

Novel Cell Encapsulation through Co-axial Electrospinning: Mimicking the Natural Tissue

Rajesh A. Pareta and Thomas J. Webster

Division of Engineering and Orthopedic Surgery, Brown University, Providence, RI, USA

Statement of Purpose: Dysfunctional central nervous system (CNS) resulting either from neurological disorders, accidents or diseases impacts all of humanity. The outcome presents a staggering health care issue with a tremendous potential for developing interventive therapies. Attempts at delivery of therapeutic molecules to the CNS have been hampered by the presence of the blood–brain barrier (BBB) — a protective cellular barrier that regulates the internal environment with a mechanism of low passive permeability combined with a highly selective transport system.

To solve this neuron transplantation has been made but the limited survivability of transplanted neurons makes current strategies of cell implantation unfeasible. While around 50% of fetal CNS cells die naturally, <5% of transplanted neurons survive. Cell encapsulation is an attractive alternative to traditional approach of cell implantations and drug delivery [1]. Cells when transplanted on their own, without being encapsulated, get tagged by antibodies and attacked by immune cells resulting in cell necrosis. Also they tend to migrate away from the site of injection. Sustained-release polymer systems offer the ability to be implanted safely and are well tolerated by the host [2]. They can be retained as a closed system within a host system and thus do not provide a conduit to contamination or infection.

The objective of this research was to generate 3-D cell encapsulated conductive scaffolds, which mimic the in-vivo conditions. These scaffolds can be used for cellular drug delivery as well as a tissue implant. The degradable polyester (PLGA) and hydrogel will ultimately lead to a full tissue regeneration and return of normal function. We have used co-axial electrospinning [3], which is capable of processing two solutions together to form cells encapsulated in microspheres in otherwise fibrous scaffold.

Methods: PLGA and carbon nanotube (CNT) solution was prepared in chloroform. Cells (PC12) were suspended uniformly (1-10 millions cells/ml) in alginate and polyethylene oxide solution. The PLGA solution and cell suspension were fed through the outer capillary and inner capillaries, respectively. In the co-axial electrospinning set-up a voltage difference of 10-20 kV was applied between the capillaries exit and collecting ground electrode. The scaffolds were collected on glass slide as well as directly deposited in the cell culture dish.

The conductivity measurements were done using a four probe method. Scaffolds were subjected to electrical stimulus. The scaffolds were maintained at standard cell culture conditions (37°C, 5% CO₂, 95% humidified air)

for various time periods. The cells were then stained and observed with confocal microscope.

Results: The PLGA shell thickness can be controlled by varying the flow rate in the outer capillary. Fig. 2 shows the PLGA shell encapsulating the cells. The cells were encapsulated in PLGA microspheres as shown in Fig. 3. In electrospinning the fibres are usually of sub-micron size, but cells are around micrometer in size. Hence when a cell goes through the capillary exit it disturbs the fibre formation momentarily and therefore a droplet (microsphere) encapsulating cells forms in otherwise nano-fibrous scaffold. This arrangement is very similar to natural organization in body.

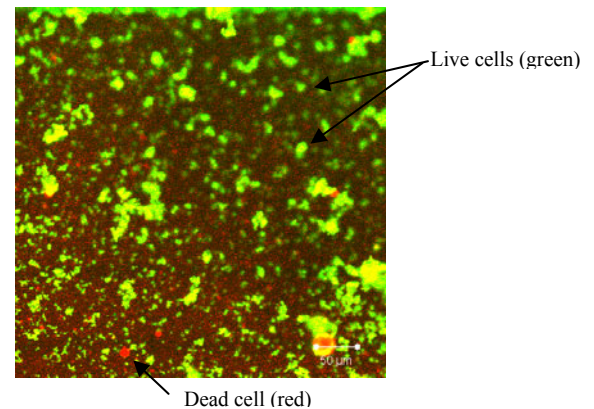


Fig. 1. Viable PC12 cells after 3 days

Conclusions: The cells were viable inside the microsphere after 3 days. Although more work needs to be completed (as in cell viability percentage and studying the various parameter effects), this process looks promising to enable one to produce a scaffold which mimics natural body tissue like organization in which cells are organized in otherwise nanofibrous extra cellular matrix.

References: 1. Stankus, J. J., Soletti, L., Fujimoto, K., Hong, Y., Vorp, D. A., and Wagner, W. R. (2007): Fabrication of cell microintegrated blood vessel constructs through electrohydrodynamic atomization. *Biomaterials* **28**, 2738–2746.

2. Winn, S. R., Aebischer, P., and Galletti, P. M. (1989): Brain tissue reaction to permselective polymer capsules. *Journal of Biomedical Materials Research* **23**, 31–44.

3. Loscertales, I. G., Barrero, A., Guerrero, I., Cortijo, R., Marquez, M., and Gañán-Calvo, A. M. (2002). Micro/Nano Encapsulation via Electrified Coaxial Liquid Jets. *Science* **295**, 1695-1998.