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Cover story

Nanocomposite microparticles for injectable cell scaffolds

More than two decades ago tissue engineering began with a simple concept of growing cells in biodegradable scaffolds to create tissue-like biomaterials. The scaffolds in early days were made of biodegradable polymers, such as poly(lactide-co-glycolide) (PLGA) and poly(lactide) (PLA), which had to be shaped into specific three-dimensional (3D) solid structures for intended applications. One of the biggest challenges in tissue engineering is to create appropriate 3D structured scaffolds favoring sufficient flow of nutrients for cell growth and at the same time controlling the release of growth stimulating compounds over several weeks. Thus, for clinical applications, it is highly attractive to develop an injectable cell scaffold that can efficiently support and enhance the cell growth for sufficient therapeutic periods.

Recent progresses in stem cell-based tissue engineering provide a great potential for development of clinically useful injectable cell scaffolds. In many previous studies, injectable cell scaffolds made of biodegradable materials have shown good properties for cell transplantation and immediate delivery of bioactive molecules. In the context of addressing the challenges associated with developing injectable scaffolds, Professor Nielsen's team reported a new kind of PLA/PLGA-based biodegradable nanocomposite microparticles as a combined drug delivery and injectable cell scaffold [1]. The delivery system is designed to achieve sustained drug release without compromising the morphology suitable for cell adhesion and growth. Biodegradable nanoparticles composed of poly(L-lactide/DL-lactide) (PLDL70) and PLGA85 with the average size of 270–300 nm were loaded with the thrombin receptor activator peptide 6 (TRAP-6) and subsequently incorporated into mPEG-PLGA microparticles by ultrasonic atomization. For proper selection of the best nanoparticulate structures, the release profiles of PLDL70 and PLGA85 nanoparticles were determined and mechanistically explained in terms of differences in crystallinity and polymer composition. The PLDL70 nanoparticles showed 30% drug release within the first 15 days and sustained release over at least 30 days. The produced nanocomposite microparticles displayed sustained drug release

identical to that of nanoparticles. This indicated the successful incorporation and preservation of nanostructures and properties in the nanocomposite particles. In addition to the sustained release properties, the composite microparticles maintained a favorable morphology for cell adhesion. In vitro, human skin fibroblasts readily attached to the composite microparticles and built up cell-particle constructs in 3 days. The good cell adhesion of human fibroblasts onto the nanocomposite microparticles indicated the cell biocompatibility necessary for a cell scaffold.

The work by Professor Nielsen's team describes a unique approach for obtaining nanocomposite microparticles as injectable cell scaffolds. The study highlights that the tailored design of biodegradable nanocomposite microparticles with a desired sustained drug release profile relies to a large extent on the characteristics of the incorporated nanoparticles. The approach gives new potential for development of injectable cell scaffolds, and the method can certainly be applied for delivery of other bioactive molecules to achieve successful autologous stem cell therapy. Formulation design and characterization of both nano- and micro-structures remain to be of major importance. Continued advances in nano/micro fabrication of diverse structures and in drug loading into nano/micro particles are expected to bring the injectable cell scaffold approach closer to clinical applications.

Reference

- [1] Y. Wen, M.R. Gallego, L.F. Nielsen, L. Jorgensen, H. Everland, E.H. Møller, H.M. Nielsen, Biodegradable nanocomposite microparticles as drug delivering injectable cell scaffolds, *J. Control. Release* 156 (1) (2011) 11–20.

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