Photopolymerized Hyaluronic Acid-based Hydrogels

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Introduction
Hyaluronic acid (HA) is a natural extracellular polysaccharide that has been extensively used for the design of cell matrices. It contains hydroxy and carboxylic groups through which modifications are possible that allow chemical cross-linking of the material and that can modulate the adhesion and proliferation of cells.

Methods
Hyaluronic acid of various molecular weights [MW: 64KDa, 234KDa] was functionalized with thiol groups in order to prepare hydrogels by photopolymerisation. Hydrogels contained 5 to 20 mg/ml of native or 10% thiolated HA (SH-HA). Poly (ethylene glycol) diacrylate (PEG-DA) was added as a comonomer in order to optimize elastic modulus and swelling behavior. Rheology measurements and degradability study were performed on the resulting gels. Also, murine fibroblasts were cultured for 9 days on top of the hydrogels. Microscopy analysis and proliferation assay were conducted every 3 days in order to assess both change in the phenotype of the cells and their proliferation on the hydrogels.

Results & Discussion
Rheology data revealed that the elastic modulus of the hydrogels were in the range of kPa which physiologically correspond to the thickness or consistency of the brain or liver tissue. Moreover when hyaluronidase was added (100U/mL) before photopolymerisation, the elastic modulus decreased by a third.

Mouse fibroblasts seeded on thiolated HA gels, showed a round shape and proliferated in clusters, which is typical of a non-cell adhesive material. But relevant changes in phenotype and proliferation were observed when the adhesive peptide GCGRGDS was incorporated at 1:100 thiol/acyrlyate into the hydrogels. The fibroblasts started spreading after only two days of culture and their proliferation rate was comparable to the one on TCPS. They were cultured for up to 9 days and reached 100% confluence.

Conclusions
Here the data suggest that thiolated HA hydrogels of soft consistency can be enzymatically biodegraded and that by incorporating and adhesive peptide it can support fibroblast adhesion and proliferation.

References

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