Studies on The Regeneration of Nerve Defects Using Poly(ε-caprolactone) Tubular Nanoweb

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1. Introduction
When compared to the central nervous system, peripheral nervous system has a greater capacity for regeneration, although complete repair is rare and, in severe injuries, functional recovery is poor. In cut injuries, the most common procedure is to suture the two nerve stumps together[1]. However, when there are large gaps, a scaffold or accessory structures are generally required to guide and protect the nerve during growth, and to provide a tension-free full regeneration of the nerve. Although nerve allografts and autografts are indicated in these cases, this strategy is usually avoided because of the high tissue morbidity, and artificial tubes have been used to guide nerve regeneration. Recently, several groups have tried to develop synthetic biodegradable polymers to build tubular prostheses to connect the proximal and distal stumps[2,3]. Their use has the advantage of avoiding a second surgery to relieve chronic nerve compression and the unavoidable tissue reaction from the implanted tissue.

Electrospinning has recently drawn strong attention in biomedical engineering, providing the basis for the fabrication of unique matrices and scaffolds for tissue engineering. The potential of applying electrospinning in vascular tissue engineering is enormous since it cannot only mimic the nanosized dimension of natural extracellular matrix but also its spatial organization on the mesoscopic scale[4].

In this study, by using special shaped collector, a small diameter biodegradable tubular scaffold was electrospun. Also, we illustrated the potential use for nerve guide regeneration of these tubular scaffolds by evaluating sciatic nerve regeneration in mice.

2. Experimental
2.1. Preparation of tubular nanoweb
Poly(ε-caprolactone) (PCL) solution with M_n of 80,000 was prepared with concentration of 10
g/\text{dL} using organic solvent mixture (7:3) of chloroform and ethanol and electrospun into nanofiber through a nozzle under the action 15 kV high electrostatic voltage. A rotating mandrel collector was placed under the spinning nozzle at a distance of 20 cm.

Then, we tested three strategies for the improvement of sciatic nerve regeneration after surgical transection: (1) PCL tubular nanoweb without cells; (2) PCL tubular nanoweb with adipose derived stem cells (ADSCs); (3) PCL tubular nanoweb with neuronal induction.

2.2. Surgical procedure

Male mice weighing 20-25 g were anesthetized by intraperitoneal injection of 3% sodium pentobarbital. The left sciatic nerve was exposed and transected at the mid-thigh position. The proximal and distal nerve stumps were place in a tubular PCL nerve guide (20 mm long), inserted 2.5 mm into it and sutured to the tube with monofilament nylon. A 15-mm gap was left between the nerve stumps. After 3 months of transplantation, the left sciatic nerves were exposed and the mid-portions of the growing nerves (corresponding to the previous gap area) were harvested and processed for assessment of cell proliferation.

3. Result and discussion

The serial semi-thin sections stained with toluidine blue-O of regenerated nerves after 3 months of the different experimental groups are shown in Figure 1. Toluidine blue-O staining showed a strong blue color with a light background in the cerebral parenchyma. In Figure 1. the mean axon counts improved significantly after 3 months in the case of PCL tubular nanowebs with neuronal induction than the nanowebs with ADSCs and pure nanowebs.

![Figure 1. Sciatric nerve stained with toluidine blue-O: a, PCL tubular nanoweb, b, PCL tubular nanoweb with ADSCs, c, PCL tubular nanoweb with neuronal induction.](image)

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5. References