Recent Advances in Stem Cell Therapy

Assay
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Heba Mohamed Ali Metwally

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List of Abbreviations

3-D	: 3-dimensional
AAR	: Alopecia areata
AGA	: Androgenic alopecia
ALL	: Acute lymphoblastic leukemia
ALS	: Amyotrophic lateral sclerosis
AML	: Acute myeloid leukemia
ANC	: Absolute neutrophil count
ANT	: Altered nuclear transfer
ATG	: Antithymocyte Globulin
BM	: Bone marrow
BMMNCs	: Bone marrow mono nuclear cells
BMP-2	: Bone morphogenetic protein-2
BMT	: Bone marrow transplantation
CML	: Chronic myelogenous leukemia
DBA	: Diamond-Blackfan anemia
DFSCs	: Stem cells the dental follicle
DMARDs	: Disease-modifying antirheumatic drugs
DMD	: Duchenne muscular dystrophy
EPCs	: Endothelial progenitor cells
ERT	: Enzyme replacement therapy
ESCs	: Embryonic stem cells
FA	: Fanconi anemia
GD	: Gaucher disease
GIT	: Gastrointestinal tract
GVHD	: Graft versus host disease
hES	: human embryonic stem cells
HLA	: Human leukocyte antigen
HPC	: Haematopoietic progenitor cell
HSC	: Hematopoietic stem cell transplantation
IL-2	: Interleukin-2
iPS	: Induced pluripotent stem cells
IVF	: In vitro fertilization

List of Abbreviations (Cont.)

Klf4	: Kruppel-like factor 4
MI	: Myocardial infarction
MPS	: Mucopolysaccharidoses
MSCs	: Mesenchymal stem cells
NCI	: National cancer institute
NPCs	: Neural precursor cells
NSCs	: Neural stem cells
Oct3/4	: Octamer ¾
PBSC	: Progenitor peripheral stem cell
PDL	: Periodontal ligament
PDLSCs	: Periodontal ligament stem cells
RA	: Rheumatoid arthritis
SAA	: Severe aplastic anemia
SCAPs	: Stem cells the apical part of the papilla
SCF	: Stem cell factor
SCF)	: Stem cell factor
SCI	: Spinal cord injury
SCNT	: Somatic Cell Nuclear Transfer
SHEDs	: Stem cells human exfoliated deciduous teeth
So.x2	: SRY-box containing gene 2
T1DM	: Type 1 diabetes mellitus
UCB	: Umbilical cord blood

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Introduction

Stem cells are cells that have the ability to differentiate into specific cell types. The two defining characteristics of a stem cell are perpetual self-renewal and the ability to differentiate into a specialized adult cell type ***(Bajada et al., 2008).***

Stem cells have many types totipotent stem cells that can become an entire human being, pluripotent stem cells that can develop into any body cell type but cannot become an entire human being, multipotent stem cells that can only differentiate into the same tissue type and unipotent stem cells that can only become one cell type but have the property of self rernwal which distinguishe them from non stem cell ***(Clark et al., 2000).***

There are two sources of stem cells: Fetal stem cells which are primitive cell types in the fetus that develop into the various organs of the body. The embryonic germ cells derived from human aborted tissue which have properties similar to stem cells isolated from the inner cell mass of blastocysts ***(Toma et al., 2002).***

Adult stem cells are specialized cells found within many tissues of the body where they function in tissue homeostasis

and repair. They are precursor cells capable of differentiation into several different cells. They have been propagated from bone marrow, liver, brain, dental pulp, hair follicles, skin, skeletal muscle, adipose tissue, and blood ***(Zuk et al., 2002).***

Diseases due to destruction and dysfunction of a certain limited number of cell types, such as diabetes mellitus (with selective damage to b-cells in Langerhans islets) or Parkinson's disease (destruction of dopaminergic neurons in substantia nigra) can be treated by transplantation of differentiated derivatives of embryonic stem cells.

Animal studies show that transplantation of pluripotent stem cells or foetal cells can successfully treat a number of chronic diseases, such as diabetes, Parkinson's disease, traumatic spinal cord injuries, Purkinje's cellular degeneration, liver failure, heart failure, Duchenne's muscular dystrophy, osteogenesis imperfecta, and others ***(Kajstura et al., 2005).***

Aim of The Work

The aim of this review is to clarify the recent development of stem cells therapy in different medical and genetic diseases and their future potential applications.

Historical review:

In the *19th century*, bone marrow (BM) was first in some way considered to be responsible for blood formation and might have healing properties and could be useful in the treatment of anemia. It was at this time, for example, that the health tonic derived from BM fats *"Virol"* became popular (Figure 1). The earliest attempts at using BM therapeutically were made in *1891* by **Brown-Sequard** and **D'Arsenoval** and reported by **Quine** in *1896*. BM was administrated orally to treat defects in blood formation ***(Quine, 1896).***

Fig. (1): (Virol) Bone marrow has nutritive properties ***(Quine, 1896).***

Further attempts using a glycerol extract of animal BM administrated orally to treat pernicious anemia were made. The rationale of treatment with BM was to provide missing nutrient ***(Fraser, 1894)***.

However, **Billings** in *1894* and **Hamilton** in *1895* attributed any positive effects of treatment to the mineral content of the elixir ***(Billings, 1894 and Hamilton, 1895)***. The first use of BM administrated by a technique likely to result in the transfer of living cells was by **Schretzenmayr** in *1937*. Patients suffering from parasitic infection were treated with intramuscular injections of freshly aspirated autologous marrow with some benefits ***(Schretzenmayr, 1937)***. Subsequently in *1944*, **Bernard** injected allogeneic BM into the medullary cavity in patients with BM deficiency but without success ***(Bernard, 1944)***.

The first clinical application of BM followed rapidly on the heels of experimental work. The first attempts to intensify antitumor treatment by myeloablative therapy and autologous marrow transplant rescue were carried out in *1956* by **Ferribee** in the United States and others in Europe ***(Kurnick et al., 1958)***. Treatment success was limited by lack of knowledge of how to administer high-dose therapy and inability to provide adequate supportive care for marrow failure. Early clinical marrow transplant attempts are well reviewed by **Pegg**. In retrospect, it appears that there may have been at least 6 patients with aplastic anemia rescued from marrow failure by marrow donation from their identical twin ***(Pegg, 1966)***.

In *1980s*, the indication for bone marrow transplantation

(BMT) expanded to include a wide variety of malignant and non-malignant disorders and donors other than human leukocyte antigen (HLA)-identical siblings, including matched but unrelated donors, have been increasingly used ***(Lehn, 1990).***

The progress in BMT was faced by the biological problems of graft versus host disease (GVHD) and BM graft rejection on one hand and the relapse of leukemia on the other hand. The introduction of cyclosporine A for GVHD prophylaxis in *1980* made BMT safer and less toxic ***(Apperley et al., 1988).***

In *1990s*, a period of increasing uses of cytokines and growth factors supported the hematological and metabolic recovery ***(Barret, 1992).***

In *2000* and beyond, it has become increasingly necessary to use the term "hematopoietic stem cell transplantation (HSCT)" rather than "bone marrow transplantation" ***(Radeva et al., 2005).***

What are stem Cells (definition)?

Stem cells are undifferentiated cells characterized by their prolonged self-renewal capacity and by their asymmetric replication. Stem cells were first identified as pluripotent cells in embryos, and these were called embryonic stem cells. It is now clear that stem cells are also present in many tissues in adult animals and contribute to the maintenance of tissue homeostasis ***(Weissman, 2000).***

Characteristics of human stem cells :

Stem cells differ from other kind of cells in the body by their unique properties of 1) Self renewal: produce progeny exactly the same as the originating cell. This trait is also true of cancer cells that divide in an uncontrolled manner, whereas stem cell division is highly regulated. 2) Being unspecialized (they are non-differentiated). 3) Plasticity (being able to give rise to specialized cell types) ***(Steindler and Pincus, 2002).***

Stem Cell Fates :

Based on the 2 defining characteristics of stem cells(unlimited self-renewal and ability to differentiate) they can be described as having 4 outcomes or fate (fig. 2):- 1)A common fate for multipotent stem cells is to remain quiescent without dividing or differentiation entiating, thus maintaining their place in the stem cell pool .An example of this stem cells in the bone marrow that activating signals from the body.

2) A second fate of stem cells is symmetric self-renewal in which 2 daughter stem cells, exactly like the parent cell, arise from cell division. This does not result in differentiated progeny but does increase the pool of stem cells from which specialized cells can develop in subsequent division. 3)The third fate, asymmetric self- renewal, occur when a stem cell divides into 2 daughter cells, one a copy of the parent, the other amore specialized cell, named somatic or progenitor cell. Asymmetric self- renewal result in the generation of differentiated progeny needed for natural tissue development\ regeneration while also maintaining the stem cell pool for the future. 4) The fourth fate is that in which a stem cell divides to produce 2 daughters both different from the parent cells ***(Molofsky et al., 2004) .***

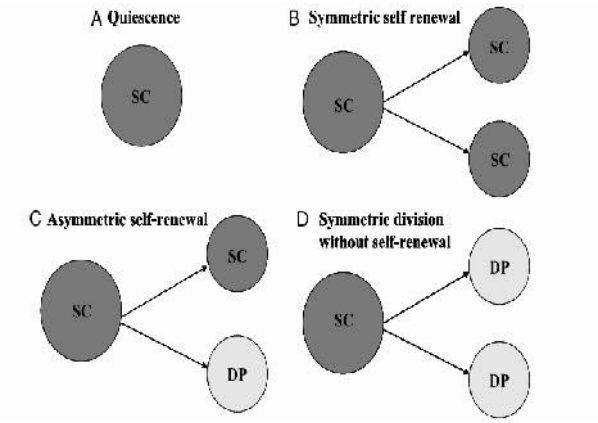

Fig. (2*): Stem cell fates. Four potential outcomes of stem cells. A, Quiescence in which a stem cell does not divide but maintains the stem cell pool. B, Symmetric self-renewal where a stem cell divides into 2 daughter stem cells increasing the stem cell pool. C, Asymmetric self-renewal in which a stem cell divides into one differentiated daughter cell and one stem cell, maintaining the stem cell pool. D, Symmetric division without self-renewal where there is a loss in the stem cell pool but results in 2 differentiated daughter cells. DP indicates differentiated progeny; SC, stem cell* ***(Molofsky et al. ,2004).***