

PERIPHERAL NERVE REPAIR WITH ALLOGENIC EPINEURAL TUBE SUPPORTED WITH BONE MARROW STROMAL CELLS (BMSC)

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Introduction: Long peripheral nerve defect repair remains a major challenge for surgeons. Allogenic epineural tubes provide unlimited source of grafting material without donor site morbidity compared to nerve autografts, the current gold standard. This study evaluates the efficacy of peripheral nerve repair with allogenic epineural tube supported with BMSC.

Material and Methods: 18 epineural tube transplantations were performed across MHC barrier from ACI (RT1^a) donor to LEW (RT1^b) recipient rats to bridge 20 mm sciatic nerve defects. In Group 1 the tube was filled with saline, in Group 2 and 3 the epineural tube was filled with $3.5-4 \times 10^6$ of PKH stained BMSC: isogenic [LEW (RT1^b)] and allogenic BMSC [ACI (RT1^a)] respectively. Animals were evaluated clinically for sensory and motor recovery (pin-prick, toe-spread test) at 3, 6, 12, 18 and 24 weeks post transplantation. Assessment at 24 weeks also included: Somatosensory Evoked Potentials (SSEP), Gastrocnemius Muscle Index (GMI), axonal counts, immunostaining for NGF and Laminin B2.

Results: 6 weeks after transplantation, Group 2 scored 3 on pin-prick, while Group 1 and Group 2 achieved the same values at 18 weeks. Group 2 revealed the best toe-spread at 24 weeks (0.75) compared to Group 1 and 3 respectively (0 and 0.25). GMI was comparable in Groups 1 and 2 (0.49 vs 0.48) and lower in Group 3 (0.43). Shortest SSEP P1 latencies were observed in the Group 2, then in Group 3 and 1 (19,6 vs 20,8 vs 21,99 ms respectively), while shortest N2 latencies were noted in Group 3 compared to Group 1 and 2 (26,9 vs 28,1 vs 28,9 ms respectively). Group 2 demonstrated decreased loss of amplitude compared to Group 1 and 2 (57 vs 40 vs 51% of control side respectively). Preliminary axonal counts showed increased number of total nerve fibers in BMSC groups compared to saline. Upregulation of NGF and Laminin B2 expression was found in the tube and correlated with double positive PKH/NGF BMSC (Fig. 1 and 2).

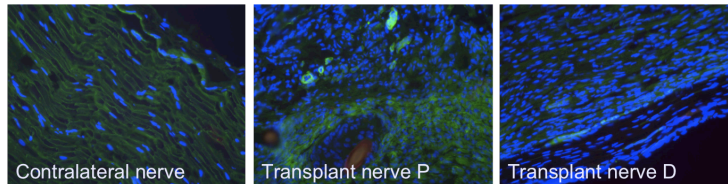


Fig.1. Laminin B2 expression in transplanted tube, contralateral nerve

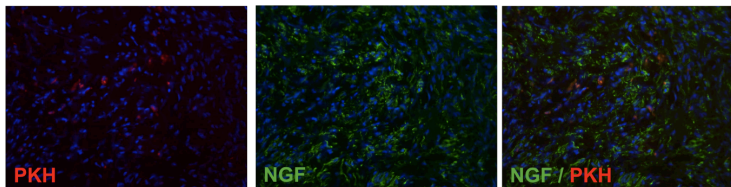


Fig.2. NGF expression and NGF/PKH positive cells in transplanted tube

Conclusions: We proved that allogenic epineural tube is a viable conduit, supporting nerve regeneration over 20 mm defect. Presence of BMSC was confirmed for 6 months inside the conduit at 6 months post transplant and correlated with expression of nerve growth factor (NGF). This study also shows the synergistic effect of allogenic epineural tube and BMSC supportive therapy on nerve regeneration as demonstrated by improved functional recovery and axonal regeneration compared to saline group.