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ACCEPTED MANUSCRIPT

Injectable hydrogel promotes early survival of induced pluripotent stem cell-derived oligodendrocytes and attenuates longterm teratoma formation in a spinal cord injury model

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ABSTRACT

Transplantation of pluripotent stem cells and their differentiated progeny has the potential to preserve or regenerate functional pathways and improve function after central nervous system injury. However, their utility has been hampered by poor survival and the potential to form tumors. Peptide-modified biomaterials influence cell adhesion, survival and differentiation *in vitro*, but their effectiveness *in vivo* remains uncertain. We synthesized a peptide-modified, minimally invasive, injectable hydrogel comprised of hyaluronan and methylcellulose to enhance the survival and differentiation of human induced pluripotent stem cell-derived oligodendrocyte progenitor cells. Cells were transplanted subacutely after a moderate clip compression rat spinal cord injury. The hydrogel, modified with the RGD peptide and platelet-derived growth factor (PDGF-A), promoted early survival and integration of grafted cells. However, prolific teratoma formation was evident when cells were transplanted in media at longer survival times, indicating that either this cell line or the way in which it was cultured is unsuitable for human use. Interestingly, teratoma formation was attenuated when cells were transplanted in the hydrogel, where most cells differentiated to a glial phenotype. Thus, this hydrogel promoted cell survival and integration, and attenuated teratoma formation by promoting cell differentiation.

Keywords: cell adhesion molecules, hydrogel, differentiation, induced pluripotent stem cells, oligodendrocytes, spinal cord injury, cell transplantation

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