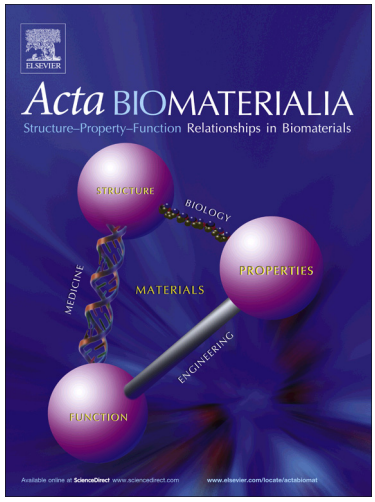

Full length article

Fibrin hydrogels as a xenofree and rapidly degradable support for transplantation of retinal pigment epithelium monolayers

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Title: Fibrin hydrogels as a xenofree and rapidly degradable support for transplantation of retinal pigment epithelium monolayers

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Abstract: (250/250)

Recent phase 1 trials of embryonic stem cell and induced pluripotent stem cell (iPSCs) derived RPE transplants for the treatment of macular degeneration have demonstrated the relative safety of this process. However, there is concern over clumping, thickening, folding, and wrinkling of the transplanted RPE. To deliver a flat RPE monolayer, current phase 1 trials are testing synthetic substrates for RPE transplantation. These substrates, however, cause localized inflammation and fibrosis in animal models due to long degradation times. Here we describe the use of thin fibrin hydrogels as a support material for the transplantation of RPE. Fibrin was formed into a mechanically rigid support that allow for easy manipulation with standard surgical instruments. Using fibrinolytic enzymes, fibrin hydrogels were degraded on the scale of hours. The rate of degradation could be controlled by varying the fibrinolytic enzyme concentration used. RPE cells degraded fibrin spontaneously. To preserve the fibrin support during differentiation of iPSCs to RPE, media was supplemented with the protease inhibitor aprotinin. iPSC-RPE on fibrin gels remained viable, generated monolayers with characteristic cobblestone appearance and dark pigmentation, and expressed mRNA and protein markers characteristic of RPE in the eye. Following differentiation of the cells, addition of fibrinolytic enzymes fully and rapidly degraded the fibrin support leaving behind an intact, viable iPSC-RPE monolayer. In conclusion, human fibrin hydrogels provide a xeno-free support on which iPSCs can be differentiated to RPE cells for transplant which can be rapidly degraded under controlled conditions using fibrinolytic enzymes without adverse effects to the cells.