Effect of Schwann Cell Survival Limiting Regeneration Across Predegenerated Isografts

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Introduction

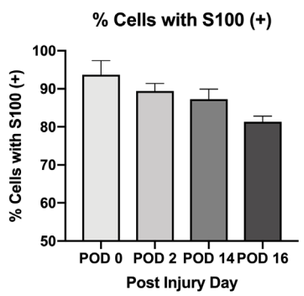
- Autografts are the gold standard to bridge a nerve gap, but limitations exist when using long nerve grafts
- It is unclear how well Schwann cells (SCs) in autografts survive and function during graft reconstruction
- To investigate the role of SC in more detail, we used conventional “fresh” isografts, as well as “predegenerated” isografts, which contain a higher number SCs, including dedifferentiated SCs with c-jun expression (repair SCs)
- We aimed to determine nerve regeneration and SC survival/status in isografts after repair

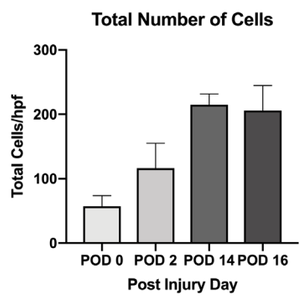
Materials and Methods

- **Predegenerated isografts** were generated by cutting proximal to site of graft harvest two weeks earlier in donor Lewis rats. Grafts were then harvested two weeks later on day of transfer (Experimental Group)
- **Fresh isografts** were harvested in donor rats on day of transfer (Control Group)
- Both groups of grafts were 1cm long and transferred to bridge a gap in recipient rats’ sciatic nerve
- Nerve regeneration was assessed using histology, muscle mass, muscle contraction force, immunohistochemical staining of neuromuscular junctions and walking track analysis at variable endpoints.

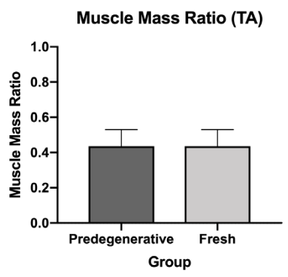
Results

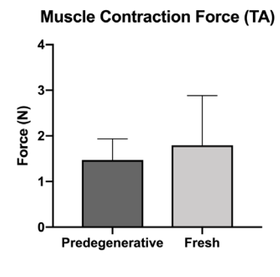
1. While the highest % of SCs is found in uninjured nerve (POD0), the total number of cells dramatically increases after injury (POD14 & POD16). Therefore, predegenerated isografts contain more cells, including SCs, prior to the grafting procedures.

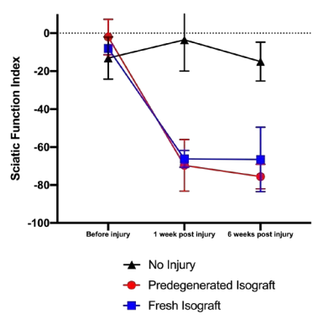


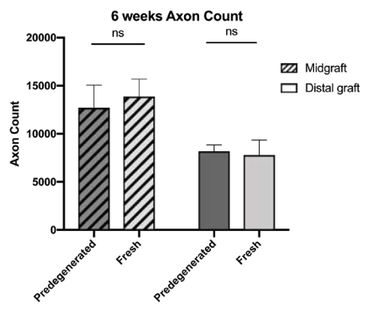


2. Yet, predegenerated isografts did not improve nerve regeneration compared to fresh isografts.

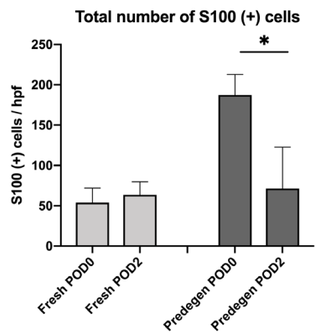


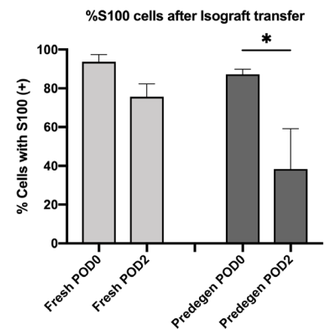


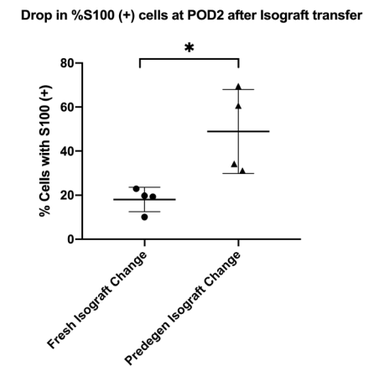




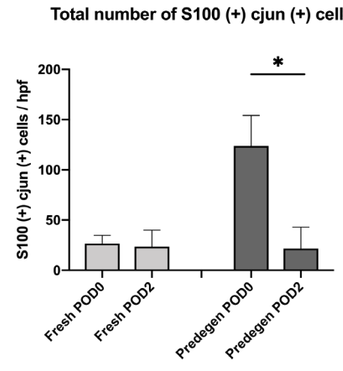
3. Significantly fewer SCs survived by 2 days following grafting when predegenerated isografts are utilized. Therefore, the benefits of using a predegenerated isograft are largely lost.

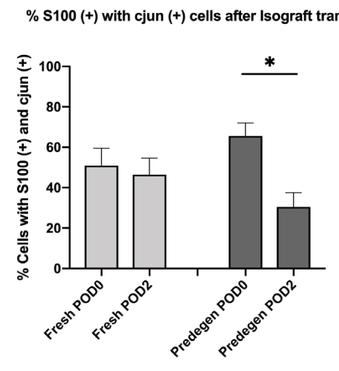


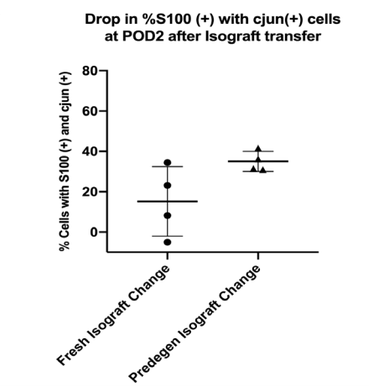




4. The quantity SCs expressing c-jun are greater in the predegenerated graft at time of nerve harvest. However, within 2 days after grafting, there is once again limited survival of these cells in the predegenerated isograft.







Conclusions

1. Nerve harvested at different days after injury are found with varying % of SCs, with fresh nerve containing the highest % of SCs of total cells. However, nerve harvested at least 14 days after injury showed increased number of cells, including SCs.
2. “Predegenerating” nerve, serving as predegenerated isografts, did not improve nerve regeneration across the isografts, despite an increased number of cells, as well as % of repair SCs (SCs expressing c-jun) contained in this specialized nerve graft.
3. This outcome may be due to less survival of SCs in the predegenerated isograft.