A 3-dimensional extracellular matrix as a delivery system for the transplantation of glioma-targeting neural stem/progenitor cells.

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Public Summary:
We report a method for suspending neural stem cells in a semisolid matrix. The approach has the potential to increase transplantation efficiency by reducing metabolic stress and providing mechanical support, especially when administered to the surgical resection cavity after brain tumor removal.

Scientific Abstract:
Neural stem/progenitor cells (NSPCs) display inherent pathotropic properties that can be exploited for targeted delivery of therapeutic genes to invasive malignancies in the central nervous system. Optimizing transplantation efficiency will be essential for developing relevant NSPC-based brain tumor therapies. To date, the real-world issue of handling and affixing NSPCs in the context of the neurosurgical resection cavity has not been addressed. Stem cell transplantation using biocompatible devices is a promising approach to counteract poor NSPC graft survival and integration in various types of neurological disorders. Here, we report the development of a 3-dimensional substrate that is based on extracellular matrix purified from tissue-engineered skin cultures (3DECM). 3DECM enables the expansion of embedded NSPCs in vitro while retaining their uncommitted differentiation status. When implanted in intracerebral glioma models, NSPCs were able to migrate out of the 3DECM to targeted glioma growing in the contralateral hemisphere, and this was more efficient than the delivery of NSPC by intracerebral injection of cell suspensions. Direct application of a 3DECM implant into a tumor resection cavity led to a marked NSPC infiltration of recurrent glioma. The semisolid consistency of the 3DECM implants allowed simple handling during the surgical procedure of intracerebral and intracavitary application and ensured continuous contact with the surrounding brain parenchyma. Here, we demonstrate proof-of-concept of a matrix-supported transplantation of tumor-targeting NSPC. The semisolid 3DECM as a delivery system for NSPC has the potential to increase transplantation efficiency by reducing metabolic stress and providing mechanical support, especially when administered to the surgical resection cavity after brain tumor removal.