Fabrication of Continuous $PDMS_{star}$-PEG Gradients for Osteochondral Regeneration

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Statement of Purpose: In tissue engineering (TE), the physical and chemical properties of a 3D material scaffold guide cell behavior and ultimate tissue regeneration (Dutta RC. Biotech. Adv. 2009;27:334-339.). The undefined cell-material relationship has resulted in the regeneration of insufficient, non-native like tissues that often fail due to insufficient mechanical properties and integration into surrounding tissue (Navarro MJR. Soc. Interface. 2008;5:1137-1158.). Thus, we propose a *combinatorial platform* adapted to prepare libraries of TE scaffolds in the form of continuous gradients towards the rapid establishment of cell-material relationships and as a potential scaffold for the regeneration of interfacial tissues (i.e. bone – cartilage interface). Herein, we report an initial "library" based on the gradual incorporation of hydrophobic, bioactive methacrylated star poly(dimethyl siloxane) ($PDMS_{star}$-MA) into a poly(ethylene glycol) diacrylate (PEG-DA) hydrogel using solvents of varying polarities (i.e. dichloromethane (DCM) and distilled water (DI-H_2O)) to extend and tune scaffold properties along a gradient **(Fig. 1)**.

Methods: This gradient scaffold is based on a gradual transition from "Low $PDMS_{star}$" (bottom) to "High $PDMS_{star}$" throughout the PEG hydrogel **(Fig. 1)**. $PDMS_{star}$-MA and PEG-DA were synthesized as previously reported (Hou Y. Biomacromolecules. 2010;11:648-656.) To fabricate the gradient, two different precursor solutions were prepared at two different ratios [(0:100)-mixing solution and (20:80)-stock solution] of $PDMS_{star}$-MA to PEG-DA in either DCM or DI-H_2O and poured into their respective chambers of a standard laboratory gradient maker (Hoefer SG 15, Amersham Biosciences). The gradient maker was connected in line to a peristaltic pump via tubing followed by a top-filling vertical mold (8 x 6 cm x 3 mm) consisting of two clamped glass slides separated by a Teflon spacer. After filling the mold, the cross-linked hydrogel was formed by immediate exposure to UV light for 6 min (alternating sides after 3 min). Upon removal from the mold, the DCM-based sheets were rinsed with DCM then air dried for 30 min to permit evaporation of DCM (leaving open pores) then (as with H_2O hydrogels) were put to soak in 60 mL DI-H_2O for 72 hr. Swelling, morphology, mechanical properties, and bioactivity were investigated by dividing the gradient scaffold into 4 "zones" and analyzing 5, 8mm discs from each zone. This was repeated for 5 scaffolds.

Results: Previous work revealed that $PDMS_{star}$ distribution and porosity can be enhanced when hydrogels are fabricated in DCM versus DI-H_2O and subsequently hydrated (Bailey BM. Acta Biomater. 2012;8:4324-4333). As $PDMS_{star}$ is bioactive and osteoinductive (Munoz-Pinto D. Tissue Eng. Part A. 2012;18:1710-1719.), its incorporation into a PEG hydrogel scaffold along a gradient permits the ability to spatially control bioactivity and osteoinductivity throughout the scaffold. This was observed by the formation of higher levels of hydroxyapatite (HAp) corresponding to increased $PDMS_{star}$ content. Swelling ratios for hydrogel scaffolds fabricated in DCM were significantly lower and varied more broadly than the corresponding scaffolds fabricated in DI-H_2O due to the dissolution and homogenous distribution of $PDMS_{star}$ in DCM enhancing its effect throughout the scaffold **(Fig. 2)**. Also noteworthy are the high modulus values achieved with the $PDMS_{star}$:PEG scaffold fabricated in DCM, which increased linearly up to 459 kPa corresponding to an increase in $PDMS_{star}$ content **(Fig. 2)**. Such high values were attributed to increased pore size resulting in increased pore wall thickness.

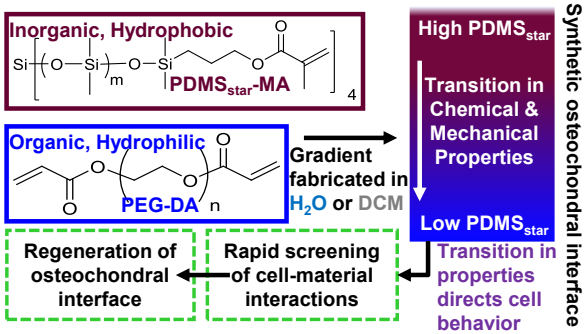

Figure 1. $PDMS_{star}$-PEG gradient scaffolds (fabricated in DCM or DI-H_2O) possessing a continuous change in bioactive, osteoinductive $PDMS_{star}$-MA.

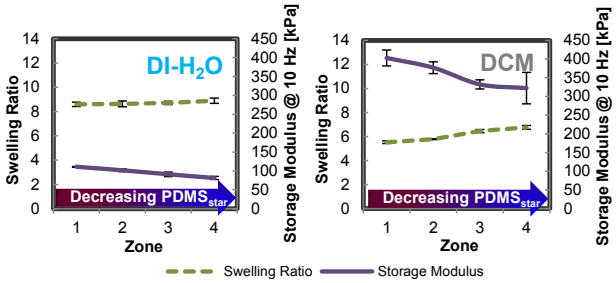

Figure 2. Modulus and swelling data are shown for both DI-H_2O (left) and DCM (right) fabricated hydrogels and reveal the ability to spatially control scaffold mechanical properties based on $PDMS_{star}$-MA content.

Conclusions: Herein, we describe an innovative, *combinatorial platform* for the fabrication of TE scaffolds that could be almost indefinitely altered. Utilizing two polymers with applicable properties in terms of TE as well as fabrication solvent, we proved the ability to expand and spatially control relevant properties throughout a single TE scaffold. This could prove beneficial as a potential method for the regeneration of a native-like osteochondral interface where there is a gradual transition in mechanical and chemical properties.