Additional file 1

Microglia-specific deletion of histone deacetylase 3 promotes inflammation resolution, white matter integrity, and functional recovery in a mouse model of traumatic brain injury

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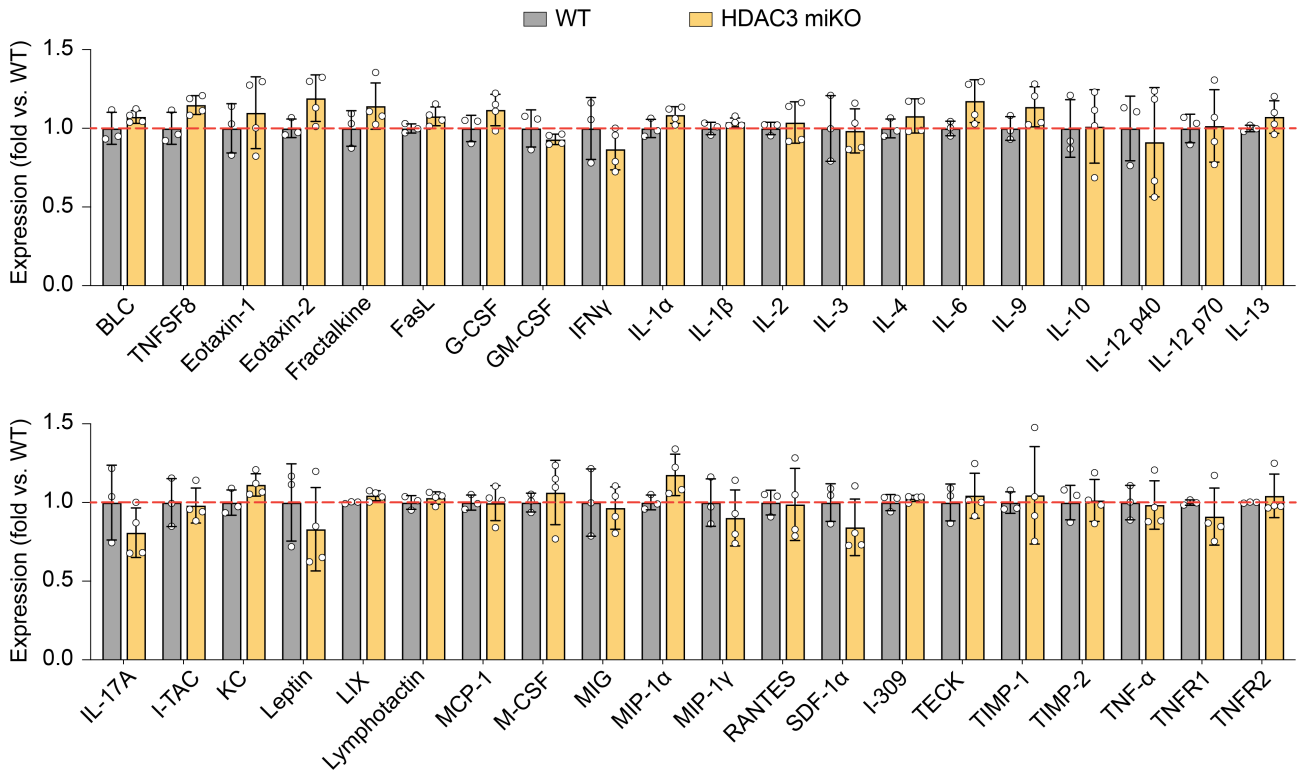

Figure S1. Microglia-specific HDAC3 knockout does not alter baseline inflammation level in the homeostatic brain.

HDAC3 miKO mice and WT mice received tamoxifen treatment for 5 days, followed by a 30-day latency. The content of 40 inflammatory cytokines was measured in the brain using an antibody array, and the data were expressed as fold changes versus WT mice. n=3 (WT) or 4 (HDAC3 miKO) mice per group. $p>0.05$ between HDAC3 miKO mice and WT mice for all markers.

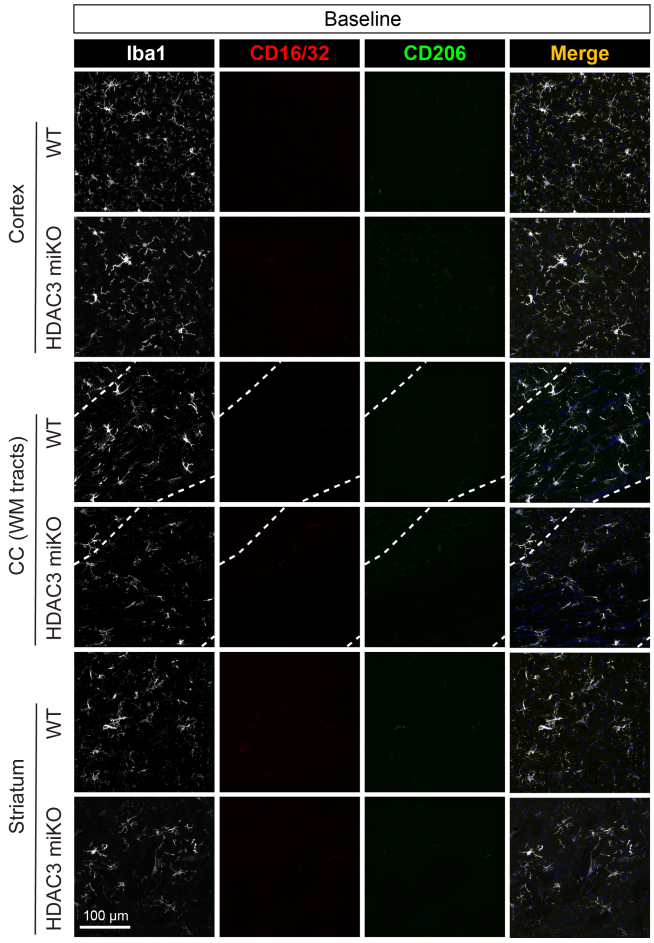

Figure S2. Microglial expression of activation markers under baseline conditions (related to Fig. 2).

The phenotype of microglia was examined in HDAC3 miKO mice and WT control mice under baseline conditions by triple-label immunostaining of CD16/32, CD206, and Iba1. Shown are images taken from the cortex, corpus callosum (CC) white matter (WM) tracts, and striatum, representative of 3 WT mice and 2 HDAC3 miKO mice. Dashed line, the boundary of CC. All microglia displayed morphology indicative of a resting/quiescent state, and there was no detectable immunosignal of the microglia activation marker CD16/32 or CD206 in the regions examined.

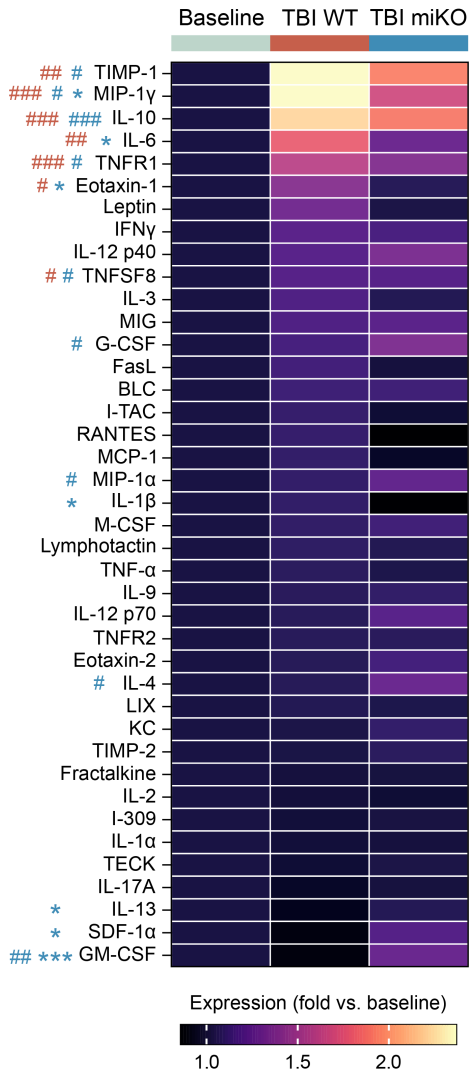

Figure S3. HDAC3 miKO promotes the resolution of inflammation in the brain after TBI (related to Fig. 3).

The content of 40 inflammatory cytokines was measured in the brain of HDAC3 miKO mice and WT mice 5 days after TBI. Heatmap shows the mean expression level in each group. The baseline control group was pooled from both WT mice and HDAC3 miKO mice, between which there was no difference (see Figure S1). n=6-7 mice per group. $^{\#}p<0.05$, $^{\#\#}p<0.01$, $^{\#\#\#}p<0.001$ TBI vs. baseline control. *p<0.05, ***p<0.001 HDAC3 miKO vs. WT after TBI.

Table S1. Key resources

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Antibodies		
CD45 Monoclonal Antibody (30-F11), eFlour 450	eBioscience	48-0451-82
CD11b Monoclonal Antibody (M1/70), APC-eFlour 780	eBioscience	47-0112-82
Ly-6G Monoclonal Antibody (1A8-Ly6g), PE	eBioscience	12-9668-82
CD11c Monoclonal Antibody (N418), PerCP-Cyanine5.5	eBioscience	45-0114-82
CD3 Monoclonal Antibody (17A2), APC	eBioscience	17-0032-82
CD19 Monoclonal Antibody (HIB19), PE-Cyanine7	eBioscience	25-0199-42
Rabbit anti-Iba1	Wako	019-19741
Rat Anti-Mouse CD16/CD32 Clone 2.4G2	BD Biosciences	553142
Mouse MMR/CD206 Antibody	R&D Systems	AF2535
Rabbit Anti-NeuN Antibody	MilliporeSigma	ABN78
Anti-Neurofilament 200 kDa Antibody, clone RT97	MilliporeSigma	MAB5262
Anti-Neurofilament H (NF-H), Nonphosphorylated Antibody (SMI-32)	BioLegend	801701
Rabbit beta Amyloid Polyclonal Antibody (CT695)	ThermoFisher	51-2700
Rat monoclonal Anti-Myelin Basic Protein antibody	Abcam	Ab7349
Chemicals, Peptides, and Recombinant Proteins		
Tamoxifen	Sigma-Aldrich	T5648
Critical Commercial Assays		
Mouse Inflammation Array C1	RayBiotech	AAM-INF-1
M.O.M. (Mouse on Mouse) Immunodetection Kit, Basic	Vector Laboratories	BMK-2202
Neural Tissue Dissociation Kit (T)	Miltenyi Biotec	130-093-231
OneComp eBeads Compensation Beads	ThermoFisher	01-1111-42
Cell Lysis Buffer	Cell Signaling Technology	9803
Halt Protease and Phosphatase Inhibitor Cocktail	ThermoFisher	78842
RNeasy Plus Micro Kit	Qiagen	74034
RT2 First Strand Kit	Qiagen	330401
RT2 SYBR Green qPCR Mastermix	Qiagen	330502
Experimental Models: Organisms/Strains		
Mouse: C57BL/6J	The Jackson Laboratory	Stock No: 000664
Mouse: B6;SJL-Tg(ACTFLPe)9205Dym/J	The Jackson Laboratory	Stock No: 003800
Mouse: B6.129P2(Cg)-*Cx3cr1*$^{tm2.1(cre/ERT2)Litt}$/WganJ	The Jackson Laboratory	Stock No: 021160
Mouse: Hdac3^{LoxP}	This paper	N/A
Oligonucleotides		

Genotyping primer: Cx3cr1^{CreER} common GAA CTA CAA TCC TTT AAG GCT CAC G	Ref. [1]	N/A
Genotyping primer: Cx3cr1^{CreER} wild type GCA GGA CCT CGG GGT AGT CAC	Ref. [1]	N/A
Genotyping primer: Cx3cr1^{CreER} mutant CAC CAG AGA CGG AAA TCC ATC G	Ref. [1]	N/A
Genotyping primer: Hdac3^{LoxP} CTG CCG TGG TAT TGG GAA TG	This paper	N/A
Genotyping primer: Hdac3^{LoxP} AGA AGG GTG CCA GTG GGT	This paper	N/A
qPCR primer: Hdac3 forward CAT CGC CTG GCA TTG ACT CAT	Ref. [2]	N/A
qPCR primer: Hdac3 reverse AAG GCA TTA AGG CTC TTG GTG	Ref. [2]	N/A
qPCR primer: Gapdh forward GTG AAG GTC GGT GTG AAC GG	Ref. [3]	N/A
qPCR primer: Gapdh reverse GTT TCC CGT TGA TGA CCA G	Ref. [3]	N/A
Software and Algorithms		
FlowJo	FlowJo, LLC	N/A
ImageJ	NIH	N/A
Imaris 9.6	Bitplane	N/A
Prism 9	GraphPad	N/A

Table S2. The numbers of mice used in this study

Figure		Fig 1		Fig 2	Fig 3		Fig 5	Fig 4-6
Assay		qPCR	IHC	IHC	Antibody array	Flow cytometry	IHC (β-APP/NF200)	Behavior, IHC, TEM and CAP
0 d	Baseline WT	6	6					
	Baseline miKO	4	5					
3 d	Baseline WT			3				
	Baseline miKO			2				
	TBI WT			6				
	TBI miKO			5				
5 d	Baseline WT				3			
	Baseline miKO				4			
	TBI WT				6	6		
	TBI miKO				6	6		
7 d	Baseline WT						4	
	Baseline miKO						4	
	TBI WT						5	
	TBI miKO						6	
42 d	Baseline WT							18
	Baseline miKO							14
	TBI WT							31
	TBI miKO							30

Table S3. Tissue samples processed in this study

Figure	Assay	Tissue type	Tissue amount per replicate	Number of replicates
1A-1B	Genotyping	Tail biopsy	2-3 mm of tail	N/A
1C-1E	qPCR	Brain Blood	7-13×10^4 cells sorted from brain or 15-20×10^4 cells sorted from blood by FACS	6 mice (WT) 4 mice (miKO)
1F-1G	IHC	Brain	25-µm thick coronal section	6 mice (WT) 5 mice (miKO)
2	IHC	Brain	25-µm thick coronal section	6 mice (WT) 5 mice (miKO)
3A-3B	Antibody array	Brain	Right cerebral hemisphere	7 mice (baseline) 6 mice (TBI WT) 6 mice (TBI miKO)
3C-3D	Flow cytometry	Brain	One cerebral hemisphere	6 mice (WT) 6 mice (miKO)
4	Behavior test	N/A	N/A	See Table S4
5	IHC	Brain	25-µm thick coronal section	See Table S4
6A-6D	TEM	Brain	50-nm section cut from 1-mm^3 tissue blocks harvested from the corpus callosum	4 mice (baseline) 4 mice (TBI WT) 3 mice (TBI miKO)
6E-6G	Electrophysiology	Brain	350-µm thick coronal slice	8 mice (baseline WT) 5 mice (baseline miKO) 8 mice (TBI WT) 8 mice (TBI miKO)

Table S4. Statistics reporting

FIGURE	SAMPLE SIZE (n)	DATA STRUCTURE	TEST USED	STATISTIC	P VALUE
1E (microglia)	6 mice (WT) 4 mice (miKO)	Normal distribution	*t* test	$t_{(8)} = 14.36$	miKO-WT < 0.0001
1E (other brain cells)	6 mice (WT) 4 mice (miKO)	Non-normal distribution	Mann-Whitney test	$U = 6$	miKO-WT = 0.2571
1E (monocytes)	6 mice (WT) 4 mice (miKO)	Normal distribution	*t* test	$t_{(8)} = 2.170$	miKO-WT = 0.0618
1G (cell number)	6 mice (WT) 5 mice (miKO)	Non-normal distribution	Mann-Whitney test	$U = 0$	miKO-WT = 0.0043
1G (cell volume)	6 mice (WT) 5 mice (miKO)	Non-normal distribution	Mann-Whitney test	$U = 4$	miKO-WT = 0.0519
1G (surface area)	6 mice (WT) 5 mice (miKO)	Normal distribution	*t* test	$t_{(9)} = 0.9470$	miKO-WT = 0.3684
1G (sphericity)	6 mice (WT) 5 mice (miKO)	Normal distribution	*t* test	$t_{(9)} = 2.448$	miKO-WT = 0.0368
1G (length A)	6 mice (WT) 5 mice (miKO)	Normal distribution	*t* test	$t_{(9)} = 0.002593$	miKO-WT = 0.9980
1G (length C)	6 mice (WT) 5 mice (miKO)	Normal distribution	*t* test	$t_{(9)} = 0.1690$	miKO-WT = 0.8695
2E (cortex)	6 mice (WT) 5 mice (miKO)	Normal distribution	Two-way ANOVA; Bonferroni *post hoc*	$F_{(1,18)} = 0.1401$	ANOVA p=0.7125 miKO-WT>0.9999 (0-400 μm) miKO-WT=0.8200 (400-800 μm)
2E (CC)	6 mice (WT) 5 mice (miKO)	Normal distribution	Two-way ANOVA; Bonferroni *post hoc*	$F_{(1,18)} = 5.335$	ANOVA p=0.0330 miKO-WT=0.1183 (0-400 μm) miKO-WT=0.4532 (400-800 μm)
2E (striatum)	6 mice (WT) 5 mice (miKO)	Normal distribution	Two-way ANOVA; Bonferroni *post hoc*	$F_{(1,18)} = 0.4746$	ANOVA p=0.4997 miKO-WT>0.9999 (0-400 μm) miKO-WT=0.5287 (400-800 μm)
2F (cortex, 0-400 μm)	6 mice (WT) 5 mice (miKO)	Normal distribution	*t* test (resting) Welch's *t* test (pro) *t* test (int) *t* test (resolving)	$t_{(9)} = 1.912$ (resting) $t_{(5.722)} = 3.505$ (pro) $t_{(9)} = 0.9953$ (int) $t_{(9)} = 2.350$ (resolving)	miKO-WT = 0.0882 (resting) miKO-WT = 0.0138 (pro) miKO-WT = 0.3456 (int) miKO-WT = 0.0433 (resolving)
2F (cortex, 400-800 μm)	6 mice (WT) 5 mice (miKO)	Normal distribution	*t* test (resting) Welch's *t* test (pro) *t* test (int) Welch's *t* test (resolving)	$t_{(9)} = 3.167$ (resting) $t_{(5.637)} = 2.679$ (pro) $t_{(9)} = 1.384$ (int) $t_{(4.665)} = 1.925$ (resolving)	miKO-WT = 0.0114 (resting) miKO-WT = 0.0389 (pro) miKO-WT = 0.1998 (int) miKO-WT = 0.1164 (resolving)
2F (CC, 0-400 μm)	6 mice (WT) 5 mice (miKO)	Normal distribution (resting, int, resolving) Non-normal distribution (pro)	*t* test (resting) Mann-Whitney test (pro) *t* test (int) *t* test (resolving)	$t_{(9)} = 2.957$ (resting) $U = 9$ (pro) $t_{(9)} = 4.446$ (int) $t_{(9)} = 0.2298$ (resolving)	miKO-WT = 0.0160 (resting) miKO-WT = 0.3290 (pro) miKO-WT = 0.0016 (int) miKO-WT = 0.8234 (resolving)
2F (CC, 400-800 μm)	6 mice (WT) 5 mice (miKO)	Normal distribution (resting, pro, resolving)	*t* test (resting) *t* test (pro) Mann-Whitney test (int) *t* test (resolving)	$t_{(9)} = 0.3967$ (resting) $t_{(9)} = 1.694$ (pro) $U = 12$ (int) $t_{(9)} = 0.8914$ (resolving)	miKO-WT = 0.7009 (resting) miKO-WT = 0.1245 (pro) miKO-WT = 0.6623 (int) miKO-WT = 0.3959 (resolving)

		Non-normal distribution (int)			
2F (striatum, 0-400 μm)	6 mice (WT) 5 mice (miKO)	Normal distribution (resting, int, resolving) Non-normal distribution (pro)	*t* test (resting) Mann-Whitney test (pro) *t* test (int) *t* test (resolving)	$t_{(9)} = 1.039$ (resting) $U = 0$ (pro) $t_{(9)} = 0.5410$ (int) $t_{(9)} = 3.105$ (resolving)	miKO-WT = 0.3260 (resting) miKO-WT = 0.0043 (pro) miKO-WT = 0.6016 (int) miKO-WT = 0.0126 (resolving)
2F (striatum, 400-800 μm)	6 mice (WT) 5 mice (miKO)	Normal distribution	*t* test (resting) *t* test (pro) *t* test (int) *t* test (resolving)	$t_{(9)} = 3.519$ (resting) $t_{(9)} = 1.744$ (pro) $t_{(9)} = 1.008$ (int) $t_{(9)} = 1.618$ (resolving)	miKO-WT = 0.0065 (resting) miKO-WT = 0.1151 (pro) miKO-WT = 0.3397 (int) miKO-WT = 0.1400 (resolving)
3B	See Figure S3 statistics				
3D (neutrophil)	6 mice (WT) 6 mice (miKO)	Non-normal distribution	Mann-Whitney test	$U = 14$	miKO- WT = 0.5887
3D (dendritic cell)	6 mice (WT) 6 mice (miKO)	Non-normal distribution	Mann-Whitney test	$U = 12$	miKO- WT = 0.3939
3D (microglia)	6 mice (WT) 6 mice (miKO)	Normal distribution	*t* test	$t_{(10)} = 6.674$	miKO-WT < 0.0001
3D (macrophage)	6 mice (WT) 6 mice (miKO)	Normal distribution	*t* test	$t_{(10)} = 0.8027$	miKO-WT = 0.4408
3D (T cell)	6 mice (WT) 6 mice (miKO)	Normal distribution	*t* test	$t_{(10)} = 1.839$	miKO-WT = 0.0958
3D (B cell)	6 mice (WT) 6 mice (miKO)	Normal distribution	*t* test	$t_{(10)} = 1.514$	miKO-WT = 0.1610
4A	9 mice (Baseline WT) 9 mice (Baseline miKO) 13 mice (TBI WT) 13 mice (TBI miKO)	Normal distribution	Two-way RM ANOVA; Bonferroni *post hoc*	$F_{(3, 40)} = 167.4$	ANOVA p < 0.0001 Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO < 0.0001 TBI miKO-TBI WT = 0.1292 Pre Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT > 0.9999 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT > 0.9999 1 day Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO < 0.0001 TBI miKO-TBI WT > 0.9999 2 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO < 0.0001 TBI miKO-TBI WT > 0.9999 3 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO < 0.0001 TBI miKO-TBI WT > 0.9999 5 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001

					TBI miKO-Baseline miKO < 0.0001 TBI miKO-TBI WT = 0.0338 7 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO < 0.0001 TBI miKO-TBI WT = 0.0338 14 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO < 0.0001 TBI miKO-TBI WT = 0.0204 21 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0032 TBI miKO-TBI WT = 0.4346 28 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0086 TBI miKO-TBI WT = 0.2034 35 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0089 TBI miKO-Baseline miKO = 0.3892 TBI miKO-TBI WT = 0.3008
4B (touch)	9 mice (Baseline WT) 9 mice (Baseline miKO) 13 mice (TBI WT) 13 mice (TBI miKO)	Normal distribution	Two-way RM ANOVA; Bonferroni *post hoc*	$F_{(3, 40)} = 17.10$	ANOVA p < 0.0001 Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0011 TBI miKO-TBI WT = 0.3624 Pre Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT > 0.9999 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT > 0.9999 3 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO < 0.0001 TBI miKO-TBI WT < 0.0001 5 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO < 0.0001 TBI miKO-TBI WT > 0.9999 7 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0003 TBI miKO-Baseline miKO = 0.0279 TBI miKO-TBI WT = 0.7382

					14 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.1012 TBI miKO-Baseline miKO = 0.1729 TBI miKO-TBI WT > 0.9999 21 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0795 TBI miKO-Baseline miKO = 0.4160 TBI miKO-TBI WT > 0.9999 28 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.7544 TBI miKO-Baseline miKO = 0.5184 TBI miKO-TBI WT > 0.9999 35 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.5424 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT > 0.9999
4B (remove)	9 mice (Baseline WT) 9 mice (Baseline miKO) 13 mice (TBI WT) 13 mice (TBI miKO)	Normal distribution	Two-way RM ANOVA; Bonferroni *post hoc*	$F_{(3, 40)} = 14.98$	ANOVA p < 0.0001 Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0030 TBI miKO-TBI WT = 0.3996 Pre Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT > 0.9999 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT > 0.9999 3 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO < 0.0001 TBI miKO-TBI WT < 0.0001 5 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO < 0.0001 TBI miKO-TBI WT > 0.9999 7 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0002 TBI miKO-Baseline miKO = 0.0174 TBI miKO-TBI WT = 0.7040 14 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.1240 TBI miKO-Baseline miKO = 0.2424 TBI miKO-TBI WT > 0.9999 21 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0316

					TBI miKO-Baseline miKO = 0.5485 TBI miKO-TBI WT = 0.7488 28 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.6076 TBI miKO-Baseline miKO = 0.6157 TBI miKO-TBI WT > 0.9999 35 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.4935 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT > 0.9999
4C	9 mice (Baseline WT) 9 mice (Baseline miKO) 13 mice (TBI WT) 13 mice (TBI miKO)	Normal distribution	Two-way RM ANOVA; Bonferroni *post hoc*	$F_{(3, 40)} = 109.6$	ANOVA p < 0.0001 Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO < 0.0001 TBI miKO-TBI WT = 0.0014 Pre Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT > 0.9999 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT > 0.9999 3 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO < 0.0001 TBI miKO-TBI WT = 0.5081 5 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO < 0.0001 TBI miKO-TBI WT > 0.9999 7 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO < 0.0001 TBI miKO-TBI WT = 0.0144 14 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO < 0.0001 TBI miKO-TBI WT = 0.0023 21 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO < 0.0001 TBI miKO-TBI WT = 0.0331 28 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO < 0.0001 TBI miKO-TBI WT < 0.0001

					35 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO < 0.0001 TBI miKO-TBI WT = 0.0037
4D (forepaw)	9 mice (Baseline WT) 9 mice (Baseline miKO) 13 mice (TBI WT) 13 mice (TBI miKO)	Normal distribution	Mixed-effects model (REML)	$F_{(3, 40)} = 42.43$	ANOVA p < 0.0001 Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0028 TBI miKO-TBI WT < 0.0001 Pre Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT > 0.9999 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT > 0.9999 3 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0003 TBI miKO-TBI WT < 0.0001 5 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0007 TBI miKO-TBI WT < 0.0001 7 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0085 TBI miKO-TBI WT < 0.0001 14 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0003 TBI miKO-TBI WT = 0.0002 21 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0919 TBI miKO-TBI WT < 0.0001 28 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.2445 TBI miKO-TBI WT = 0.0002 35 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.1098 TBI miKO-TBI WT = 0.0211
4D (hindpaw)	9 mice (Baseline WT)	Normal distribution	Mixed-effects model (REML)	$F_{(3, 40)} = 42.87$	ANOVA p < 0.0001 Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001

	9 mice (Baseline miKO) 13 mice (TBI WT) 13 mice (TBI miKO)				TBI miKO-Baseline miKO = 0.0003 TBI miKO-TBI WT < 0.0001 Pre Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT > 0.9999 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT > 0.9999 3 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0057 TBI miKO-TBI WT = 0.0005 5 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0155 TBI miKO-TBI WT < 0.0001 7 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0054 TBI miKO-TBI WT = 0.0477 14 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0015 TBI miKO-TBI WT = 0.0089 21 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.6530 TBI miKO-TBI WT < 0.0001 28 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0039 TBI miKO-TBI WT = 0.1273 35 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0003 TBI miKO-Baseline miKO = 0.0551 TBI miKO-TBI WT = 0.6653
4E (learning)	7 mice (Baseline WT) 6 mice (Baseline miKO) 13 mice (TBI WT) 13 mice (TBI miKO)	Normal distribution	Two-way RM ANOVA; Bonferroni *post hoc*	$F_{(3, 35)} = 7.514$	ANOVA p = 0.0005 Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0720 TBI miKO-Baseline miKO = 0.0432 TBI miKO-TBI WT = 0.1880 29 days Baseline miKO-Baseline WT = 0.0719 TBI WT-Baseline WT > 0.9999 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT = 0.5646

					30 days Baseline miKO-Baseline WT = 0.8350 TBI WT-Baseline WT = 0.0036 TBI miKO-Baseline miKO = 0.3235 TBI miKO-TBI WT > 0.9999 31 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT > 0.9999 TBI miKO-Baseline miKO = 0.0610 TBI miKO-TBI WT = 0.2238 32 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT > 0.9999 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT > 0.9999 33 days Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT > 0.9999 TBI miKO-Baseline miKO = 0.4299 TBI miKO-TBI WT > 0.9999
4E (target quadrant time)	7 mice (Baseline WT) 6 mice (Baseline miKO) 13 mice (TBI WT) 13 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(3, 35)} = 6.370$	ANOVA p = 0.0015 Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0349 TBI miKO-Baseline miKO = 0.1083 TBI miKO-TBI WT = 0.3615
4E (platform crossing)	7 mice (Baseline WT) 6 mice (Baseline miKO) 13 mice (TBI WT) 13 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(3, 35)} = 3.912$	ANOVA p = 0.0165 Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0401 TBI miKO-Baseline miKO = 0.6230 TBI miKO-TBI WT > 0.9999
4E (speed)	7 mice (Baseline WT) 6 mice (Baseline miKO) 13 mice (TBI WT) 13 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(3, 35)} = 0.2992$	ANOVA p = 0.8257 Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT > 0.9999 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT > 0.9999
5C	5 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	Two-way ANOVA; Bonferroni *post hoc*	$F_{(1, 18)} = 10.42$	ANOVA p = 0.0047 TBI miKO - TBI WT = 0.0004 (CC) TBI miKO - TBI WT > 0.9999 (STR)
5E (7 days cortex)	4 mice (Baseline WT) 4 mice (Baseline miKO) 5 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(3, 15)} = 3.475$	ANOVA p = 0.0428 Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0938 TBI miKO-Baseline miKO = 0.8406 TBI miKO-TBI WT > 0.9999
5E (7 days CC)	4 mice (Baseline WT)	Non-normal distribution	One-way ANOVA on	$H_{(3)} = 5.623$	ANOVA p = 0.1315 Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.4688

	4 mice (Baseline miKO) 5 mice (TBI WT) 6 mice (TBI miKO)		ranks (Kruskal-Wallis test); Dunn's *post hoc*		TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT > 0.9999
5E (7 days striatum)	4 mice (Baseline WT) 4 mice (Baseline miKO) 5 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(3, 15)} = 14.11$	ANOVA p = 0.0001 Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0009 TBI miKO-Baseline miKO = 0.0050 TBI miKO-TBI WT > 0.9999
5E (42 days cortex)	4 mice (Baseline WT) 4 mice (Baseline miKO) 5 mice (TBI WT) 5 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(3, 14)} = 7.814$	ANOVA p = 0.0026 Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0160 TBI miKO-Baseline miKO = 0.0514 TBI miKO-TBI WT > 0.9999
5E (42 days CC)	4 mice (Baseline WT) 4 mice (Baseline miKO) 5 mice (TBI WT) 5 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(3, 14)} = 34.35$	ANOVA p < 0.0001 Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0001 TBI miKO-TBI WT = 0.3410
5E (42 days striatum)	4 mice (Baseline WT) 4 mice (Baseline miKO) 5 mice (TBI WT) 5 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(3, 14)} = 12.67$	ANOVA p = 0.0003 Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0010 TBI miKO-Baseline miKO = 0.0564 TBI miKO-TBI WT = 0.2383
5G (% axons)	4 mice (Baseline WT) 4 mice (Baseline miKO) 5 mice (TBI WT) 5 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(3, 14)} = 18.48$	ANOVA p < 0.0001 Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0002 TBI miKO-Baseline miKO = 0.0147 TBI miKO-TBI WT = 0.0707
5G (% baseline)	5 mice (TBI WT) 5 mice (TBI miKO)	Normal distribution	*t* test	$t_{(8)} = 2.475$	TBI miKO-TBI WT = 0.0384
5H	12 mice (TBI WT) 12 mice (TBI miKO)	Normal distribution	*t* test	$t_{(22)} = 2.480$	TBI miKO-TBI WT = 0.0213
6B (myelinated)	4 mice (TBI WT) 3 mice (TBI miKO)	Normal distribution	*t* test	$t_{(5)} = 0.08965$	TBI miKO-TBI WT = 0.9320
6B (demyelinated)	4 mice (TBI WT) 3 mice (TBI miKO)	Normal distribution	*t* test	$t_{(5)} = 0.3944$	TBI miKO-TBI WT = 0.7096

6C (%)	4 mice (TBI WT) 3 mice (TBI miKO)	Normal distribution	*t* test	$t_{(5)} = 3.589$	TBI miKO-TBI WT = 0.0157
6C (number per FOV)	4 mice (TBI WT) 3 mice (TBI miKO)	Normal distribution	Two-way ANOVA; Bonferroni *post hoc*	$F_{(2, 15)} = 19.72$	ANOVA p < 0.0001 TBI miKO - TBI WT > 0.9999 (outfolds) TBI miKO - TBI WT < 0.0001 (splitting) TBI miKO - TBI WT = 0.7510 (vacuolization)
6D	4 mice (Baseline) 4 mice (TBI WT) 3 mice (TBI miKO)	Normal distribution	Two-way ANOVA; Bonferroni *post hoc*	$F_{(2, 24)} = 82.45$	ANOVA p < 0.0001 0.2-0.4 TBI WT - Baseline < 0.0001 TBI miKO - Baseline = 0.0001 TBI miKO - TBI WT = 0.0651 0.4-0.6 TBI miKO - Baseline < 0.0001 TBI miKO - Baseline = 0.0024 TBI miKO - TBI WT = 0.0217 > 0.6 TBI miKO - Baseline < 0.0001 TBI miKO - Baseline = 0.0645 TBI miKO - TBI WT = 0.0021
6G (0.75 mm N1)	8 mice (Baseline WT) 5 mice (Baseline miKO) 8 mice (TBI WT) 8 mice (TBI miKO)	Normal distribution	Two-way ANOVA; Bonferroni *post hoc*	$F_{(3, 225)} = 34.91$	ANOVA p < 0.0001 Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT < 0.0001 0 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT > 0.9999 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT > 0.9999 250 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0011 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT = 0.1807 500 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0008 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT = 0.0576 750 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0014 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT = 0.0222 1000 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0018 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT = 0.0185

					1250 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0032 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT = 0.0605 1500 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0052 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT = 0.0513 1750 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0084 TBI miKO-Baseline miKO = 0.8700 TBI miKO-TBI WT = 0.0440 2000 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0091 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT = 0.0243
6G (0.75 mm N2)	8 mice (Baseline WT) 5 mice (Baseline miKO) 8 mice (TBI WT) 8 mice (TBI miKO)	Normal distribution	Two-way ANOVA; Bonferroni *post hoc*	$F_{(3, 225)} = 102.1$	ANOVA p < 0.0001 Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO < 0.0001 TBI miKO-TBI WT < 0.0001 0 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT > 0.9999 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT > 0.9999 250 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.2090 TBI miKO-TBI WT > 0.9999 500 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0032 TBI miKO-TBI WT = 0.4927 750 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0077 TBI miKO-TBI WT = 0.1973 1000 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0060 TBI miKO-TBI WT = 0.1943 1250 μA Baseline miKO-Baseline WT > 0.9999

					TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0072 TBI miKO-TBI WT = 0.2768 1500 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0144 TBI miKO-TBI WT = 0.3282 1750 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0100 TBI miKO-TBI WT = 0.2582 2000 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0147 TBI miKO-TBI WT = 0.1732
6G (1 mm N1)	8 mice (Baseline WT) 5 mice (Baseline miKO) 8 mice (TBI WT) 8 mice (TBI miKO)	Normal distribution	Two-way ANOVA; Bonferroni *post hoc*	$F_{(3, 225)} = 46.75$	ANOVA p < 0.0001 Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0023 TBI miKO-TBI WT < 0.0001 0 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT > 0.9999 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT > 0.9999 250 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0003 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT = 0.4661 500 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0001 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT = 0.1302 750 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0004 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT = 0.1245 1000 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0001 TBI miKO-Baseline miKO = 0.7784 TBI miKO-TBI WT = 0.0792 1250 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0005 TBI miKO-Baseline miKO = 0.8038 TBI miKO-TBI WT = 0.1200

					1500 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0004 TBI miKO-Baseline miKO = 0.6088 TBI miKO-TBI WT = 0.1469 1750 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0009 TBI miKO-Baseline miKO = 0.8700 TBI miKO-TBI WT = 0.1344 2000 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT = 0.0011 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT = 0.1147
6G (1mm N2)	8 mice (Baseline WT) 5 mice (Baseline miKO) 8 mice (TBI WT) 8 mice (TBI miKO)	Normal distribution	Two-way ANOVA; Bonferroni *post hoc*	$F_{(3, 225)} = 107.7$	ANOVA p < 0.0001 Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO < 0.0001 TBI miKO-TBI WT < 0.0001 0 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT > 0.9999 TBI miKO-Baseline miKO > 0.9999 TBI miKO-TBI WT > 0.9999 250 μA Baseline miKO-Baseline WT = 0.5633 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.1112 TBI miKO-TBI WT > 0.9999 500 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0716 TBI miKO-TBI WT = 0.1388 750 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0348 TBI miKO-TBI WT = 0.0658 1000 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0402 TBI miKO-TBI WT = 0.0321 1250 μA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0286 TBI miKO-TBI WT = 0.0422 1500 μA Baseline miKO-Baseline WT > 0.9999

					TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0076 TBI miKO-TBI WT = 0.0239 1750 µA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0159 TBI miKO-TBI WT = 0.0536 2000 µA Baseline miKO-Baseline WT > 0.9999 TBI WT-Baseline WT < 0.0001 TBI miKO-Baseline miKO = 0.0146 TBI miKO-TBI WT = 0.0821
S1	3 mice (WT) 4 mice (miKO)	Normal distribution Non-normal distribution (G-CSF, IL-2, IL-4, I-309, TNFR2)	*t* test Mann-Whitney test (G-CSF, IL-2, IL-4, I-309, TNFR2)	$t_{(5)}$ = 1.327 (BLC) $t_{(5)}$ = 2.446 (TNFSF8) $t_{(5)}$ = 0.6449 (Eotaxin-1) $t_{(5)}$ = 2.094 (Eotaxin-2) $t_{(5)}$ = 1.385 (FasL) $t_{(5)}$ = 2.019 (fractalkine) U = 2 (G-CSF) $t_{(5)}$ = 1.155 (GM-CSF) $t_{(5)}$ = 1.071 (IFNγ) $t_{(5)}$ = 2.035 (IL-1α) $t_{(5)}$ = 1.540 (IL-1β) U = 6 (IL-2) $t_{(5)}$ = 0.1200 (IL-3) U = 3 (IL-4) $t_{(5)}$ = 2.086 (IL-6) $t_{(5)}$ = 1.638 (IL-9) $t_{(5)}$ = 0.07522 (IL-10) $t_{(5)}$ = 0.3819 (IL-12 p40) $t_{(5)}$ = 0.1104 (IL-12 p70) $t_{(5)}$ = 1.177 (IL-13) $t_{(5)}$ = 1.299 (IL-17A) $t_{(5)}$ = 0.1916 (I-TAC) $t_{(5)}$ = 1.961 (KC) $t_{(5)}$ = 0.8649 (Leptin) $t_{(5)}$ = 2.304 (LIX) $t_{(5)}$ = 0.9250 (Lymphotactin) $t_{(5)}$ = 0.04243 (MCP-1) $t_{(5)}$ = 0.5086 (M-CSF) $t_{(5)}$ = 0.2656 (MIG) $t_{(5)}$ = 2.169 (MIP-1α) $t_{(5)}$ = 0.7612 (MIP-1γ)	miKO-WT = 0.2417 (BLC) miKO-WT = 0.0582 (TNFSF8) miKO-WT = 0.5474 (Eotaxin-1) miKO-WT = 0.0904 (Eotaxin-2) miKO-WT = 0.2248 (FasL) miKO-WT = 0.0995 (fractalkine) miKO-WT = 0.2286 (G-CSF) miKO-WT = 0.3003 (GM-CSF) miKO-WT = 0.3329 (IFNγ) miKO-WT = 0.0975 (IL-1α) miKO-WT = 0.1843 (IL-1β) miKO-WT > 0.9999 (IL-2) miKO-WT = 0.9092 (IL-3) miKO-WT = 0.4000 (IL-4) miKO-WT = 0.0913 (IL-6) miKO-WT = 0.1624 (IL-9) miKO-WT = 0.9430 (IL-10) miKO-WT = 0.7182 (IL-12 p40) miKO-WT = 0.9164 (IL-12 p70) miKO-WT = 0.2922 (IL-13) miKO-WT = 0.2508 (IL-17A) miKO-WT = 0.8556 (I-TAC) miKO-WT = 0.1071 (KC) miKO-WT = 0.4266 (Leptin) miKO-WT = 0.0694 (LIX) miKO-WT = 0.3974 (Lymphotactin) miKO-WT = 0.9678 (MCP-1) miKO-WT = 0.6326 (M-CSF) miKO-WT = 0.8011 (MIG) miKO-WT = 0.0822 (MIP-1α) miKO-WT = 0.4809 (MIP-1γ) miKO-WT = 0.9318 (RANTES) miKO-WT = 0.2501 (SDF-1α) miKO-WT = 0.2286 (I-309) miKO-WT = 0.6831 (TECK) miKO-WT = 0.8140 (TIMP-1) miKO-WT = 0.8920 (TIMP-2) miKO-WT = 0.8855 (TNF-α) miKO-WT = 0.4471 (TNFR1) miKO-WT = 0.4000 (TNFR2)

				$t_{(5)}$ = 0.08992 (RANTES) $t_{(5)}$ = 1.301 (SDF-1α) U = 2 (I-309) $t_{(5)}$ = 0.4330 (TECK) $t_{(5)}$ = 0.2480 (TIMP-1) $t_{(5)}$ = 0.1428 (TIMP-2) $t_{(5)}$ = 0.1515 (TNF-α) $t_{(5)}$ = 0.8247 (TNFR1) U = 3 (TNFR2)	
S2 (TIMP-1)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)}$ = 10.09	ANOVA p = 0.0015 TBI WT-Baseline = 0.0014 TBI miKO-Baseline = 0.0288 TBI miKO-TBI WT = 0.5614
S2 (MIP-1γ)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)}$ = 15.21	ANOVA p = 0.0002 TBI WT-Baseline = 0.0001 TBI miKO-Baseline = 0.0483 TBI miKO-TBI WT = 0.0454
S2 (IL-10)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)}$ = 26.18	ANOVA p < 0.0001 TBI WT-Baseline < 0.0001 TBI miKO-Baseline = 0.0004 TBI miKO-TBI WT = 0.2582
S2 (IL-6)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)}$ = 9.400	ANOVA p = 0.0020 TBI WT-Baseline = 0.0017 TBI miKO-Baseline = 0.5020 TBI miKO-TBI WT = 0.0433
S2 (TNFR1)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)}$ = 15.02	ANOVA p = 0.0002 TBI WT-Baseline = 0.0002 TBI miKO-Baseline = 0.0113 TBI miKO-TBI WT = 0.2157
S2 (Eotaxin-1)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)}$ = 6.052	ANOVA p = 0.0110 TBI WT-Baseline = 0.0153 TBI miKO-Baseline > 0.9999 TBI miKO-TBI WT = 0.0419
S2 (Leptin)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)}$ = 2.632	ANOVA p = 0.1027 TBI WT-Baseline = 0.1664 TBI miKO-Baseline > 0.9999 TBI miKO-TBI WT = 0.2163
S2 (IFNγ)	7 mice (Baseline) 6 mice (TBI WT)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)}$ = 1.317	ANOVA p = 0.2953 TBI WT-Baseline = 0.4215 TBI miKO-Baseline= 0.8119 TBI miKO-TBI WT > 0.9999

	6 mice (TBI miKO)				
S2 (IL-12 p40)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 1.890$	ANOVA p = 0.1833 TBI WT-Baseline = 0.7734 TBI miKO-Baseline = 0.2199 TBI miKO-TBI WT > 0.9999
S2 (TNFSF8)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 5.610$	ANOVA p = 0.0143 TBI WT-Baseline = 0.0347 TBI miKO-Baseline = 0.0329 TBI miKO-TBI WT > 0.9999
S2 (IL-3)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 1.772$	ANOVA p = 0.2018 TBI WT-Baseline = 0.2664 TBI miKO-Baseline > 0.9999 TBI miKO-TBI WT = 0.5626
S2 (MIG)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 1.745$	ANOVA p = 0.2062 TBI WT-Baseline = 0.5277 TBI miKO-Baseline = 0.3061 TBI miKO-TBI WT > 0.9999
S2 (G-CSF)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 4.680$	ANOVA p = 0.0251 TBI WT-Baseline = 0.6348 TBI miKO-Baseline = 0.0226 TBI miKO-TBI WT = 0.3302
S2 (Fasl)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 2.082$	ANOVA p = 0.1572 TBI WT-Baseline = 0.3144 TBI miKO-Baseline > 0.9999 TBI miKO-TBI WT = 0.2573
S2 (BLC)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 3.525$	ANOVA p = 0.0539 TBI WT-Baseline = 0.1184 TBI miKO-Baseline = 0.1065 TBI miKO-TBI WT > 0.9999
S2 (I-TAC)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 1.817$	ANOVA p = 0.1945 TBI WT-Baseline = 0.5151 TBI miKO-Baseline > 0.9999 TBI miKO-TBI WT = 0.2629
S2 (RANTES)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 2.126$	ANOVA p = 0.1518 TBI WT-Baseline > 0.9999 TBI miKO-Baseline = 0.6431 TBI miKO-TBI WT = 0.1734
S2 (MCP-1)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 2.435$	ANOVA p = 0.1193 TBI WT-Baseline = 0.6015 TBI miKO-Baseline > 0.9999 TBI miKO-TBI WT = 0.1298

S2 (MIP-1α)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 4.267$	ANOVA p = 0.0327 TBI WT-Baseline = 0.9150 TBI miKO-Baseline = 0.0311 TBI miKO-TBI WT = 0.2836
S2 (IL-1β)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 6.018$	ANOVA p = 0.0113 TBI WT-Baseline = 0.6090 TBI miKO-Baseline = 0.1211 TBI miKO-TBI WT = 0.0103
S2 (M-CSF)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 2.133$	ANOVA p = 0.1510 TBI WT-Baseline = 0.6137 TBI miKO-Baseline = 0.1822 TBI miKO-TBI WT > 0.9999
S2 (Lymphotactin)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 1.367$	ANOVA p = 0.2832 TBI WT-Baseline = 0.3533 TBI miKO-Baseline > 0.9999 TBI miKO-TBI WT > 0.9999
S2 (TNF-α)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 0.3230$	ANOVA p = 0.7286 TBI WT-Baseline > 0.9999 TBI miKO-Baseline > 0.9999 TBI miKO-TBI WT > 0.9999
S2 (IL-9)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 0.3981$	ANOVA p = 0.6781 TBI WT-Baseline > 0.9999 TBI miKO-Baseline > 0.9999 TBI miKO-TBI WT > 0.9999
S2 (IL-12 p70)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 1.613$	ANOVA p = 0.2301 TBI WT-Baseline > 0.9999 TBI miKO-Baseline= 0.2990 TBI miKO-TBI WT = 0.6772
S2 (TNFR2)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Non-normal distribution	One-way ANOVA on ranks (Kruskal-Wallis test); Dunn's *post hoc*	$H_{(2)} = 3.910$	ANOVA p = 0.1422 TBI WT-Baseline = 0.1440 TBI miKO-Baseline > 0.9999 TBI miKO-TBI WT = 0.9147
S2 (Eotaxin-2)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Non-normal distribution	One-way ANOVA on ranks (Kruskal-Wallis test); Dunn's *post hoc*	$H_{(2)} = 2.383$	ANOVA p = 0.3154 TBI WT-Baseline > 0.9999 TBI miKO-Baseline = 0.3848 TBI miKO-TBI WT > 0.9999
S2 (IL-4)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 5.884$	ANOVA p = 0.0121 TBI WT-Baseline > 0.9999 TBI miKO-Baseline = 0.0146 TBI miKO-TBI WT = 0.0586
S2 (LIX)	7 mice (Baseline)	Non-normal distribution	One-way ANOVA on	$H_{(2)} = 1.231$	ANOVA p = 0.5565 TBI WT-Baseline = 0.9245

	6 mice (TBI WT) 6 mice (TBI miKO)		ranks (Kruskal-Wallis test); Dunn's *post hoc*		TBI miKO-Baseline > 0.9999 TBI miKO-TBI WT > 0.9999
S2 (KC)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 1.968$	ANOVA p = 0.1721 TBI WT-Baseline > 0.9999 TBI miKO-Baseline= 0.2434 TBI miKO-TBI WT = 0.4201
S2 (TIMP-2)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 0.4612$	ANOVA p = 0.6386 TBI WT-Baseline > 0.9999 TBI miKO-Baseline > 0.9999 TBI miKO-TBI WT > 0.9999
S2 (Fractalkine)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 0.04304$	ANOVA p = 0.9580 TBI WT-Baseline > 0.9999 TBI miKO-Baseline > 0.9999 TBI miKO-TBI WT > 0.9999
S2 (IL-2)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 0.1173$	ANOVA p = 0.8900 TBI WT-Baseline > 0.9999 TBI miKO-Baseline > 0.9999 TBI miKO-TBI WT > 0.9999
S2 (I-309)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Non-normal distribution	One-way ANOVA on ranks (Kruskal-Wallis test); Dunn's *post hoc*	$H_{(2)} = 1.420$	ANOVA p = 0.5080 TBI WT-Baseline = 0.7155 TBI miKO-Baseline > 0.9999 TBI miKO-TBI WT > 0.9999
S2 (IL-1α)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 0.09920$	ANOVA p = 0.9061 TBI WT-Baseline > 0.9999 TBI miKO-Baseline > 0.9999 TBI miKO-TBI WT > 0.9999
S2 (TECK)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 0.1090$	ANOVA p = 0.8974 TBI WT-Baseline > 0.9999 TBI miKO-Baseline > 0.9999 TBI miKO-TBI WT > 0.9999
S2 (IL-17A)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 0.2218$	ANOVA p = 0.8035 TBI WT-Baseline > 0.9999. TBI miKO-Baseline > 0.9999 TBI miKO-TBI WT > 0.9999
S2 (IL13)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Non-normal distribution	One-way ANOVA on ranks (Kruskal-Wallis test); Dunn's *post hoc*	$H_{(2)} = 9.129$	ANOVA p = 0.0051 TBI WT-Baseline = 0.0906 TBI miKO-Baseline > 0.9999 TBI miKO-TBI WT = 0.0104
S2 (SDF-1α)	7 mice (Baseline) 6 mice (TBI WT)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 5.197$	ANOVA p = 0.0182 TBI WT-Baseline = 0.7182 TBI miKO-Baseline= 0.1610 TBI miKO-TBI WT = 0.0173

	6 mice (TBI miKO)				
S2 (GM-CSF)	7 mice (Baseline) 6 mice (TBI WT) 6 mice (TBI miKO)	Normal distribution	One-way ANOVA; Bonferroni *post hoc*	$F_{(2, 16)} = 20.23$	ANOVA $p < 0.0001$ TBI WT-Baseline = 0.2146 TBI miKO-Baseline= 0.0011 TBI miKO-TBI WT < 0.0001

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