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Over-expression of *Oct4* and *Sox2* transcription factors enhances differentiation of human umbilical cord blood cells *in vivo*

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ABSTRACT

Gene and cell-based therapies comprise innovative aspects of regenerative medicine. Even though stem cells represent a highly potential therapeutic strategy, their wide-spread exploitation is marred by ethical concerns, potential for malignant transformation and a plethora of other technical issues, largely restricting their use to experimental studies. Utilizing genetically modified human umbilical cord blood mono-nuclear cells (hUCB-MCs), this communication reports enhanced differentiation of transplants in a mouse model of amyotrophic lateral sclerosis (ALS). Over-expressing *Oct4* and *Sox2* induced production of neural marker PGP9.5, as well as transformation of hUCB-MCs into micro-glial and endothelial lines in ALS spinal cords. In addition to producing new nerve cells, providing degenerated areas with trophic factors and neo-vascularisation might prevent and even reverse progressive loss of moto-neurons and skeletal muscle paralysis.

1. Introduction

Regeneration is a fundamental feature of a living organism, responsible for the restoration of tissues during vital activity as well as after injures induced by endogenous and exogenous factors. Stimulation of the regeneration is inherently related to the life quality in patients with degenerative diseases, ischemic damages and traumatic injuries. Development of new technologies, such as gene and cell therapies, gave rise to the new findings, demonstrating the capability of these methods to stimulate the process of regeneration. Furthermore, preclinical trials and clinical application of the high technologies resulted from new discoveries in physics and chemistry have a great potential for the development of the regenerative medicine.

Organ allografting (for instance, heart, kidney or liver transplantation) is now accepted as a routine method in the clinical practice, while cell transplantation (bone marrow transplantation, peripheral and umbilical cord blood mononuclear cells transplantation) is mainly restricted to the therapy of blood disorders, for example, anaemia, hemoblastosis and cancer chemotherapy. Extensive research in the field of cellular therapy revealed its high efficiency in the stimulation of regeneration in the affected organs. However, advances in the field of stem cell therapy are mainly in the experimental studies because of ethical issues (the use of embryo and fetus derived cells), a risk of malignant transformation of transplanted stem cells, recipient infection with unknown pathogens from human donors and animal derived products used in cell culture, immune response to allogeneic cells. Thus, the cells subjected to the transplantation must have predictable and reproducible characteristics, namely – retain their viability; actively proliferate to produce a sufficient number of cells for the regeneration of injured tissues; be capable to integrate with host cells; differentiate into required cell types; restore a tissue structure and form a guide pathway for the regenerating axons; participate in re-myelination; produce the trophic and neuroprotective factors; stimulate neurite outgrowth and re-establishment of an intracellular contacts.

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