Growth and differentiaion of adult neural progenitor cells in a novel three-dimensional implantable fibrin matrix

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The extracellular matrix (ECM) of the brain is a complex milieu of proteins and proteoglycans that, with the glial cells, forms a type of three-dimensional scaffolding for the neurons, their dendrites and axons. Potential treatments of Parkinson's disease via the surgical transplantation into the brain of stem cells, neural progenitor cells, and other predifferentiated species all depend on the presumed ability of such cells to survive the physical shock of cannulated infusive delivery, integrate themselves within the enviornment, and establish and sustain patterns of growth and differentiation that will lead to the desired dopaminergic phenotype. However, the profound difficulties associated with transplanted cells and their attempts to adapt to and thrive within the new environment results in cell survival rates that are typically less than 5%. Many investigators are developing strategies for improving the survival statistics, and a number of them involve evaluation of cell and growth factor delivery methodologies that use as the test specimens samples of plated cells, often situated on a two-dimensional planar surface. Much can be learned from such studies since the cells are easy to access and image. However, the extrapolation of findings from two-dimensional *in vitro* experiments may be difficult and extrapolations could be improved by investigating influences on cell survival by culturing cells in a 3-D environment.

Toward that end, a three-dimensional, self-assembled fibrin matrix has been developed as an *in vitro* test bed for the growth and differentiation of adult neural progenitor cells intended for CNS implantation for the treatment of neurodegenerative disorders. Neurospheres obtained from adult autopsy brain or temporal lobectomy surgeries were placed in a fibrin/plasma gel matrix and subsequently underwent morphological changes with extension of cellular processes. This novel biomaterial holds the promise of providing the type of sheltered environment and scaffolding that can maximize the potential for survival and optimize differentiation for cells implanted into the CNS, although major questions remain regarding optimization of fibrin matrix structure and the potential effect of orientation of fibrin fibers on guidance of neural processes. Also, matricies other than fibrin that might better mimic the true extracellular matrix of the central nervous system need to be studied.