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Effects of Intramuscular Administration of Platelet-Rich Plasma on Denervated Muscle After Peripheral Nerve Injury

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Faculty Disclosure Information

Nothing to disclosure

Introduction

- **Peripheral nerve injuries (PNI)** are one of the most prevalent injuries of the musculoskeletal system (more 10^6 per year).

- Following peripheral nerve injury, prolonged **denervation of the muscle** prevents adequate reinnervation, even if nerve repair is carried out.

- Muscle deterioration and atrophy, and loss of function **worsen as denervation is prolonged**, which may prevent adequate reinnervation after nerve repair.

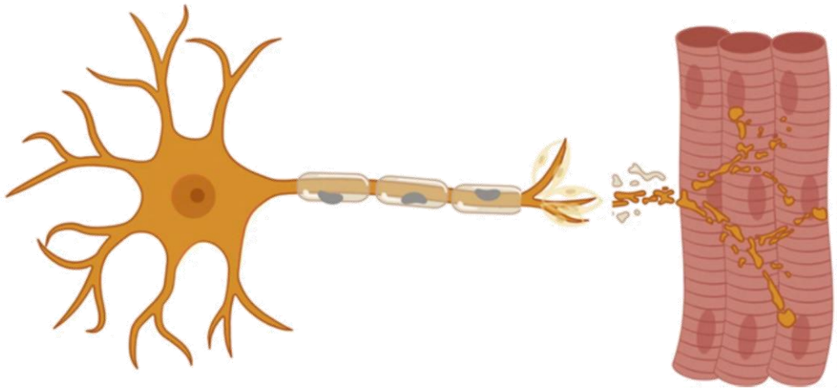
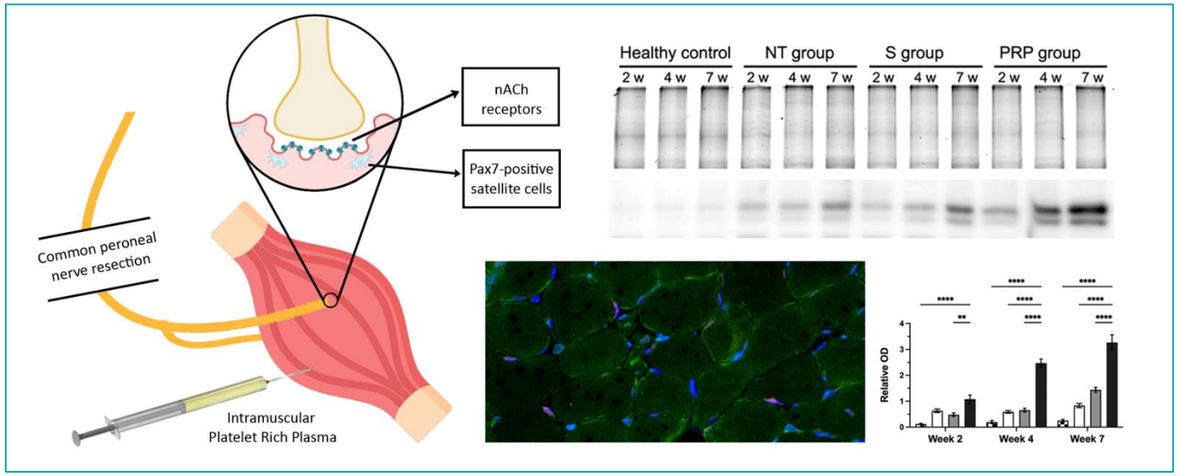


Image modified from Fissel et al. J Neuroinflammation. 2021 Mar 15;18(1):71. doi: 10.1186/s12974-021-02121-2.

Objective

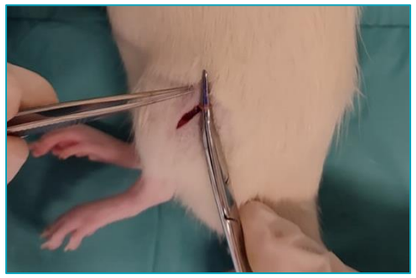
- Analyze the **effect of intramuscular injection of Platelet Rich Plasma (PRP) in a denervated muscle** due to peripheral nerve injury.

- The hypothesis of this study is based on exploiting the biological action and stimulation of **PRP to attenuate the effects generated in the muscle** by the denervation induced after peripheral nerve injury.

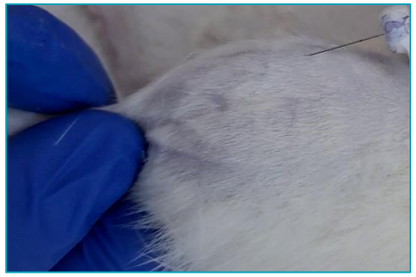


Methods

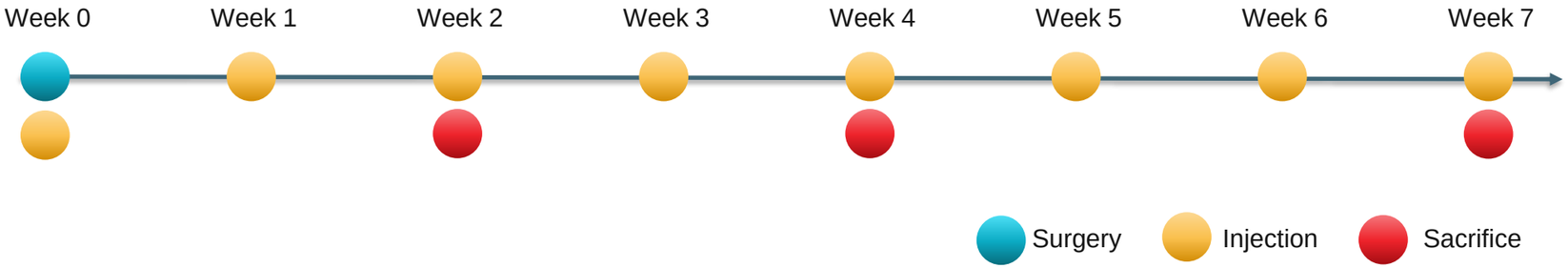
- An irreversible PNI was generated in the **common peroneal nerve** of 80 Wistar rats by nerve.



- Animals were divided into thre groups (N=18): **non-treatment (NT), saline (S) and PRP (PRP)**. Additional group for obtaining PRP (N= 26).

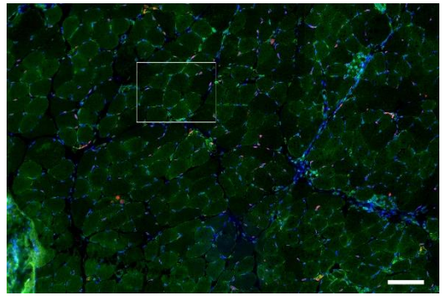


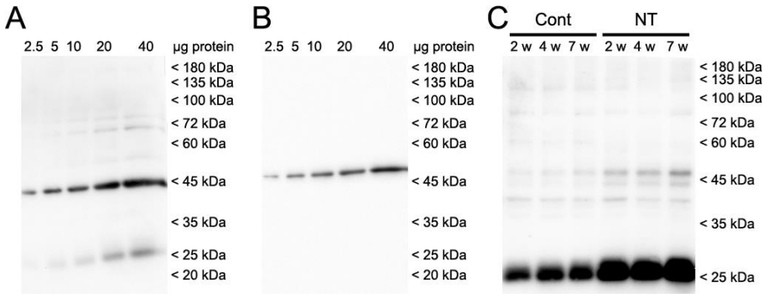
- **200 uL** of saline (S group) and PRP (PRP group) were infiltrated **intramuscularly into the tibialis anterior muscle on a weekly basis**, from surgery to sacrifice (at 2, 4 and 7 weeks)



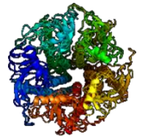
Methods

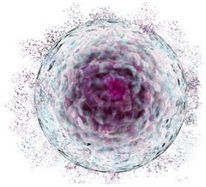
- Muscles were weighted and histologically processed for immunofluorescence and Western blotting.





- Effects on nicotinic acetylcholine receptor (nAChR) and satellite cells (SC).





- Comparisons were performed by two-way analysis of variance (ANOVA).

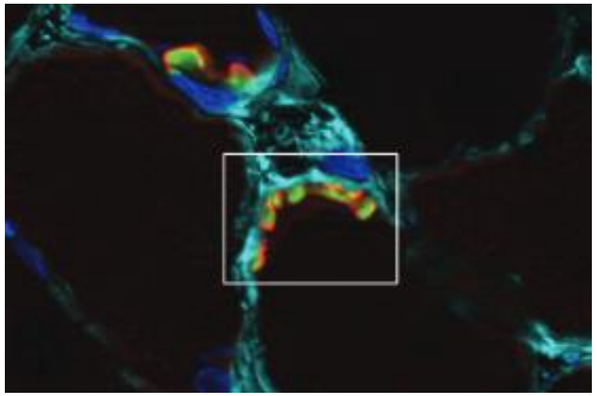
Results

Table S2. Characteristics of Platelet Rich-Plasm	
1. PRP Preparation	
Initial blood volume	5 mL per donor animal
Anticoagulant	Sodium citrate 3.8% (wt/V)
System	Close
Centrifugation	Yes
number	1
speed	300 g / 8 min
Final PRP volume	2 mL
2. PRP Characteristics	
PRP Type	812-00-11
MPV	7.5 ± 0.2 fL
Red Blood Cells	$0.03 \times 10^6/\mu L$
White Blood Cells	$0.03 \times 10^3/\mu L$
Activation	$CaCl_2$ (10% wt/vol)
3. Application Characteristics	
Formulation type	Liquid
Administration route	Intramuscular
Dosage	1 injection per week
Volume	200 µL
Dose (range of platelets)	1.7×10^8 - 3.1×10^8
Tissue	Muscle (tibialis anterior muscle)
Pathology	Denervated muscle
Animal	Wistar Rat

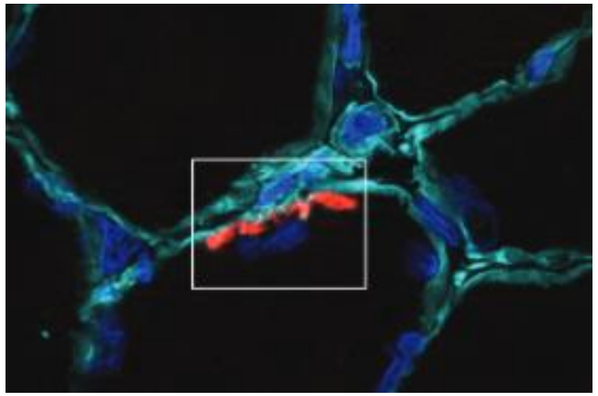
The mean platelet concentration of PRP was **1202.7×103 ± 335.8** platelets/µL, achieving a **platelet enrichment of 1.5 times** the blood platelet concentration, **without leukocytes and erythrocytes.**

Results - Denervation generation

The **effectiveness of denervation** was confirmed by analyzing the motor end plates through a combination of synaptophysin and α-bungarotoxin immunostaining, showing the **absence of presynaptic synaptophysin signal in denervated muscles** even 7 weeks post-denervation.



Healthy control



NT Group

α-bungarotoxin (postsynaptic membrane)

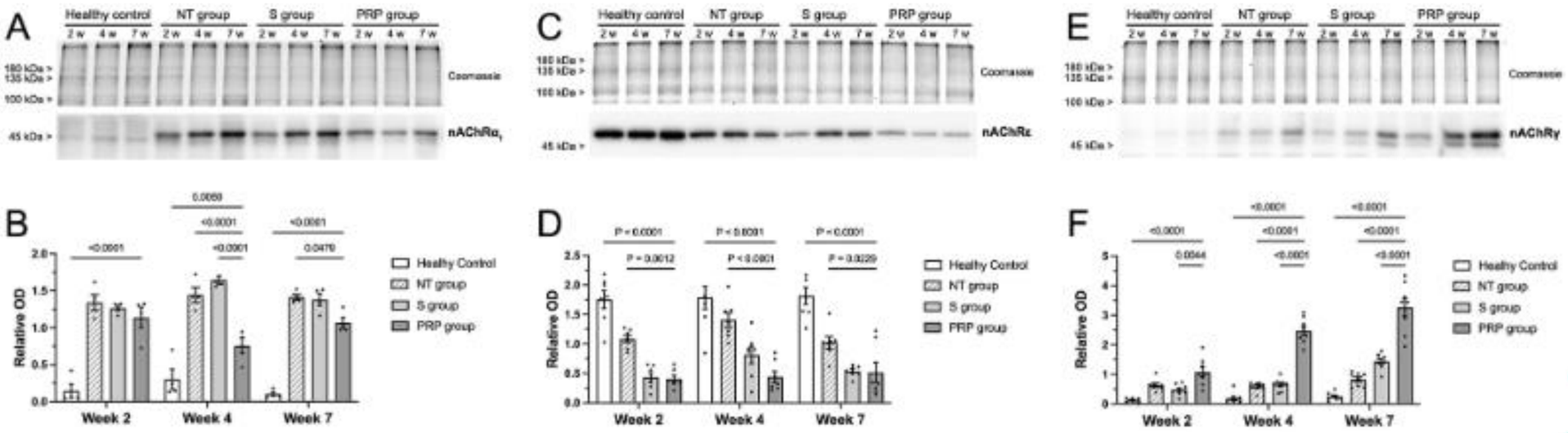
Synaptophysin (presynaptic membrane)

Laminin (muscle fiber boundarie)

Hoechst (nucleous)

Absence of synaptophysin signal (green) in denervated muscle (Nt Group), confirming effective and irreversible denervation.

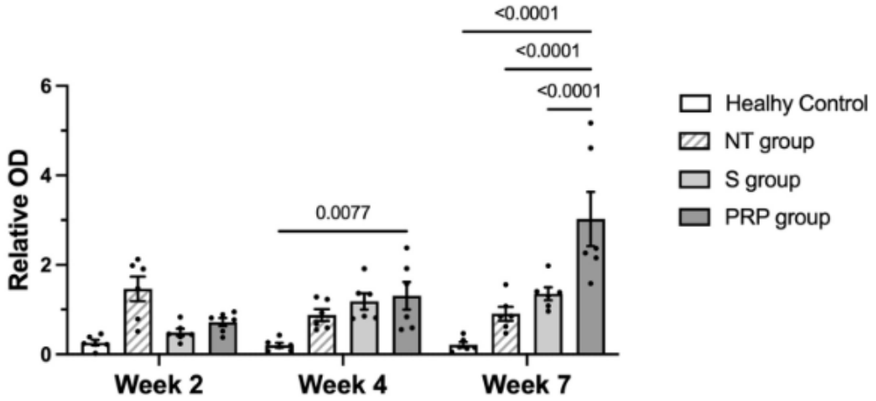
Results - Acetylcholine receptors

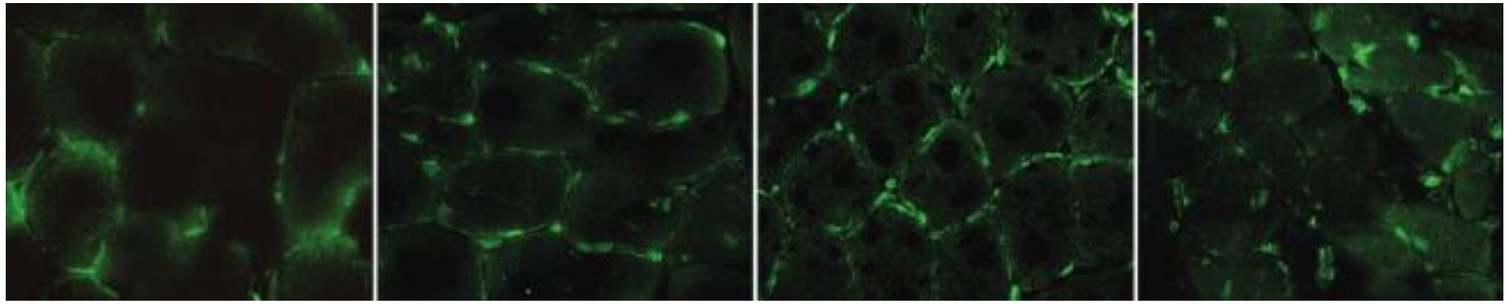


The **PRP group** showed changes in the nAChR clusters of the NMJ, with a **significant decrease in the ε subunit (adult type) (C-D)** and a **significant increase in the γ subunit (fetal type) (E-F),** compared to the other groups ($p < 0.05$).

Results - Satellite Cells

The **PRP group** also showed **significantly higher levels of the protein Pax7** ($p < 0.05$), indicating SCs stimulation.



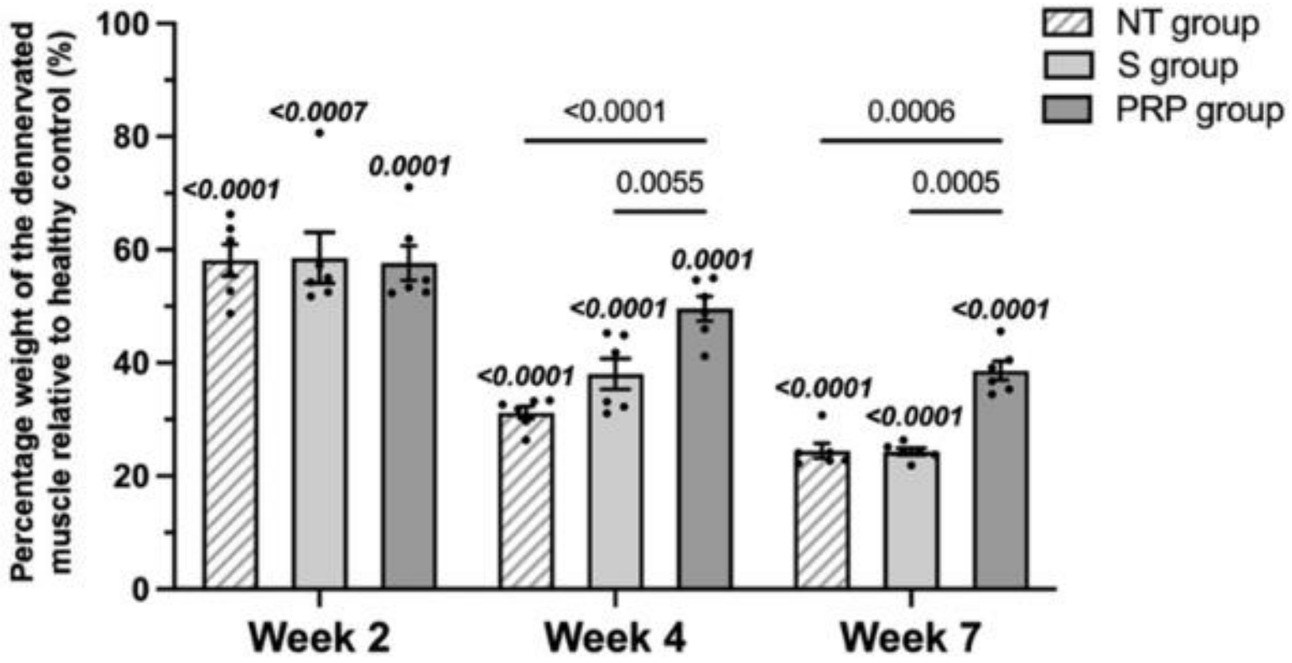


Healthy control | NT Group | Saline Group | PRP Group

Immunofluorescence of Pax7- positive cells at 7-weeks after surgery.

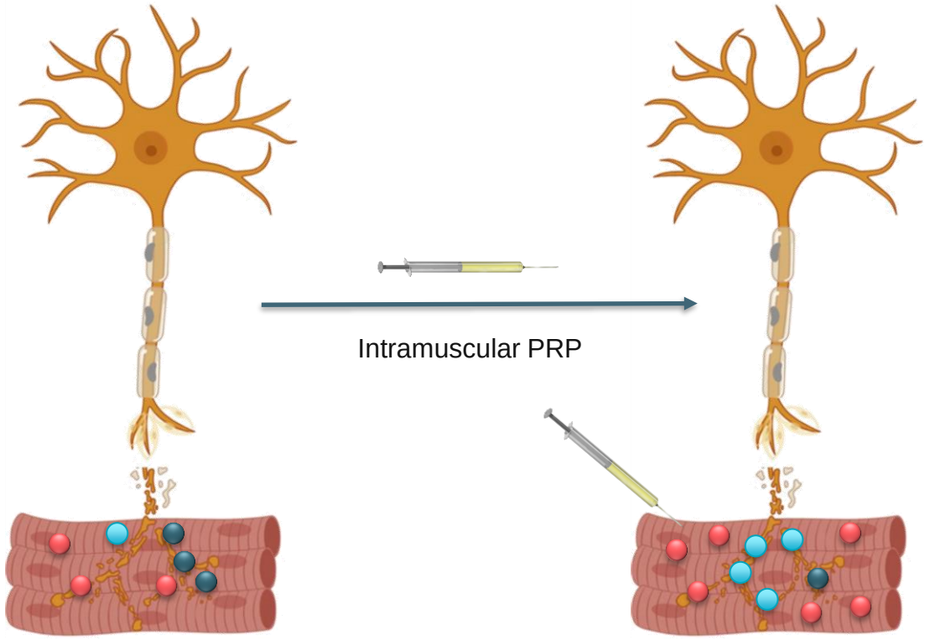
Results - Muscle weight

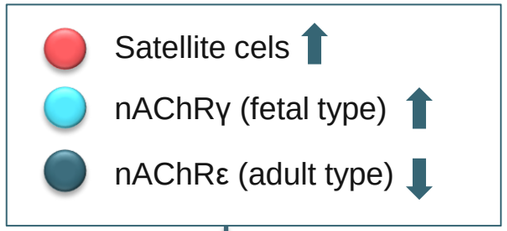
PRP group suffered less and slower weight loss than the control groups (saline and no-treatment), suggesting less muscle atrophy ($p < 0.05$).



Conclusion

The findings suggest the importance of **treating the denervated muscle as a consequence of injury to the nerve that innervates** it, as well as the nerve itself. It **could promote a faster and more effective reinnervation**, enhancing and accelerating the process that would improve the patient's clinical outcomes.





State to favor reinnervation

References

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4. Soldado F, et al. Effects of intramuscular administration of Platelet-Rich Plasma on denervated muscle after peripheral nerve injury. Connect Tissue Res. 2025 Jan;66(1):10-25.