Hyaluronic Acid-Based Hydrogels as Scaffolds for Stem Cells to Differentiate Into Neuronal Cells

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Introduction. Neurological damages in the central nervous system can disrupt the receiving and transmission of information through the body, and thus affect an individual's motor, sensory and autonomic functions. Currently, there is no cure for such patients since the lost functions could not be completely restored using current clinically available treatments. However, with the advances in the understanding of the disease processes, and tissue engineering, it is very promising that the lost or damaged neural tissues can be regenerated by engineered scaffolds. In this study, we have developed hyaluronic acid (HA) based hydrogels as scaffolds for stem cell growth and differentiation into neuronal cells for treating ocular diseases.

Materials and Methods. A serial of hyaluronic acid monomers are synthesized by conjugating 2-aminoethyl methacrylate (AEMA) to hyaluronic acid with different molecular weights (i.e. 6400, 16000 and 66000). The synthesized monomers are further used to make hyaluronic acid hydrogels using UV polymerization technique. The chemical structures of the monomers and the hydrogels are characterized using ATR-FTIR. The storage and loss moduli of these hydrogels are characterized using rheometer and dynamic mechanical analyzer (DMA). The degradation of these hydrogels is investigated using ATR-FTIR and rheometer. The cytotoxicity of the HA-AEMA macromers to neuron-like PC-12 cells and stem cells is evaluated using MTT assay. PC-12 cells and neural stem cells are encapsulated into the hydrogels in situ during the photo-polymerization. The cell viability of the encapsulated cells are assessed using LIVE/DEAD® cell assay. In the presence of nerve growth factor (NGF), the differentiation of the stem cells into neuronal cells inside the hydrogels in terms of neurite length and number is currently being studied.

Results and Discussion. ATR-FTIR measurements confirm the successful synthesis of HA-AEMA monomers and HA hydrogels (see Figure 1). The storage and loss modulus studies show that the substitution of the AEMA component in the hydrogel affects the rheological properties of the hydrogel. MTT data indicate that the HA-AEMA macromers are not toxic to both PC-12 and stem cells at concentration of 3 wt%. LIVE/DEAD cell staining results suggest that PC-12 and stem cells can survive after being encapsulated in the hydrogels during the UV-polymerization process. In the presence of NGF, the stem cells can potentially differentiate into neuronal cells inside the developed HA hydrogels.

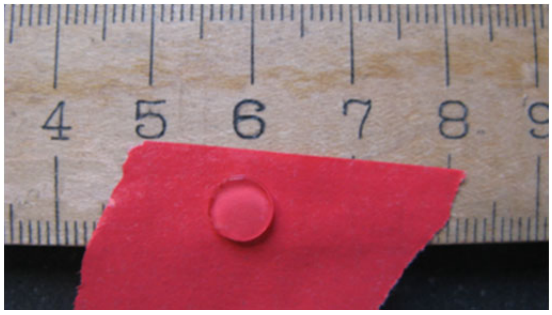

Figure 1. HA hydrogel is successfully produced using UV-polymerization

Conclusion. HA hydrogels containing AEMA can be developed to have different mechanical properties to control differentiation of stem cells into neuronal cells which will have significant impact on neuronal regeneration in treating ocular diseases.