

## EPINEURAL SHEATH PATCH AND BONE MARROW STROMAL CELLS (BMSC) PROMOTE REGENERATION IN DORSAL ROOT GANGLION INJURY IN RAT

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**Introduction:** Cytokine expression and neuroglial activation in compressed or inflamed dorsal root ganglion (DRG) are the underlying causes of painful radiculopathy. Epineural sheath and BMSC demonstrated neuroregenerative potential in peripheral nerve repair. The goal of this study is to evaluate the role of the epineural sheath and BMSC in DRG inflammation. We hypothesize that epineural sheath seeded with BMSC can provide a unique environment for regeneration after nerve root injury.

**Material and Methods:** A lumbar hemilaminectomy exposing the left L4 DRG and nerve root was performed in 24 rats. Three 3mm pieces of 4-0 chromic-gut suture were placed on the exposed DRG. The right side of the spine was left undisturbed. Animals were re-operated 3 days after initial surgery. Four procedures were investigated: Group I: wound was inspected, chromic-gut was left in place; Group II: chromic-gut was removed; Group III: chromic-gut was removed, DRG was wrapped, without compression, with epineural sheath harvested from sciatic nerve of the donor rat; Group IV: chromic-gut was removed, DRG was wrapped with epineural sheath seeded with BMSC previously cocultured in-vitro for 14 days and stained with PKH dye. Outcome was assessed at 1,2,3,7,14,28 days after the second surgery by somatosensory evoked potentials (SSEP) and immunostaining for VEGF and GFAP expression in harvested bilateral DRG and epineural sheath.

**Results:** Group II showed prolongation of P1 and N2 latencies from day 7 to 28, compared to stable latencies in Group III and IV. In Group III at day 1 100% of neurons expressed VEGF while at day 28 the number of VEGF positive neurons decreased to 23% compared to Group II (78% vs 60% respectively). In Group I 85% of DRG neurons were VEGF positive at 24hrs and reached 98% at 28. The highest VEGF expression in the epineural sheath was observed at day 7. At day 2 Group I and II operated side showed an increase in number of GFAP positive satellite cells (SC) (80% and 66% respectively) compared to Group III (32%). VEGF and GFAP expression decreased over time in contralateral DRG (Fig.1). Preliminary results from Group IV showed the presence of viable BMSC, expressing GFAP and VEGF, in the patch and wrapped DRG at 28 days (Fig.2).

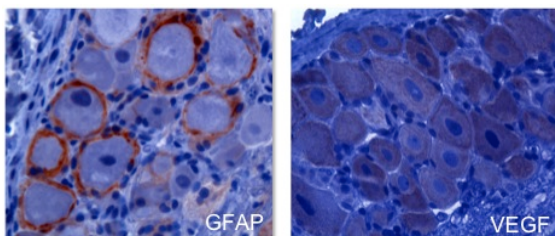


Fig. 1. GFAP and VEGF expression in DRG.

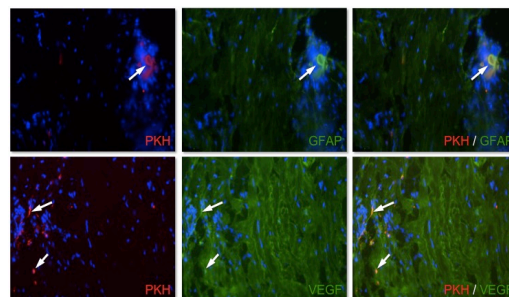


Fig. 2. BMSC expressing VEGF and GFAP in DRG

**Conclusions:** Epineural sheath patch demonstrated neuroprotective properties in the DRG inflammation model. This was confirmed by improvement in functional recovery by SSEP testing and correlated with decreased expression of GFAP in SC in early phase of inflammation and by heightened expression of VEGF in epineural sheath 7 days after the inflammatory insult. BMSC enhance the neuroregenerative potential of epineural sheath patch.