Artificial Nerve Conduits Made with Photo-cross-linked Hyaluronic Acid

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The achievement of peripheral nerve regeneration through biodegradable tubular conduits is at the frontier of nerve repair surgery. In principle, a biodegradable conduit should maintain its structural integrity, permit cell adhesion and infiltration, and subsequent tissue in-growth during the nerve regeneration process. Many conduits using bioresorbable materials, such as polyglycolic acid, collagens, chitosan, poly L-lactic acid and polycaprolactone have been developed, however, none of these materials have been proven to act as an agent to aid nerve growth and repair. Yoshihito Sakai and a team of engineers at Nagoya University School of Medicine in Japan in collaboration with the Seikagaku Corporation have fabricated new artificial nerve conduits made with hyaluronic acid (HA) that facilitate a pathway for cellular and axonal in-growth during peripheral nerve regeneration, identifying viability of disseminated Schwann cells and neuron cells into HA conduits *in vitro*.

Fig. 2. Macroscopic appearance of the HA conduit.

To Fabricate the HA Conduits, the HA derivative was dissolved in water at a concentration of 4.0 wt%, and the solution was poured into polydimethylsiloxane (PDMS) mold. The mold was exposed to ultraviolet (UV) light at -20 degrees C for 15 minutes. The UV-iradiated gellous intermediate was freeze-dried and the final product was stored with desiccant at R.T. before it could be used.

For experimentation, Schwann cells were harvested from dorsal root ganglia (DRG) and sciatic nerves of 6 week old female rats, weighing about 200g under anesthesia. The nerves were de-sheathed and dissociated into single cells with the use of centrifuge and gentle trituration with a fire-polished Pateur pipette. 0.8% collagen gel was filled with the dissociated Schwann cells and inserted into the photo-cross-linked HA conduits to be incubated for 3 weeks.

Throughout the 3 week experimental period, the HA conduits remained circular with a round lumen, and construct of cell-conduits maintained the size and shape of the original architecture of the tube. Scanning Electron Microscope (SEM) micrographs showed cell adhesion to the conduit surfaces and migration into the porous matrix. Cell growth and neurite outgrowth were observed serially and obviously after the 3 week incubation as well.

These findings provide the feasibility of using the HA conduits for better cell adhesion and differentiation, leading to axonal regeneration in peripheral nerve reconstruction. Further improvement and investigation of the conduits stability and biocompatibility will be needed to decide the suitable design for artificial nerve conduit clinically.

Reference:

Sakai, Y., Matsuyama, Y., Takahashi, K., Sato, T., Hattori, T., Nakashima, S., Ishiguro N., New artificial nerve conduits made with photocrosslinked hyaluronic acid for peripheral nerve regeneration; *Bio-Medical Materials & Engineering,* 2007, Vol. 17 Issue 3