Bone and Cartilage Repair Using Stem Cells

Essay

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بسم الله الرحمن الرحيم

﴿ فَأَمَّا الزَّبَدُ فَيَذْهَبُ جُفَاءً وأَمَّا مَا يَنفَعُ النَّاسَ فَيَمْكُثُ فِي الأَرْضِ ﴾

صدق الله العظيم

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Mohamed Ali Shafik

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AC : anterior capsular layer
ACI : Autologous chondrocytes implantation
ADAMTS : Adisintegrin and metalloproteinase with thrombopondin motifs
AF : annulus fibrosus
BM : Bone marrow
BMP : Bone morphogenic protein
BMSCs : Bone marrow stem cells
DMD : Duchenne muscular dystrophy
DMEM : Dulbecco's modified Eagle's medium
ES : Embryonic stem
FCS : Fetal cord serum
FP : fat pad
FBS : Fetal bovine serum
HA : hydroxyapatite
HLA : Human leucocyte antigen
IGF-1 : Insulin like growth factor-1
IL : Interleukin
IVD : Intervertebral disc
LUC : luciferase
MCP-1 : chemokine monocyte chemoattractant protein-1
MMP : Matrix metalloproteinase
MSCs : Mesenchymal stem cells
NP : Nucleus pulposus
OI : Osteogenesis imperfecta
OA : osteoarthritis
PCR : Polymerase chain reaction
PL : Patellar ligament
PBS : Phosphate buffered saline
PB-MSCs : peripheral blood mesenchymal stem cells
PLA : Processed liposuction aspirate

TGF-beta : Transforming growth factor-beta
UCB :Umbilical cord blood
UCE :Umbilical cord epithelium
VEGF : Vascular endothelial growth factor

Introduction

To restore skeleton function in the field of orthopaedics, bone tissue regeneration remains an important challenge. Spinal fusion, augmentation of fracture healing, and reconstruction of bone defects resulting from trauma, tumour, infections, biochemical disorders, or abnormal skeletal development are clinical situations in which surgical intervention is required. The types of graft materials available to treat such problems essentially include autologous bone , allogeneic bone, and demineralised bone matrices, as well as a wide range of synthetic biomaterials such as metals, ceramics, polymers, and composites[(1)].

Until recently, the use of autologous bone grafts has been the number one choice for bone repair and regeneration. A patient's own bone lacks immunogenicity and provides bone-forming cells, which are directly delivered at the implant site. Moreover, autologous bone grafts recruit mesenchymal cells and induce them to differentiate into osteogenic cells through exposure to osteoinductive growth factors. Although there are many advantages to using autologous bone, there are major drawbacks to the harvesting procedure, and for centuries there has been a search for alternatives[(1)].

Lesions in cartilage are a significant problem in medical practice, with approximately one million patients treated annually in USA. It is well known that lesions that are confined to the articular cartilage alone have little or no capacity to heal. In general, the patients become symptomatic and a significant progression to osteoarthritis is possible.

However, those lesions that penetrate the subchondral bone have access to bone marrow space and chondroprogeinator cells and therefore have a limited repair capacity[2].

Tissue engineering is a multidisciplinary area of research aimed at the regeneration of tissues and the restoration of the function of organs by the implantation of cells or tissues grown outside the body, or by the stimulation of cells to grow into an implanted matrix.The general principle of tissue engineering involves the combination of living cells with a natural or synthetic support, or scaffold, to produce a three-dimensional living tissue construct which is functionally, structurally and mechanically equal to, if not better than, that which it has been designed to replace[3].

Stem cells are unspecialised cells, which have the ability to renew themselves indefinitely, and under appropriate conditions can give rise to a variety of mature cell types in the human body. Some stem cells can give rise to a wide range of mature cell types, whereas others give rise to only a few. Stem cells can be derived from a variety of sources including early embryos, fetal tissue, and some adult tissues, of which bone marrow and blood are the best known examples. Hence, there are two populations of stem cells: embryonic and adult stem cells[4].

There is great interest in the biology of adult stem cells because of their capacity to self-renew and their high plasticity. These traits enable adult stem cells to produce diverse mature cell progenitors that actively participate in the maintenance of homeostatic processes by replenishing the cells that repopulate the tissues/organs during a lifespan and regenerate damaged tissues during injury. In general, embryonic, fetal, and adult stem cells show several common

functional properties. Common properties include their high self-renewal capacity and potential to generate differentiated cell progenitors of different lineages under simplified culture conditions in vitro and after transplantation in the host in vivo. More particularly, the establishment of the functional properties of stem cells and their progenitors in vitro and in vivo has indicated that they may contribute to the regeneration of damaged tissues. Therefore, the use of stem cells and their progenitors is a promising strategy in cellular and genetic therapies for multiple degenerative disorders[5].

Aim of the Work

To review the literature about the issues concerning stem cell researches, as well as the potential therapeutic use of these cells in orthopaedic surgery.

Stem Cell Biology

A stem cell is a cell that has the ability to divide for indefinite periods - often throughout the life of an organism. The stem cells, when provided with the right signals, have the potential to differentiate into different types of cells that constitute an organism. These cells when differentiated can have a characteristic shape and specialized functions, such as heart cells, skin cells or nerve cells. In short, stem cells have two distinctive properties, one they can make identical copies of themselves for a long period of time (self renewal) and two give rise to mature cells that have a characteristic morphology[6].

They were initially named plastic-adherent cells or colony-forming-unit fibroblasts and subsequently named either marrow stromal cells or mesenchymal stem cells (MSCs) [7].

Typically a stem cell generates an intermediate cell type or different cell types prior to achieving a mature differentiated state. The intermediate cell is called a 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 committed meaning that they tend to differentiate only along a particular cellular development pathway, however, some recent studies have shown that this may not be as definitive as was once thought. Their use in orthopedics has gained a significant

momentum in past few years and the field is witnessing some path breaking research currently [6].

Stem cells can be distinguished from progenitor cells by their capacity for both self-renewal and multilineage differentiation, whereas progenitor cells are capable only of multilineage differentiation without self-renewal. It is this capacity for self-renewal that makes stem cells particularly useful for transplantation medicine, because this in theory could provide an unlimited supply of donor material. Moreover, stem cells and their differentiated derivatives possess much higher proliferative and regenerative potential compared with mature differentiated somatic cells. This in turn is more likely to guarantee adequate regeneration and cell turnover at the transplantation site for an extended period of time, possibly a lifetime [8].

Stem cells and progenitor cell populations are part of continuous systems involving cell loss and regeneration in virtually all human tissues that consist of ongoing generation of new cells and the orderly transition of cells from one state to another. This turnover is most evident in the lining cells of the gastrointestinal tract (every three days) or dermis (every fourteen days). In musculoskeletal tissues, turnover is much slower and has been best characterized in bone, where the cells that give rise to and support bone tissue progress through a series of stages beginning upstream with the stem cell. Stem cells give rise to progenitor cells, which progress to become

pre-osteoblasts and then osteoblasts. Osteoblasts represent yet another transit population, with a life span of only about forty days, and give rise to both the matrix of new bone tissue and the downstream cells that comprise bone tissue (i.e., osteocytes and bone-lining cells). As osteoblasts reach the end of their functional life, they have three possible fates: they may become osteocytes, they may become lining cells on the surface of mature bone, or they may die by means of apoptosis. As an osteocyte or a lining cell, the same cell may survive for a mean of twenty years or more in human cortical bone, until the region of bone in which it resides is remodeled by another wave of stem cell function. Bone repair and regeneration following a fracture or a bone-grafting procedure follow the same steps. The same principles apply to cells in muscle, tendon, ligament, and cartilage [9].

Stem cell self-renewal:

One of the defining characteristics of stem cells is their self-renewal potential, the ability to generate identical copies of themselves through mitotic division over extended time periods (even the entire lifetime of an organism). The absolute selfrenewal potential of MSCs remains an open question, due in large part to the different methods employed to derive populations of MSCs and the varying approaches used to evaluate their selfrenewal capacity (Fig 1) [10].