CURRENT AND FUTURE APPLICATIONS OF STEM CELLS IN SURGERY

Essay

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بسم الله الرحمن الرحيم

" قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ"

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LIST OF ABBREVIATIONS

Abbreviations	Words
ABI	Ankle Brachial Index
ADSCs	Adipose-Derived Stem Cells
AKI	Acute Kidney Injury
ALCAM	Activated Leukocyte Cell Adhesion Molecule
Allo-SCT	Allogeneic Stem Cell Transplantation
ASCs	Adult Stem Cells
AT-SCs	Adipose Tissue-Derived Stromal Cells
auto-HSCT	Autologous Hematopoietic Stem Cell
BCSCs	Breast Cancer Stem Cells
BM	Bone Marrow
BM-EPCs	Bone-Marrow Derived Endothelial Progenitor
BM-MNCs	Bone-Marrow-Derived Mononuclear Cells
BMP	Bone Morphogenetic Protein
BMSCs	Bone Marrow–Derived Stem Cells
CAL	Cell-Assisted Lipotransfer
CD	Crohn’s Disease
CDAI	Crohn's Disease Activity Index
CEA	Cultured Epithelial Autografts
CLI	Critical Limb Ischemia

CMV	Cytomegalovirus
CSCs	Cancer Stem Cells
DFUs	Diabetic foot ulcers
DMSO	Dimethyl Sulfoxide
eASC	Expanded Mesenchymal Stem Cells
EBs	Embryoid Bodies
ECCO	European Crohn's and Colitis Organisation
ECs	Endothelial Cell
EF	Engraftment Failure
EPCs	Endothelial Progenitor Cells
EpSCs	Epidermal Stem Cells
ESCs	Embryonic Stem Cells
FCS	Fetal Calf Serum
FGF	Fibroblast Growth Factor
G-CSF	Granulocyte Colony-Stimulating Factor
GIT	Gastrointestinal Tract
GMCSF	Granulocyte Monocyte Colony-Stimulating
GVHD	Graft Versus-Host Disease
GVT	Graft-Versus-Tumor
HaploSCT	Haploidentical Stem Cell Transplantation
hESCs	Human Embryonic Stem Cells
HLA	Human Leukocyte Antigen

HPCs	Hepatic Progenitor Cells
HSCs	Haematopoietic Stem Cells
HSCT	Hematopoietic Stem Cell Transplantation
ICM	Inner cell mass
IL-8	Interleukin-8
iPS	Induced Pluripotent Stem
ISSCR	International Society For Stem Cell Research
IVF	In Vitro Fertilization
LIF	Leukemia Inhibitory Factor
LNGFR	Low Affinity Nerve Growth Factor Receptor
MEFs	Mouse Embryonic Fibroblasts
MOF	Multi-Organ Failure
mPB	Mobilized Peripheral Blood
MRI	Magnetic Resonance Imaging
MSCs	Mesenchymal Stem Cells
non-ESCs	Non-Embryonic Stem Cells
OA	Osteoarthritis
OI	Osteogenesis Imperfecta
ONFH	Osteonecrosis Of The Femoral Head
PAD	Peripheral Arterial Disease
PB	Peripheral Blood
PBSCs	Peripheral Blood Stem Cells

PC	Pancreatic Cancer
pESCs	Parthenogenetic Embryonic Stem Cells
PLA	Processed Lipoaspirate
POF	Premature Ovarian Failure
PPAR-γ	Peroxisome Proliferator-Activated Receptor
SCNT	Somatic Cell Nuclear Transfer
SCT	Stem Cell Transplantation
SDF	Stromal Cell Derived Factor
SF	Sulforaphane
SO	Sorafenib
SVF	Stromal Vascular Fraction
TBSA	Total Body Surface Area
TGF	Transforming Growth Factor
TGF-β	Transforming Growth Factor –Beta
TNF	Tumour Necrosis Factor
UCB	Umbilical Cord Blood
UCSCs	Umbilical Cord Stem Cells
VEGF	Vascular Endothelial Growth Factor

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INTRODUCTION

The whole idea is amazing! If you were to lose, say an arm in a car accident, medical professionals may one day be able to simply grow it back. If you ever need a transplant, you can replace the bad organ with a new one grown from your own cells. That means no more worrying about transplant rejection. Unfortunately, though, studies up to date have been largely inconclusive and there are still many areas of research on regeneration that require further investigation ***(Eggleson, 2012)***.

Stem cells are defined functionally as cells that can generate daughter cells identical to the mother (self-renewal) as well as the ability to generate differentiated cells ***(Mummery, 2011)***.

Intense research on stem cells during the last decades has provided important information on developmental, morphological and physiological processes that govern tissue and organ formation, maintenance, regeneration and repair after injuries ***(Bryder et al., 2006)***.

Stem cells can be classified into four broad types 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 types can be grouped into subtypes ***(Lee & Bongso, 2005)***.

Embryonic stem cell (ESCs) research offers much hope for alleviating the human suffering brought on by the ravages of disease and injury. The main goal is to identify the mechanisms that govern cell differentiation and to turn these cells into specific cell types that can be used for treating debilitating and life-threatening diseases and injuries ***(Siegel, 2013)***.

Technology of induced pluripotent stem (iPS) cells provides researchers with a unique tool to obtain disease-specific stem cells for the study and possible treatment of degenerative disorders with autologous cells in a more ethical way ***(Stadtfeld and Hochedlinger, 2010)***.

Progress in basic stem cell biology is challenged by the wide range of observable stem cell phenotypes documented in literature, coupled with the diversity of biologically influential components in the stem cell microenvironment. These issues are only amplified when one endeavors to create stem cell therapies or functional human tissues for clinical use ***(Healy et al., 2013)***.

In the field of surgery, stem cells could be used for treatment of inflammatory bowel diseases (IBD) ***(Cassinott et al., 2008)*** and liver failure ***(Boulter et al., 2012)***. Stem cells could serve as the treatment of diseases affecting the whole skeleton such as osteogenesis imperfecta (OI) ***(Evans, 2012)***.

Stem cells can be used for soft tissue replacement and treatment of burns and skin ulcers ***(Butler et al., 2010)***.Stem cells have the potential for prevention of amputation of the limbs in diabetes and critical ischemia by stimulation of angiogenesis ***(Lee et al., 2011)***

Since the discovery of stem cells is a real revolution in the field of medical sciences because of its unique properties, this essay spots light on these cells, their types and ways to benefit from them in the field of surgery. We will also focus on hopes offered by the special use of stem cells in the field of cell-based treatments. We will also stress on ethical and legal controversy raised around it.

AIM OF THE WORK

The aim of this work is to spot light on stem cells as regard history, its unique properties, to stress upon the current uses of stem cells in surgery, the future challenge and the limitations.

STEM CELL BASICS

Stem cells are defined functionally as cells that can generate daughter cells identical to the mother (self-renewal) as well as the ability to generate differentiated cells ***(Mummery, 2011)***.

They are also capable of regenerating tissues. There are two main types of stem cells, embryonic and non-embryonic. ESCs are pluripotent because they can differentiate into all cell types. Non-embryonic stem cells (non-ESC) are multipotent because their potential to differentiate into cell types is more limited. ESCs are more prevalent and more able to differentiate spontaneously than non-ESCs ***(Tuch, 2006)***.

Under some specific conditions, stem cells can be induced to differentiate into various functional cell lineages, including adipocytes, chondrocytes, osteoblasts, smooth muscle cells, cardiomyocytes, neurons and hepatocytes ***(Lin et al., 2011)***.

The medical community has become very interested in the potential applications of stem cells in regenerative medicine. These potential applications may involve tissue engineering, genetic engineering, and other techniques to repair, replace or regenerate failing tissues and organs ***(Hug, 2005)***.

Progress in basic stem cell biology is challenged by the wide range of observable stem cell phenotypes documented in literature, coupled with the diversity of biologically influential components in the stem cell microenvironment. These issues are only amplified when one endeavors to create stem cell therapies or functional human tissues for clinical use ***(Healy et al., 2013)***.

Classification of Stem Cells

I. Types of stem cells according to origin

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

a) Stem cells from embryos,
b) Stem cells from the fetus,
c) Stem cells from the umbilical cord,
d) Stem cells from the adult.

Each type can be grouped into subtypes ***(Lee and Bongso, 2005)***.

A. Embryonic stem cells (ESCs)

The discovery of ESCs has been one of the most exciting developments in the biological sciences in the past decade ***(Hug, 2005)***.

These cells are derived from inner cell mass (ICM) of mammalian blastocysts (which are masses of cells developing at the 5th-6th day from the fertilized ova) ***(Figure 1)***.If the blastocyst implants into the uterus, ICM will develop into a fetus, while the surrounding trophoblast will develop into the placenta ***(Tuch, 2006)***.

They have the ability to grow indefinitely while maintaining pluripotency and have the ability to differentiate into cells of all three germ layers ***(Vidarsson et al., 2010)***.

They possess a nearly unlimited self-renewal capacity and developmental potential to differentiate into virtually any cell type of an organism. ESC lines, which have recently been derived, may additionally serve as an unlimited source of cells for regenerative medicine ***(Wobus and Boheler, 2005)***.