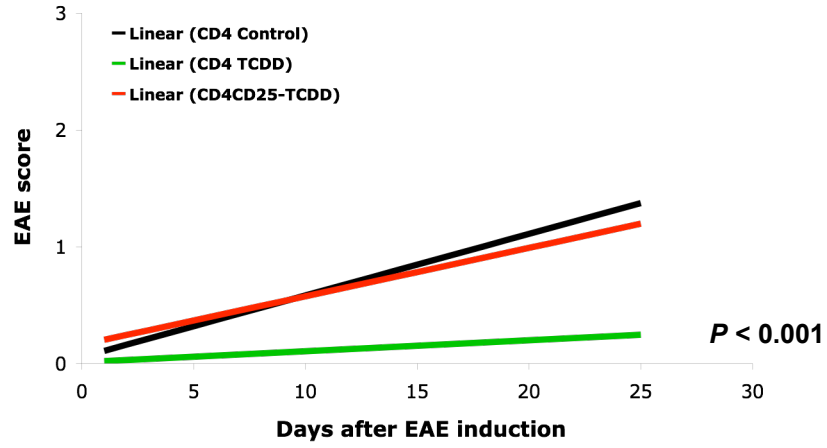
Supplementary Figure 5



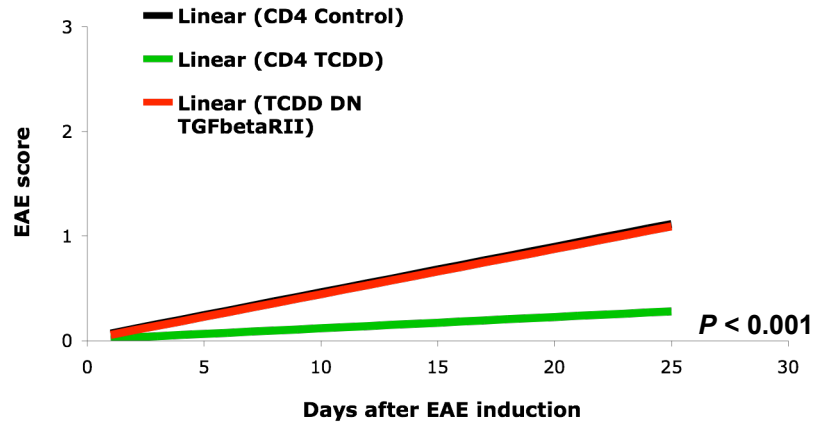
Supplementary Figure 6



Supplementary Figure 7

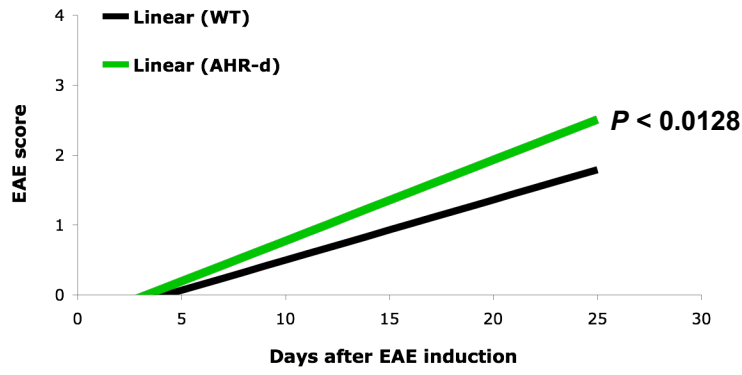


Supplementary Figure 8

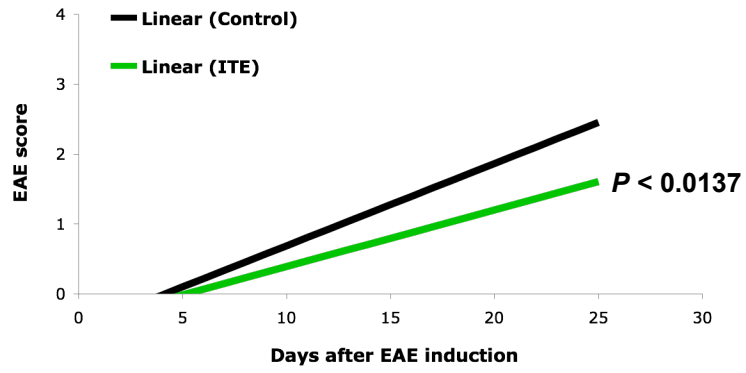


Supplementary Figure 9

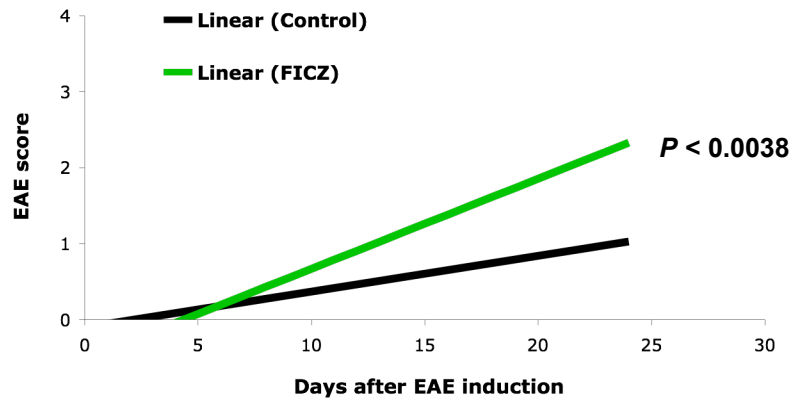




Supplementary Figure 10



Supplementary Figure 11



Supplementary Figure 12

## Legends to Supplementary Figures

**Supplementary Figure 1. AHR binding sites in the *foxp3* locus.** (a) Schematic representation of the *foxp3* gene. Arrows indicate location of PCR primers used in ChIP assays, exons are depicted in red, with their number indicated below them. (b) Sequence comparison of FoxP3 genes of zebrafish, human and mouse around the CABS. The stars indicate identity. (c) Sequences corresponding to NCABS-1, -2 and -3. (d) ChIP analysis of the interaction of AHR to the CABS and NCABS in *foxp3* and *cyp1a1* in thymic CD4<sup>+</sup> T cells from TCDD- or control-treated mice.

**Supplementary Figure 2. Effects of AHR modulation on pre-existing T<sub>reg</sub>.** (a) CD4<sup>+</sup> Foxp3:GFP<sup>+</sup> T<sub>reg</sub> were FACS-sorted from naive Foxp3<sup>gfp</sup> mice and the effect of AHR-inactivation with resveratrol on the suppressive activity was assayed using CD4<sup>+</sup> Foxp3:GFP<sup>-</sup> cells activated with antibodies to CD3 as effector T cells in the presence of resveratrol. Cell proliferation is indicated as cpm + s.d. in triplicate wells. (b) CD4<sup>+</sup> Foxp3:GFP<sup>+</sup> T<sub>reg</sub> and CD4<sup>+</sup> Foxp3:GFP<sup>-</sup> T cells were FACS-sorted from naive Foxp3<sup>gfp</sup> mice and the effect of AHR activation with TCDD on the proliferation was studied. Cell proliferation is indicated as cpm + s.d. in triplicate wells. (c) CD4<sup>+</sup> Foxp3:GFP<sup>+</sup> T<sub>reg</sub> were FACS-sorted from naive Foxp3<sup>gfp</sup> mice and the effect of AHR-activation with TCDD on the suppressive activity was assayed using CD4<sup>+</sup> Foxp3:GFP<sup>-</sup> cells activated with antibodies to CD3 as effector T cells in the presence of resveratrol. Cell proliferation is indicated as cpm + s.d. in triplicate wells.

**Supplementary Figure 3. Dose-dependent suppression of EAE by TCDD.** Linear regression analysis of EAE in C57BL/6 mice treated with 1, 0.1 or 0.01 µg/mouse of

TCDD, or with the vehicle corn oil (control).  $P < 0.0001$  when the slope of the TCDD 1  $\mu\text{g}$  group was compared to that of the Control, TCDD 0.1  $\mu\text{g}$  or TCDD 0.01  $\mu\text{g}$  groups.

**Supplementary Figure 4. AHR activation by TCDD inhibits CNS inflammation, demyelination and axonal loss.** Quantification of the cellular infiltrate, demyelination and axonal loss on the spinal cord of TCDD-treated and control mice. Spinal cords were taken on day 19 after EAE induction and stained with hematoxylin & eosin, luxol fast blue or silver stain to quantify the cellular infiltrate (a), demyelination (b) and axonal loss (c), respectively. The effect of TCDD-treatment was analyzed using Student's *t*-test.

**Supplementary Figure 5. Inhibition of EAE by TCDD is mediated by AHR.** Linear regression analysis of EAE in WT and AHR-d mice treated with 1  $\mu\text{g}/\text{mouse}$  of TCDD or corn oil (Control).  $P < 0.0001$  when the slope of the WT TCDD group was compared to that of the WT Control, AHR-d TCDD groups.

**Supplementary Figure 6. Inhibition of EAE by TCDD is mediated by AHR.** (a) Heatmap depicting the antibody response to myelin antigens on day 21 after EAE induction as measured on antigen microarrays. Each column represents a serum sample, color-coded at the bottom to indicate whether it corresponds to a TCDD or control sample. Only significantly down-regulated antibody reactivities are shown ( $n = 10$ , *t*-test FDR  $< 0.05$ ), according to the colorimetric scale on the right. (b) Proliferative response to antibodies to CD3 of lymph node cells taken from TCDD or control treated animals 10 days after immunization with MOG<sub>35-55</sub>/CFA. Cell

proliferation is indicated as cpm + s.d. in triplicate wells. (c) Recall cytokine response to MOG<sub>35-55</sub> of CD4<sup>+</sup>Foxp3:GFP<sup>-</sup> lymph node cells taken from TCDD or control treated Foxp3<sup>gfp</sup> mice 10 days after immunization with MOG<sub>35-55</sub>/CFA. Cytokine secretion is expressed as pg/ml in triplicate wells.

**Supplementary Figure 7. Effect of AHR activation by TCDD on T<sub>reg</sub> depleted mice.**

Foxp3<sup>gfp</sup> mice were treated with an antibody to CD25 (PC61) to deplete T<sub>reg</sub> cells, treated with TCDD (1 µg/mouse) or oil and then EAE was induced with MOG<sub>35-55</sub>/CFA. (a) Foxp3:GFP<sup>+</sup> fraction in the CD4<sup>+</sup> T cell gate in the peripheral blood. Significantly higher levels CD4<sup>+</sup> Foxp3:GFP<sup>+</sup> T<sub>reg</sub> were detected in the TCDD-treated group 7 days after treatment with TCDD ( $P < 0.04$ , Student's *t*-test,  $n = 4-5$ ). (b) Clinical EAE scores. TCDD-treated mice showed a significant delay in the onset of EAE ( $P = 0.03$ , Student's *t*-test,  $n = 9$ ). (c and d) Draining lymph node cells were recovered on day 18, stimulated with PMA/ionomycin and stained for CD4 and intracellular IL-17 and IFN $\gamma$ . The numbers in the quadrants show percentages of cytokine positive cells in the CD4<sup>+</sup>Foxp3:GFP<sup>-</sup> T cell gate. Treatment with TCDD led to a significant decrease in the frequency of CD4<sup>+</sup> IL-17<sup>+</sup> T cells ( $P = 0.03$ , Student's *t*-test,  $n = 4$ ).

**Supplementary Figure 8. Transfer of protection of EAE by TCDD with CD4<sup>+</sup> T cells.** Linear regression analysis of EAE in WT mice transferred with CD4<sup>+</sup> T cells prepared from control (corn oil) treated mice (CD4 Control), or with CD4<sup>+</sup> T cells (CD4 TCDD) or CD4<sup>+</sup>CD25<sup>-</sup> (CD4CD25- TCDD) T cells from TCDD-treated mice.

$P < 0.001$  when the slope of the CD4 TCDD group was compared to that of the CD4 Control or CD4CD25- TCDD groups.

**Supplementary Figure 9. CD4<sup>+</sup>-transferred protection from EAE requires TGFbRII signalling.** Linear regression analysis of EAE in WT mice and DN TGFbeta RII transferred with CD4<sup>+</sup> T cells prepared from TCDD or control (corn oil) treated mice.  $P < 0.001$  when the slope of the CD4 TCDD group was compared to that of the CD4 Control or TCDD DN TGFbetaRII groups.

**Supplementary Figure 10. Augmented EAE in AHR-d mice.** Linear regression analysis of EAE in WT and AHR-d mice (control).  $P < 0.0128$  when the slopes of the AHR-d and WT groups were compared.

**Supplementary Figure 11. Amelioration of EAE by the AHR endogenous ligand ITE.** Linear regression analysis of EAE in mice treated with ITE (100  $\mu\text{g}/\text{mouse}/\text{day}$ ) or vehicle (Control).  $P < 0.0137$  when the slopes of the ITE and Control groups were compared.

**Supplementary Figure 12. Exacerbation of EAE by the AHR endogenous ligand FICZ.** Linear regression analysis of EAE in mice treated with FICZ (1  $\mu\text{g}/\text{mouse}$ ) or vehicle (corn oil).  $P < 0.0038$  when the slopes of the FICZ and Control groups were compared.