Characterizing the Evolution of Gel Scaffolds Using Passive Microrheology

The evolution of gel scaffolds has implications in potential applications. Due to gel versatility, these materials are used in applications that range from home care products to synthetic materials that enhance wound healing. To meet the need of this broad range of applications, we must first understand the change in material properties and scaffold structure during gelation and degradation. We will discuss the characterization of two gel systems: a hydrogenated castor oil (HCO) colloidal gel and an enzymatically degradable human mesenchymal stem cell (hMSC)-laden poly(ethylene glycol) (PEG)-peptide scaffold. In this work, we use multiple particle tracking microrheology (MPT) to measure dynamic material properties during critical phase transitions. MPT measures the thermal motion of embedded probe particles to measure rheological properties. HCO is a rheological modifier used in commercial products, including fabric and home care products. Of concern in the design is whether the gradient that induces phase change can overcome any processing history, particularly due to shear stress. In this work, we characterize HCO evolution due to a osmotic pressure gradient with MPT, μrheology, MPT in a microfluidic device, and bulk rheology. MPT measures that the scaffold structure varies when a single sample is gelled or degraded. To determine whether this is due to colloidal rearrangement during phase transitions or processing history we develop a new microfluidic device for μrheology measurements. This two-level device creates equal pressure around the HCO sample locking it in place when solvent is exchanged and also imparts minimal shear on the sample. μrheology measurements of consecutive phase changes of HCO are taken starting with both a sheared solution of HCO and an un-sheared HCO gel. Samples are measured during 4 – 9 phase transitions and return to the same equilibrium properties. Bulk rheological measurements support these results. We conclude that equilibrium structures depend on the shear history of the starting material, which can have implications in end use products made with this colloidal gel scaffolds. hMSCs are critical players in wound healing. During wound healing, hMSCs are called to the wound by chemical cues in the environment. In response, they migrate out of their niche and traverse mechanically distinct microenvironments to reach the wound. At the injury, they are active in all phases of healing, regulating inflammation. To enhance wound healing, implantable synthetic hydrogels are designed to mimic in vivo microenvironments to deliver hMSCs to the surrounding tissue. It is still not understood how cells re-engineer their microenvironments during motility and how the microenvironment influences cellular degradation strategies. Our approach uses MPT to characterize the pericellular region during cellular remodeling and degradation in a synthetic hydrogel scaffold. The material hMSCs are encapsulated in is degraded by cell secreted matrix metalloproteinases (MMPs). We measure that hMSCs degrade a gradient into the material with the largest degradation furthest from the cell and are not motile. The hMSC then degrades the entire scaffold and move at twice the speed generally reported for hMSC motility.

From these measurements, we hypothesize that hMSCs are secreting tissue inhibitors of metalloproteinases (TIMPs), which inhibit MMP activity and enzymatic degradation directly around the cell. Inhibition of TIMPs results in the opposite degradation profile and enhanced hMSC motility. This work provides a strategy to enhance hMSC motility in an implantable wound healing scaffold to more effectively deliver these cells to wounds to begin the healing process.

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