

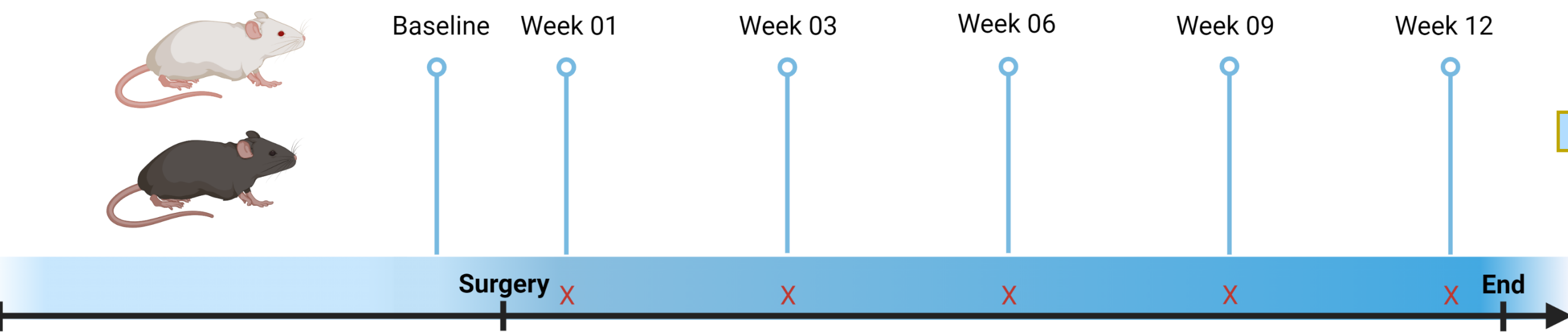
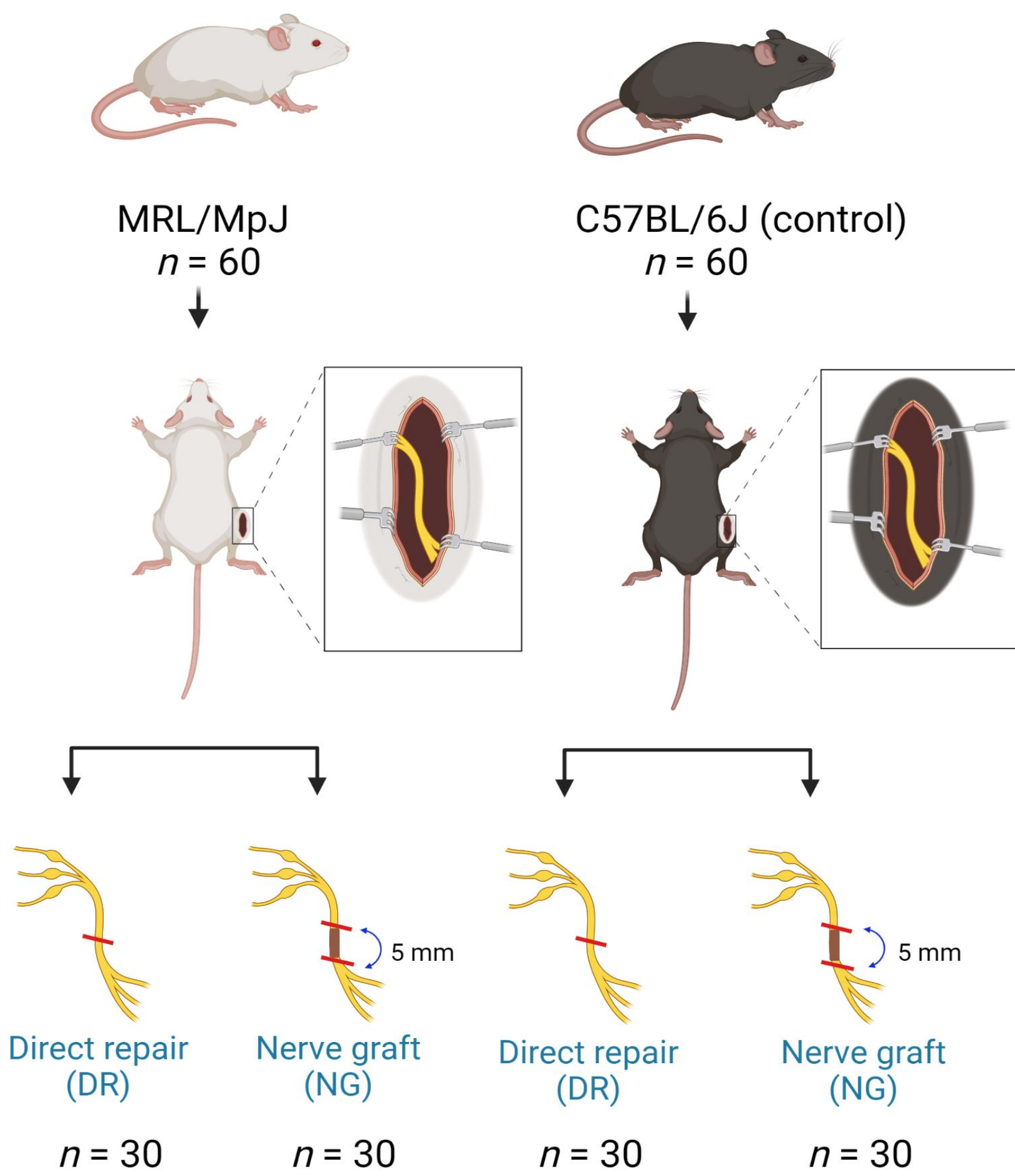
Peripheral Nerve Regeneration in MRL/MpJ Mice

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Introduction

- Peripheral nerve injury outcomes remains largely unchanged over decades
- Following transection, scar formation creates a physical barrier to axonal regeneration and could be a key element that explains suboptimal outcomes in peripheral nerve injuries including those treated with autologous nerve grafts
- MRL/MpJ mice strain demonstrated healing with no or minimal scar formation in ear and tendon wounds but its nerve regeneration abilities remain unclear
- We investigated whether MRL/MpJ mice would demonstrate improved functional and histomorphology outcomes compared to control strain following repair of nerve injury with either direct repair or nerve grafting

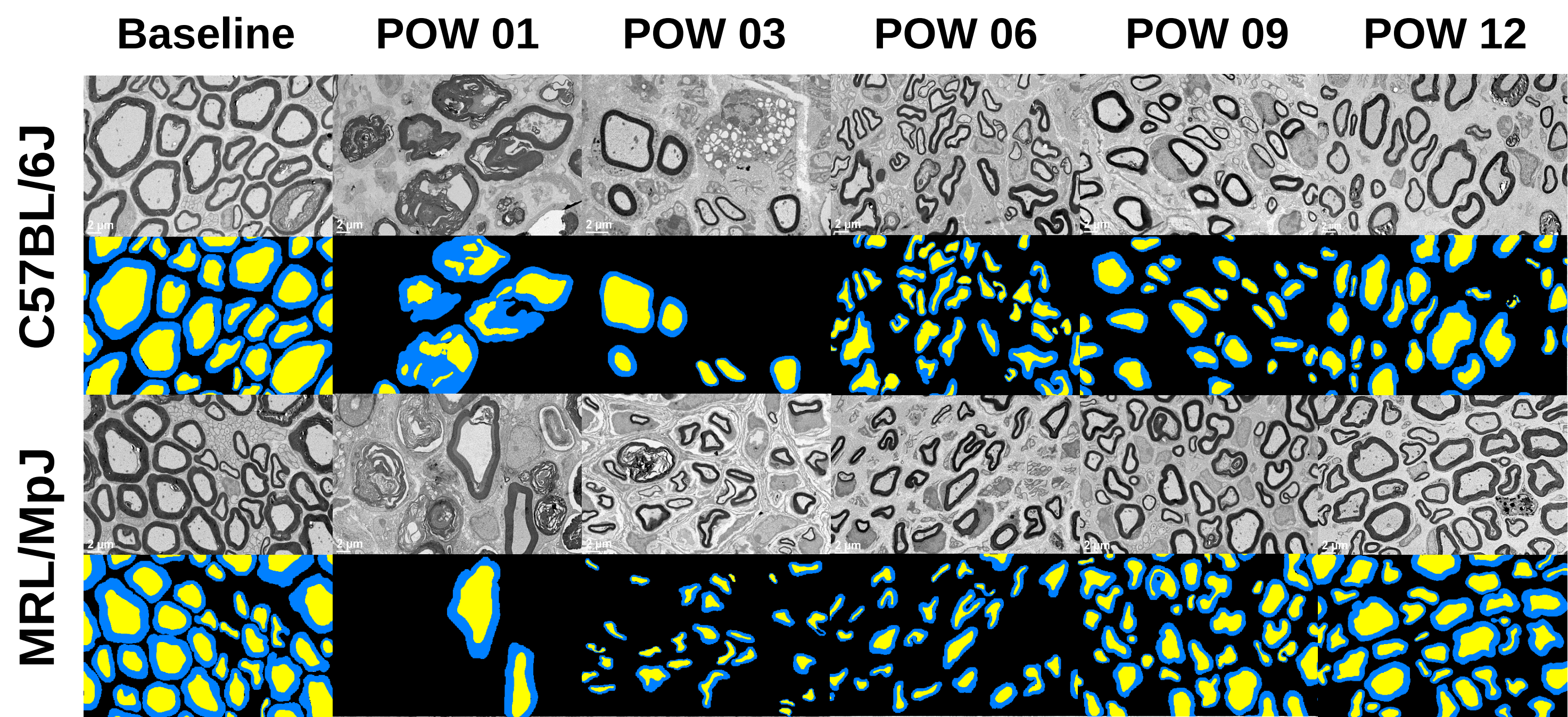
Methods



- Functional outcome measures:**
 - Sciatic Function Index
- Histomorphology measures:**
 - Axon Count
 - Axon:Myelin Ratio (G Ratio)
 - Axon:ECM Ratio

Results

Outcome	Group	Strain	Baseline		Week 01		Week 03		Week 06		Week 09		Week 12	
			Mean (SD)	p value	Mean (SD)	p value	Mean (SD)	p value	Mean (SD)	p value	Mean (SD)	p value	Mean (SD)	p value
Sciatic Nerve Index (SFI)	Direct Repair	C57BL/6	-8.37 (12.0)	0.15	-71.84 (13.9)	<0.0001	-69.43 (14.5)	0.0015	-65.28 (14.5)	0.0256	-67.48 (13.4)	0.0388	-67.32 (11.0)	0.0168
		MRL/MpJ	-5.45 (12.2)		-61.08 (9.6)		-59.8 (14.6)		-56.78 (13.9)		-54.85 (17.3)		-52.16 (16.6)	
	Nerve Graft	C57BL/6	-7.16 (16.6)	0.17	-72.26 (13.8)	0.0301	-69.33 (12.9)	0.0164	-73.41 (12.0)	<0.0001	-65.77 (12.6)	0.0499	-67.66 (9.4)	0.0412
		MRL/MpJ	-10.43 (11.7)		-66.63 (13.7)		-62.72 (14.6)		-56.25 (13.9)		-54.09 (23.8)		-56.78 (16.5)	
Axon Count	Direct Repair	C57BL/6	2381 (486)	0.42	524 (139)	0.0042	1931 (375)	0.0493	2830 (613)	<0.0001	2901 (760)	0.0052	2760 (524)	0.0164
		MRL/MpJ	2233 (361)		400 (102)		1611 (551)		1684 (354)		2094 (857)		2303 (561)	
	Nerve Graft	C57BL/6	2360 (484)	0.23	353 (102)	0.45	1111 (459)	0.87	2427 (652)	0.0004	2492 (591)	0.0398	2822 (873)	0.0446
		MRL/MpJ	2401 (423)		326 (102)		1087 (429)		1509 (790)		2048 (488)		2264 (726)	
G Ratio	Direct Repair	C57BL/6	0.65 (0.03)	0.48	-	-	0.74 (0.06)	0.0086	0.66 (0.06)	0.0079	0.71 (0.05)	0.0059	0.72 (0.04)	0.0136
		MRL/MpJ	0.64 (0.05)		-		0.63 (0.10)		0.57 (0.08)		0.64 (0.06)		0.63 (0.09)	
	Nerve Graft	C57BL/6	0.63 (0.04)	0.23	-	-	0.75 (0.07)	0.0037	0.66 (0.06)	0.0438	0.68 (0.06)	0.0356	0.72 (0.08)	0.0243
		MRL/MpJ	0.66 (0.05)		-		0.65 (0.07)		0.60 (0.07)		0.60 (0.09)		0.65 (0.05)	
Axon:ECM	Direct Repair	C57BL/6	2.61 (0.46)	0.48	-	-	0.17 (0.06)	0.35	0.28 (0.06)	0.0064	0.46 (0.06)	0.0003	0.79 (0.12)	<0.0001
		MRL/MpJ	2.67 (0.42)		-		0.20 (0.02)		0.59 (0.08)		0.76 (0.09)		1.17 (0.02)	
	Nerve Graft	C57BL/6	2.58 (0.37)	0.42	-	-	0.09 (0.02)	0.95	0.26 (0.10)	0.0461	0.31 (0.07)	0.0034	0.38 (0.03)	<0.0001
		MRL/MpJ	2.63 (0.41)		-		0.09 (0.14)		0.40 (0.08)		0.54 (0.16)		1.08 (0.07)	



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Conclusions

- MRL/MpJ mice demonstrate superior regenerative ability than C57BL/6 mice
- Despite having fewer regenerating axons, there are better functional outcomes that can be attributed to improved myelination
- Future work focusing on a mechanistic that targets nerve scarring is warranted