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Role of Stem Cells in Rheumatic Disorders

An essay Submitted For Partial Fulfillment of the Requirements of M.Sc. Degree in Physical Medicine, Rheumatology and Rehabilitation

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والتأهيل

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Summary

Research on stem cells is advancing knowledge about how an organism develops from a single cell and how healthy cells replace damaged cells in adult organisms. This promising area of science is also leading scientists to investigate the possibility of cell-based therapies to treat disease, which is often referred to as regenerative or reparative medicine (Sabrina et al, 2009).

Stem cells exhibit multilineage differentiation capacity, and are able to generate progenitors with restricted developmental potential, including fibroblast, osteoblast, adipocyte and chondrocyte progenitors. These cells are unique cells possessing two main features. The first is self-renewal ability, and the second is the ability to give rise to differentiating cells (Bacigalupo, 2004).

The source of adult stem cells remains a controversy. They can be harvested from aborted fetuses, umbilical cord blood, or adult tissues. During development, stem cells progress towards cell specific lineages through progenitors, mature into differentiated cell types, and assemble to form tissues. The most accepted hypothesis suggests that the stem cells are somehow set-aside during the fetal development and restrained from differentiating (Schuldiner et al, 2002).

Biomaterials are frequently used in regenerative medicine. They act as artificial extracellular matrix (scaffolds) with distinct mechanical and biological properties or as carriers for drugs and bioactive molecules (Sabrina et al, 2009).

Many organic biomaterials have been investigated for scaffold formation. These are either **naturally derived** as collagen, fibrin, agarose, alginate, gelatin, silk or hyaluronic acid, or **synthetically produced**. Synthetically produced organic biomaterials are mainly polyhydroxyacids as polyglycolide or polylactide (Sabrina et al, 2009).

The usefulness of MSCs for cartilage repair has been demonstrated in studies with animal models. The disorder in osteoarthritis seems to

بسْمِ اللهِ الرَّحْمَٰن الرَّحْيم

(وَقُلْ رَبِّ زِدْنِي عِلْمًا)

صَدَقَ اللهُ العَظِيمْ

سُورَةْ طه : (١١٤)

Dedication

To my Parents

To my Husband

To my children

Thank you
for all the support you have given me all along

Ola Elsaka
2011

Acknowledgement

First and foremost, I would like to express my greatest and deepest thanks to **Allah**, the most merciful, for giving me the power to go through, and the strength to complete this work.

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Contents

List of Abbreviations

(ACI): Autologous chondrocytes implantation.
(ADAMTs): A disintegrin and matalloprotease with thrombospondin motifs).
(ANAs): antinuclear auto-antibodies.
(ANCA): anti-neutrophil cytoplasmic antibodies.
(ASCT): autologous stem cell transplantation.
(BMDCs): bone marrow derived cells.
(CBEs): cord-blood-derived embryonic-like stem cells.
(EBMT): European group for blood and marrow transplant.
(ECM): Extracellular matrix.
(EP): end plates.
(ESCs): embryonic stem cells.
(EULAR): European league against rheumatism.
(GVHD): Greft-vers-host diseases.
(HDIT): high dose immunosuppressive therapy.
(HSCs): Hematopoietic stem cells
(HUCB): Human umbilical cord blood stem cells
(ICM): Inner cell mass
(iPSC): induced pluripotent stem cells.
(IVD): Intervertebral disc.
(JCA): Juvenil chronic arthritis.
(LBP): low back pain.
(MDSCs): muscle derived side population cells.
(MHC): Major histo-compitability complex.
(MMPs): Matrix metalloproteinases.
(MSCs): Mesenchymal Stem Cells
(mSP): muscle side population.
(NICD): notch intracellular domain.
(NP): nucleus pulposus.
(PLA): Processed liposuction aspirate.
(RA): rheumatoid arthritis.
(SDF-1): stromal-derived factor 1.
(SLE): systemic lupus erythematosus.
(SSc): systemic sclerosis.
(TBI): total body irradiation.
(TNFα): tumor necrosis factor-α.
(USSC): unrestricted somatic stem cell.

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Introduction

Introduction

Research on stem cells is advancing knowledge about how an organism develops from a single cell and how healthy cells replace damaged cells in adult organisms. This promising area of science is also leading scientists to investigate the possibility of cell-based therapies to treat disease, which is often referred to as regenerative or reparative medicine (Sabrina et al, 2009).

Stem cells exhibit multilineage differentiation capacity, and are able to generate progenitors with restricted developmental potential, including fibroblast, osteoblast, adipocyte and chondrocyte progenitors. These cells are unique cells possessing two main features. The first is self-renewal ability, and the second is the ability to give rise to differentiating cells. In general stem cells can be divided into two categories. ***The first category is embryonic stem cells (ES)***, which together with the totipotent zygote present a cell population able to give rise to a multitude of cell types and tissues. ***The second category is adult stem cells***. They constitute adult tissues and give rise to differentiated tissue-specialized cells, and are responsible for the regenerative capacities of tissues. Generally adult stem cells present a more limited range of differentiation lineages. Compared to embryonic stem cells adult stem cells are preferable for therapeutic purposes since they are considered safer for implantation, with lesser proliferation capacity and tumorogenecity. Adult stem cells are also easier to differentiate to specific lineages, while embryonic stem cells can give a wide range of tissues following local implantation (Bacigalupo, 2004).

Mesenchymal Stem Cells (MSCs) and ***Hematopoietic stem cells*** (HSCs) are varieties of adult stem cells, and can be isolated from the bone marrow and expanded in culture. They represent an attractive and promising field in tissue regeneration and

engineering for treatment applications in a wide range of Rheumatologic disorders (Pountos and Giannoudis, 2005).

Donated organs and tissues are often used to replace diseased or destroyed tissue, but the need for transplantable tissues and organs exceeds the available supply. Stem cells when directed to differentiate into specific cell types, offer the possibility of a renewable source of replacing cells and tissues to treat diseases including rheumatoid arthritis, osteoarthritis, muscle dystrophy, systemic lupus erythematosis, systemic vasculitis, systemic sclerosis and juvenile chronic arthritis (Bethesda and Maryland, 2006).

Stem cells are one of the most attractive areas of biology. But like many growing fields of scientific investigation, research on stem cells raises scientific questions as rapidly as it generate new discoveries (Bethesda and Maryland, 2006).

Aim of the essay

The aim of this essay is to review the literatures about the stem cells and its role in management of different rheumatic disorders.

Materials and methods

Collection of literatures related to the stem cell therapy from references, papers, articles and the internet.

Stem Cell Biology

- Definitions.
- Types of stem cells.
- The unique properties of all stem cells.
- The differentiation potential of stem cells.
- Stem cell plasticity.
- Applications of stem cells in regenerative medicine.
- Biomaterials in regenerative medicine.

Stem Cell Biology

Stem cells represent the basic building blocks of human development. They have the capability to transform into all the specialized tissues and organs that make up the human body (Thomson et al, 1998).

☒ Definitions:

Stem cells are cells that have the ability to divide for indefinite periods often throughout the life of an organism. Stem cells, when provided with the correct signals, they acquire the potential to differentiate into different types of cells. These cells when differentiated, can have a characteristic shape and specialized functions, such as bone, heart, skin or nerve cells. They have two distinctive unique properties, ***first*** they can make identical copies of themselves for a long period of time (self-renewal) and ***second,*** they give rises to mature cells that have a characteristic morphology (Harley et al, 2001).

Stem cells generate different intermediate cell types prior to achieving a mature differentiated state. The intermediate cell is called ***precursor*** *or* ***progenitor cell***. Precursor or progenitor cells in fetus or adults are partly differentiated cells and eventually divide and give rise to mature differentiated cell. These cells are often devoted which means that they tend to differentiate only along a particular cellular development pathway (Anderson et al, 2001).

Stem cells can be distinguished from progenitor cells by their capacity for both self-renewal and multi-lineage differentiation, whereas progenitors are capable only of multi-lineage differentiation without self-renewal. The capacity for self-renewal is the property that makes stem cells particularly useful for transplantation medicine, as this; in theory; can provide an unlimited supply donor material (Weissman, 2000).