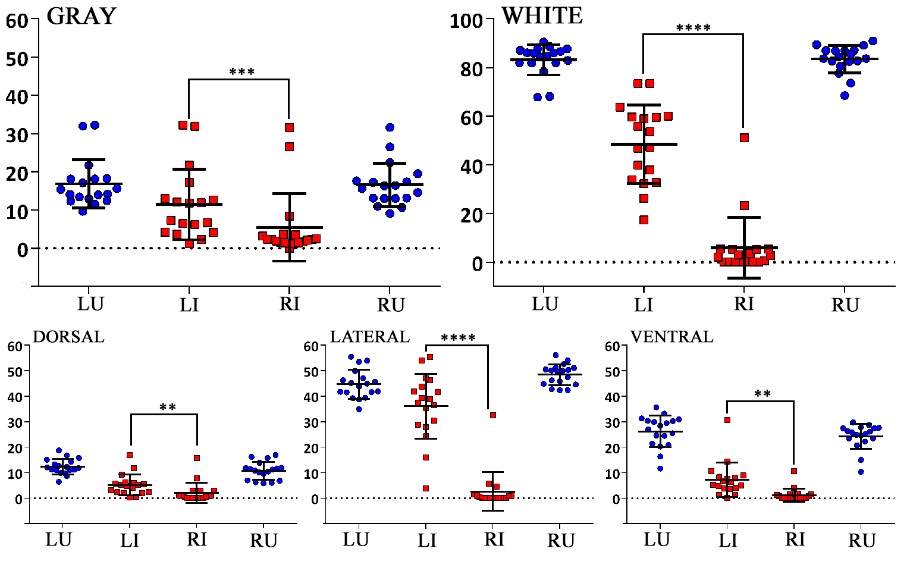
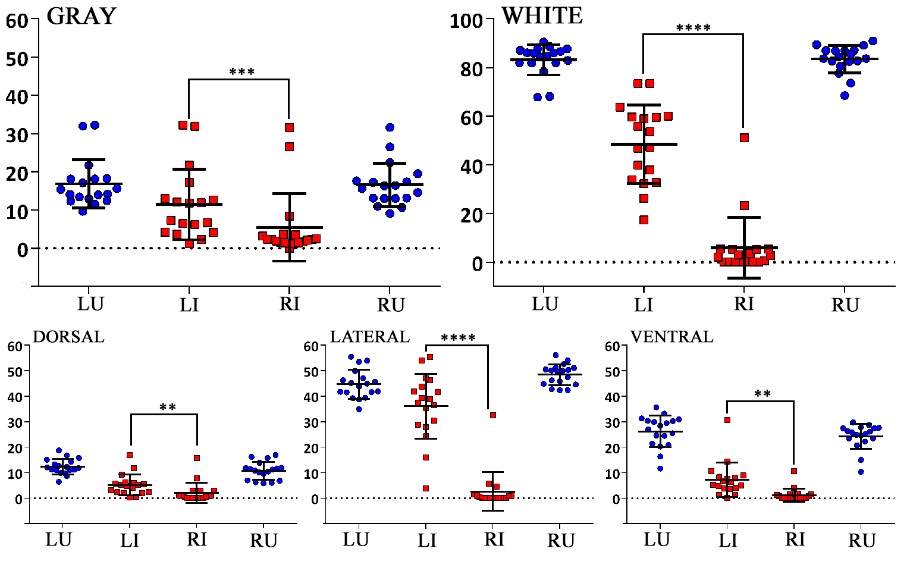
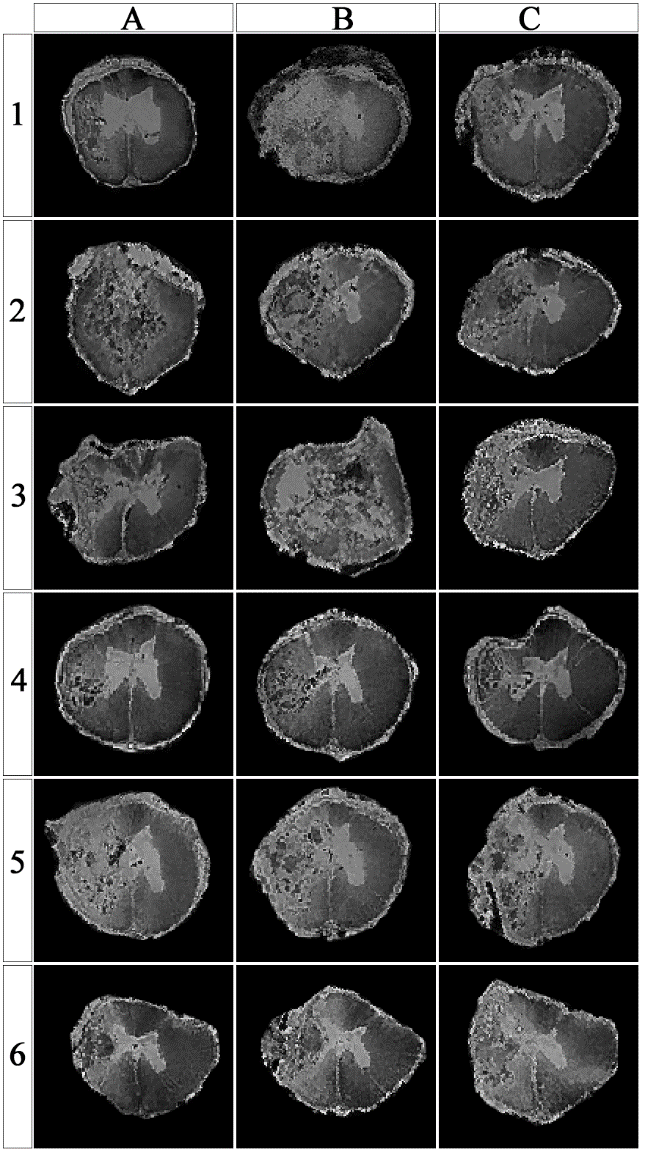
**Immune Responses to Autologous Schwann Cell Grafts in a Minipig Spinal Cord Injury Hemicontusion Model**

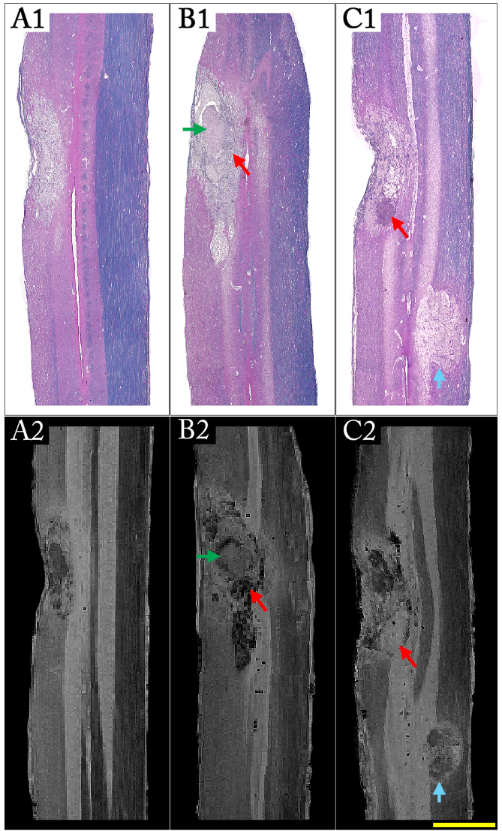
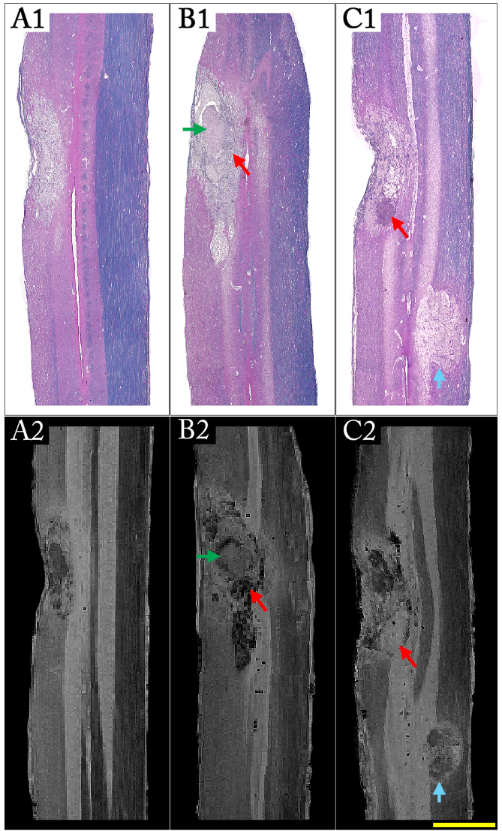
Santamaria, A.J.; Benavides, F.D.; Nunez, Y.; Brooks, A.; Solano, J.P. (U. of Miami, The Miami Project to Cure Paralysis); Rosenberg, J.T. (NHMFL); Grant, S.C. (Florida State U., Chemical & Biomedical Engineering, NHMFL) and Guest, J.D. (U. of Miami, Neurological Surgery and The Miami Project to Cure Paralysis)

**Fig. 1** Ex-vivo MRI show left-sided distribution of injuries, and area quantification.



**Introduction**

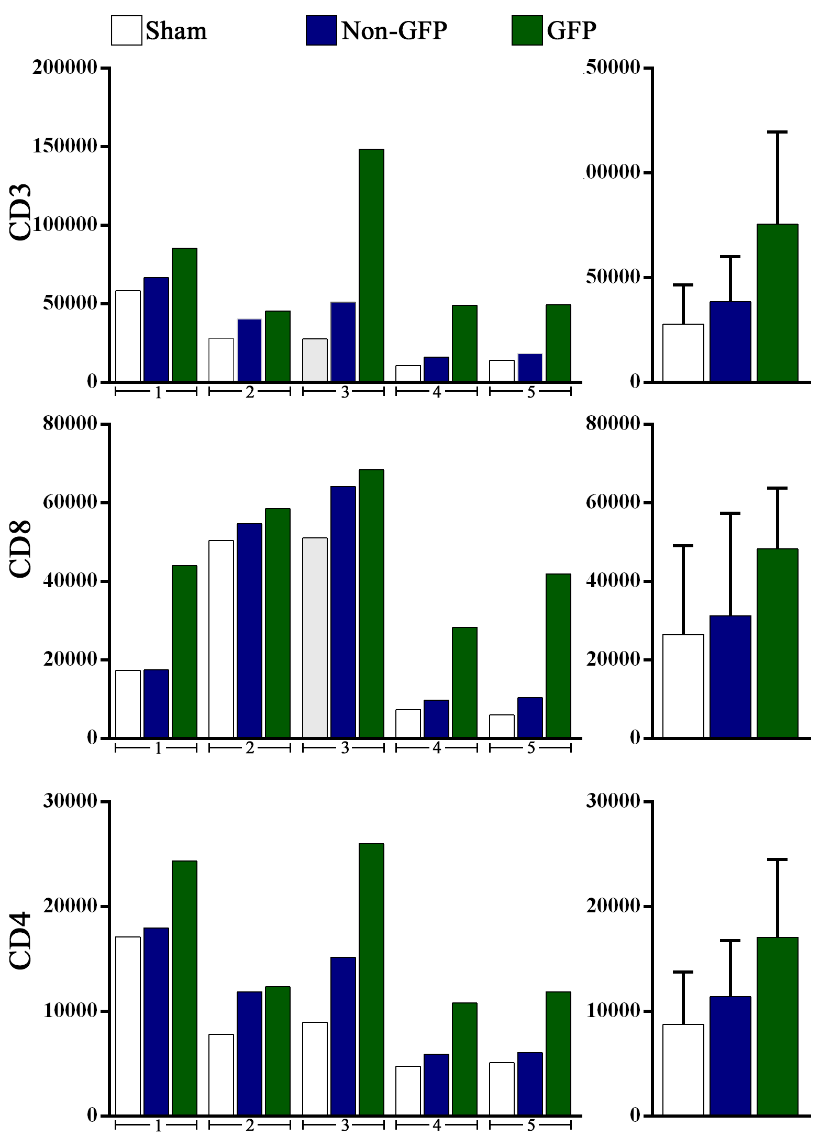
Autologous Schwann cells (aSC) from sural nerves are expanded, and purified for testing in a Phase 1 human clinical trial after SCI (ClinicalTrials.gov Identifier: NCT01739023). Observations from preclinical pivotal studies in minipigs included a robust lymphocytic response related to transplanted GFP-transfected cells. Formation of lymphoid follicular structures has been reported before in a mouse model after SCI through B cell activation as a systemic autoimmune response, with enhanced lymphopoiesis in bone marrow and spleen, higher circulation of IgG and IgM antibodies[1], and declines in locomotor function[2]. This has never been reported after cell transplantation for SCI. It is naive to assume that transplantation of artificially manufactured autologous cells into a site different from that of origin will not elicit an immune response. A triple-hemicontusion minipig model was used to assess these responses and their association with SCI and viral cell transfection.



**Fig. 2** Visualization of injury and transplant sites through MRI shows faithful histological comparison.

**Methods**

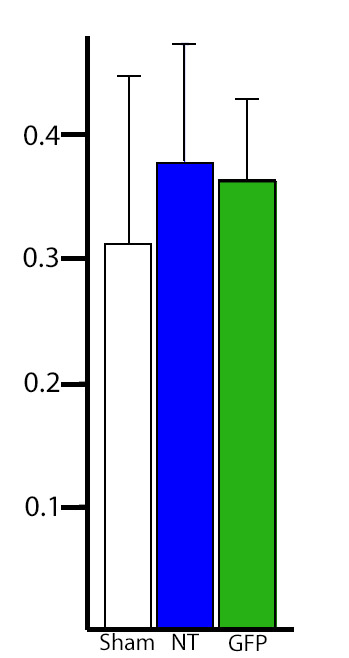
5 Female Yucatan minipigs underwent 3 left hemi-contusion injuries at T6, T9 and T12. A nerve was extracted to derive aSC, and preparations were divided into a GFP-transfected and non-transfected products. After 52 ± 2.1 days transplants were delivered through myelotomy directly into the injury cavities (100,000 cells/μl) until extrusion was observed. Animals survived for additional 70 days before perfusion. Spinal cords were dissected and submitted to the NHMFL Tallahassee facility for ex-vivo MRI scanning with the 11.75 T magnet. High resolution 3D gradient recalled echo (GRE) sequence was used for assessment. Specimens were then returned for histological analysis to The Miami Project.



**Fig. 3** Quantification of lymphocytic populations within groups.

**Results**

The triple injury hemicontusion paradigm allowed an animal number reduction by preserving uninjured right sided parenchyma in all epicenters assessed **Fig. 1,** identification of the transplants and lymphocytic reaction through MRI as a faithful histologic comparison **Fig. 2,** quantification of greater quantities of inflammatory cells within GFP transfected transplants **Fig. 3**, and visualization of smallest injury cavities in non-transfected transplants though Fractional anisotropy evaluation **Fig. 4**.



**Fig. 4** Fractional anisotropy differences between groups.

**Conclusions**

Detection of prominent lymphocytic responses in aSC transplanted sites was higher, additionally non-transfected transplants showed better integration with axonal and astrocytic elements. Fractional anisotropy was similar between transplanted groups and higher as compared to sham injuries. High field *ex-vivo* MRI showed excellent correlation to the injury histological outcomes with unexpected identification of cellular transplants location and distribution.

**Acknowledgements**

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**References**

[1] Ankeny, D.P., *et al*., J Neurochem, **99**, 1073-87 (2006). [2] Ankeny, D.P., *et al.,* J Clin Invest, **119**, 2990-9 (2009).