
Supplementary information

**Suppression of proteolipid protein rescues
Pelizaeus–Merzbacher disease**

In the format provided by the
authors and unedited

SUPPLEMENTARY TABLE 1

PLP1 mutation	Patient #	Motor function	Cognitive function	Death	Ref.
Frameshift and early termination codon (c.4delG) <i>Protein absence confirmed by western blot</i>	1	Wheelchair bound at 35 with spasticity in all limbs	No intellectual disability and verbally communicated into mid-20s. Cooperative, alert, and aware of surroundings in adulthood.	Age 47	^{1,2}
	2	Wheelchair bound at 37 with spasticity in all limbs	No intellectual disability and verbally communicated into mid-20s. Cooperative, alert, and aware of surroundings in adulthood.	Age 49	
	3	Walked from age 4-12, spasticity in all limbs at age 25	Language delay. At 22 communicated, was cooperative, and alert. At 25 could follow commands, count, and distinguish colors.	Age 34	
	4	Wheelchair bound at 17, gait deterioration starting at age 8, and spasticity in legs but not arms.	Able to read, follow commands, and perform arithmetic.	None reported	
Frameshift and early termination codon c.191+1G>A <i>No biochemical analysis</i>	1	Walked from age 6-9. Spastic with cerebellar dysfunction.	Attends normal school and can read and write.	None reported	³
Loss of start codon (c.3G>A) <i>No biochemical analysis</i>	1	Early life motor dysfunction with spasticity in arms and legs. Further decline at age 33.	Early life intellectual disability. Further decline at age 33.	None reported	^{2,4}
	2	Early life hypertonia and spasticity in arms and legs. Wheelchair bound at 6.	Language delay. Moderately retarded development.	None reported	
	3	Never walked and spasticity in legs by age 1, progressing to arms with age.	Mild cognitive deficits at age 20.	None reported	⁵

Table S1.

Table containing details of published reports of *PLP1*-null patients.

SUPPLEMENTARY TABLE 2

Mouse	Genotype	<i>Plp1</i> exon 3 indels
1	Wild-type	81bp deletion (29%) 2bp insertion (71%)
2	Wild-type	86bp deletion (61%) 1bp insertion (39%)
3	Wild-type	1bp insertion (100%)
4	<i>jimpy</i>	80bp deletion (100%)
5	Wild-type	83bp deletion (100%)
6	Wild-type	1bp deletion (100%)
7	Wild-type	1bp insertion (26%)

Table S2.

Table showing the on-target mutations for sgRNAs 3 and 7 after electroporation into mouse zygotes and measured by high-throughput sequencing of tail tip DNA from founder animals. Mouse number 4, a *jimpy* male with a complex deletion including 80-bp of total deleted sequence in *Plp1* exon 3, served as the founder for the CR-*impy* cohort.

SUPPLEMENTARY TABLE 3

Protein Group	982
Protein ID	700
Accession	P60202 MYPR_MOUSE
Coverage (%)	7
#Peptides	2
PTM	Carbamidomethylation
WT Intensity	7.75E+08
<i>jimpy</i> Intensity	6.27E+06
CR-<i>impy</i> Intensity	0
Avg. Mass	30077
Description	Myelin proteolipid protein OS=Mus musculus OX=10090 GN=Plp1 PE=1 SV=2

Table S3.

Table showing quantification of PLP signal intensities from LC-MS/MS analysis of wild type (WT), *jimpy*, and CR-*impy* samples. PLP protein were decreased over 100-fold in *jimpy* compared to wild-type and undetectable in CR-*impy*.

SUPPLEMENTARY TABLE 4

Sequencing primers			
PCR amplicon	Genomic Location	Forward Primer	Reverse Primer
<i>jimpy</i> mutation	<i>Plp1</i> intron 4 - exon 5	AACGCAAAGCAGCACATTTCA	AGTGCAGCTCTGGGGTTAAT
CR- <i>impy</i> mutation	<i>Plp1</i> exon 3	TCTGTCTGTCCATGCAGGATT	GACACACCCGCTCCAAGAA
qPCR primers			
Gene	Forward primer	Reverse primer	Probe (5'FAM; 3'TAMRA)
<i>Plp1</i>	CTGATGCCAGAATGTATGGTGT	AGGTGGAAGGTCATTTGGAAC	TGCAGATGGACAGAAGGTTGGAGC
<i>Gfap</i>	GAAACCAGCCTGGACACCAA	TCCACAGTCTTTACCACGATGTTT	TCCGTGTGAGAAGGCCACCTCAAGA
<i>Aif1</i>	TGGTCCCCCAGCCAAGA	CCCACCGTGTGACATCCA	AGCTATCTCCGAGCTGCCCTGATTGG
<i>Cd68</i>	TGGCGGTGGAATACAATGTG	GATGAATTCTGCGCCATGAA	CCTCCACAGGCAGCACAGTGG
Gene	Forward primer	Reverse primer	Probe (5'FAM; 3'IBFQ)
<i>Xylt1</i>	AAGTCTTCAAGGTCGCAAGTC	CAAAAGACCACCAAAGTTCCG	CCCAGTCAG/ZEN/TGCCAACCTAGAA
<i>Scfd1</i>	CGGAGTAATGACAGCTCAGTT	CCTTGCTTTGCCTTTATGTAGTC	AAGACAATG/ZEN/GCCTCTTGGAAATGGACT
<i>Tpk1</i>	CAAGCCACTCACATCACTCC	CACCAGCTCCCTTCCATTC	TCTCTCATC/ZEN/TACCTCCTCCAACCCG

Table S4.
Table listing all PCR primers.

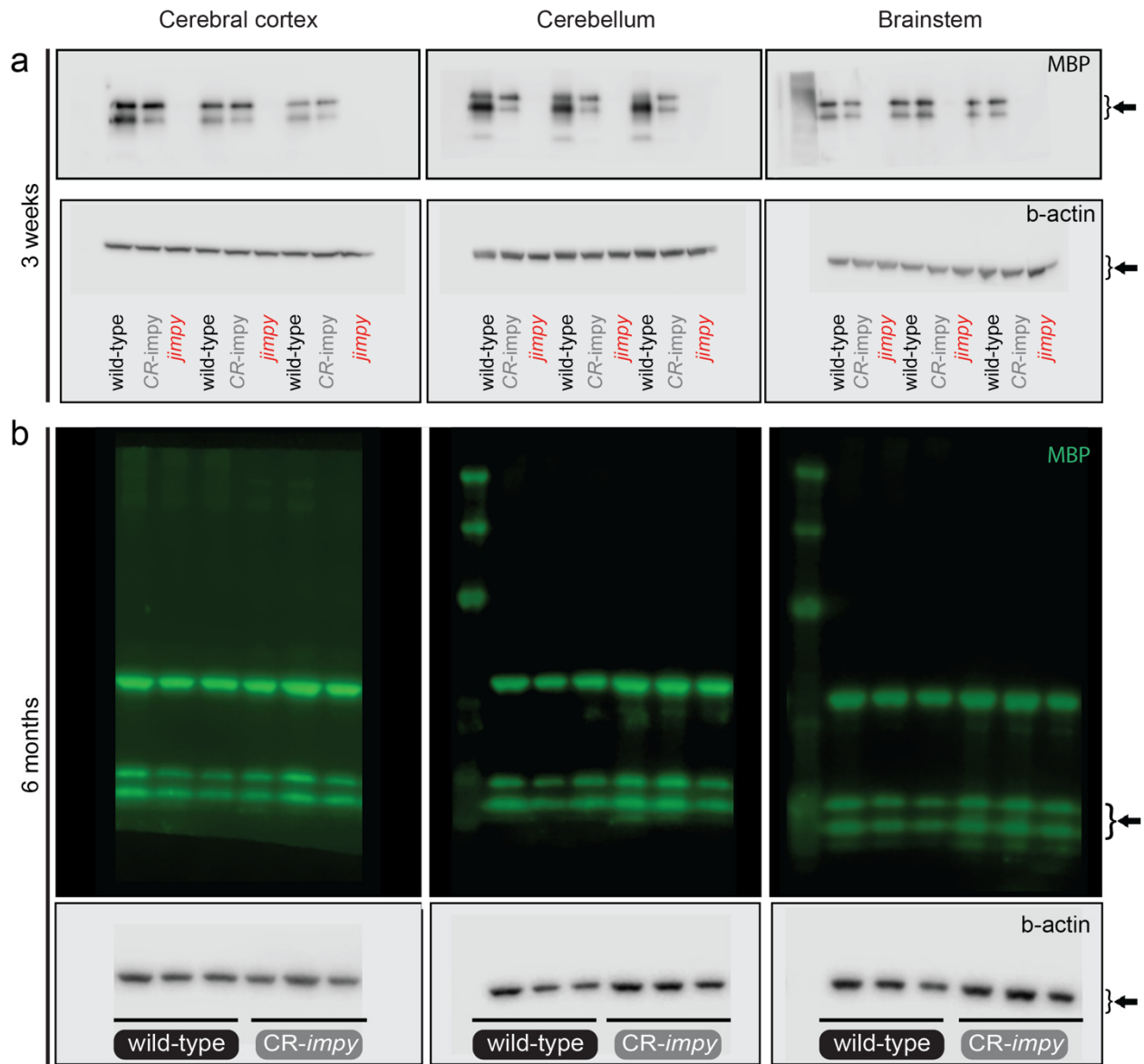
SUPPLEMENTARY DATA 1

Metadata for mouse CRISPR survival cohort from Elitt et al.										mean time to fall (seconds)				total distance traveled (meters)			
Identifier	Date of birth	Date of death	Euthanized at		Genotype	Phenotype	Censored (Y/N)	Censor Reason	Rotarod				Open field				
			18 month endpoint?	Lifespan (days)					3 wk	2 mo	6 mo	18 mo	3 wk	2 mo	6 mo	18 mo	
CR200301	11/13/2016	4/22/2018	n	525	wild-type	none	N		69.3	70.9	61.8		22.8	17.9	12.5		
CR200090	11/13/2016	5/14/2018	y	547	wild-type	none	N		144.0	104.1	60.1	43.0	17.0	17.4	10.8	13.2	
CR200091	11/13/2016	5/14/2018	y	547	wild-type	none	N		81.3	103.4	77.5	61.3	19.3	18.8	10.2	15.4	
CR200302	11/15/2016	12/5/2017	n	385	CR-impv	none	N		100.7	120.9	108.0		10.9	15.0	15.5		
CR200303	11/15/2016	12/28/2017	n	408	CR-impv	none	N		115.3	138.0	74.2		8.6	14.3	17.7		
CR200304	11/15/2016	5/6/2018	n	537	CR-impv	none	N		95.7	138.3	55.2		13.7	11.0	11.5		
CR200092	11/15/2016	5/14/2018	y	545	CR-impv	none	N		139.4	106.3	66.2	16.3	10.1	10.2	10.5	7.3	
CR200093	11/15/2016	5/14/2018	y	545	CR-impv	none	N		72.7	117.7	116.3	29.2	17.1	7.9	17.3	22.0	
CR200305	11/15/2016	12/8/2016	n	23	impv	severe	N		39.1				3.9				
CR200306	11/15/2016	12/7/2016	n	22	impv	severe	N		21.0				2.4				
CR200307	11/15/2016	12/9/2016	n	24	impv	severe	N		20.7				1.0				
CR200308	11/15/2016	12/5/2016	n	20	impv	severe	N		12.9				5.5				
CR200309	11/15/2016	12/6/2016	n	21	impv	severe	N		4.7				6.8				
CR200310	11/16/2016	12/17/2016	n	31	impv	severe	N		38.7				0.4				
CR200311	11/16/2016	12/10/2016	n	24	impv	severe	N		31.9				0.6				
CR200312	11/17/2016	4/30/2018	n	529	wild-type	none	N		101.6	84.7	52.9		19.0	7.0	8.1		
CR200096	11/17/2016	5/14/2018	y	543	wild-type	none	N		93.0	219.3	125.7	29.1	20.0	25.7	12.7	12.5	
CR200313	11/17/2016	3/27/2018	n	495	wild-type	none	N		156.7	70.4	52.6		14.4	17.0	9.3		
CR200097	11/17/2016	5/14/2018	y	543	wild-type	none	N		55.9	86.0	118.8	71.9	15.6	18.0	25.1	14.1	
CR200094	11/18/2016	5/14/2018	y	542	CR-impv	none	N		65.8	74.0	111.1	16.3	22.5	15.8	16.2	7.2	
CR200314	11/18/2016	3/19/2018	n	486	CR-impv	none	N		69.6	71.3	90.9		21.1	17.0	15.5		
CR200095	11/18/2016	5/14/2018	y	542	CR-impv	none	N		110.1	128.3	148.1	29.2	19.1	26.4	19.6	27.6	
CR200315	11/26/2016	12/22/2016	n	26	impv	severe	N		2.7				1.8				
CR200316	11/26/2016	12/18/2016	n	22	impv	severe	N		27.3				0.5				
CR200317	11/26/2016	12/18/2016	n	22	impv	severe	N		24.2				0.9				
CR200318	11/26/2016	12/20/2016	n	24	impv	severe	N		26.9				1.2				
CR200319	11/26/2016	12/19/2016	n	23	impv	severe	N		41.4				1.0				
CR200320	12/12/2016	1/5/2017	n	24	impv	severe	N										
CR200321	12/12/2016	12/31/2016	n	19	impv	severe	N										
CR200322	12/12/2016	11/16/2017	n	339	CR-impv	none	N			102.9	88.2			25.2	26.0		
CR200323	12/12/2016	6/27/2018	y	562	CR-impv	none	N			81.1	89.4	43.9		15.4	17.8	19.6	
CR200324	3/30/2017	4/20/2017	n	21	impv	severe	N										
CR200325	3/30/2017	4/20/2017	n	21	impv	severe	N										
CR200326	3/30/2017	4/26/2017	n	27	impv	severe	N										
CR200327	3/30/2017	4/24/2017	n	25	impv	severe	N										
CR200328	11/13/2016	10/1/2017	n	322	wild-type	none	Y	Euthanized inadvertently	92.7	135.4	63.5		31.8	18.3	8.9		
CR200329	11/13/2016	10/1/2017	n	322	wild-type	none	Y	Euthanized inadvertently	148.7	126.7	102.4		18.6	13.8	6.7		
CR200330	11/13/2016	10/1/2017	n	322	wild-type	none	Y	Euthanized inadvertently	85.7	109.3	120.0		15.3	19.4	19.1		
CR200081	11/15/2016	6/1/2017	n	198	wild-type	none	Y	Tissue collection	196.0	160.7	145.0		13.5	20.9	10.3		
CR200082	11/15/2016	6/1/2017	n	198	CR-impv	none	Y	Tissue collection	132.3	91.5	99.1		13.5	15.1	20.3		
CR200083	11/15/2016	6/2/2017	n	199	CR-impv	none	Y	Tissue collection	120.5	93.6	96.9		21.5	23.7	25.2		
CR200084	11/15/2016	6/2/2017	n	199	wild-type	none	Y	Tissue collection	170.4	137.7	78.6		23.7	11.5	7.3		
CR200061	11/15/2016	5/25/2017	n	191	CR-impv	none	Y	Tissue collection	102.5	111.7	105.4		21.1	12.2	16.2		
CR200062	11/15/2016	5/25/2017	n	191	CR-impv	none	Y	Tissue collection	56.4	122.4	63.4		13.3	15.1	18.3		
CR200063	11/15/2016	5/25/2017	n	191	wild-type	none	Y	Tissue collection	109.3	115.3	57.3		26.3	26.3	10.8		
CR200064	11/15/2016	5/25/2017	n	191	wild-type	none	Y	Tissue collection	88.7	101.3	82.0		17.4	15.6	8.0		
CR200065	11/16/2016	5/30/2017	n	195	CR-impv	none	Y	Tissue collection	42.5	100.8	131.3		10.0	6.4	6.7		
CR200075	11/17/2016	5/31/2017	n	195	wild-type	none	Y	Tissue collection	82.1	32.1	23.3		24.0	21.3	21.1		
CR200076	11/17/2016	5/31/2017	n	195	wild-type	none	Y	Tissue collection	162.8	70.8	98.9		20.5	11.6	9.4		
CR200077	11/17/2016	5/31/2017	n	195	wild-type	none	Y	Tissue collection	120.6	95.5	108.5		20.5	26.0	14.1		
CR200078	11/18/2016	6/13/2017	n	207	CR-impv	none	Y	Tissue collection	40.5	102.0	97.6		19.7	13.0	7.8		
CR200079	11/18/2016	6/13/2017	n	207	wild-type	none	Y	Tissue collection	82.2	130.0	77.2		12.8	15.6	3.8		
CR200080	11/18/2016	6/12/2017	n	206	CR-impv	none	Y	Tissue collection	87.0	78.1	63.5		26.3	18.6	15.8		
CR200085	11/18/2016	6/12/2017	n	206	wild-type	none	Y	Tissue collection	75.8	113.4	104.0		19.7	9.3	8.3		
CR200071	11/18/2016	6/12/2017	n	206	CR-impv	none	Y	Tissue collection	59.0	142.3	134.3		8.0	16.5	8.3		
CR200086	11/18/2016	6/13/2017	n	207	wild-type	none	Y	Tissue collection	79.7	112.2	100.1		14.3	8.512	12.0		
CR200098	11/18/2016	6/13/2017	n	207	wild-type	none	Y	Tissue collection	90.6	130.3	115.3		17.9	19.54	13.0		
CR200066	11/19/2016	5/30/2017	n	192	CR-impv	none	Y	Tissue collection	88.4	124.4	82.9		14.0	14.136	0.6		
CR200067	11/19/2016	5/30/2017	n	192	CR-impv	none	Y	Tissue collection	131.7	146.0	68.2		11.6	13.449	9.8		
CR200068	11/19/2016	5/30/2017	n	192	wild-type	none	Y	Tissue collection	82.5	119.3	126.1		14.1	20.689	14.5		
CR200069	11/22/2016	5/30/2017	n	189	wild-type	none	Y	Tissue collection	88.4	67.0	41.5		19.0	9.404	8.4		
CR200070	11/22/2016	5/30/2017	n	189	wild-type	none	Y	Tissue collection	88.3	80.6	77.4		20.1	9.051	5.2		
CR200072	11/22/2016	6/1/2017	n	191	wild-type	none	Y	Tissue collection	110.7	170.0	124.3		21.7	19.759	11.8		
CR200073	11/22/2016	6/1/2017	n	191	wild-type	none	Y	Tissue collection	145.0	152.3	116.1		13.5	22.028	11.4		
CR200331	11/26/2016	5/23/2017	n	178	CR-impv	none	Y	Euthanized inadvertently	110.0	196.0			24.3	16.452			
CR200074	12/12/2016	6/1/2017	n	171	CR-impv	none	Y	Tissue collection		94.2				23.557			

Supplementary Data 1.

Metadata for all mice in Kaplan-Meier survival plot in Fig. 1b. Also included are raw data values for rotarod and open field assays in Fig. 1k-l.

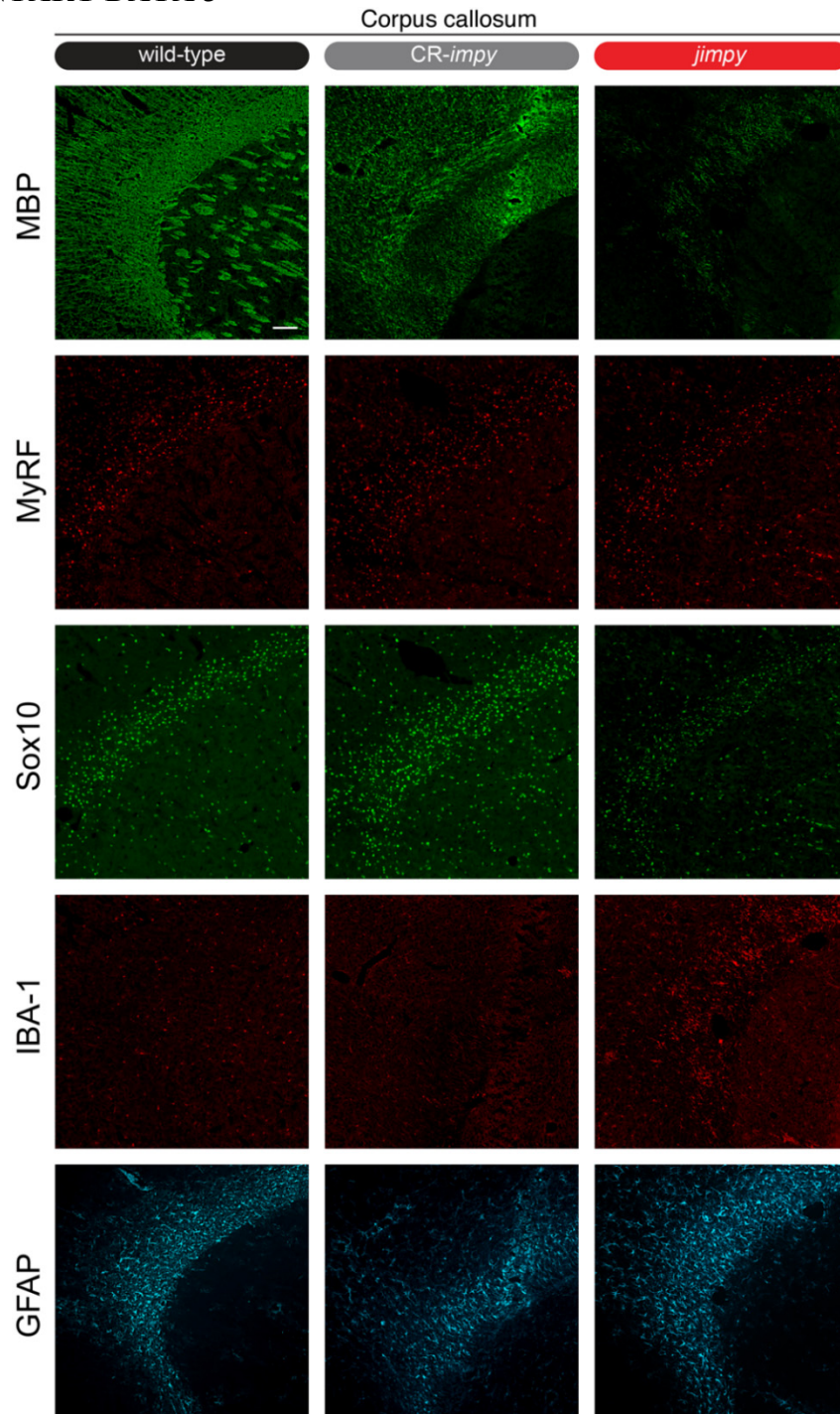
SUPPLEMENTARY DATA 2



Supplementary Data 2.

a-b, Labeled raw images of western blots for all samples in Extended Data Fig. 2, b, d. The upper bands in the fluorescent blots in (b) are carry over from chemiluminescent detection of B-actin (bottom panel).

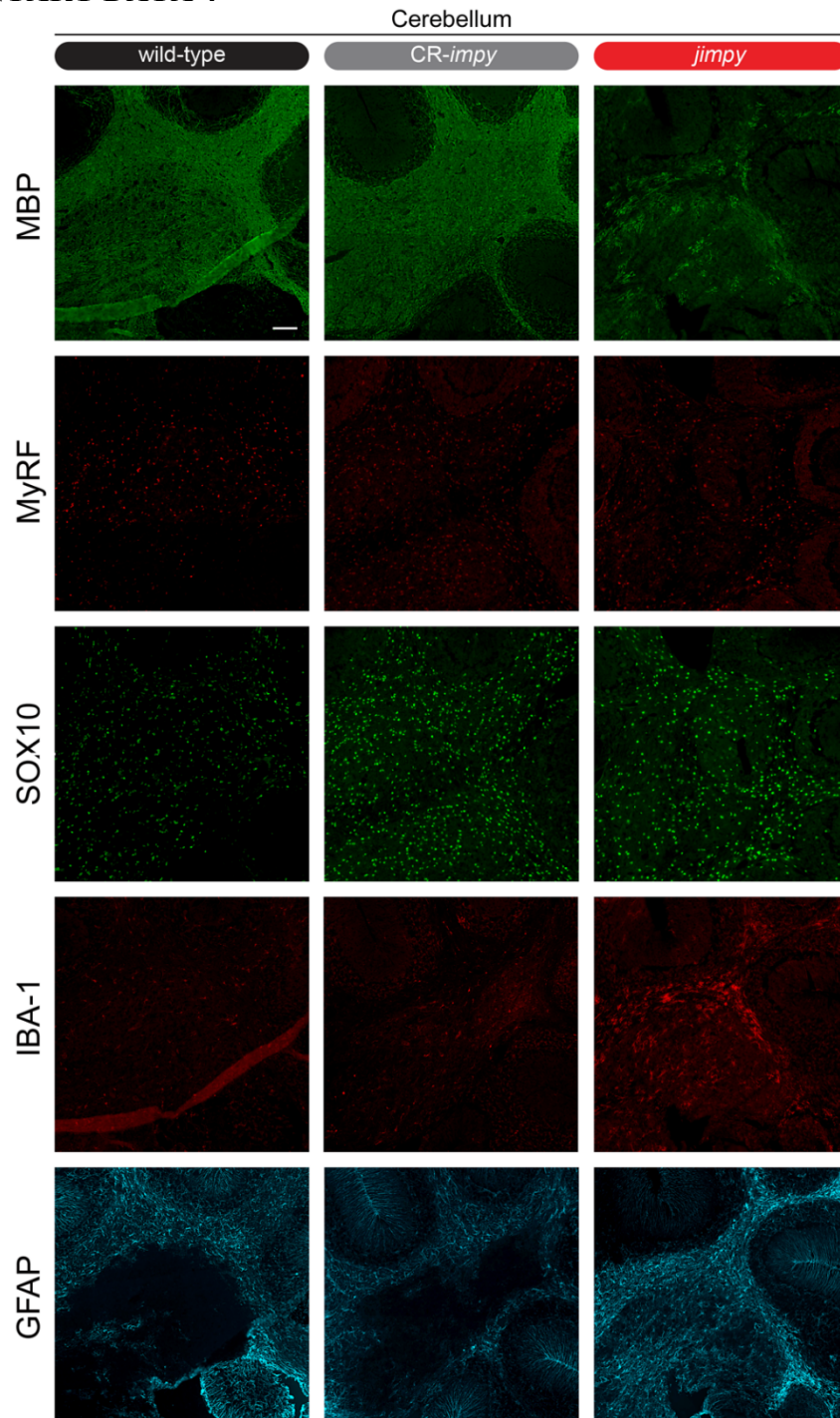
SUPPLEMENTARY DATA 3



Supplementary Data 3.

Representative source immunohistochemical images for counts in Fig. 1d and Extended Data Fig. 3c,d of corpus callosum from 3-week old wild-type, CR-*impy*, and *jimpy* mice showing MBP, MyRF, and Sox10, IBA-1, or GFAP. Replicate images generated for each biological replicate in Fig. 1d and Extended Data Fig. 3c,d. Scale bar, 100 μ m.

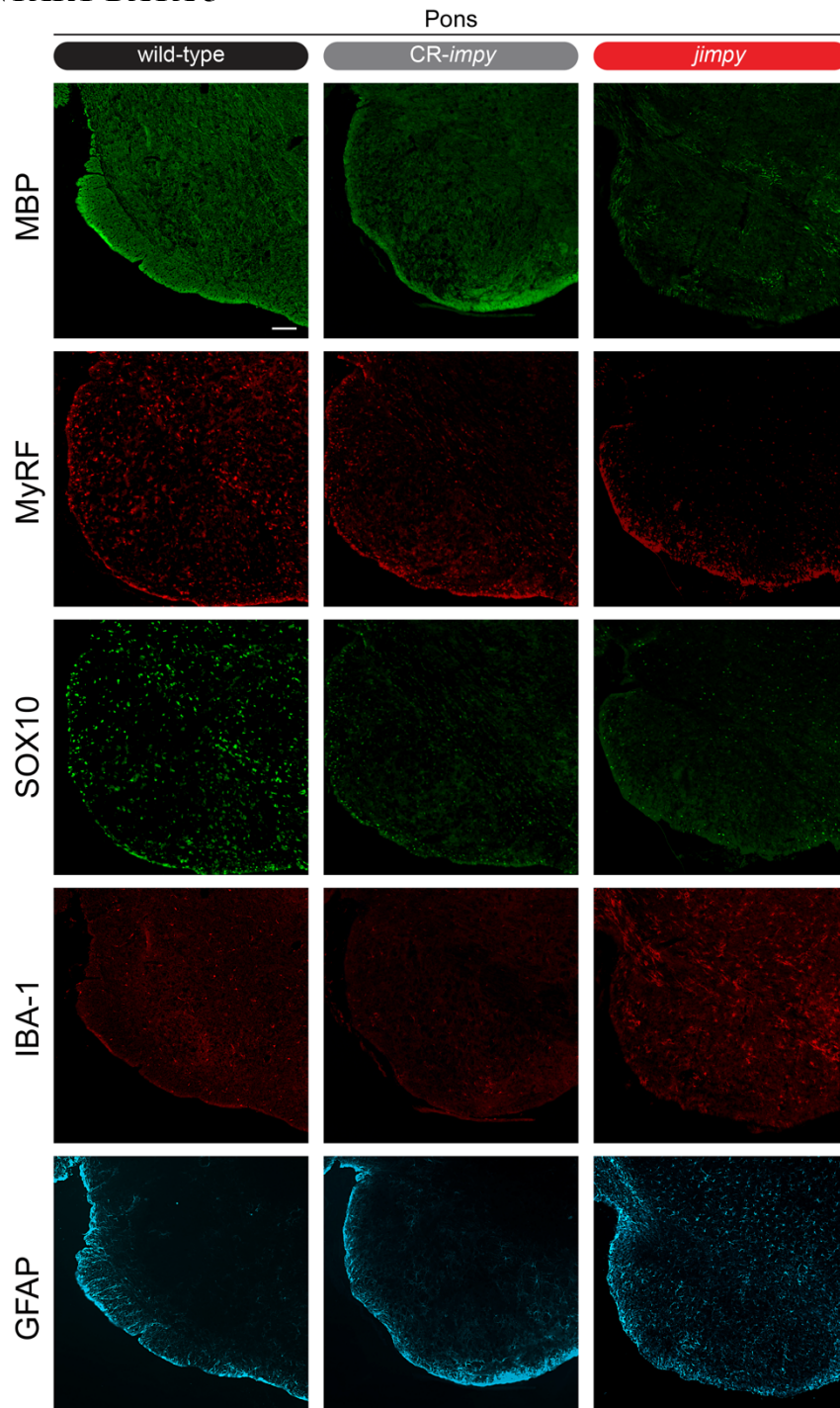
SUPPLEMENTARY DATA 4



Supplementary Data 4.

Representative source immunohistochemical images for counts in Fig. 1d,e and Extended Data Fig. 3c,d of cerebellum from 3-week old wild-type, CR-*impy*, and *jimpy* mice showing MBP, MyRF, and Sox10, IBA-1, or GFAP. Replicate images generated for each biological replicate in Fig. 1d and Extended Data Fig. 3c,d. Scale bar, 100 μ m.

SUPPLEMENTARY DATA 5



Supplementary Data 5.

Representative source immunohistochemical images for counts in Fig. 1d,e and Extended Data Fig. 3c,d of pons from 3-week old wild-type, CR-*impy*, and *jimpy* mice showing MBP, MyRF, and Sox10, IBA-1, or GFAP. Replicate images generated for each biological replicate in Fig. 1d and Extended Data Fig. 3c,d. Scale bar, 100 μ m.

SUPPLEMENTARY DATA 6

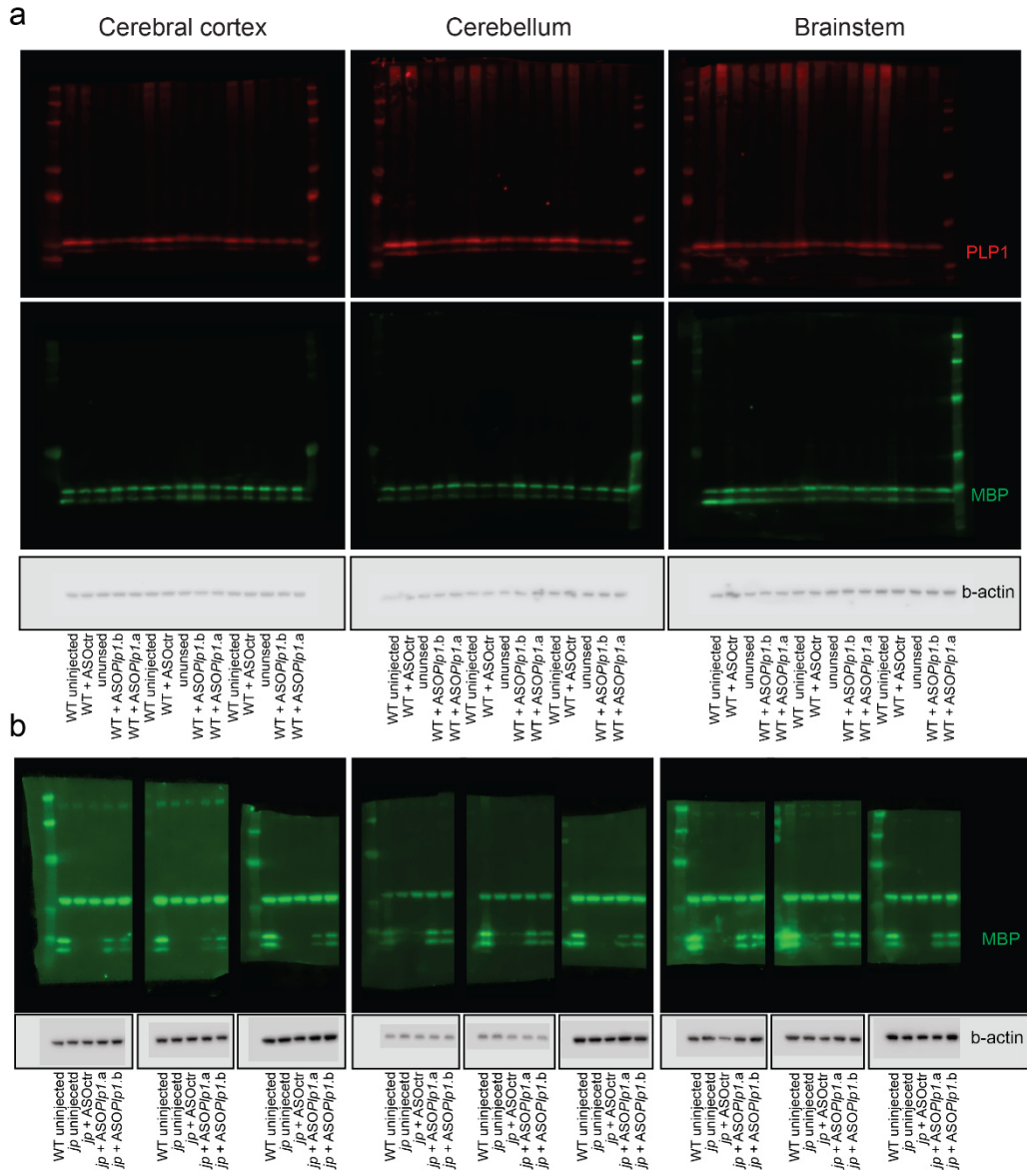
Metadata for mouse ASO survival cohort from Elitt et al.

Identifier	Date of birth	Date of death	Euthanized at 8 month endpoint?	Lifespan (days)	Genotype	Treatment	Phenotype	Additional phenotype notes	mean time to fall (seconds)			total distance traveled (meters)		
									Rotarod 2 mo	Rotarod 4 mo	Rotarod 6 mo	Open field 2 mo	Open field 4 mo	Open field 6 mo
ASO00091	11/23/17	7/20/18	y	239	<i>jimpy</i>	ASO P1p1.a	mild	Periorbital area inflammation, left eye	32.9	22.4	5.6	22.0	18.0	18.0
ASO00095	11/23/17	7/20/18	y	239	<i>jimpy</i>	ASO P1p1.a	mild	Periorbital area inflammation, bilateral	22.3	24.6	unable to train	19.6	13.7	14.0
ASO00051	12/7/17	12/28/17	n	21	<i>jimpy</i>	uninjected	severe							
ASO00052	12/7/17	12/28/17	n	21	<i>jimpy</i>	ASO control	severe							
ASO00053	12/7/17	12/29/17	n	22	<i>jimpy</i>	ASO control	severe							
ASO00054	12/7/17	12/27/17	n	20	<i>jimpy</i>	ASO control	severe							
ASO00055	12/8/17	12/24/17	n	16	<i>jimpy</i>	uninjected	severe							
ASO00056	12/8/17	12/27/17	n	19	<i>jimpy</i>	uninjected	severe							
ASO00057	12/11/17	12/26/17	n	15	<i>jimpy</i>	uninjected	severe							
ASO00058	12/5/17	12/25/17	n	20	<i>jimpy</i>	uninjected	severe							
ASO00059	12/5/17	12/25/17	n	20	<i>jimpy</i>	uninjected	severe							
ASO000S10	12/8/17	12/28/17	n	20	<i>jimpy</i>	uninjected	severe	Found with hind-limb paralysis, required euthanization						
ASO000S11	12/8/17	12/30/17	n	22	<i>jimpy</i>	uninjected	severe							
ASO000S12	12/8/17	12/28/17	n	20	<i>jimpy</i>	uninjected	severe	Found with hind-limb paralysis, required euthanization						
AS000103	12/27/17	8/27/18	y	243	<i>jimpy</i>	ASO P1p1.b	mild	Periorbital area inflammation, right eye	unable to train	unable to train	unable to train	13.2	6.2	4.3
AS000104	12/27/17	8/27/18	y	243	<i>jimpy</i>	ASO P1p1.b	mild		39.4	49.5	27.8	14.5	9.0	11.3
ASO000S13	12/27/17	1/18/18	n	22	<i>jimpy</i>	uninjected	severe							
AS000105b	12/28/17	8/27/18	y	242	<i>jimpy</i>	ASO P1p1.b	mild		51.5	37.2	36.9	13.8	12.7	8.8
AS000106	12/28/17	8/27/18	y	242	<i>jimpy</i>	ASO P1p1.b	mild		34.7	27.4	37.2	15.0	15.5	8.9
AS000107	12/30/17	8/27/18	y	240	<i>jimpy</i>	ASO P1p1.a	mild		unable to train	unable to train	unable to train	11.3	15.7	12.8
AS000108	12/30/17	8/27/18	y	240	<i>jimpy</i>	ASO P1p1.a	mild	Periorbital area inflammation, bilateral	unable to train	17.0	unable to train	10.1	15.1	18.5
AS000109	12/31/17	8/27/18	y	239	<i>jimpy</i>	ASO P1p1.a	mild		14.3	34.1	3.3	15.1	14.2	10.7
ASO000S14	12/18/17	1/5/18	n	18	<i>jimpy</i>	uninjected	severe							
ASO000S15	12/18/17	1/5/18	n	18	<i>jimpy</i>	uninjected	severe							
ASO000S16	12/18/17	1/4/18	n	17	<i>jimpy</i>	uninjected	severe							
ASO000S17	1/6/18	1/25/18	n	19	<i>jimpy</i>	ASO control	severe							
ASO000S18	1/6/18	1/25/18	n	19	<i>jimpy</i>	ASO control	severe							
ASO000S19	12/29/17	1/18/18	n	20	<i>jimpy</i>	uninjected	severe							
AS000115	1/22/18	9/7/18	y	228	<i>jimpy</i>	ASO P1p1.b	mild		41.9	19.2	8.1	11.9	8.4	3.3
ASO000S20	1/22/18	3/30/18	n	67	<i>jimpy</i>	ASO P1p1.b	mild		31.1	dead	dead	20.5	dead	dead
AS000117	1/22/18	9/7/18	y	228	<i>jimpy</i>	ASO P1p1.b	mild		40.1	unable to train	unable to train	14.8	16.4	18.6
AS000110	1/18/18	9/17/18	y	242	<i>jimpy</i>	ASO P1p1.b	mild	Upper back inflammation	unable to train	unable to train	unable to train	23.9	25.2	17.3
ASO00096	12/7/17	7/23/18	y	228	wild-type	ASO control	none							
ASO00097	12/7/17	7/23/18	y	228	wild-type	ASO control	none							
ASO00099	12/7/17	7/23/18	y	228	wild-type	ASO control	none							
AS000100	12/5/17	7/23/18	y	230	wild-type	uninjected	none		111.1	110.8	63.7	8.2	1.4	3.9
AS000101	12/5/17	7/23/18	y	230	wild-type	uninjected	none		76.8	94.9	64.6	12.0	3.3	2.9
AS000102	12/5/17	7/23/18	y	230	wild-type	uninjected	none		53.1	54.3	67.0	8.0	7.9	3.8
AS000111	1/19/18	9/17/18	y	241	wild-type	uninjected	none		84.0	80.5	67.4	37.2	32.9	21.7
AS000112	1/19/18	9/17/18	y	241	wild-type	uninjected	none		107.0	61.0	76.3	17.9	7.5	6.2
AS000122	4/5/18	12/14/18	y	253	wild-type	ASO control	none				3.7			14.3
AS000123	4/5/18	12/14/18	y	253	wild-type	ASO control	none				18.3			1.8
AS000124	4/5/18	12/14/18	y	253	wild-type	ASO control	none				89.4			20.5
AS000125	4/5/18	12/14/18	y	253	wild-type	ASO control	none				107.1			13.2
AS000126	4/13/18	12/13/18	y	244	wild-type	ASO control	none				123.7			13.0
AS000127	4/13/18	12/13/18	y	244	wild-type	ASO control	none				45.4			20.4
AS000128	4/14/18	12/14/18	y	244	wild-type	ASO control	none							
ASO000S21	5/4/18	12/14/18	y	224	wild-type	ASO control	none							
ASO000S22	5/4/18	12/14/18	y	224	wild-type	ASO control	none							

Supplementary Data 6.

Table of metadata for all mice in Kaplan-Meier survival plot in Fig. 3b. We noted 5 of 13 of ASO-injected *jimpy* mice in our survival cohort developed periorbital or upper back skin inflammation. The underlying cause of this is unknown as it was not observed in ASO-injected wild-type littermates. Also included are raw data values for rotarod and open field assays in Fig. 4a, b.

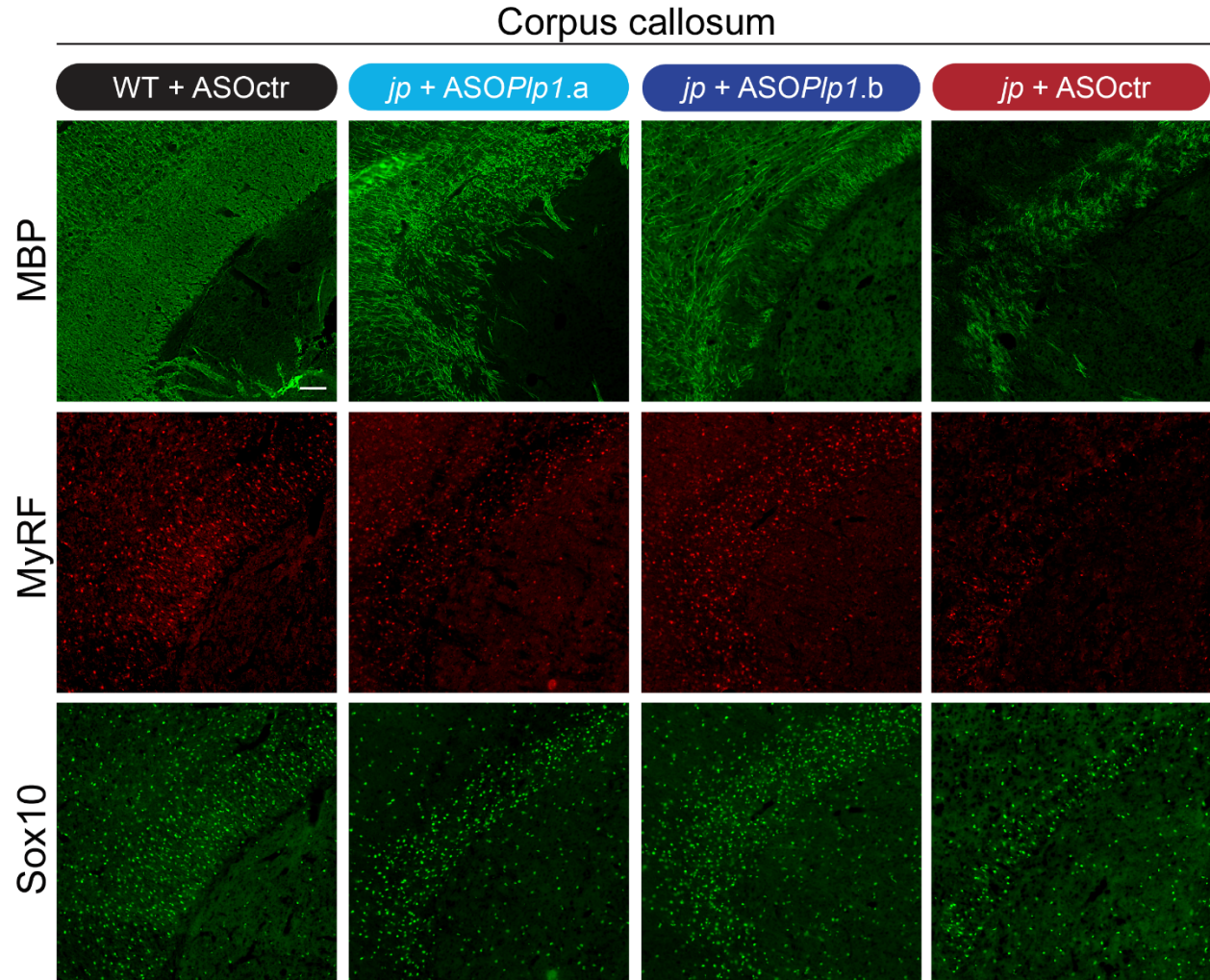
SUPPLEMENTARY DATA 7



Supplementary Data 7.

a-b, Labeled raw images of western blots for all samples in Fig. 2g and Extended Data Fig. 7a, c. The upper bands in the fluorescent blots in **(b)** are carry over from chemiluminescent detection of B-actin (bottom panel).

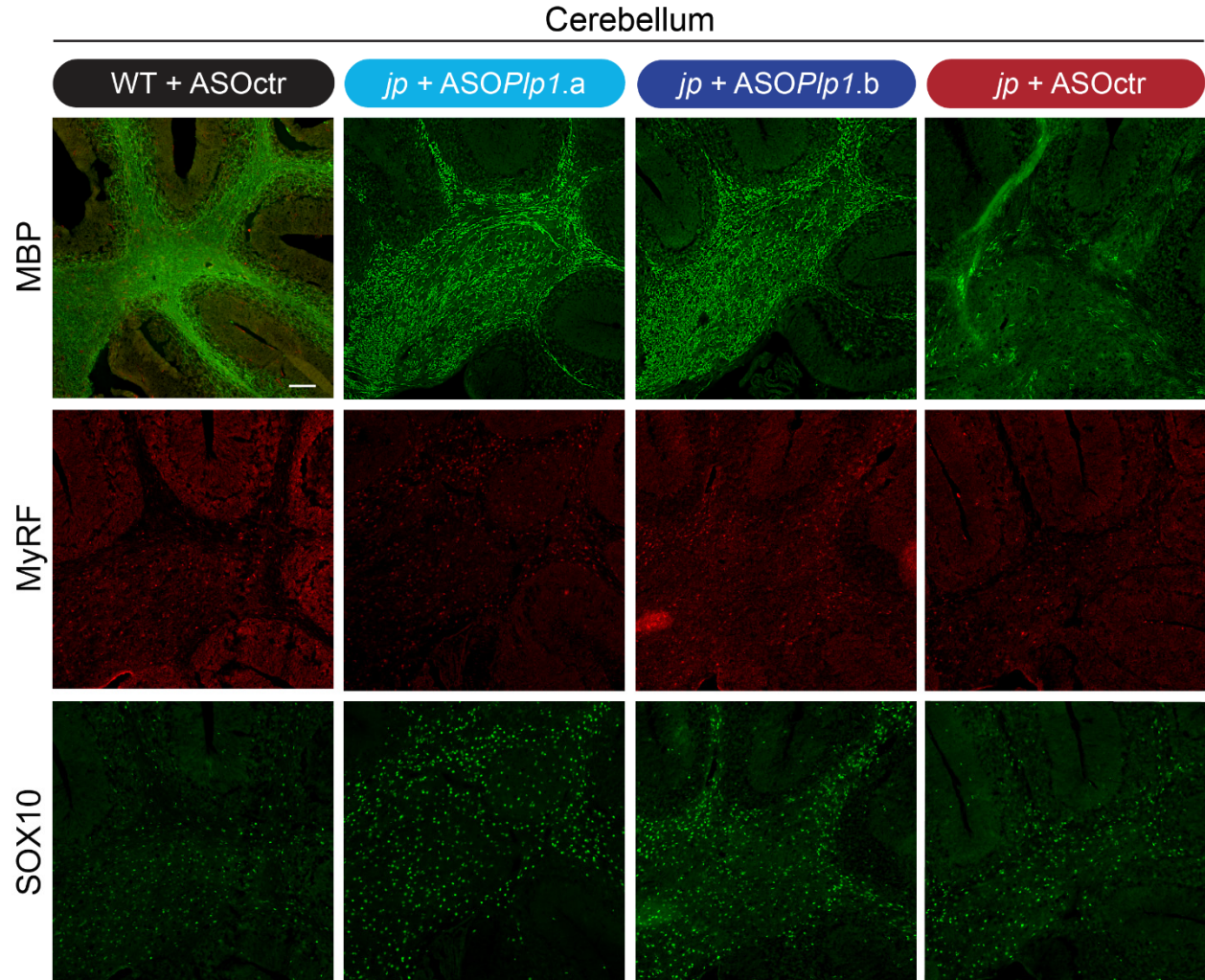
SUPPLEMENTARY DATA 8



Supplementary Data 8.

Representative source immunohistochemical images for counts in Fig. 3e,f of corpus callosum from mice, 3 weeks post-ASO injection (30ug dose at birth), showing MBP, MyRF, and Sox10. Replicate images generated for each biological replicate in Fig. 3e,f. Scale bar, 100µm.

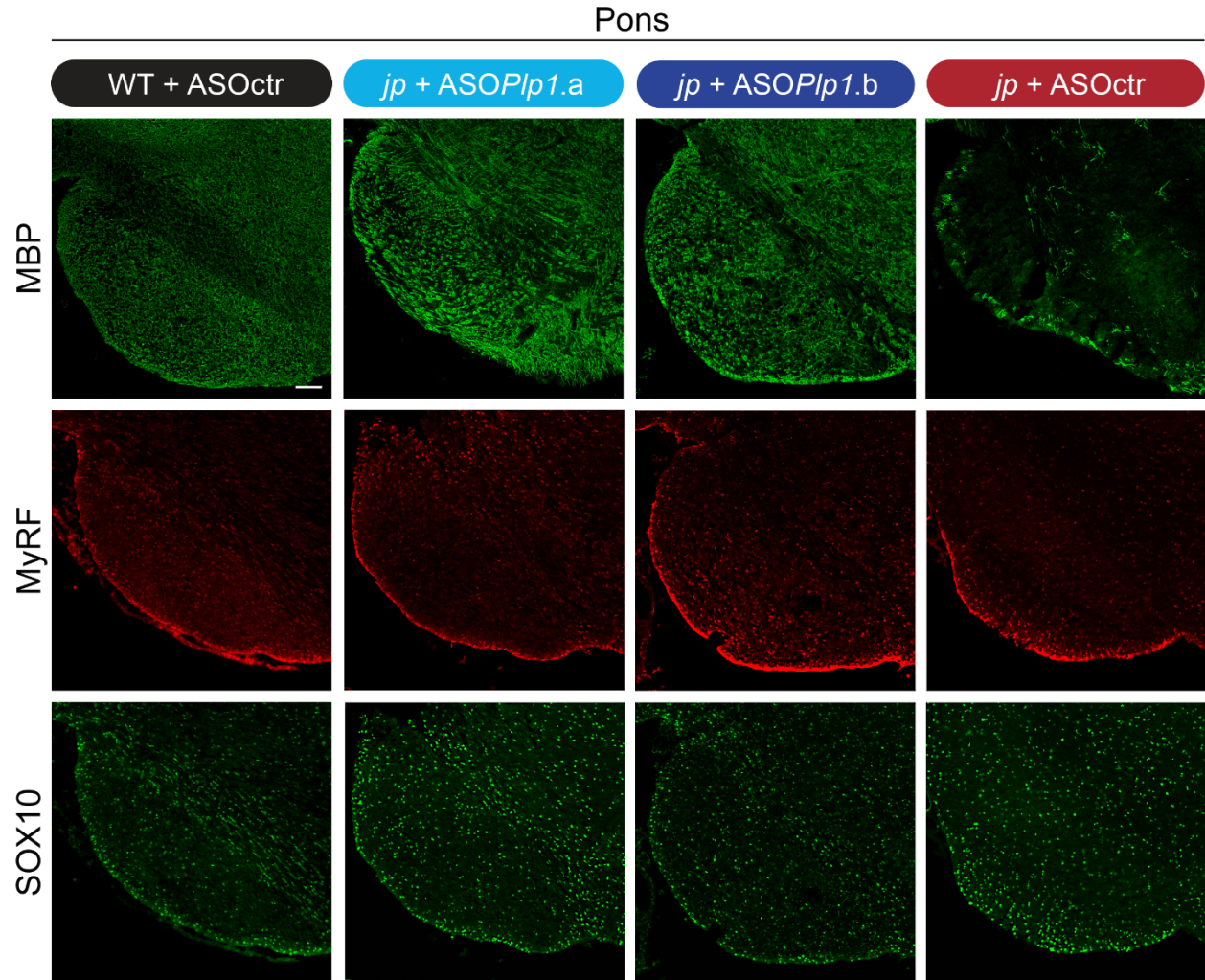
SUPPLEMENTARY DATA 9



Supplementary Data 9.

Representative source immunohistochemical images for counts in Fig. 3e,f of cerebellum from 3-week old mice injected at postnatal day 0 with the indicated ASOs showing MBP, MyRF, and Sox10. Replicate images generated for each biological replicate in Fig. 3e,f. Scale bar, 100 μ m.

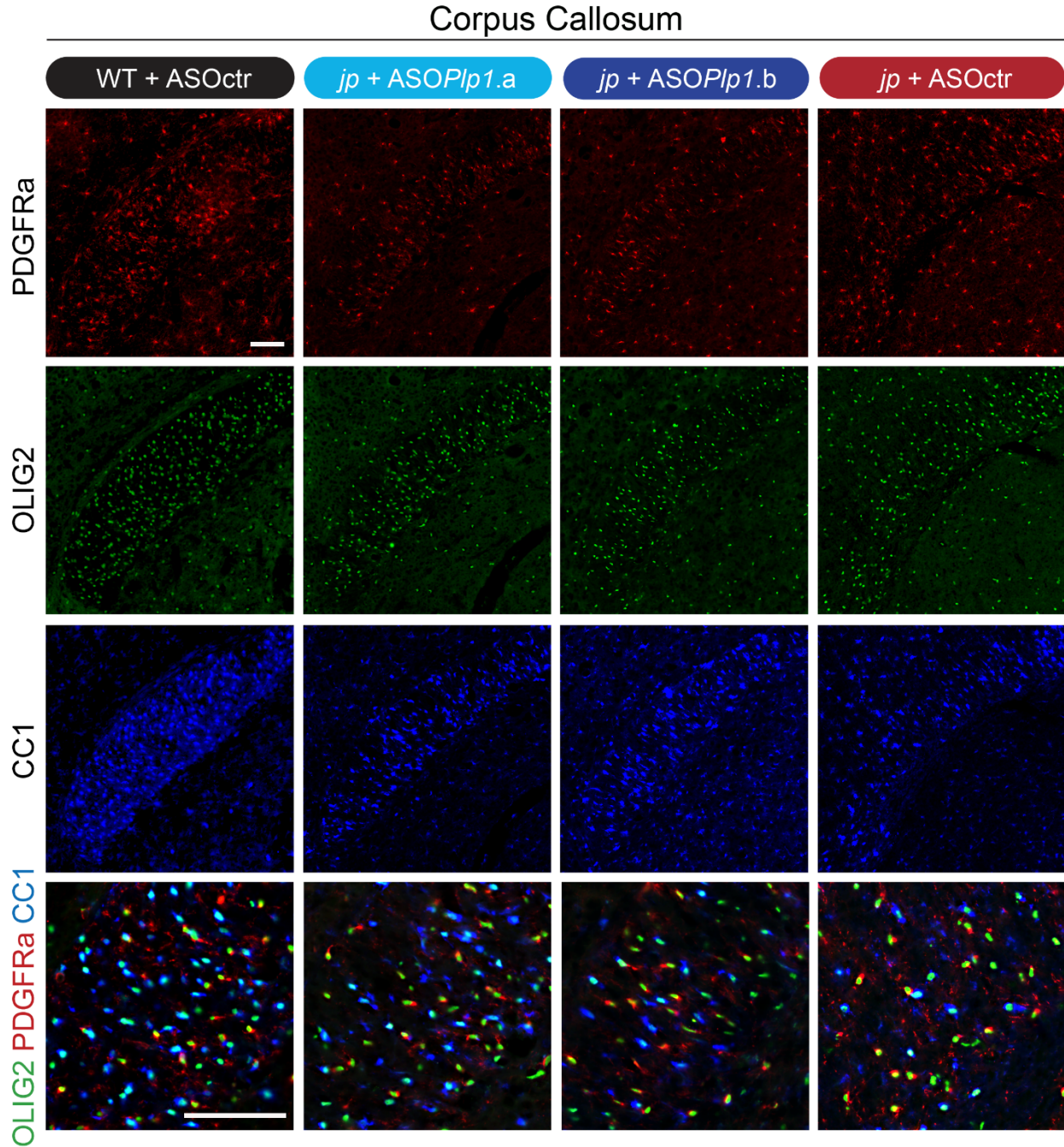
SUPPLEMENTARY DATA 10



Supplementary Data 10.

Representative source immunohistochemical images for counts in Fig. 3e,f of pons from mice, 3 weeks post-ASO injection (30ug dose at birth), showing MBP, MyRF, and Sox10. Replicate images generated for each biological replicate in Fig. 3e,f. Scale bar, 100 μ m.

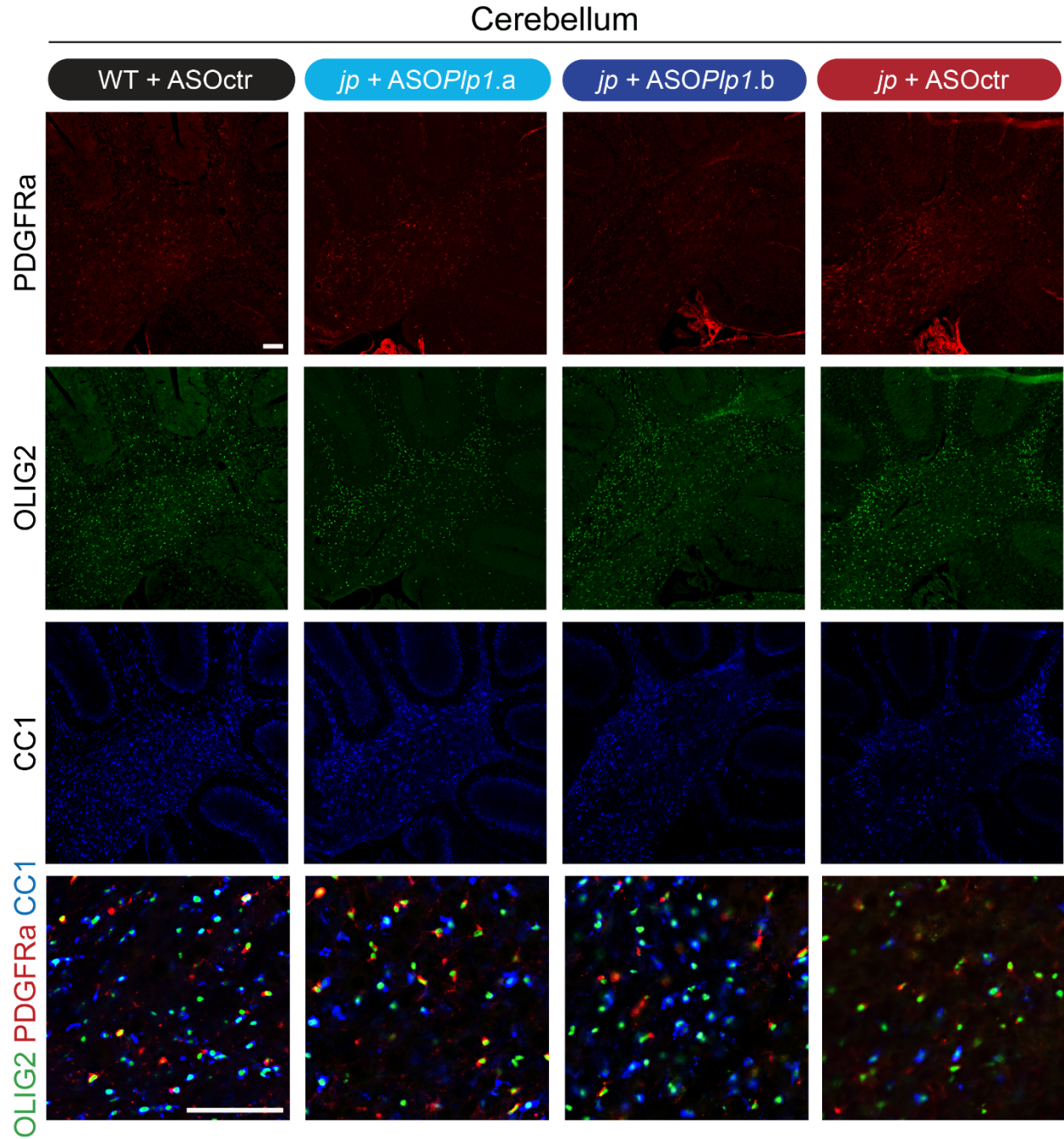
SUPPLEMENTARY DATA 11



Supplementary Data 11.

Representative source immunohistochemical images for counts in Extended Data Fig. 7f-h of corpus callosum from mice, 3 weeks post-ASO injection (30ug dose at birth), showing PDGFR α , Olig2, and CC1. Replicate images generated for each biological replicate in Extended Data Fig. 7f-h. Scale bar, 100 μ m.

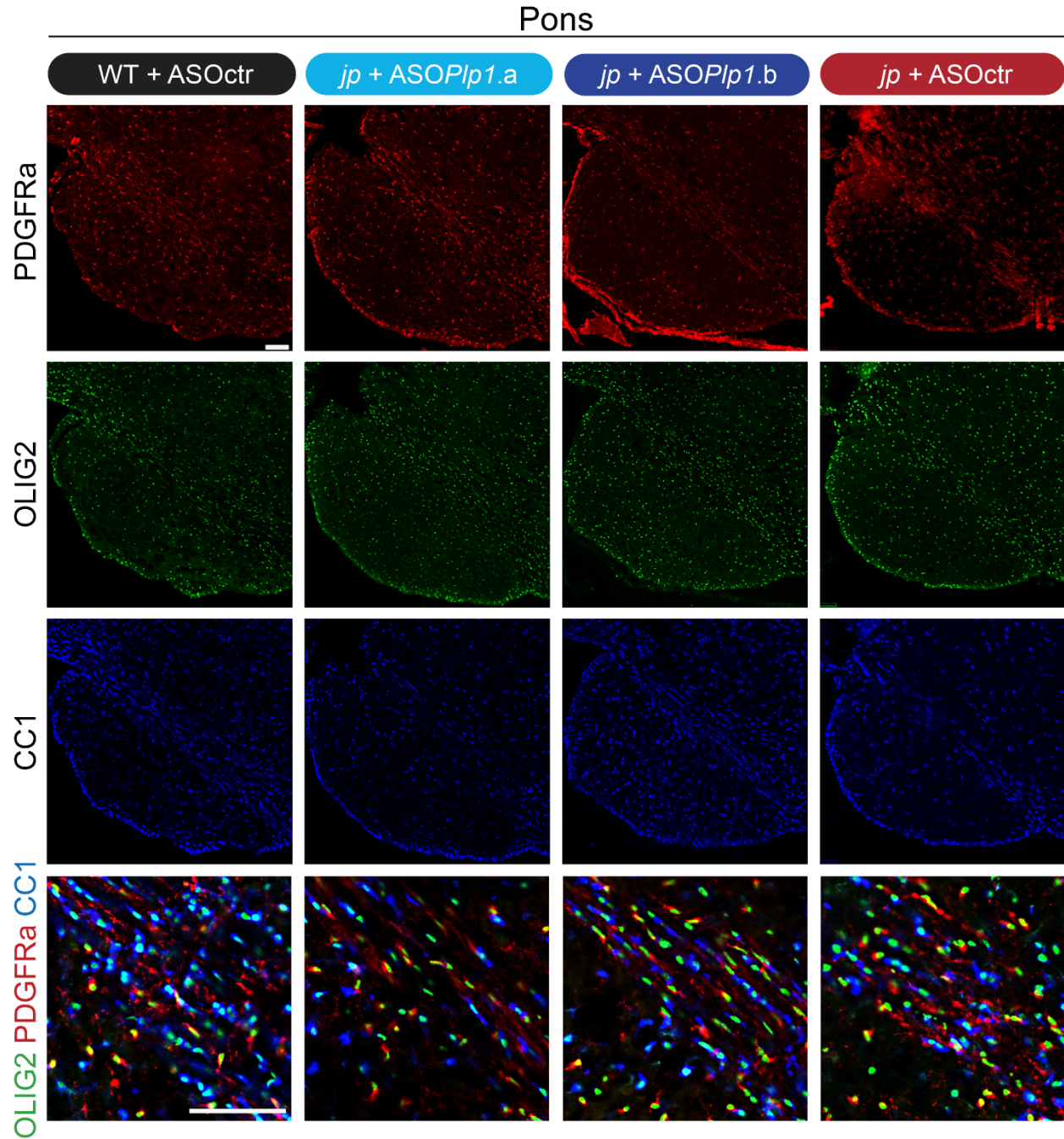
SUPPLEMENTARY DATA 12



Supplementary Data 12.

Representative source immunohistochemical images for counts in Extended Data Fig. 7f-h of cerebellum from mice, 3 weeks post-ASO injection (30 μ g dose at birth), showing PDGFR α , Olig2, and CC1. Replicate images generated for each biological replicate in Extended Data Fig. 7f-h. Scale bar, 100 μ m.

SUPPLEMENTARY DATA 13



Supplementary Data 13.

Representative source immunohistochemical images for counts in Extended Data Fig. 7f-h of pons collected from mice, 3 weeks post-ASO injection (30ug dose at birth), showing PDGFR α , Olig2, and CC1. Replicate images generated for each biological replicate in Extended Data Fig. 7f-h. Scale bar, 100 μ m.

SUPPLEMENTARY DATA 14

Analyzed breath number in different conditions

	Normal Air	5% CO ₂	10.5% O ₂
WT + ASOctr	18,194 (n=10)	7,556 (n=9)	2,471 (n=12)
<i>jp</i> + ASOctr	8,980 (n=10)	4,787 (n=8)	1,836 (n=8)
<i>jp</i> + ASOP <i>p</i> 1.b	7,175 (n=8)	6,573 (n=8)	1,846 (n=9)

Supplementary Data 14.

Cumulative analyzed breaths from mice, 3 weeks post-ASO injection (30ug dose at birth), after exposure to normal air, 5% CO₂, and 10.5% O₂. n corresponds to the number of individual mice analyzed in each cohort.

Supplementary References

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- 4 Sistermans, E. A. *et al.* A (G-to-A) mutation in the initiation codon of the proteolipid protein gene causing a relatively mild form of Pelizaeus-Merzbacher disease in a Dutch family. *Hum Genet* **97**, 337-339 (1996).
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