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$PDMS_{star}$–PEG hydrogels prepared via solvent-induced phase separation (SIPS) and their potential utility as tissue engineering scaffolds

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ABSTRACT

Inorganic–organic hydrogels based on methacrylated star polydimethylsiloxane ($PDMS_{star}$-MA) and diacrylated poly(ethylene glycol) (PEG-DA) macromers were prepared via solvent-induced phase separation (SIPS). The macromers were combined in a dichloromethane precursor solution and sequentially photopolymerized, dried and hydrated. The chemical and physical properties of the hydrogels were further tailored by varying the number average molecular weight (M_n) of PEG-DA (M_n = 3.4k and 6k g mol^{-1}) as well as the weight percent ratio of $PDMS_{star}$-MA (M_n = 7k g mol^{-1}) to PEG-DA from 0:100 to 20:80. Compared to analogous hydrogels fabricated from aqueous precursor solutions, SIPS produced hydrogels with a macroporous morphology, a more even distribution of $PDMS_{star}$-MA, increased modulus and enhanced degradation rates. The morphology, swelling ratio, mechanical properties, bioactivity, non-specific protein adhesion, controlled introduction of cell adhesion, and cytocompatibility of the hydrogels were characterized. As a result of their tunable properties, this library of hydrogels is useful to study material-guided cell behavior and ultimate tissue regeneration.

1. Introduction

In tissue engineering, the properties of the three-dimensional scaffold guide both cell behavior and ultimate tissue regeneration [1–5]. The physical properties of scaffolds known to impact cell behavior include modulus [6–9] and morphology (e.g. porosity) [10–19]. In addition, scaffold chemical properties influence cell behavior, including bioactivity [20–22], chemical functionality [23], hydrophobicity [24–26] and related hydration (i.e. swelling) [6,27]. Therefore, a library of scaffolds having precisely tunable physical and chemical properties over a broad range would be a valuable tool to probe material-guided cell behavior and enable the regeneration of functional tissues.

Poly(ethylene glycol) diacrylate (PEG-DA) hydrogels are extensively utilized as scaffolds for the regeneration of numerous types of tissues [28–34]. Their resistance to protein and cell adhesion in the absence of cell adhesive ligands makes them particularly useful in studying cell–material interactions [28,29,35–37]. Thus, changes in cell behavior may be related to an associated material property change. However, PEG-DA hydrogels display a limited range of physical as well as chemical properties, restricting their utility for such studies. For instance, the modulus of PEG-DA hydrogels may be tuned over a somewhat narrow range by altering the crosslink density (i.e. the PEG-DA number average molecular weight, M_n) or the weight percent (wt.%) concentration of PEG-DA in the aqueous precursor solution [31,38]. However, these alterations simultaneously produce changes in swelling, thereby restricting the ability to uncouple the effects of the modulus and swelling on cellular response [39]. While morphological changes in general alter cell behavior [40–42], a macroporous hydrogel morphology has shown particular utility in tissue regeneration [18,43,44]. PEG-DA (M_n = 3.4k and 6k g mol^{-1}) hydrogels fabricated by the photopolymerization of aqueous precursor solutions exhibit pores smaller than ~5–10 μm [45]. Several strategies have been explored to produce macroporous PEG-DA hydrogels, including salt leaching [46,47], gas foaming [48] and cryogelation [49,50]. However, difficulty in leaching porogens (salt leaching), high temperatures or low pressures (gas foaming) and extremely low temperatures (cryogelation) [51] limit these techniques.

In general, the chemical nature of hydrogel scaffolds has been shown to have a significant impact on cell behavior [20,24,52–54]. Alterations to the chemical nature of PEG-DA hydrogels have been largely limited to those that increase the rate of degradation. For instance, polyester segments [55,56] and enzymatically unstable peptides [37,57] have been introduced to enhance the otherwise limited degradation rate of PEG-DA hydrogels. The impact of chemical functionality incorporated into

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