Guiding Regeneration Gel (GRG) for Growth and Repair of Peripheral Nerves

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Abstract

Massive regional losses of peripheral nerve always require surgical procedure for its reconnection. The current common clinical treatment option is an autologous nerve graft ("gold standard" treatment), in spite having many drawbacks.

Recent developments in our laboratories seem to offer an alternative to the above "gold standard" treatment, the employment of a GRG-guided regeneration gel. The gel functions as a stimulator for both neurogenesis of rat cerebral stem cells in culture, and support axonal growth upon placing the GRG in vivo, within neuroconduits, ranging from the proximal to the distal nerve stumps, bridging gaps of massive regional losses in injured/complete transected rat sciatic peripheral nerve. The goals are increasing gap distances, as well shorten the period of recovery.

Background

Peripheral nerve injuries result in considerable disability associated with loss of sensory and motor functions and in some cases intractable pain leading to social and economical burden on the society.

Traumatic injuries of peripheral nerves represent a major cause for morbidity and disability affecting about 3% of all trauma patients. In cases of peripheral nerve injuries with a nerve defect more than 2 cm, autologous nerve grafting is the treatment of choice. However, the outcome of such neural repair is often unsatisfactory.

Materials

An innovative Guiding Regenerative Gel (GRG) invented by our research team is a special milieu that increases nerve growth and promotes recovery, aiming, ultimately, at restoring the function of a torn nerve. The GRG is composed of:
1) anti-oxidants, found to exhibit high anti-inflammatory activities;
2) synthetic laminin peptides, which act as a scaffold for the nerve fibers to grow along; and
3) hyaluronic acid, which is highly hydrated and contributes to the success of survival, growth and regeneration of nerve fibers by protecting them from drying.

In vivo experimental model: Standard rat peripheral nerve injury model
Surgical procedure

Segment of sciatic nerve removed and 15mm* gap was reconnected with 17mm conduit (tube) to align both nerve ends
Experiment groups
1. Tube filled with GRG
2. Autologous nerve graft (gold standard control)
3. Empty tube (control)

Creating nerve damage — Nerve reconstruction using tube

Results

On a pilot pre-clinical study, we evaluated the efficacy of GRG in promoting axonal growth in peripheral nerves with massive loss defect after autologous nerve graft (gold standard) and a 17 mm long implementation of tube, with and without GRG (Rochkind and Nevo, Biomed Res Int. 2014).

Histological observation of the nerves showed no axonal growth through the tube in the empty tube group (regeneration within the empty tube in rats is possible only when the gap is smaller than 7mm). Whereas, in the group treated with a tube filled with GRG, growth of myelinated axons and continuation of axonal sprouting through the tube to the distal part of the nerve was observed. Moreover, the histological pictures of the GRG group versus autologous nerve transplanted group showed no significant differences between both groups.

Conclusions

GRG filled tube enabled regeneration of a major nerve loss defect, which was impossible when bridging with an empty tube.
GRG was shown to enable nerve regeneration at least as good as with autologous nerve graft ('gold standard' treatment)
GRG enables a simpler and cheaper alternative to current treatment of major nerve loss, which comprises majority of peripheral nerve injury cases.
This data emphasizes, that the GRG enabled optimal axonal regeneration as compared to gold standard.

References: Rochkind S, Nevo Z. Recovery of peripheral nerve with massive loss defect by tissue engineered guiding regenerative gel. Biomed Res Int. 2014.