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Supplemental information

Characterization of AAV-mediated dorsal root ganglionopathy

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Table S1: Test article release data

Vector	Concentration (GC/mL)[A]		In vitro potency[B]		Endotoxin[C]	Bioburden[D]	AAV Purity[E]	
	At release	7 Months	At release	6 Months			At release	6 Months
AAV9.hCLN2-CEX	3.1×10^{13}	3.0×10^{13}	82%	98%	< 0.01 EU/mL	< 10 CFU/1 mL	98%	99%
AAV9.hCLN2-UC	3.1×10^{13}	3.2×10^{13}	91%	103%	< 0.01 EU/mL	< 10 CFU/1 mL	98%	99%
AAV9.hCLN2-AEX	3.1×10^{13}	3.0×10^{13}	76%	91%	< 0.01 EU/mL	< 10 CFU/1 mL	98%	99%
AAV9.hCLN2-AEX	1.1×10^{14}	1.1×10^{14}	75%	84%	0.11 EU/mL	< 10 CFU/1 mL	98%	99%
AAV9.Null	2.8×10^{13}	2.7×10^{13}	NA	NA	0.02 EU/mL	< 10 CFU/1 mL	98%	99%

A: transgene ddPCR; B: HEK293 Transduction followed by TPP1 enzymatic activity assay; C: Endosafe; D: USP <61> Membrane Filtration; E: SDS-CGE.

Table S2: Summary Incidence of Histopathology

Vector	Control	AAV9.hCLN2-CEX	AAV9.hCLN2-UC	AAV9.hCLN2-AEX	AAV9.hCLN2-AEX	Null
Dose (GC/animal)	**0**	**3.1×10^{13}**	**3.1×10^{13}**	**3.1×10^{13}**	**1.1×10^{14}**	**2.8×10^{13}**
Number of animals	**2/sex**	**2/sex**	**2/sex**	**2/sex**	**2/sex**	**2/sex**
Observation						
Brain						
-Perivascular mononuclear infiltrate in the meninges	0/4	4/4	4/4	3/4	4/4	1/4
-Neuronal degeneration	0/4	0/4	0/4	1/4	2/4	0/4
-Neuronal necrosis in the cerebellum	0/4	1/4	0/4	1/4	1/4	0/4
-Gliosis/microgliosis in multiple brain levels	2/4	4/4	4/4	4/4	4/4	0/4[a]
Dorsal Root Ganglia						
-Increased cellularity	1/4	4/4	4/4	3/4	4/4	2/4
-Neuronal degeneration	1.4	4/4	4/4	3/4	4/4	0/4
-Glial hypertrophy/hyperplasia	0/4	1/4	2/4	3/4	3/4	
Spinal Nerve Roots						
-Increased cellularity	0/4	3/4	2/4	4/4	4/4	0/4
-Degeneration	0/4	3/4	3/4	4/4	4/4	0/4
Sciatic Nerve						
-Degeneration	0/4	3/4	4/4	3/4	4/4	2/4
Spinal Cord						
-Degeneration of dorsal tracts	1/4	3/4	4/4	3/4	4/4	0/4
-Gliosis of gray matter	0/4	1/4	2/4	1/4	4/4	0/4
a: Noted in medulla oblongata only						

Table S3: Individual Histopathology – Brain

Treatment Group	Control				AAV9.hCLN2-CEX				AAV9.hCLN2-UC				AAV9.hCLN2-AEX				AAV9.hCLN2-AEX				Null			
Dose (GC/animal)	**0**				**3.1×10^{13}**				**3.1×10^{13}**				**3.1×10^{13}**				**1.1×10^{14}**				**2.8×10^{13}**			
Animal Number	**1**	**2**	**13**	**14**	**5**	**6**	**17**	**18**	**7**	**8**	**19**	**20**	**3**	**4**	**15A**	**16**	**9A**	**10**	**21**	**22**	**11**	**12**	**23**	**24**
Observation																								
Brain																								
-Perivascular mononuclear infiltrate in the meninges	-	-	-	-	2	3	2	2	2	2	2	2	2	2	1	-	2	2	2	2	-	-	-	2
-Neuronal degeneration	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-	-	-	1	2	-	-	-	-
-Neuronal necrosis in the cerebellum	-	-	-	-	-	-	1	-	-	-	-	-	1	-	-	-				1	-	-	-	-
-Gliosis/microgliosis in multiple brain levels[B]	-	1	2	3	2	2	3	2	2	2	3	3	2	1	3	1	2	3	4	3			2[A]	

Severity Grades: 1: Minimal; 2: Mild; 3: Moderate; 4: Marked; 5: Severe
A: Microgliosis in in Medulla Oblongata only
B: Highest severity grading only
- : Not observed

Table S4: Individual Histopathology – Spinal Cord

Treatment Group	Control				AAV9.hCLN2-CEX				AAV9.hCLN2-UC				AAV9.hCLN2-AEX				AAV9.hCLN2-AEX				Null			
Dose (GC/animal)	0				3.1×10^{13}				3.1×10^{13}				3.1×10^{13}				1.1×10^{14}				2.8×10^{13}			
Animal Number	1	2	13	14	5	6	17	18	7	8	19	20	3	4	15A	16	9A	10	21	22	11	12	23	24
Observation																								
Spinal Cord (Cervical)																								
-Degeneration of dorsal tracts	-	1	-	-	1	2	1	-	1	-	2	2	1	-	2	1	2	1	2	2	-	-	-	-
-Gliosis of gray matter	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-	-	2	-	-	-	-
Spinal Cord (Thoracic)																								
-Degeneration of dorsal tracts	-	-	-	-	1	2	1	-	-	1	2	-	2	-	2	1	2	1	2	2	-	-	-	-
-Gliosis of gray matter	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2	-	-	1	2	2	-	-	-	-
Spinal Cord (Lumbar)																								
-Degeneration of dorsal tracts	-	-	-	-	-	3	2	-	2	1	3	2	-	-	3	3	3	3	3	3	-	-	-	-
-Gliosis of gray matter	-	-	-	-	-	-	-	-	-	-	2	2	1	-	-	-	2	2	3	3	-	-	-	-
Spinal Cord (Lumbosacral)																								
-Degeneration of dorsal tracts	-	-	-	-	1	-	-	-	-	2	2	2	-	-	3	3	2	3	3	3	-	-	-	-
-Gliosis of gray matter	-	-	-	-	-	-	1	-	-	-	2	2	-	-	1	-	2	-	3	2	-	-	-	-
Spinal Nerve Roots (Cervical)																								
-Increased cellularity	-	-	-	-	-	-	-	-	-	-	2	-	-	-	1	-	3	-	-	1	-	-	-	-
-Degeneration	-	-	-	-	-	-	-	-	-	-	3	-	-	-	-	-	-	-	1	-	-	-	-	-
Spinal Nerve Roots (Thoracic)																								
-Increased cellularity	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-	-	-	-
-Degeneration	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	2	-	-	-	-
Spinal Nerve Roots (Lumbar)																								
-Increased cellularity	-	-	-	-	-	2	-	-	-	-	3	3	-	-	-	-	3	2	3	3	-	-	-	-
-Degeneration	-	-	-	-	-	-	-	-	-	-	3	5	-	-	-	-	3	2	3	4	-	-	-	-
Spinal Nerve Roots (Lumbosacral)																								
-Increased cellularity	-	-	-	-	3	3	3	-	-	-	3	3	2	3	2	3	3	3	3	3	-	-	-	-
-Degeneration	-	-	-	-	4	4	4	-	-	2	4	5	3	4	3	4	4	4	4	4	-	-	-	-

Severity Grades: 1: Minimal; 2: Mild; 3: Moderate; 4: Marked; 5: Severe
- : Not observed

Table S5: Individual Histopathology – Dorsal Root Ganglion

Treatment Group	Control				AAV9.hCLN2-CEX				AAV9.hCLN2-UC				AAV9.hCLN2-AEX				AAV9.hCLN2-AEX				Null			
Dose (GC/animal)	0				3.1×10^{13}				3.1×10^{13}				3.1×10^{13}				1.1×10^{14}				2.8×10^{13}			
Animal Number	1	2	13	14	5	6	17	18	7	8	19	20	3	4	15A	16	9A	10	21	22	11	12	23	24
Observation																								
Dorsal Root Ganglion (Cervical)																								
-Increased cellularity	-	-	-	-	-	-	1	-	-	-	2	-	-	1	1	-	3	-	2	3	-	-	-	-
-Neuronal degeneration	-	-	-	-	-	-	-	-	-	-	1	-	-	-	-	-	2	-	1	2	-	-	-	-
-Glial hypertrophy/hyperplasia	-	-	-	-	-	-	-	-	-	-	1	-	-	-	-	-	1	-	-	-	-	-	-	-
Dorsal Root Ganglion (Thoracic)																								
-Increased cellularity	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-	1	1	2	2	-	-	-	-
-Neuronal degeneration	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1	-	2	1	-	-	-	-
-Glial hypertrophy/hyperplasia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Dorsal Root Ganglion (Lumbar)																								
-Increased cellularity	-	-	-	-	1	2	2	-	-	1	3	3	1	-	1	-	1	2	4	3	-	-	-	-
-Neuronal degeneration	-	-	-	-	1	-	-	-	-	-	2	3	-	-	-	-	1	1	3	3	-	-	-	-
-Glial hypertrophy/hyperplasia	-	-	-	-	-	-	-	-	-	-	-	1	-	-	-	-	-	-	2	-	-	-	-	-
Dorsal Root Ganglion (Lumbosacral)																								
-Increased cellularity	-	-	1	-	4	4	3	2	2	3	3	4	3	3	3	-	3	3	4	3	-	2	1	-
-Neuronal degeneration	-	-	1	-	2	2	2	1	1	2	2	2	2	2	1	-	2	1	3	2	-	-	-	-
-Glial hypertrophy/hyperplasia	-	-	-	-	2	-	-	-	-	-	-	2	2	1	2	-	-	-	-	1	-	-	-	-
Nerve (sciatic)																								
-Degeneration	-	-	-	-	4	3	1	-	1	1	3	4	3	-	3	2	3	3	3	4	1	-	-	2

Severity Grades: 1: Minimal; 2: Mild; 3: Moderate; 4: Marked; 5: Severe
- : Not observed

Table S6: Peripheral Nerve Conduction – Sural (sensory) nerve conduction velocity

Group	Bsl NCV L (m/s) Mean±Std Dev		Mo1 NCV L (m/s) Mean±Std Dev		p-value[1]	Bsl NCV R(m/s) Mean±Std Dev		Mo1 NCV R (m/s) Mean±Std Dev		p-value[1]
1	30.0	±0.8	31.8	±3.0	0.30	29.8	±1.3	30.3	±1.3	0.59
2	32.3	±1.3	32.5	±1.0	0.77	31.8	±0.5	32.0	±0.8	0.62
3	30.8	±1.5	31.0	±1.4	0.82	30.3	±0.5	31.0	±0.6	0.54
4	31.3	±1.3	32.0	±1.2	0.41	31.3	±1.3	32.0	±1.3	0.79
5	30.8	±1.0	31.0	±1.2	0.75	30.8	±1.0	31.0	±1.3	0.77
6	31.0	±1.2	30.8	±1.0	0.75	30.5	±1.0	30.8	±1.7	0.13

[1]two tailed Student's t-test; normal sural NCV in primates recorded at the digital branches is > 30 m/s; minimal sural velocity varies depending on the recording location between 30 m/s and 45 m/s.

Bsl=baseline; Mo1= Day 28±1 timepoint; L=left; R=right; NCV=nerve conduction velocity

Table S7: Peripheral Nerve Conduction – Sural (sensory) SNAP amplitude

Group	Bsl SNAP Amp L (µV) Mean±Std Dev		Mo1 SNAP Amp L (µV) Mean±Std Dev		p-value[1]	Bsl SNAP Amp R (µV) Mean±Std Dev		Mo1 SNAP Amp R (µV) Mean±Std Dev		p-value[1]
1	10.6	±5.8	10.1	±3.3	0.88	±11.1	±6.8	11.0	±6.1	0.98
2	14.8	±3.2	13.6	±3.9	0.66	8.3	±4.7	8.5	±5.2	0.96
3	11.4	±6.4	11.0	±4.2	0.93	15.6	±6.0	16.1	±5.1	0.91
4	15.5	±8.1	14.5	±6.6	0.85	13.6	±7.6	13.1	±5.7	0.92
5	7.5	±2.9	9.4	±4.6	0.52	20.1	±9.2	19.7	±7.5	0.94
6	24.7	±15.1	18.2	±9.8	0.49	12.2	±5.8	12.7	±6.0	0.90

[1]two tailed Student's t-test

Bsl=baseline; Mo1= Day 28±1 timepoint; L=left; R=right; SNAP=sensory nerve action potential

Table S8: Peripheral Nerve Conduction – Radial (sensory) nerve conduction velocity

Group	Bsl NCV L (m/s) Mean±Std Dev		Mo1 NCV L (m/s) Mean±Std Dev		p-value[1]	Bsl NCV R(m/s) Mean±Std Dev		Mo1 NCV R (m/s) Mean±Std Dev		p-value[1]
1	58.5	±2.4	61.0	±4.2	0.34	59.5	±3.3	61.0	±3.8	0.58
2	61.3	±4.3	61.5	±3.8	0.93	61.3	±4.3	62.0	±4.0	0.81
3	62.8	±1.0	62.8	±1.5	1.00	61.8	±1.7	62.8	±1.2	0.27
4	63.5	±1.7	63.8	±0.5	0.79	63.0	±2.0	63.8	±2.4	0.13
5	62.5	±1.9	63.0	±1.2	0.67	62.0	±1.6	63.0	±3.0	0.09
6	62.5	±1.9	63.0	±2.0	0.73	62.5	±1.9	63.0	±3.0	1.00

[1]two tailed Student's t-test; normal radial NCV in primates is > 50 m/s

Bsl=baseline; Mo1= Day 28±1 timepoint; L=left; R=right; NCV=nerve conduction velocity

Table S9: Peripheral Nerve Conduction – Radial (sensory) SNAP amplitude

Group	Bsl SNAP Amp L (µV) Mean±Std Dev		Mo1 SNAP Amp L (µV) Mean±Std Dev		p-value[1]	Bsl SNAP Amp R (µV) Mean±Std Dev		Mo1 SNAP Amp R (µV) Mean±Std Dev		p-value[1]
1	50.2	±12.1	49.8	±10.8	0.96	45.3	±19.6	51.6	±13.2	0.61
2	37.2	±8.2	40.1	±8.1	0.63	33.1	±11.7	46.8	±20.4	0.29
3	34.1	±11.4	45.4	±14.2	0.26	38.1	±21.2	38.6	±15.1	0.97
4	30.8	±15.1	37.2	±4.4	0.45	35.8	±11.9	40.4	±9.9	0.57
5	59.2	±12.4	40.4	±13.3	0.08	54.2	±13.1	40.4	±8.1	0.12
6	34.7	±14.2	36.6	±10.6	0.83	42.5	±33.5	37.5	±7.6	0.78
[1]two tailed Student's t-test										

Bsl=baseline; Mo1= Day 28±1 timepoint; L=left; R=right; SNAP=sensory nerve action potential

Table S10: Peripheral Nerve Conduction – Fibular/peroneal (sensory) nerve conduction velocity

Group	Bsl NCV L (m/s) Mean±Std Dev		Mo1 NCV L (m/s) Mean±Std Dev		p-value[1]	Bsl NCV R(m/s) Mean±Std Dev		Mo1 NCV R (m/s) Mean±Std Dev		p-value[1]
1	63.5	±2.5	64.0	±2.9	0.80	62.8	±1.9	63.0	±3.9	0.91
2	61.3	±2.5	61.0	±2.2	0.88	62.0	±2.8	63.0	±2.0	0.58
3	61.3	±2.1	61.8	±2.9	0.79	61.3	±2.1	61.8	±1.7	0.39
4	61.8	±2.9	61.0	±2.4	0.70	61.0	±2.4	61.0	±0.0	1.00
5	62.5	±1.7	61.8	±1.5	0.54	63.3	±2.2	61.8	±3.4	0.64
6	61.3	±2.1	61.8	±1.5	0.71	61.3	±2.1	61.8	±3.3	0.29
[1]two tailed Student's t-test; normal peroneal NCV in primates is > 50 m/s										

Bsl=baseline; Mo1= Day 28±1 timepoint; L=left; R=right; NCV=nerve conduction velocity

Table S11: Peripheral Nerve Conduction – Fibular/peroneal (sensory) SNAP amplitude

Group	Bsl SNAP Amp L (µV) Mean±Std Dev		Mo1 SNAP Amp L (µV) Mean±Std Dev		p-value[1]	Bsl SNAP Amp R (µV) Mean±Std Dev		Mo1 SNAP Amp R (µV) Mean±Std Dev		p-value[1]
1	21.6	±8.3	21.0	±9.7	0.92	23.6	±9.3	20.4	±6.3	0.59
2	14.6	±6.2	16.2	±4.8	0.69	14.7	±4.1	15.3	±3.8	0.82
3	12.9	±2.6	13.1	±4.1	0.91	17.5	±8.9	17.0	±4.0	0.91
4	13.7	±5.3	14.7	±4.4	0.79	13.9	±5.6	14.1	±3.8	0.96
5	25.0	±10.3	20.0	±7.8	0.47	24.2	±7.1	20.8	±4.9	0.47
6	13.2	±6.7	13.6	±4.8	0.93	15.3	±8.9	15.4	±8.2	0.98
[1]two tailed Student's t-test										

Bsl=baseline; Mo1= Day 28±1 timepoint; L=left; R=right; SNAP=sensory nerve action potential

Table S12: Peripheral Nerve Conduction – Femoral (sensory) nerve conduction velocity

Group	Bsl NCV L (m/s) Mean±Std Dev		Mo1 NCV L (m/s) Mean±Std Dev		p-value[1]	Bsl NCV R (m/s) Mean±Std Dev		Mo1 NCV R (m/s) Mean±Std Dev		p-value[1]
1	31.0	±1.2	32.3	±1.9	0.30	32.0	±1.4	31.0	±1.4	0.36
2	32.3	±1.7	32.0	±0.8	0.80	31.8	±0.5	32.8	±0.5	0.03*↑
3	32.5	±1.0	34.3	±2.2	0.20	32.3	±1.0	34.3	±0.8	0.70
4	31.5	±1.0	32.3	±1.0	0.32	32.0	±0.8	32.3	±3.4	0.50
5	32.0	±0.0	32.0	±0.0	-	32.3	±0.6	32.0	±1.0	0.81
6	32.3	±2.4	32.8	±1.7	0.74	33.3	±2.1	32.8	±0.5	1.00
↑=NCV increased compared to baseline; [1]two tailed Student's t-test; *$p \leq 0.05$; normal femoral NCV in primates is > 30 m/s										

Bsl=baseline; Mo1= Day 28±1 timepoint; L=left; R=right; NCV=nerve conduction velocity

Table S13: Peripheral Nerve Conduction – Femoral (sensory) SNAP amplitude

Group	Bsl SNAP Amp L (µV) Mean±Std Dev		Mo1 SNAP Amp L (µV) Mean±Std Dev		p-value[1]	Bsl SNAP Amp R (µV) Mean±Std Dev		Mo1 SNAP Amp R (µV) Mean±Std Dev		p-value[1]
1	15.4	±2.3	13.3	±1.2	0.17	14.9	±3.4	12.5	±2.0	0.27
2	13.5	±3.4	13.9	±2.2	0.85	13.1	±2.4	13.0	±2.3	0.97
3	12.2	±1.8	12.5	±2.3	0.86	11.6	±0.7	12.0	±2.7	0.82
4	13.5	±2.3	13.8	±2.0	0.85	13.2	±2.3	12.9	±0.6	0.84
5	14.8	±1.3	14.2	±1.3	0.62	15.4	±2.6	15.1	±3.6	0.91
6	14.7	±4.4	15.0	±2.8	0.93	14.9	±3.0	13.9	±1.7	0.58
[1]two tailed Student's t-test										

Bsl=baseline; Mo1= Day 28±1 timepoint; L=left; R=right; SNAP=sensory nerve action potential

Table S14: Peripheral Nerve Conduction – Tibial (motor) nerve conduction velocity

Group	Bsl NCV L (m/s) Mean±Std Dev		Mo1 NCV L (m/s) Mean±Std Dev		p-value[1]	Bsl NCV R (m/s) Mean±Std Dev		Mo1 NCV R (m/s) Mean±Std Dev		p-value
1	73.8	±7.6	78.8	±6.3	0.35	73.8	±8.0	78.0	±5.4	0.47
2	80.0	±1.6	81.8	±2.4	0.27	80.0	±1.9	82.0	±3.6	0.26
3	81.0	±1.2	82.3	±2.1	0.33	81.0	±1.2	81.0	±1.2	1.00
4	81.8	±2.9	84.0	±6.4	0.54	81.8	±2.9	82.3	±3.7	0.84
5	82.0	±0.0	84.0	±4.0	0.36	82.0	±0.0	84.5	±2.9	0.13
6	77.0	±1.4	80.5	±1.9	0.03*↑	77.0	±1.4	82.3	±2.1	0.01*↑
↑=NCV increased compared to baseline; [1]two tailed Student's t-test; *$p \leq 0.05$; normal tibial NCV in primates is > 60 m/s										

Bsl=baseline; Mo1= Day 28±1 timepoint; L=left; R=right; NCV=nerve conduction velocity

Table S15: Peripheral Nerve Conduction – Tibial (motor) CMAP amplitude and duration at Hock

Group	Bsl CMAP Amp L (mV) Mean±Std Dev		Mo1 CMAP Amp L (mV) Mean±Std Dev		p-value[1]	Bsl CMAP Dur L (ms) Mean±Std Dev		Mo1 CMAP Dur L (ms) Mean±Std Dev		p-value
1	10.0	±3.2	6.3	±2.4	0.11	2.8	±1.1	3.0	±0.8	0.81
2	11.4	±4.7	8.9	±3.9	0.46	2.1	±0.3	2.1	±0.2	0.86
3	6.4	±3.3	7.3	±2.2	0.66	2.5	±0.3	2.5	±0.5	0.91
4	12.7	±6.9	7.9	±2.1	0.23	2.6	±0.5	2.5	±0.4	0.56
5	9.5	±6.0	6.6	±2.3	0.40	2.0	±0.5	2.1	±0.3	0.76
6	5.7	±3.7	6.4	±3.8	0.81	2.8	±1.0	7.4	±0.5	0.63
[1]two tailed Student's t-test										

Bsl=baseline; Mo1= Day 28±1 timepoint; L=left; CMAP=compound muscle action potential

Table S16: Peripheral Nerve Conduction – Tibial (motor) CMAP amplitude and duration at Popliteal Fossa

Group	Bsl CMAP Amp L (mV) Mean±Std Dev		Mo1 CMAP Amp L (mV) Mean±Std Dev		p-value[1]	Bsl CMAP Dur L (ms) Mean±Std Dev		Mo1 CMAP Dur L (ms) Mean±Std Dev		p-value
1	6.8	±3.7	4.5	±2.2	0.33	3.6	±1.3	2.3	±0.8	0.15
2	7.6	±2.9	9.4	±4.0	0.50	1.9	±0.1	2.2	±0.3	0.03[2]
3	5.2	±1.8	6.6	±2.2	0.36	2.3	±0.3	2.6	±0.7	0.50
4	11.4	±4.4	6.4	±1.8	0.08	2.1	±0.4	2.1	±0.8	0.97
5	5.7	±3.7	5.9	±2.4	0.93	1.8	±0.5	2.0	±0.3	0.59
6	4.9	±3.4	7.4	±4.6	0.41	2.9	±1.6	2.5	±0.5	0.66
[1]two tailed Student's t-test; [2] change not considered physiologically relevant										

Bsl=baseline; Mo1= Day 28±1 timepoint; L=left; CMAP=compound muscle action potential

Table S17: Intraepidermal Nerve Fiber Density

Group	Dose (GC/animal)	Animal	In-life Density (nerve fibers/mm)	Post-Life Density (nerve fibers/mm)	In-life compared to Post-Life (p-value)
Control	**0**	**1**	61.52	49.87	
		2	46.85	52.64	
		13	59.96	63.19	
		14	67.29	55.74	
		Average	**58.91**	**55.36**	**0.5038**
		Std Dev	**8.63**	**5.74**	
AAV9.hCLN2-CEX	**3.1×10^{13}**	**5**	52.08	29.88	
		6	59.87	25.23	
		17	62.25	56.47	
		18	43.56	42.32	
		Average	**54.44**	**38.48**	**0.1292**
		Std Dev	**8.45**	**14.00**	
AAV9.hCLN2-UC	**3.1×10^{13}**	**7**	66.60	41.24	
		8	76.05	57.28	
		19	47.63	47.48	
		20	66.80	42.91	
		Average	**64.27**	**47.23**	**0.0607**
		Std Dev	**11.94**	**7.2**	
AAV9.hCLN2-AEX	**3.1×10^{13}**	**3**	52.08	29.88	
		4	59.87	25.23	
		15A	62.25	56.47	
		16	43.56	42.32	
		Average	**47.25**	**45.51**	**0.6657**
		Std Dev	**6.63**	**13.41**	
AAV9.hCLN2-AEX	**1.1×10^{14}**	**9A**	-	40.35	
		10	41.63	45.1	
		21	33.72	49.94	
		22	62.79	44.27	
		Average	**46.05**	**44.92**	**0.9728**
		Std Dev	**15.03**	**3.94**	
Null	**2.8×10^{13}**	**11**	71.24	41.56	
		12	42.17	42.83	
		23	40.55	-	
		24	36.17	47.44	
		Average	**47.53**	**43.94**	**0.6773**
		Std Dev	**16.01**	**3.09**	

Data were statistically analyzed using a standard t-test. The resulting p-values of the standard t-test are reported as "In-Life Compared to Post-Life" in the data table. The t-test was two-tailed (meaning no hypothesis was made on which group was expected to have the highest values), and independent (meaning the data did not rely on the data from other groups). Statistical analyses were performed comparing test article-dosed groups against their sex-matched controls. A p value <0.05 was considered statistically significant.

Table S18: Individual MRI Data – Dorsal Spinal Cord

Group	Animal	Time	Axial-Diffusion (mm^2/s)	FA (N/A)	Mean Diffusivity (mm^2/s)	Radial-Diffusion (mm^2/s)	STIR-Intensity	s2neuroT2TFE Intensity
1	1	Baseline	0.00120075	0.377746	0.000829654	0.000644096	216.222	572.333
	2	Baseline	0.00186243	0.442552	0.0012299	0.000913626	207.813	495.034
	13	Baseline	0.00358588	0.352199	0.00255417	0.0020383	-	468.361
	14	Baseline	0.0017107	0.588897	0.000989876	0.000629458	187.589	493.697
		Mean	**0.0021**	**0.4403**	**0.0014**	**0.0011**	**203.8747**	**507.3563**
		Std Dev	**0.0010**	**0.1061**	**0.0008**	**0.0007**	**14.7172**	**45.0223**
	1	4 Weeks	0.00130688	0.388437	0.000901472	0.000698771	217.213	495.091
	2	4 Weeks	0.00147402	0.498117	0.000940103	0.000673108	199.007	392.891
	13	4 Weeks	0.00228556	0.482422	0.00144598	0.00102615	245.646	657.755
	14	4 Weeks	0.00209573	0.496266	0.0013433	0.000967106	220.331	479.323
		Mean	**0.0018**	**0.4663**	**0.0012**	**0.0008**	**220.5493**	**506.2650**
		Std Dev	**0.0005**	**0.0524**	**0.0003**	**0.0002**	**19.1928**	**110.5345**
		p-value	0.4776	0.6162	0.4988	0.5130	0.5757	0.9879
5	10	Baseline	0.00160139	0.433951	0.00106099	0.0007908	180.545	205.222
	21	Baseline	0.00300759	0.439511	0.00197255	0.00145504	-	446.847
	22	Baseline	0.00246861	0.34194	0.00180666	0.00147568	220.601	465.851
		Mean	**0.0024**	**0.4051**	**0.0016**	**0.0012**	**200.5730**	**372.6400**
		Std Dev	**0.0007**	**0.0548**	**0.0005**	**0.0004**	**28.3239**	**145.2993**
	9A	4 Weeks	0.00128445	0.335336	0.000908114	0.000719929	233.449	465.97
	10	4 Weeks	0.00145124	0.359459	0.0010285	0.000817113	207.915	537.373
	21	4 Weeks	0.00201447	0.380451	0.00141343	0.00111291	295.743	505.945
	22	4 Weeks	0.00155738	0.352179	0.00110892	0.000884648	228.73	427.006
		Mean	**0.0016**	**0.3569**	**0.0011**	**0.0009**	**241.4593**	**484.0735**
		Std Dev	**0.0003**	**0.0187**	**0.0002**	**0.0002**	**37.8512**	**47.9709**
		p-value	0.1254	0.2554	0.1680	0.2339	0.3162	0.4009

FA: Fractional anisotropy
Data were statistically analyzed using a standard t-test. Statistical analyses were performed comparing groups against their baseline. A p value <0.05 was considered statistically significant.

Table S19: Individual MRI Data – L3

Group	Animal	Time	Axial-Diffusion (mm^2/s)	FA (N/A)	Mean Diffusivity (mm^2/s)	Radial-Diffusion (mm^2/s)	STIR-Intensity	s2neuroT2TFE-Intensity
1	1	Baseline	0.00254818	0.419432	0.00171813	0.0013031	229.884	311.782
	2	Baseline	0.00210474	0.306864	0.00163338	0.0013977	182.754	298.096
	13	Baseline	0.00177128	0.358492	0.00140381	0.00122006	-	286.552
	14	Baseline	0.00274187	0.325031	0.00207462	0.00174102	273.909	373.61
		Mean	**0.0023**	**0.3525**	**0.0017**	**0.0014**	**228.8490**	**317.5100**
		Std Dev	**0.0004**	**0.0495**	**0.0003**	**0.0002**	**45.5863**	**38.7957**
	1	4 Weeks	0.00137762	0.461512	0.000956394	0.000745762	149.698	306.284
	2	4 Weeks	0.00193208	0.35845	0.0014947	0.00127597	156.513	285.009
	13	4 Weeks	0.00251558	0.297468	0.00198014	0.00171238	209.127	357.326
	14	4 Weeks	0.00217019	0.332149	0.00161341	0.00133503	256.08	347.454
		Mean	**0.0020**	**0.3624**	**0.0015**	**0.0013**	**192.8545**	**324.0183**
		Std Dev	**0.0005**	**0.0706**	**0.0004**	**0.0004**	**49.8178**	**34.1314**
		p-value	0.5192	0.7228	0.5434	0.5681	0.1681	0.7852
5	10	Baseline	0.00195684	0.325297	0.00154283	0.0013358	119.781	249.798
	21	Baseline	0.00212273	0.387806	0.00150558	0.001197	-	305.819
	22	Baseline	0.00131334	0.482013	0.00094252	0.000757093	186.584	275.208
		Mean	**0.0018**	**0.3984**	**0.0013**	**0.0011**	**153.1825**	**276.9417**
		Std Dev	**0.0004**	**0.0789**	**0.0003**	**0.0003**	**47.2369**	**28.0507**
	9A	4 Weeks	0.00148586	0.431432	0.00105765	0.000843535	181.999	294.449
	10	4 Weeks	0.00213318	0.376377	0.00154507	0.001251	185.483	345.032
	21	4 Weeks	0.00200624	0.36973	0.00145237	0.00117542	155.303	362.748
	22	4 Weeks	0.00202447	0.363506	0.00147571	0.00120129	189.642	402.046
		Mean	**0.0019**	**0.3853**	**0.0014**	**0.0011**	**178.1068**	**351.0688**
		Std Dev	**0.0003**	**0.0312**	**0.0002**	**0.0002**	**15.5202**	**44.6368**
		p-value	0.4000	0.6212	0.4804	0.5692	0.4704	**0.0441**

FA: Fractional anisotropy
Data were statistically analyzed using a standard t-test. Statistical analyses were performed comparing groups against their baseline. A p value <0.05 was considered statistically significant.

Table S20: Individual MRI Data – L4

Group	Animal	Time	Axial-Diffusion (mm^2/s)	FA (N/A)	Mean Diffusivity (mm^2/s)	Radial-Diffusion (mm^2/s)	STIR-Intensity	s2neuroT2TFE-Intensity
1	1	Baseline	0.00164009	0.480537	0.00109337	0.000820004	140.605	312.313
	2	Baseline	0.00183719	0.387882	0.00130171	0.00103396	145.795	329.708
	13	Baseline	0.00161384	0.388804	0.00122764	0.00103453	-	301.515
	14	Baseline	0.00232294	0.349862	0.00171092	0.00140491	194.55	345.484
		Mean	**0.0019**	**0.4018**	**0.0013**	**0.0011**	**160.3167**	**322.2550**
		Std Dev	**0.0003**	**0.0556**	**0.0003**	**0.0002**	**29.7603**	**19.3574**
	1	4 Weeks	0.00158203	0.451504	0.00109979	0.000858655	154.637	332.698
	2	4 Weeks	0.00195503	0.427391	0.00134453	0.00103925	155.568	356.948
	13	4 Weeks	0.00241949	0.369827	0.00176532	0.00143822	197.872	359.617
	14	4 Weeks	0.00166999	0.38537	0.00123614	0.0010192	212.727	325.864
		Mean	**0.0019**	**0.4085**	**0.0014**	**0.0011**	**180.2010**	**343.7818**
		Std Dev	**0.0004**	**0.0376**	**0.0003**	**0.0002**	**29.6114**	**17.0098**
		p-value	0.8708	0.7311	0.9008	0.9296	**0.0288**	0.2707
5	10	Baseline	0.0018994	0.390417	0.00142887	0.00119359	132.279	301.655
	21	Baseline	0.00161676	0.497399	0.00106419	0.000787914	-	300.433
	22	Baseline	0.00115742	0.503597	0.000801095	0.00062291	153.137	290.143
		Mean	**0.0016**	**0.4638**	**0.0011**	**0.0009**	**142.7080**	**297.4103**
		Std Dev	**0.0004**	**0.0636**	**0.0003**	**0.0003**	**14.7488**	**6.3233**
	9A	4 Weeks	0.00168598	0.445452	0.00113229	0.000855428	192.15	343.738
	10	4 Weeks	0.0021749	0.409252	0.00150562	0.00117096	191.293	393.707
	21	4 Weeks	0.00191731	0.367454	0.00136742	0.00109246	191.423	402.882
	22	4 Weeks	0.00205229	0.371177	0.00146943	0.00117797	203.456	420.291
		Mean	**0.0020**	**0.3983**	**0.0014**	**0.0011**	**194.5805**	**390.1545**
		Std Dev	**0.0002**	**0.0367**	**0.0002**	**0.0002**	**5.9290**	**32.8497**
		p-value	0.1364	0.2460	0.1798	0.2372	0.0505	**0.0109**

FA: Fractional anisotropy
Data were statistically analyzed using a standard t-test. Statistical analyses were performed comparing groups against their baseline. A p value <0.05 was considered statistically significant.

Table S21: Individual MRI Data – L5

Group	Animal	Time	Axial-Diffusion (mm^2/s)	FA (N/A)	Mean Diffusivity (mm^2/s)	Radial-Diffusion (mm^2/s)	STIR-Intensity	s2neuroT2TFE-Intensity
1	1	Baseline	0.00171802	0.513196	0.00108433	0.000767472	136.523	307.388
	2	Baseline	0.00183058	0.477933	0.00119043	0.000870346	146.86	335.953
	13	Baseline	0.00119133	0.534825	0.000793294	0.000594253	-	293.161
	14	Baseline	0.00202071	0.475374	0.00130486	0.000946939	163.455	388.222
		Mean	**0.0017**	**0.5003**	**0.0011**	**0.0008**	**148.9460**	**331.1810**
		Std Dev	**0.0004**	**0.0288**	**0.0002**	**0.0002**	**13.5866**	**41.9844**
	1	4 Weeks	0.00178225	0.514975	0.00113855	0.000816686	189.72	340.438
	2	4 Weeks	0.00202022	0.451508	0.00134671	0.00100994	198.558	394.455
	13	4 Weeks	0.002171	0.443973	0.00146674	0.00111458	198.43	373.173
	14	4 Weeks	0.00191686	0.45356	0.0013009	0.000992919	231.89	384.967
		Mean	**0.0020**	**0.4660**	**0.0013**	**0.0010**	**204.6495**	**373.2583**
		Std Dev	**0.0002**	**0.0329**	**0.0001**	**0.0001**	**18.6255**	**23.5483**
		p-value	0.3243	0.1818	0.2502	0.1923	**0.0085**	0.1003
5	10	Baseline	0.00179584	0.42432	0.00125173	0.000979678	142.24	309.457
	21	Baseline	0.00164786	0.640985	0.000893478	0.000516288	-	344.361
	22	Baseline	0.00132893	0.510176	0.000874912	0.000647898	155.895	311.214
		Mean	**0.0016**	**0.5252**	**0.0010**	**0.0007**	**149.0675**	**321.6773**
		Std Dev	**0.0002**	**0.1091**	**0.0002**	**0.0002**	**9.6555**	**19.6643**
	9A	4 Weeks	0.00158349	0.446996	0.0010521	0.000786382	243.059	368.202
	10	4 Weeks	0.00194564	0.427661	0.00131997	0.00100711	194.482	392.925
	21	4 Weeks	0.00179698	0.428462	0.00122466	0.000938493	204.062	397.044
	22	4 Weeks	0.00186158	0.453116	0.00123514	0.000921888	199.246	408.704
		Mean	**0.0018**	**0.4391**	**0.0012**	**0.0009**	**210.2123**	**391.7188**
		Std Dev	**0.0002**	**0.0129**	**0.0001**	**0.0001**	**22.2444**	**17.0426**
		p-value	0.1622	0.3015	0.1123	0.1712	0.0590	**0.0277**

FA: Fractional anisotropy
Data were statistically analyzed using a standard t-test. Statistical analyses were performed comparing groups against their baseline. A p value <0.05 was considered statistically significant.

Table S22: Individual MRI Data – L6

Group	Animal	Time	Axial-Diffusion (mm^2/s)	FA (N/A)	Mean Diffusivity (mm^2/s)	Radial-Diffusion (mm^2/s)	STIR-Intensity	s2neuroT2TFE-Intensity
1	1	Baseline	0.00159837	0.554987	0.00099051	0.000686566	156.526	338.848
	2	Baseline	0.00187633	0.530051	0.00115788	0.000798624	139.23	330.96
	13	Baseline	0.00143129	0.531231	0.000934308	0.000685796	-	273.402
	14	Baseline	0.0017205	0.494426	0.00109932	0.000788728	143.242	330.732
		Mean	**0.0017**	**0.5277**	**0.0010**	**0.0007**	**146.3327**	**318.4855**
		Std Dev	**0.0002**	**0.0250**	**0.0001**	**0.0001**	**9.0527**	**30.2916**
	1	4 Weeks	0.00158257	0.468136	0.00105818	0.000795969	196.544	355.668
	2	4 Weeks	0.00204625	0.513793	0.00131583	0.000950595	194.136	370.981
	13	4 Weeks	0.00196683	0.342915	0.00144639	0.00118614	193.588	340.436
	14	4 Weeks	0.00183349	0.454908	0.00124615	0.000952471	201.097	334.271
		Mean	**0.0019**	**0.4449**	**0.0013**	**0.0010**	**196.3413**	**350.3390**
		Std Dev	**0.0002**	**0.0725**	**0.0002**	**0.0002**	**3.4206**	**16.4392**
		p-value	0.1881	0.1185	0.1117	0.0833	0.0115	0.1065
5	10	Baseline	0.00174956	0.484861	0.00115743	0.000861361	172.861	350.049
	21	Baseline	0.0012488	0.643431	0.000679148	0.000394318	-	236.313
	22	Baseline	0.00129135	0.519297	0.000856608	0.000639229	112.58	235.083
		Mean	**0.0014**	**0.5492**	**0.0009**	**0.0006**	**142.7205**	**273.8150**
		Std Dev	**0.0003**	**0.0834**	**0.0002**	**0.0002**	**42.6251**	**66.0234**
	9A	4 Weeks	0.00153564	0.49319	0.000999931	0.000732061	233.007	332.064
	10	4 Weeks	0.00200311	0.377531	0.00142451	0.00113518	248.734	455.517
	21	4 Weeks	0.00146819	0.477278	0.000973735	0.000726497	179.968	334.797
	22	4 Weeks	0.00148491	0.464362	0.00100701	0.00076803	185.793	341.016
		Mean	**0.0016**	**0.4531**	**0.0011**	**0.0008**	**211.8755**	**365.8485**
		Std Dev	**0.0003**	**0.0517**	**0.0002**	**0.0002**	**34.1735**	**59.8962**
		p-value	**0.0061**	0.0764	**0.0330**	0.0559	**0.0114**	**0.0005**

FA: Fractional anisotropy
Data were statistically analyzed using a standard t-test. Statistical analyses were performed comparing groups against their baseline. A p value <0.05 was considered statistically significant.

Table S23: Individual MRI Data – S1

Group	Animal	Time	Axial-Diffusion (mm^2/s)	FA (N/A)	Mean Diffusivity (mm^2/s)	Radial-Diffusion (mm^2/s)	STIR-Intensity	s2neuroT2TFE-Intensity
1	1	Baseline	0.0011955	0.55935	0.000753139	0.000531953	109.41	209.57
	2	Baseline	0.00172125	0.467917	0.00114881	0.000862576	131.155	251.252
	13	Baseline	0.00232384	0.353559	0.00178701	0.00151858	-	193.181
	14	Baseline	0.0021569	0.384207	0.00154465	0.00123854	121.182	212.754
		Mean	**0.0018**	**0.4413**	**0.0013**	**0.0010**	**120.5823**	**216.6893**
		Std Dev	**0.0005**	**0.0924**	**0.0005**	**0.0004**	**10.8849**	**24.5858**
	1	4 Weeks	0.00142078	0.543375	0.000919433	0.000668729	164.744	265.131
	2	4 Weeks	0.00214313	0.416873	0.00147262	0.00113735	172.768	248.894
	13	4 Weeks	0.0020714	0.353963	0.00159736	0.00136031	159.208	243.89
	14	4 Weeks	0.00176136	0.442727	0.00123325	0.0009692	165.035	214.852
		Mean	**0.0018**	**0.4392**	**0.0013**	**0.0010**	**165.4388**	**243.1918**
		Std Dev	**0.0003**	**0.0788**	**0.0003**	**0.0003**	**5.5733**	**20.9561**
		p-value	0.9992	0.9350	0.9865	0.9767	**0.0081**	0.1845
5	10	Baseline	0.00154917	0.494586	0.00100629	0.000734857	135.906	269.179
	21	Baseline	0.00137954	0.466893	0.000939643	0.000719699	-	228.3
	22	Baseline	0.0013289	0.40992	0.000973975	0.00079648	88.1247	189.545
		Mean	**0.0014**	**0.4571**	**0.0010**	**0.0008**	**112.0154**	**229.0080**
		Std Dev	**0.0001**	**0.0432**	**0.0000**	**0.0000**	**33.7865**	**39.8217**
	9A	4 Weeks	0.0013591	0.447335	0.000926135	0.000709627	169.354	278.679
	10	4 Weeks	0.00172692	0.456323	0.0011691	0.000890175	180.634	358.432
	21	4 Weeks	0.00131021	0.403115	0.0009632	0.00078967	140.735	293.472
	22	4 Weeks	0.00126738	0.501476	0.00085969	0.000655813	141.119	251.492
		Mean	**0.0014**	**0.4521**	**0.0010**	**0.0008**	**157.9605**	**295.5188**
		Std Dev	**0.0002**	**0.0403**	**0.0001**	**0.0001**	**20.2011**	**45.4026**
		p-value	0.8649	0.9487	0.7922	0.7789	0.0537	**0.0140**

FA: Fractional anisotropy
Data were statistically analyzed using a standard t-test. Statistical analyses were performed comparing groups against their baseline. A p value <0.05 was considered statistically significant.

Table S24: Individual MRI Data – Gluteal Muscle (DSC to L4)

Group	Animal	Time	DSC STIR-Intensity	DSC s2neuroT2TFE-Intensity	L3 STIR-Intensity	L3 s2neuroT2TFE-Intensity	L4 STIR-Intensity	L4 s2neuroT2TFE-Intensity
1	1	Baseline	3.43437	1.48109	3.65137	0.806832	2.23331	0.808207
	2	Baseline	3.60879	1.37875	3.17363	0.830246	2.53181	0.918291
	13	Baseline	-	1.53009	-	0.936134	-	0.985017
	14	Baseline	3.2428	1.40563	4.73498	1.06372	3.36314	0.983643
		Mean	**3.4287**	**1.4489**	**3.8533**	**0.9092**	**2.7094**	**0.9238**
		Std Dev	**0.1831**	**0.0693**	**0.8000**	**0.1174**	**0.5855**	**0.0831**
	1	4 Weeks	3.28416	1.28797	2.26336	0.796788	2.33803	0.865505
	2	4 Weeks	3.04539	1.03978	2.3951	0.75427	2.38064	0.944656
	13	4 Weeks	4.12499	1.88083	3.51175	1.02176	3.32274	1.02831
	14	4 Weeks	2.93215	1.36376	3.4079	0.988569	2.83095	0.927141
		Mean	**3.3467**	**1.3931**	**2.8945**	**0.8903**	**2.7181**	**0.9414**
		Std Dev	**0.5392**	**0.3534**	**0.6563**	**0.1344**	**0.4607**	**0.0671**
		p-value	0.105	0.732	**0.027**	0.654	0.407	0.539
5	10	Baseline	3.31741	0.635745	2.20092	0.773837	2.43055	0.934481
	21	Baseline	-	1.28355	-	0.878451	-	0.86298
	22	Baseline	4.18192	1.4706	3.53705	0.868781	2.903	0.915927
		Mean	**3.7497**	**1.1300**	**2.8690**	**0.8404**	**2.6668**	**0.9045**
		Std Dev	**0.6113**	**0.4381**	**0.9448**	**0.0578**	**0.3341**	**0.0371**
	9A	4 Weeks	3.85957	1.51491	3.00896	0.95728	3.17679	1.11752
	10	4 Weeks	3.5417	1.42865	3.15959	0.917294	3.25856	1.0467
	21	4 Weeks	4.79143	1.50695	2.51612	1.08044	3.1013	1.19997
	22	4 Weeks	3.23813	1.16273	2.68475	1.09477	2.88031	1.14445
		Mean	**3.8577**	**1.4033**	**2.8424**	**1.0124**	**3.1042**	**1.1272**
		Std Dev	**0.6722**	**0.1650**	**0.2942**	**0.0885**	**0.1625**	**0.0637**
		p-value	0.649	0.535	0.963	**0.016**	0.517	**0.074**

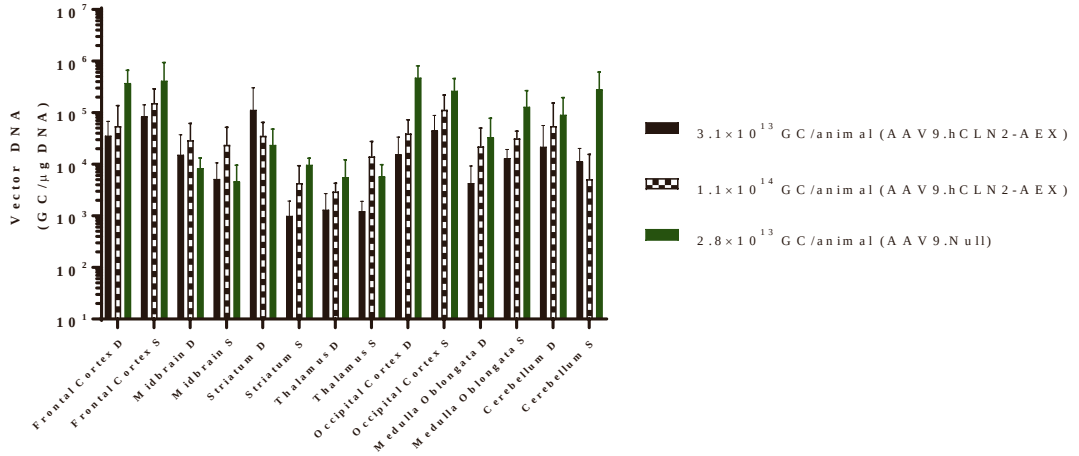
DSC: Dorsal Spinal Cord
STIR intensity and S2 neuro intensity normalized to gluteal muscle.
Data were statistically analyzed using a standard t-test. Statistical analyses were performed comparing groups against their baseline. A p value <0.05 was considered statistically significant.

Table S25: Individual MRI Data – Gluteal Muscle (L5 to S1)

Group	Animal	Time	L5 STIR-Intensity	L5 s2neuroT2TFE-Intensity	L6 STIR-Intensity	L6 s2neuroT2TFE-Intensity	S1 STIR-Intensity	S1 s2neuroT2TFE-Intensity
1	1	Baseline	2.16848	0.795463	2.48618	0.876876	1.73781	0.542327
	2	Baseline	2.55031	0.935684	2.41781	0.921776	2.27758	0.699777
	13	Baseline	-	0.957725	-	0.893177	-	0.631103
	14	Baseline	2.8256	1.10532	2.47619	0.941641	2.09484	0.605741
		Mean	**2.5148**	**0.9485**	**2.4601**	**0.9084**	**2.0367**	**0.6197**
		Std Dev	**0.3300**	**0.1268**	**0.0369**	**0.0289**	**0.2745**	**0.0651**
	1	4 Weeks	2.86848	0.885639	2.97165	0.925261	2.49085	0.689731
	2	4 Weeks	3.03851	1.04392	2.97084	0.981793	2.64385	0.658694
	13	4 Weeks	3.33212	1.06708	3.25081	0.973466	2.67348	0.697397
	14	4 Weeks	3.08598	1.0953	2.67618	0.951062	2.19627	0.611293
		Mean	**3.0813**	**1.0230**	**2.9674**	**0.9579**	**2.5011**	**0.6643**
		Std Dev	**0.1915**	**0.0939**	**0.2346**	**0.0253**	**0.2184**	**0.0391**
		p-value	0.063	**0.080**	0.062	**0.045**	0.164	0.354
5	10	Baseline	2.61358	0.958652	3.17622	1.0844	2.4972	0.833875
	21	Baseline	-	0.989162	-	0.678798	-	0.65578
	22	Baseline	2.95529	0.982443	2.13418	0.742113	1.67057	0.598358
		Mean	**2.7844**	**0.9768**	**2.6552**	**0.8351**	**2.0839**	**0.6960**
		Std Dev	**0.2416**	**0.0160**	**0.7368**	**0.2182**	**0.5845**	**0.1228**
	9A	4 Weeks	4.01846	1.19706	3.85226	1.07957	2.79991	0.90601
	10	4 Weeks	3.31287	1.04462	4.23702	1.21103	3.07698	0.95292
	21	4 Weeks	3.30607	1.18259	2.91573	0.997184	2.28009	0.8741
	22	4 Weeks	2.82072	1.11289	2.63026	0.92858	1.99781	0.684808
		Mean	**3.3645**	**1.1343**	**3.4088**	**1.0541**	**2.5387**	**0.8545**
		Std Dev	**0.4931**	**0.0702**	**0.7598**	**0.1215**	**0.4890**	**0.1176**
		p-value	0.621	**0.048**	0.222	0.065	0.173	**0.071**

DSC: Dorsal Spinal Cord
STIR intensity and S2 neuro intensity normalized to gluteal muscle.
Data were statistically analyzed using a standard t-test. Statistical analyses were performed comparing groups against their baseline. A p value <0.05 was considered statistically significant.

A



B

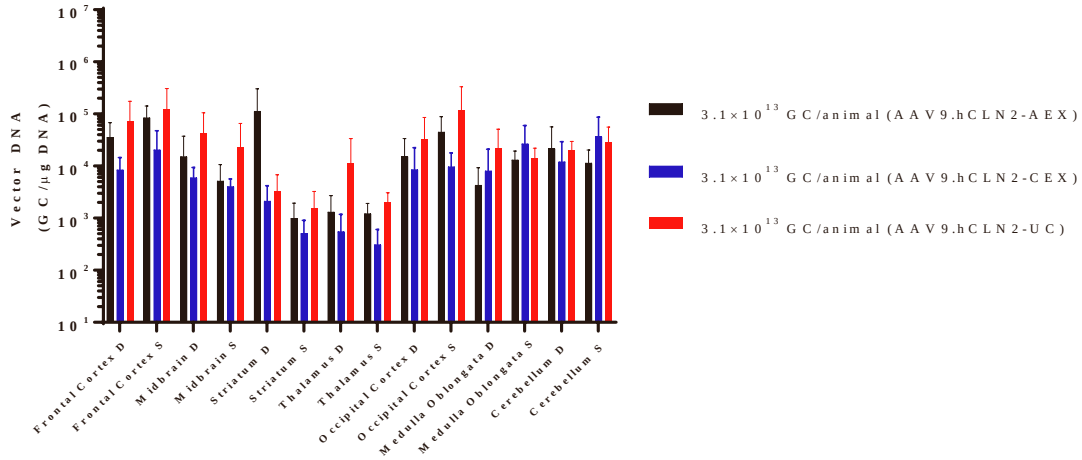


Figure S1: Biodistribution within deep and superficial layers of the brain with AAV9.hCLN2 or AAV9.Null. (A) AAV9.hCLN2 at different dose levels alongside AAV9.Null vector and (B) AAV9.hCLN2 prepared by different manufacturing processes. Vector DNA measured by qPCR from 4-mm round samples of frontal cortex, occipital cortex, cerebellum, striatum, medulla oblongata, midbrain and thalamus. One sample from each area was superficial (<3 mm deep) and the other sample from each area was deep (>3 mm deep). Results are shown as averages per group with standard deviations as error bars.

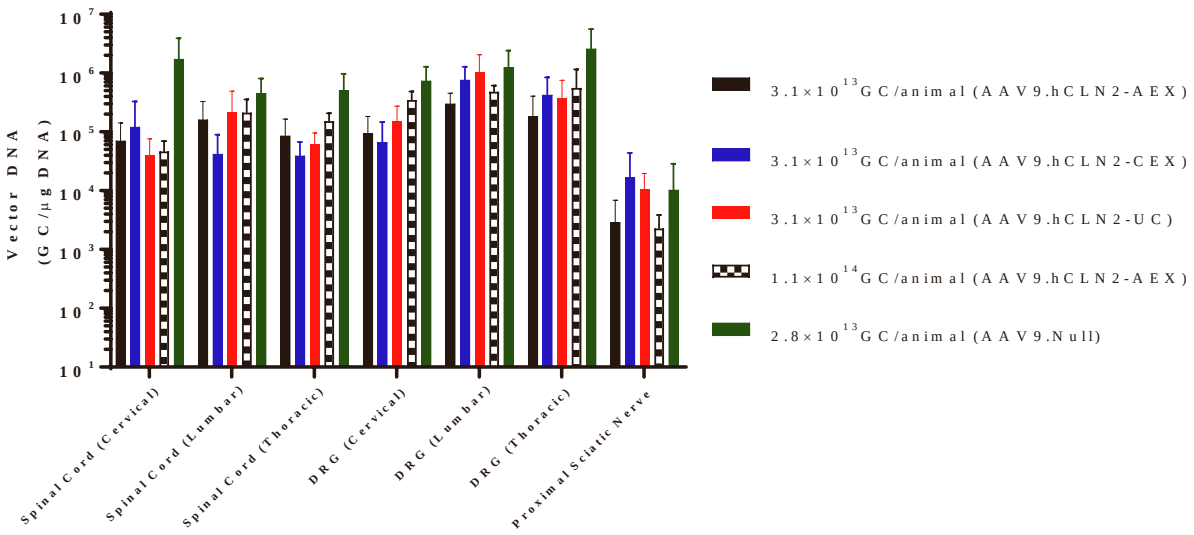


Figure S2: Biodistribution within spinal cord, DRG and sciatic nerve. At necropsy, samples of the spinal cord and DRG were collected and vector DNA measured by qPCR. Results are shown as averages per group with standard deviations as error bars.

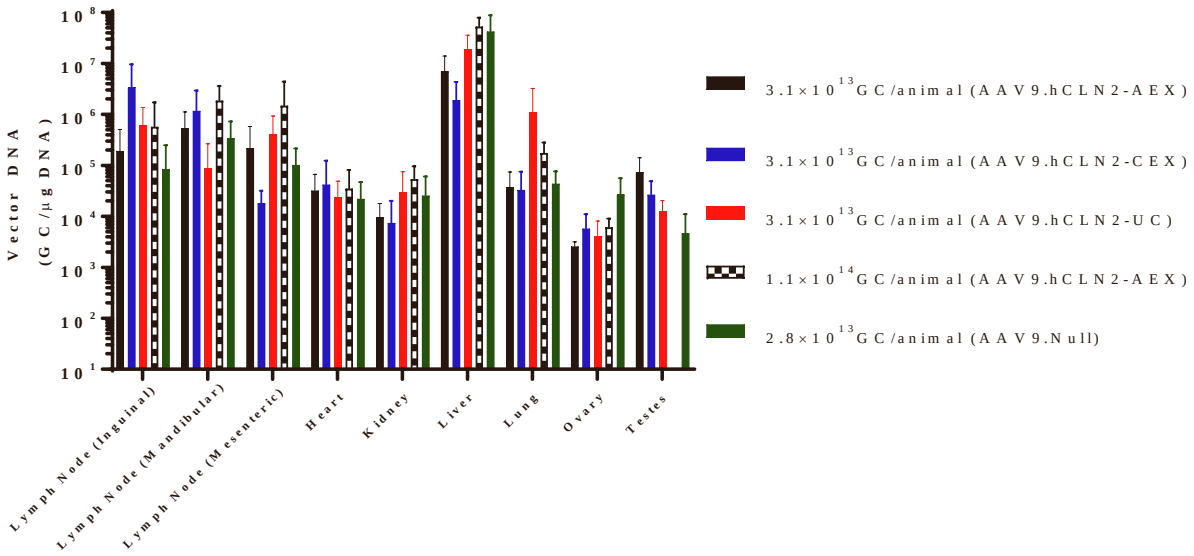


Figure S3: Biodistribution within peripheral tissue. At necropsy, samples of tissue were collected and vector DNA measured by qPCR. Results are shown as averages per group with standard deviations as error bars.

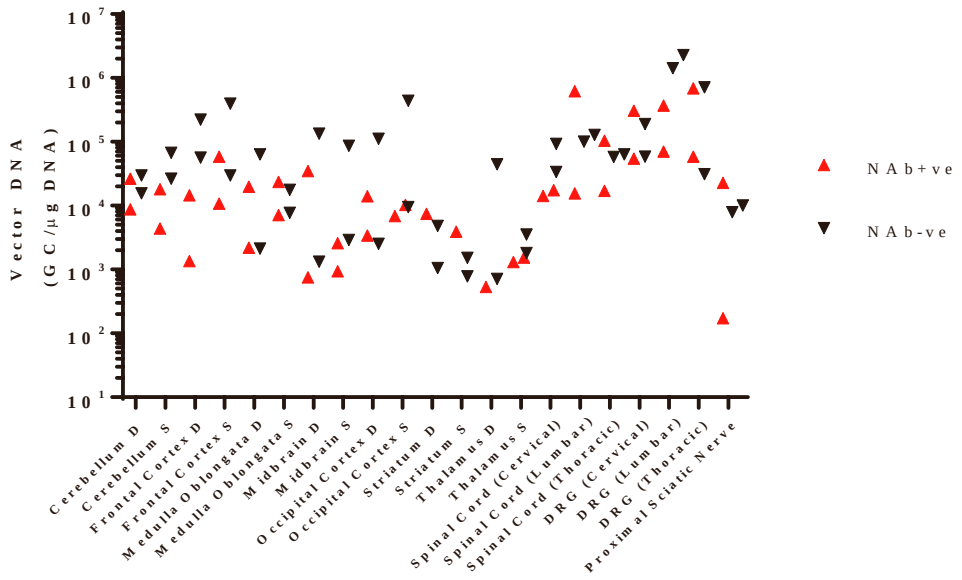


Figure S4. Comparison of intra-group biodistribution (CNS and PNS) of anti-AAV9 neutralizing antibody (NAb) positive or negative animals administered 3.1×10^{13} GC/animal AAV9.hCLN2-AEX. At necropsy, samples of tissue were collected and vector DNA measured by qPCR. Results are shown as individual values of two animals that were either NAb positive (titers of 5 and 3) or NAb negative on Day 1 prior to dosing.

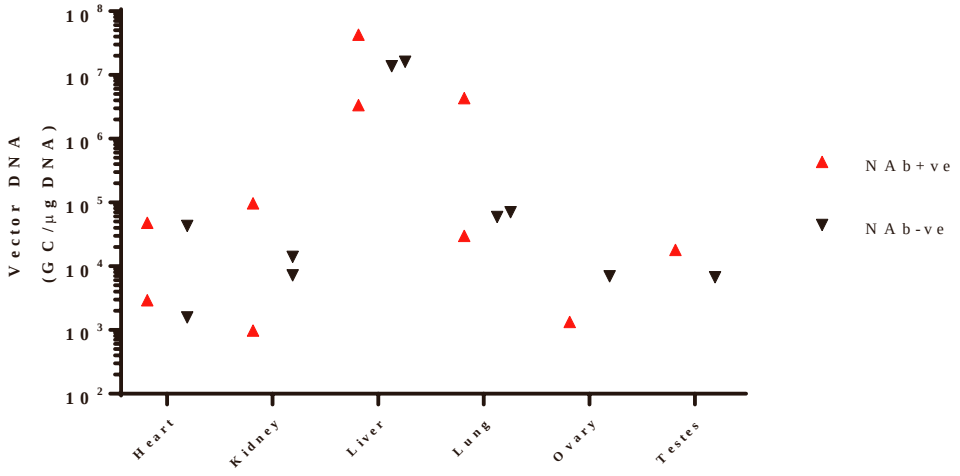


Figure S5. Comparison of intra-group biodistribution (peripheral) of anti-AAV9 neutralizing antibody (NAb) positive or negative animals administered 3.1×10^{13} GC/animal AAV9.hCLN2-AEX. At necropsy, samples of tissue were collected and vector DNA measured by qPCR. Results are shown as individual values of two animals that were either NAb positive (titers of 5 and 3) or NAb negative on Day 1 prior to dosing.

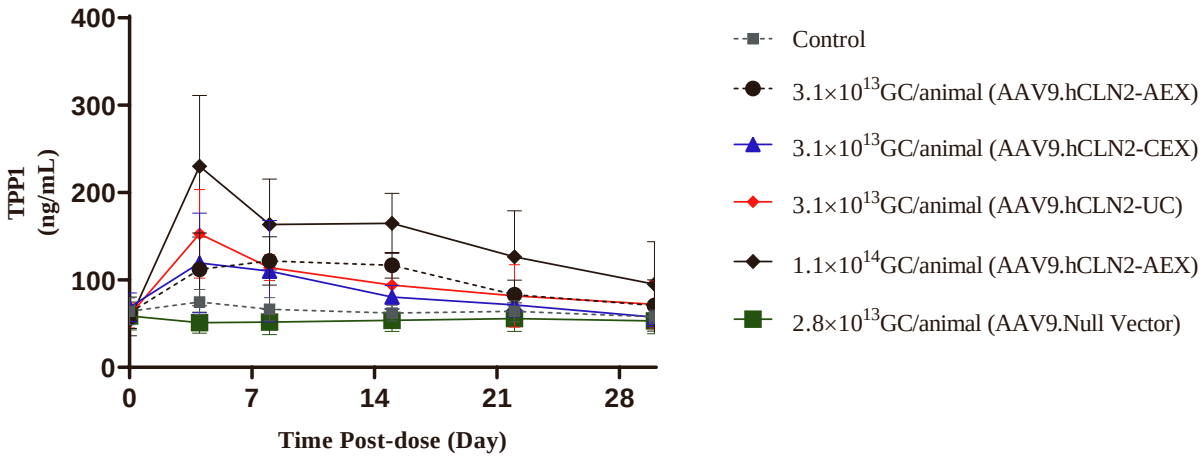


Figure S6: Serum TPP1 concentrations. Samples of blood were collected on Days 1 (prior to dosing), 4, 8, 15, 22 and prior to necropsy for serum TPP1 concentration. TPP1 concentration was determined by an electrochemiluminescent (ECL) immunoassay implemented using the Meso Scale Discovery (MSD) platform. Results are shown as averages per group with standard deviations as error bars.

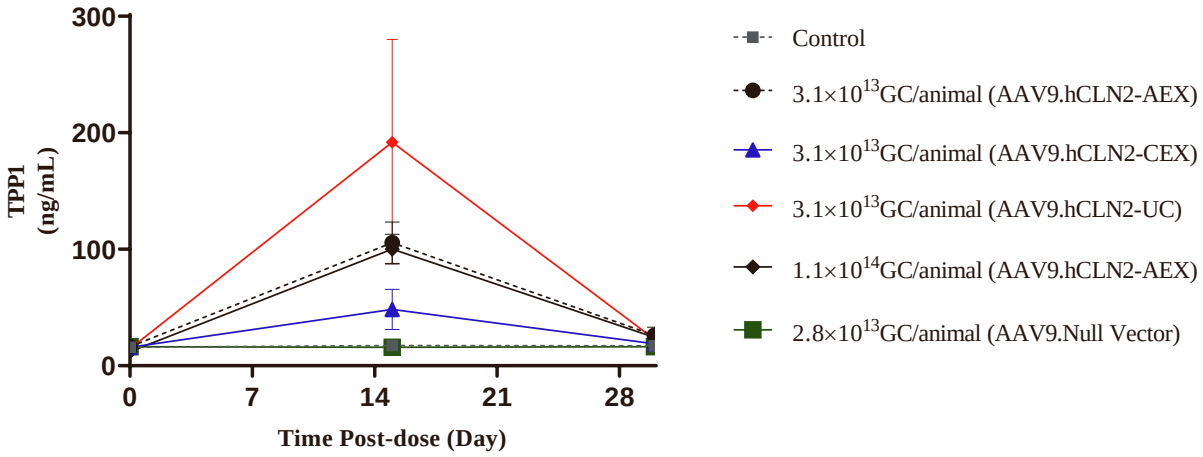


Figure S7: CSF TPP1 concentrations. CSF was collected on Days 1 [prior to dosing], 15 and prior to necropsy for TPP1 concentration. TPP1 concentration was determined by an electrochemiluminescent (ECL) immunoassay implemented using the Meso Scale Discovery (MSD) platform.

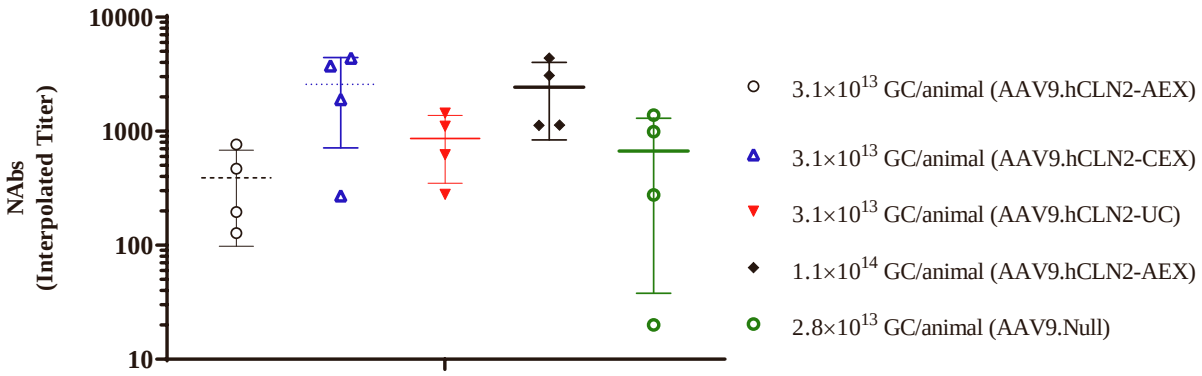


Figure S8: Serum NAb titers on Day 30. Serum was collected prior to necropsy to detect the presence of anti-AAV9-neutralizing antibodies (NAbs) using a cell-based method.

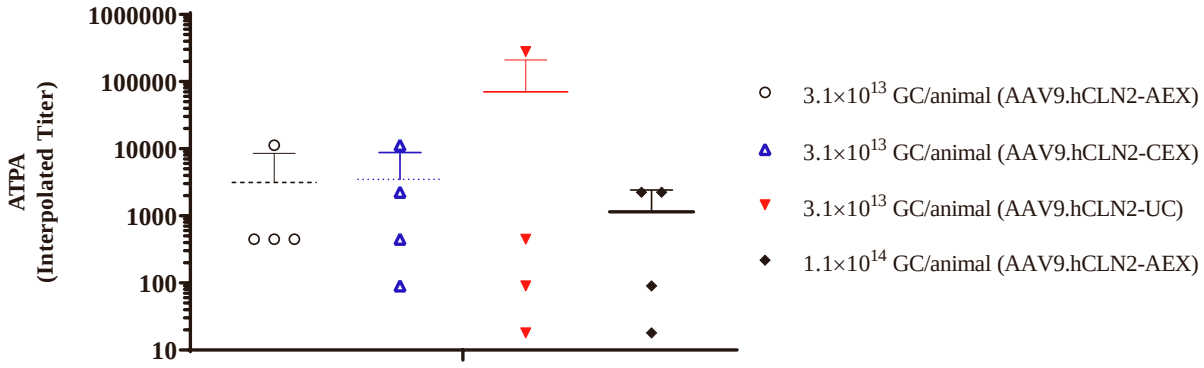


Figure S9: Serum ATPA titers on Day 30. Serum was collected prior to necropsy to detect the presence of anti-transgene product antibodies (ATPAs) using a solution bridging ECL immunoassay with the MSD platform.

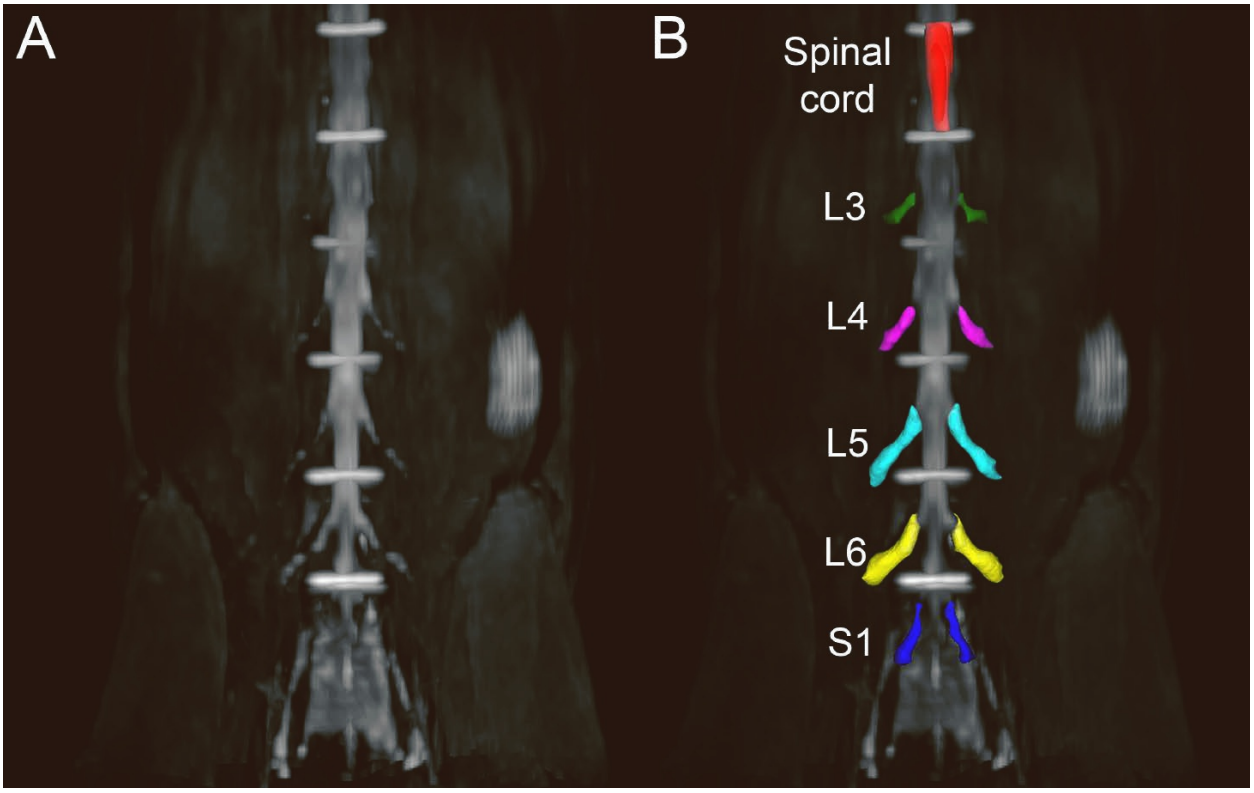


Figure S10. MRI region of interest (ROI) from L3 to S1. Dorsal plane maximum intensity projection T2-weighted anatomical images of the lumbosacral spine of a cynomolgus monkey (A) overlain with regions of interest used to measure quantitative results for the L3-S1 spinal nerve pairs and lumbar spinal cord (B).