

longer, a wide variety of differentiated derivatives can be observed in the culture. Thereafter, with some modifications depending on the desired tissue types, many culture systems have been developed and widely used as developmental models of cardiogenic,^{8,9} myogenic,¹⁰ hematopoietic,¹¹ neurogenic,¹² and epithelial,¹³ differentiation.

ES cells are not the only type which can differentiate into a variety of tissue types in vitro; ES-derived cells can also integrate into the hosts and function well. It was reported that differentiated ES cells co-cultured with stromal cells could repopulate myeloid, erythroid, and lymphoid lineages in lethally irradiated mice.¹⁴ Most recently, in a rat model that mimics human myelin disease, it was shown that ES cell-derived glial precursors interact with host neurons and efficiently myelinate axons in the brain and spinal cord.¹⁵ McDonald and his group also transplanted ES-derived neural precursors into a rat spinal cord 9 days after traumatic injury. It was demonstrated that transplanted rats showed hindlimb weight support and partial hindlimb coordination.¹⁶

Human pluripotent stem cell lines, like their mouse counterparts, are established from primordial germ cells and blastocysts, respectively. Human embryonic germ cells are derived from PGCs of 5 to 9 weeks postfertilization on mouse STO fibroblast in the presence of human recombinant leukemia inhibitory factor, human recombinant basic fibroblast growth factor, and forskolin, while human embryonic stem cells are established from the inner cell mass of blastocysts. Both types of culture are karyotypically normal through extensive passages. The blastocyst-derived cells produce teratomas which contain all 3 germ layers derivatives after injection into severe combined immunodeficient (SCID) mice. As for germ-cell-derived cultures, embryoid bodies which formed spontaneously in culture tested positive for markers representative of mesodermal, ectodermal, and endodermal lineages. These data strongly suggest the pluripotency of these human stem cells.

The derivation of human pluripotent stem cells soon raised whole new expectations for transplantation therapies. Assuming these human stem cells are similar to their mouse counterparts with respect to

pluripotency, they will revolutionize our ways of understanding human embryogenesis, specific gene functions involved in differentiation pathways, drug and teratogen testing, and most importantly, of providing unlimited sources of cells for cell transplantation and tissue replacement. Based on the successful experiences from mouse ES cells, it is reasonable to speculate on the potential of human pluripotent stem cells in tissue transplantation therapies.

There is no doubt that human pluripotential stem cells have enormous potential for both clinical application and biomedical research. However, there are still many challenges such as ethical considerations which lie ahead. A more efficient, reliable protocol needs to be developed for further expansion of these human stem cells. Mechanisms and pathways involved in lineage-specific differentiation from human stem cells also need to be further refined. Efforts should be made to minimize the immunorejection caused by engraftment of stem cell derivatives, perhaps by the concept of "herapeutic cloning" discussed previously. With the collaboration of experts in this field, hopefully one day we can fully explore the true potential of these human pluripotential stem cells.

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