Nanostructure Processing of Advanced Biomaterials and Biosystems

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Nanostructured materials are of interest for a variety of applications. Through controlled synthesis in reverse microemulsions, my laboratory has achieved polymeric nanoparticles for the glucose-sensitive delivery of insulin. These stimuli-responsive materials allow for the appropriate insulin delivery to diabetic patients only when their blood sugar levels are high, without the need for external blood sugar monitoring. The nanoparticles are small enough to escape macrophage digestion, and provide for enhanced systemic absorption and bioavailability.

We have also developed targeted and stimuli-responsive polymers as chemotherapeutic delivery systems. The polymeric nanoparticles are engineered with both temperature and pH sensitivities, and would only release paclitaxel rapidly at a low pH at body temperature, i.e. tumor or endosomal conditions. In addition, the polymer is substituted with a galactose functional group to target the high surface concentration of asialoglycoprotein receptors on hepatocytes in hepatocellular carcinoma. This material provides for the effective delivery of paclitaxel, reducing its LC_{50} by almost 3 orders of magnitude in the target cells.

We have generated apatite-polymer nanocomposite particles for the sustained, zero-order delivery of protein therapeutics. By adsorbing valuable bone morphogenetic proteins on carbonated apatite nanocrystals that are then encapsulated within biodegradable polymeric microparticles, we are able to achieve the controlled release of growth factors for the bone healing process over an extended period of time.

Nanoporous polymers have been synthesized using bicontinuous microemulsion polymerization as drug-loaded contact lenses. The nanostructured channels allow for the loading of drugs such as glaucoma medication, antibiotics, and artificial tears. The nanoporous polymeric contact lenses enable the sustained release of various ophthalmic drugs for hours or days in contrast to eye drops.

Nanostructure processing has been employed in tissue engineering and artificial implant applications as well. For example, we have prepared collagen-apatite nanofoam for orthopedic implants and bone scaffolds. Highly porous, sponge-like collagen constitutes the organic matrix component. A mixture of carbonated and hydroxy apatite nanocrystals are synthesized to mimic the biomineral phase of bone. The collagen-apatite nanofoam has been processed to provide a hierarchical porosity that resembles the microstructure of natural bone. The material demonstrates tunable mechanical properties and excellent bioactivity.

We have also created scaffolds for soft tissues using fibers prepared by interfacial polyelectrolyte complexation. The latter is room-temperature, aqueous, pH-neutral process, unlike most conventional fiber fabrication processes. It allows for the incorporation of biomolecules, without compromising their activities. Nanocomposites of chitosan-alginate fibers and nanoparticles can be achieved with multiple functionalities. For example, silica has been incorporated in the fibers to increase the hydrophobicity and mechanical strength of the fibers. Cell-adhesive peptide sequences and extracellular matrix molecules have also been introduced into the fibers for enhanced cell adhesion and proliferation. The fibrous scaffolds have been successfully applied as a delivery vehicle for differentiated stem cells for liver tissue engineering.

Lastly, nanotechnology has been combined with microfabrication to establish organ assist devices with functionalized materials characteristics and microfluidics control. For example, we have developed various microstructures in kidney-specific dimensions and shapes. These structures can be used as bioartificial renal assist microdevices, and may serve as three-dimensional templates for tissue engineering.