1. Can the changes in the gel architecture that result in making gel relaxation time close to that of viscoelastic tissues be made simultaneously while keeping the gel Young’s modulus constant? Explain.

Different changes could be made in the gel architecture to allow tuning the stress relaxation time close to the ones observed in viscoelastic tissues while maintaining the gel Young’s modulus constant:

1. Lowering the molecular weight of alginate hydrogel in combination with different crosslinking densities of calcium reduces entanglement and network connectivity and produces faster stress relaxation. Introducing PEG spacers in the gel architecture further increases the rate of stress relaxation.
2. Any reduction in the initial gel’s Youn’s modulus resulting from the reduction in gel molecular weight can be compensated by increasing ionic crosslinking using calcium.
3. Discuss the main features of osteogenic differentiation of stem cells sitting on modified gels of greater stiffness.

At higher gel stiffness (17 kPa vs. 9 kPa), almost no adipogenic differentiation is observed, while stiff alginate gels (~17 kPa) that relax stress fast show significant osteogenic differentiation.

In addition, osteogenic differentiation in modified gels of greater stiffness and fast-relaxing gels, form an interconnected, mineralized, collagen-I-rich matrix and result in bone-forming activity.

1. What changes in the gel architecture result in making gel relaxation time close to that of viscoelastic tissues?

Lowering the molecular weight of the alginate gel, crosslinked by calcium, which decreases entanglement and connectivity, coupled with small PEG pacers which prevent ionic crosslinking between alginate chains, increase the rate of relaxation time; the relaxation time was successfully reduced from T1/2 of about 103 seconds to 10 similar to rates observed for viscoelastic tissues such as liver, brain and fracture haematoma.

1. Sketch the main steps of cell/ECM interaction in the cases of elastic and viscoelastic matrices.

A diagram of a diagram of a cell

AI-generated content may be incorrect.

1. Do stem cells sitting on the modified gels significantly increase their spreading and proliferation? Explain.

Similar to 3T3s , faster stress relaxation with modified gels increased cell spreading and proliferation (different initial elastic moduli, RGD ligand density, and rate of stress relation, Supplementary Fig. 7).

Experiments showed, that with faster relaxation time, 3T3 cells in alginate gels with two RGD concentrations (150 μm and 1,500 μM RGD) significantly spread with almost a doubling of the smallest bounding boxes containing the 3T3 cells and about 70% of increased proliferation when relaxation time went from 3,300s to 70s. Cell spreading and proliferation were suppressed with gels with longer stress relaxation (T ½ ~ 1h).