The Use of Stem Cells in Soft Tissue Repair in Orthopaedics

Essay

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LIST OF ABBREVIATIONS

ACL : Anterior crutiate ligament

ADSC : Adipose derived stem cells

bACL : bioengineered Anterior Cruciate Ligament

bFGF : Basic fibroblast growth factor

BMC : Bone marrow cells

CFU-F : Fibroblast colony forming unit

DMEM : Dulbecco's Modified Eagles Media

DMD : Duchenne muscular dystrophy

D-PBS : Dulbecco's phosphate buffered saline

ECCs : Embryonic carcinoma cells

EDTA : Ethylene Diamine Tetraacetic Acid

EGCs : Embyonic germ cells

ESC : Embryonic stem cells

FBS : Fetal Bovine Serum

FGF-2 : fibroblast growth factor 2

FSK : Forskolin Growth Factor

GFP : green fluorescent protein

HLA : Human leucocyte antigen

HLFs : Human Ligament Fibroblasts

hSCs : Hematopioetic stem cells
ICM : Inner cell mass

IL-4 : interleukin 4

MCL : Medial Collateral Ligament

MDSC : Muscle derived stem cells

MDX : Muscle dystrophin deficiency

M-MLCs : MSC-derived muscle lineage cells

MPCs : muscle precursor cells

MSC :Mesenchymal stem cells

M-Sch : Mesenchymal Stem Cell-derived Schwann cells

NRPs : neuronal-restricted-precursor

NSCs : Neural Stem Cells

OTJ : **Osteotendinous Junction**

PBS : phosphate-buffered saline

PDGF-B : Platelet-derived growth factor beta

SD rats : Sprague-Dawley rats

RT–PCR : Reverse Transcription and Polymerase Reaction

SCI : Spinal cord injury

SKPs : skin derived precursors

SKP-SCs : skin derived precursors -derived Schwann cells

SOD1 :superoxide dismutase 1 gene

TGFbeta : transforming growth factor beta

TNF-alpha : tumor necrosis factor alpha

VEGF : vascular endothelial growth factor

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INTRODUCTION

As individuals grow older & lead more active life styles, orthopaedic surgeons are increasingly being called on to use their surgical techniques to improve patients' quality of life. Earlier solutions to orthopaedic disorders required the use of instrumentation to improve the mechanical environment for orthopedic tissues. Newer research has aimed to improve biologic environment for healing. One area that has shown a promising future is the use of stem cells to regenerate or repair tissues. (1)

In several branches of medicine such as cardiac surgery, plastic surgery, angiology, and abdominal surgery, tissue engineering approaches to enhance repair have been employed. Orthopedic surgery has also benefited from tissue engineering in many areas, including repair of long bone defect and cartilage defects. Ligaments and tendons, with impaired ability to fully heal lend themselves well to tissue engineering applications. (2)

Stem cells are cells characterized by the ability to renew themselves through mitotic cell division and differentiating into a diverse range of specialized cell types. They may be totipotent , pleuripotent or multipotent depending on type. Only the embryo is totipotent. The embryonic stem cells (ESC) are pleuripotent as they are capable of differentiating into many tissue types, wheras differentiation of adult stem cells is generally resticted to the tissue in which they reside, as with hepatocytes in the liver and haemopiotic stem cells in blood. (3) Mesenchymal stem cells (MSCs) are present in a variety of tissues during

human development, and in adults they are prevalent in bone marrow. From that readily available source, MSCs can be isolated, expanded in culture, and stimulated to differentiate into bone, cartilage, muscle, marrow stroma, tendon, fat and a variety of other connective tissues. [4]

The use of adult mesenchymal stem cells (MSCs) has been studied as a platform for tendon healing. [5] Experimental models have shown better histological and biomechanical properties in tendon defects following the implantation of bone marrow-derived mesenchymal stem cell-seeded scaffolds as compared with scaffolds alone. [6] These cells have the promise of differentiating into fibroblastic ligament- or tendon-forming tissue when influenced by appropriate biochemical and mechanical strain effects. [7]

Cell-based therapies involving stem cells as well as other forms of implantable scaffolding have been shown to facilitate axonal regeneration and remyelination after spinal cord injury in animal models. [8]

Transplanted mesenchymal stem cells could survive and proliferate in the meniscal defects in the organ culture model. In a clinical situation, mesenchymal stem cell transplantation is a promising new clinical strategy for the treatment of meniscal tears in the avascular zone. [9]

The use of muscle derived stem cells (MDSCs) to repair defects in articular cartilage and bone and to repair skeletal muscle injury is discussed. MDSCs may play a big role in healing skeletal muscle injuries. [10]

AIM OF THE WORK

The aim of this study is to review the recent literatures regarding the potential therapeutic use of stem cells in tendons , ligaments , muscles & other soft tissue injuries in orthopaedics & the researches concerning them.

Basics of Stem Cells

Basics of stem cells

Definition :

Stem cells are unspecialized cells in the human body that are capable of becoming specialized cells, each with new specialized cell functions. The best example of a stem cell is the bone marrow stem cell that is unspecialized and able to specialize into blood cells, such as white blood cells and red blood cells, and these new cell types have special functions, such as being able to produce antibodies, act as scavengers to combat infection and transport gases [(3)].

Thus, stem cells can develop into mature cells that have characteristic shapes and specialized functions, such as heart, skin, or nerve cells. They have the ability to divide or self-replicate for long periods; this replication may continue throughout the life of the living body. Stem cells can form many different types of cells that make up an organism. The ability to divide and form other cells is called "differentiation". Another term that is used to describe this power to differentiate , the power even to change from one type of cell to another is "plasticity" [(11)].

WHY ARE STEM CELLS IMPORTANT?

Stem cells have three important characteristics that distinguish them from other cells:

1. They are unspecialized cells that renew themselves for long periods through cell division. They do not have any tissue-specific functions that allow them to perform specialized functions. For example, a single stem cell cannot beat with another heart cell; it cannot communicate with other cells, as nerves cells do.

2. Under certain conditions stem cells can be induced to become cells with special functions, such as cells of the heart muscle or insulin-producing cells of the pancreas. Unlike muscle, blood, or nerve cells, they can replicate themselves many times,a process called proliferation. A starting line of stem cells can proliferate in the laboratory for many months and yield millions of cells. If this happens over a long period of time, the process is called self-renewal.

3. Stem cells give rise to specialized cells. When this occurs, the process is called differentiation . Signals from both inside and outside the cell may trigger this differentiation. Genes control the internal signals. External signals include chemicals secreted by other cells, physical contact with other cells, and certain molecules called growth factors.

A future is envisioned in which stem cells may be used in treating diseases such as Parkinson's disease, diabetes, and heart disease. Such cell-based therapies form the basis of a new field of generative or reparative medicine . In addition, these therapies may be used for screening new drugs and understanding birth defects [11] .

Classification and Sources of Stem Cells :

Stem cells can be classified into four broad types based on their origin:

-stem cells from embryos;

-stem cells from the fetus;

-stem cells from the umbilical cord;

-and stem cells from the adult.

Each of these can be grouped into subtypes (Fig. 1). Some believe that adult and fetal stem cells evolved from embryonic stem cells and the few stem cells observed in adult organs are the remnants of original embryonic stem cells that gave up in the race to differentiate into