

## **Nogo Receptors Contribute to Parallel Growth of Regenerating Axons on Spinal Cord White Matter**

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**Introduction:** Following trauma, axonal regeneration along CNS white matter is usually abortive. However, *in vitro* studies demonstrate that axonal growth will occur with a trajectory parallel to the underlying fiber tract. This observation has led to the hypothesis that myelin associated inhibitor molecules constrain, but do not prevent, axonal regeneration through interaction with membrane receptors (eg., Nogo Receptor [NgR]) on the growing neurite. To explore this hypothesis, dissociated neurons were cultured on spinal cord white matter in the absence or presence of NEP1-40, an antagonist of NgR.

**Methods:** Lumbar sympathetic chain ganglia were dissected from 10-day-old Leghorn chicken embryos, dissociated, and cultured on longitudinal cryostat sections of adult rat thoracic spinal cord. At the time of culture, as well as on post-culture day 3, the cultures were treated with either a low or high concentration of the NgR antagonist NEP1-40, a scrambled sequence control peptide, or vehicle. After 7 days, all cultures were stained with vital dye to visualize the growing neurites using a Nikon Diaphot fluorescent microscope.

**Results:** The extent of parallel growth (isotropism) of neurites was evaluated using Fourier spectrometry or a blinded rank order analysis. The data were analyzed with an ANOVA or Kruskal-Wallis test, respectively. Neurites in cultures treated with the antagonist NEP1-40 exhibited significantly less isotropism than vehicle- or scrambled peptide-treated cultures. This difference was greatest with the high concentration of NEP1-40. In addition, neurite outgrowth and orientation did not differ significantly between vehicle control and scrambled peptide control treatments.

**Conclusions:** These findings implicate the interaction between myelin associated inhibitors and NgR in mediating the parallel orientation of axonal regeneration on white matter. Gaining a clear understanding of the phenomena involved in this process could ultimately prove beneficial towards the treatment of patients with lesions of the central nervous system.