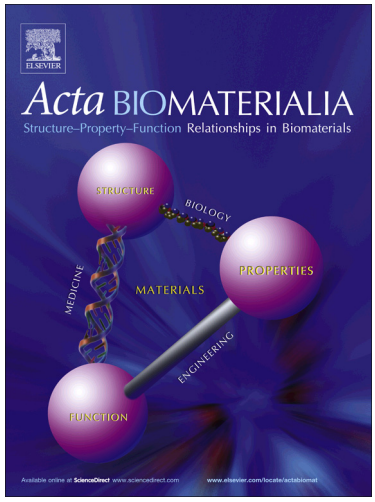

Full length article

Independent control of matrix adhesiveness and stiffness within a 3D self-assembling peptide hydrogel

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Title: Independent control of matrix adhesiveness and stiffness within a 3D self-assembling peptide hydrogel

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Keywords: self-assembling peptide; 3D cell culture; human mesenchymal stem cell differentiation; matrix stiffness; RGD concentration

Abstract

A cell's insoluble microenvironment has increasingly been shown to exert influence on its function. In particular, matrix stiffness and adhesiveness strongly impact behaviors such as cell spreading and differentiation, but materials that allow for independent control of these parameters within a fibrous, stromal-like microenvironment are very limited. In the current work, we devise a self-assembling peptide (SAP) system that facilitates user-friendly control of matrix stiffness and RGD (Arg–Gly–Asp) concentration within a hydrogel possessing a microarchitecture similar to stromal extracellular matrix. In this system, the RGD-modified SAP sequence KFE-RGD and the scrambled sequence KFE-RDG can be directly swapped for one another to change RGD concentration at a given matrix stiffness and total peptide concentration. Stiffness is controlled by altering total peptide concentration, and the unmodified base peptide KFE-8 can be included to further increase this stiffness range due to its higher modulus. With this tunable system, we demonstrate that human mesenchymal stem cell morphology and differentiation are influenced by both gel stiffness and the presence of functional cell binding sites in 3D culture. Specifically, cells 24 hours after encapsulation were only able to spread out in stiffer matrices containing KFE-RGD. Upon addition of soluble adipogenic factors, soft gels facilitated the greatest adipogenesis as determined by the presence of lipid vacuoles and PPARγ-2 expression, while increasing KFE-RGD concentration at a given stiffness had a negative effect on adipogenesis. This three-component hydrogel system thus allows for systematic investigation of matrix stiffness and RGD concentration on cell behavior within a fibrous, three-dimensional matrix.