Systematic optimization of an engineered hydrogel allows for selective control of human neural stem cell survival and differentiation after transplantation in the stroke brain.

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Public Summary:

Stem cell therapies have shown promise in promoting recovery from a stroke but have been limited by poor stem cell survival and differentiation in cell cultures. We have developed a hydrogel that has the consistency of Jello and provides the cells with a soft substrate on which to grow that also contains growth factors that are easy for cells to absorb. The hydrogel promotes better transplant stem cell survival and differentiation to adult cells that are in significant numbers and ready to use therapeutically.

Scientific Abstract:

Stem cell therapies have shown promise in promoting recovery in stroke but have been limited by poor cell survival and differentiation. We have developed a hyaluronic acid (HA)-based self-polymerizing hydrogel that serves as a platform for adhesion of structural motifs and a depot release for growth factors to promote transplant stem cell survival and differentiation. We took an iterative approach in optimizing the complex combination of mechanical, biochemical and biological properties of an HA cell scaffold. First, we optimized stiffness for a minimal reaction of adjacent brain to the transplant. Next hydrogel crosslinkers sensitive to matrix metalloproteinases (MMP) were incorporated as they promoted vascularization. Finally, candidate adhesion motifs and growth factors were systemically changed in vitro using a design of experiment approach to optimize stem cell survival or proliferation. The optimized HA hydrogel, tested in vivo, promoted survival of encapsulated human neural progenitor cells (iPS-NPCs) after transplantation into the stroke core and differentially tuned transplanted cell fate through the promotion of glial, neuronal or immature/progenitor states. This HA hydrogel can be tracked in vivo with MRI. A hydrogel can serve as a therapeutic adjunct in a stem cell therapy through selective control of stem cell survival and differentiation in vivo.

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