Abstract of Presentation

Presentation Title

Cell Therapy in Parkinson's Disease- Embryonic Stem Cell-derived neurons

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Abstract

One of the major impediments in stem cell-based regenerative therapy is the risk of tumor development. Human embryonic stem cells (hESC) maintain high proliferative capacity and form teratomas upon ectopic injection. Thus, any prospective clinical use of hESC or hESC-derived differentiated cells will heavily depend on the ability of researchers to develop tumor-risk free cell populations. Cell therapy for Parkinson's disease is no exception. The limited effectiveness of the conventional pharmaceutical treatment and the common adverse effects over prolonged use pointed to regenerative cell therapy as an alternative. Clinical trials with fetal mesencephalic grafts showed promising improvements in Parkinson patients and provided the proof-of-principal for cell replacement therapy, but issues of embryonic tissue availability, difficulties in standardization and ethical aspects stressed the need for alternative neuron resources. Our group and several other groups worldwide, have developed protocols for derivation of dopaminergic (DA) neurons from pluripotent stem cells. These protocols enrich neural cultures for DA neurons but always yield mixed cell populations that contain minuscule numbers of undifferentiated and/ or highly proliferative early neural progenitors. The proliferative cells can and often do give rise to development of teratomas or bulky neural tumors following transplantation. We propose a novel strategy to overcome this problem by developing a combined selection method that uses a screening of laminin-derived peptide library to formulate unique ECM-mimetic substrates that preferentially support neuronal growth but not proliferation. This will be reinforced by selection and elimination method that exploits dynamic changes in cellular properties of neurons at different maturation stages. Our method does not involve any genetic manipulation and can be applied in large-scale cell preparations. Nonetheless, using cultures of well-developed neurons for transplantation poses a new problem of increased vulnerability and low survival rates following the process of harvesting and grafting. To resolve this, we propose to utilize ECM-mimetic scaffolding materials based on laminin peptide conjugates with chitosan and alginate to recreate a protective microenvironment at the site of transplantation and enhance cell survival and integration.

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Combining the capabilities and expertise of the Japanese group in laminin peptide biology and matrix preparations with the Israeli experience and knowledge in embryonic stem cell biology, neuron derivation and Parkinson's disease research is expected to devise selection and protection methods for producing tumor risk-free cell preparations suitable for regenerative cell therapy for Parkinson's disease, and to extend the research capabilities and fields of interest of both groups.