In vitro Attractiveness and Deviation of Superparamagnetic Iron Oxide Stem Cells towards Magnetic Field

Thesis

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In Internal Medicine

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List of Abbreviations

Abb.	Full term
AF	Amniotic fluid
ASCs	Adult stem cells
BAL	Bronchoalveolar lavage
CD	Chron's disease
CK	Cytokeratin
CK-9	Cytokeratin-9
CMV	Cytomegalovirus
CNS-SCs	Central nervous system stem cells
CS	Cyclosporine
DAH	Diffuse alveolar haemorrhage
DM	Diabetes mellitus
ERC	Endometrial regenerative cells
ESCs	Embryonic stem cells
FACS	Fluorescence activated cell sorting
GFP	Green fluorescent protein
GVHD	Gastrointestinal Graft-versus-Host Disease
HAPC	Human activated protein C
HHV-6	Human herpes virus-6
HSCs	Haematopoietic stem cells
IBD	Inflammatory bowel disease
IBL	Interpapillary basal layer
ICCs	Intestinal crypt cells
ICM	Inner cell mass
IMS	Immuno magnetic separation
IVF	InVitro fertilization

LIF	Leukemia inhibitory factor
MAPCs	Multipotent adult progenitor cells
MIBE	Measles inclusion body encephalitis
MSCs	Mesenchymal stem cells
ngn-3	Neurogenin-3-positive cells
PBL	Papillary basal layer
Pdx-1	Pancreatic duodenal homeobox factor
PP	Pancreatic polypeptide
RSV	Respiratory syncytial virus
SPIO	Superparamagnetic iron oxide
TBI	Total body irradiation
TNF	Tumor necrosis factor
TSC	Totipotent stem cells
TS-SCs	Tissue specific stem cells
UACL	Ulcer associated cell lineage
UC	Ulcerative colitis
VOD	Veno-occlusive disease

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INTRODUCTION

Mesenchyme is embryonic connective tissue that is derived from the mesoderm and that differentiates into hematopoietic and connective tissue, whereas MSCs do not differentiate into hematopoietic cells ***(Porcellini Adolfo et al., 2011)***.

Because the cells, called MSCs by many labs today, can encompass multipotent cells derived from other non-marrow tissues, such as umbilical cord blood, adipose tissue, adult muscle, corneal stroma ***(Branch et al., 2012)***.

Adipose tissue is one of the richest sources of MSCs. When compared to bone marrow, there is more than 500 times more stem cells in 1 gram of fat when compared to 1 gram of aspirated bone marrow. Adipose stem cells are currently actively being researched in clinical trials for treatment in a variety of diseases.

The presence of MSCs in peripheral blood has been controversial. However, a few groups have successfully isolated MSCs from human peripheral blood and been able to expand them in culture ***(J Orthop Res et al., 2012)***.

Detection

A cell can be classified as an MSC if it shows plastic adherent properties under normal culture conditions and has a fibroblast-like morphology. In fact, some argue that MSCs and fibroblasts are functionally identical ***(Hematti et al., 2005)***. Furthermore, MSCs can undergo osteogenic, adipogenic and chondrogenic differentiation ex-vivo. The cultured MSCs also express on their surface CD73, CD90 and CD105, while lacking the expression of CD11b, CD14, CD19, CD34, CD45, CD79a and HLA-DR surface markers ***(Dominici et al., 2006)***.

Differentiation capacity

MSCs have a great capacity for self-renewal while maintaining their multipotency. Beyond that, there is little that can be definitively said. The standard test to confirm multipotency is differentiation of the cells into osteoblasts, adipocytes, and chondrocytes as well as myocytes and neurons. MSCs have been seen to even differentiate into neuron-like cells ***(Jiang et al., 2002),*** but there is lingering doubt whether the MSC-derived neurons are functional ***(Franco Lambert et al., 2009)***. The degree to which the culture will differentiate varies among individuals and how differentiation is induced, e.g., chemical vs. mechanical; ***(Engler et al., 2006).***

AIM OF THE WORK

To study deviation and attractiveness of superparamagnetic iron oxide stem cells toward magnetic field in-vitro.

Chapter One

GENERAL FEATURES OF STEM CELLS

1- Introduction

A stem cell is a special kind of cell that has a unique capacity to renew itself and to give rise to specialized cell types. Although most cells of the body, such as heart cells or skin cells, are committed to conduct a specific function, a stem cell is uncommitted and remains uncommitted, until it receives a signal to develop into a specialized cell. Their proliferative capacity combined with the ability to become specialized makes stem cells unique ***(Slack, 2000)***. Stem cells play a key role in tissue homeostasis and renewal after damage. Stem cells clarify the nature and the pathophysiology of several human diseases and can find new treatments for pathologies, such as cancers, degenerative, autoimmune and genetic disorders, that are currently untreatable ***(Weissman, 2002).***

Morphology

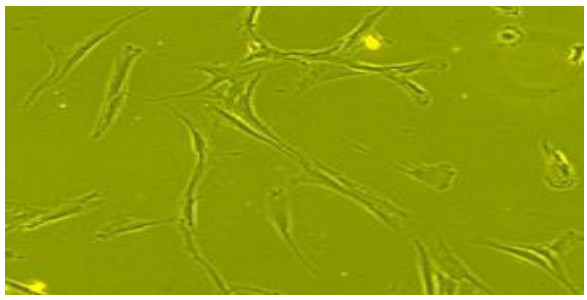

Fig. (1): Human bone marrow derived Mesenchymal stem cell showing fibroblast like morphology seen under phase contrast microscope (carl zeiss axiovert 40 CFL) at 63 x magnification ***(Ryan et al., 2005).***

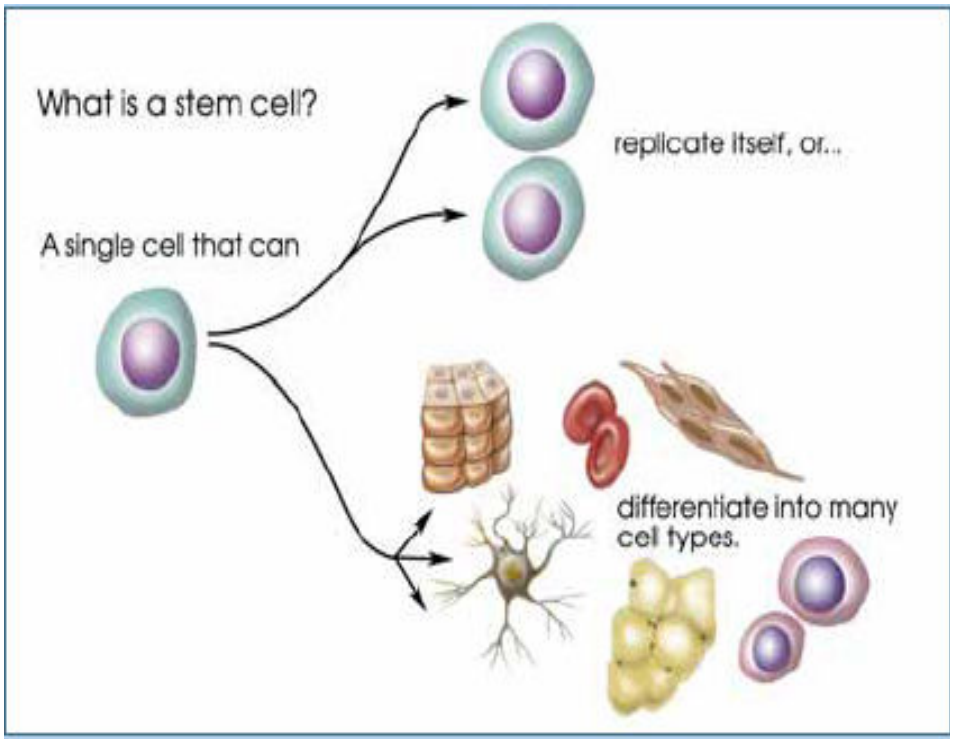

Fig. (2): What is stem cell? ***(Chandross, 2001).***

2- Properties of a Stem Cell

A- Stem cells can divide and renew themselves

Stem cells are capable of making identical copies of themselves for the life time of the organism. This property is referred to as "self-renewal." Stem cells usually divide to generate progenitor or precursor cells, which then differentiate or develop into "mature" cell types that have characteristic shapes and specialized functions, e.g., muscle cell contraction or nerve cell signaling ***(Chandross et al., 2001)***.

B- Stem Cells are Unspecialized

The unspecialized nature of stem cells is an important one. It means that stem cells lack the specific parts that allow them to perform specialized functions in the body. A stem cell is an undifferentiated (unspecialized) cell that occurs in a differentiated (specialized) tissue.

C- Stem Cells Can Give Rise to Specialized Cells

Differentiation is the process by which an unspecialized cell (such as a stem cell) becomes specialized into one of the many cells that make up the body. During differentiation, certain genes become activated and other genes become inactivated in a regulated fashion. As a result, a differentiated cell develops specific structures and performs certain functions.

For example, a mature, differentiated nerve cell has thin, fiber-like projections that send and receive the electrochemical signals that permit the nerve cell to communicate with other nerve cells. In the laboratory, a stem cell can be manipulated to become specialized or partially specialized cell types (e.g., heart muscle, nerve, or pancreatic cells) and this is known as directed differentiation ***(Slack, 2000).***

3- Potency definition

***Potency*:** It is the potential to differentiate into different cell types (Figure 2).

Totipotent stem cells are produced from the fusion of an egg and sperm cell. Cells produced by the first few divisions of the fertilized egg are also totipotent. These cells can differentiate into embryonic and extraembryonic cell ***(Tuch, 2006).***

Pluripotent stem cells are the descendants of totipotent cells and can differentiate into cells derived from any of the three germ layers ***(Hans, 2007).***

Multipotent stem cells can produce only cells of a closely related family of cells (e.g. hematopoietic stem cells differentiate into red blood cells, white blood cells, platelets. . .) ***(Hans, 2007)***.

Unipotent stem cells can produce only one cell type, but have the property of self-renewal which distinguishes them from non-stem cells e.g. muscle stem cells ***(Ulloa et al., 2005).***