



ISSN (E): 2277- 7695
 ISSN (P): 2349-8242
 NAAS Rating: 5.03
 TPI 2019; 8(3): 434-436
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 www.thepharmajournal.com
 Received: 16-01-2019
 Accepted: 20-02-2019

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Stem cells in cancer therapy

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Abstract

Over 30 years stem cells are been used as replacement of blood and immune systems damaged by the cancer cells during treatment of cancer by chemotherapy or radiotherapy. Aside from it immune constitution, the stem cells have been reported to contribute in the tissue generation and act as carrying vehicles in the treatments. When stem cells are penetrate into cancer tumors and metastatic divisions, shows anti cancer activity on targeted sites.

Keywords: chemotherapy, radiotherapy, tissue generation, cancer tumor, metastasis

1. Introduction

Stem cells can be divided into main three categories: embryonic, germinal, and somatic. Embryonic stem cells (ESCs) originate from the inner cell mass of the blastocyst. ESCs are have supreme and have unlimited duplicatelife span, which is due to their telomerase expression [1]. Germinal stem cells are derived from primary germinal layers of embryo. They differentiate into parent cells to produce specific organ cells. Somatic or adult stem cells are progenitor cells as they are less totipotent i.e. less replicative life span than ESCs. They exist in mature tissues such as hematopoietic, neural, and gastrointestinal and tissues. The most commonly used adult stem cells (ASCs) derived from bone marrow are haemopoietic stem cells (HSCs) and other primitive progenitor cells including mesenchymal stem cells (MSCs) and multipotent adult progenitor cells (MAPCs) [2].

2. Source of stem cells for cancer therapy

ESCs are the derived from the stem cells and they have the greater totipotency and infinity life span compared to ASCs with shorter totipotency and limited life span.

Whenever, use of ESCs has Alternatives (Department of Health, UK, National Institutes of Health and International Society for Stem Cell Research) and their use for research and therapeutic purposes are restricted [3].

Stem cells with higher totipotency have been shown to be more tumorigenic in mice [4].

ESCs are derived from the pre implanted human embryo, then it took the risk to collapsing the embryo, Mostly ASCs are derived from the tissues i.e bones synovial fluid, teeth, brain, blood vessels and umbilical cord blood [5].

Mostly, ASCs are derived from the bone marrow and peripheral blood.

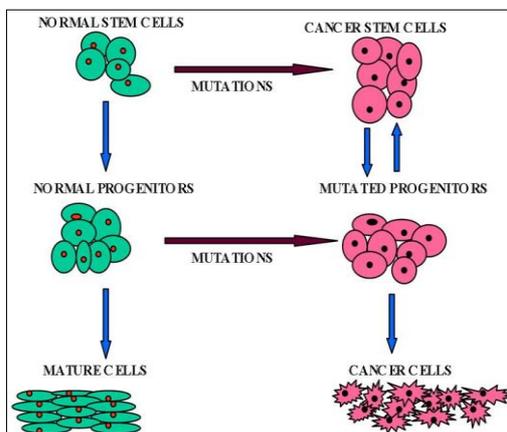


Fig 1: hypothesis about origin of cancer stem cells.

3. Life span of ASC

The majority of the stem cells in clinical area is the life span of the stem cells ESCs are shows good performance due to their unspecified duplicate life span due to their telomerase expression [6]. Theoretically the use in clinical area is very much restricted. Most of ASC do not shows proper telomerase activity and they cannot prevent the loss of telomerase.

Role of purging in the isolation of stem cells

The isolation of stem cells from the denoting donor is best method, in which 30% of population are eligible, due to shortage of donors and age limitations [7]. Stem cells from independent source are easily exist but they carry the risk of coincidence of normal deteriorate of cancer. In population of patients with breast cancer, PBSC transplantation has been related to a rapid and sustained hematogenic conjoin and has shown to be less contaminated than bone marrow stem cells [8]. There was however no overall improvement in survival outcome.

The contaminations of the gain of stem cells with tumour cells have been major problem which reported by the many studies however the effect on clinical cell therapy has been less effective.

Someone procedures are used in an attempt to remove these contaminant cancer cells from stem cells. clinical trials with various in laboratory and biological conditions to rid the stem cells such as using monoclonal antibodies, continuous flow immune adsorption technique, use of rituximab, pulsed electric field, and hyperthermia. Aminoethyl Thio Phosphate has been shown to protect normal haematopoietic progenitor cells from damage by alkylating agents used for rid of stem cells. The double procedure using 'CD34+' and 'CD19-' double selection method for purging is reported to be better than single procedure in the poor prediction lymphoproliferative disorders, but it is associated with increased risk of life-threatening infections.

3.1 Mechanism

The stem cells including ES, CSCs, and iPSs can be differentiated into cardiomyocytes after transplantation and restore contractile function. They also can be differentiated into endothelial cells and promote angiogenesis, turn part of the damaged heart muscle alive, and limit scar expansion. Stem cells including BMC and ADSCs trans differentiate into cardiomyocytes [9]. *In vivo*, but no one has yet observed that MSCs give rise to fully differentiated and functional cardiomyocytes *in vivo*. With the discovery of paracrine effect of the stem cell, many studies have confirmed that stem cell therapy of heart failure depends on the mechanism, mainly in the promotion of angiogenesis, against myocardial apoptosis, immune regulation, and so on.

(1) The autocrine or paracrine growth factor such as vascular endothelial growth factor (VEGF) promotes reconstruction of myocardial vascular network. VEGF can increase permeability of capillary wall, activate matrix metalloproteinase, and promote endothelial cell proliferation and migration. It is one of the most important angiogenesis factors. Research has shown that sustained high expression of VEGF, cooperated with the other angiogenesis factors (such as bFGF), may promote the formation of smooth muscle cells, participate in the "arteriogenesis". Process, and improve myocardial ischemia. Tangetal. Confirmed capillary proliferation in the areas of acute myocardial infarction and surrounding area after stem cell transplantation.

(2) MSCs transplantation inhibits the activation of NF- κ B, attenuates the protein production of TNF- α and IL-6, and increases anti-inflammatory cytokines IL-10 expression. As proinflammatory cytokines, TNF- α and IL-6 have a toxic effect on myocardial cells, can inhibit the cardiac contractile function, and induce apoptosis of cardiomyocyte. In addition, they can regulate the expression of monocyte chemoattractant protein, vascular endothelial cellular adhesion molecule to chemotaxis of inflammatory cells into myocardial tissue, increase myocardial tissue inflammatory responses, and thus promote the progress of ventricular remodeling after AMI. As an anti-inflammatory cytokine, IL-10 may be expressed by monocytes, macrophages, cardiac cells, and so on. Through inhibition of NF- κ B activity to decrease TNF- α and IL-6 expression, it can also inhibit the inflammatory response to some degree.

(3) Cardiomyocyte hypertrophy and the extracellular matrix deposition play major roles in the remodeling of non infarcted myocardium [10]. Pathologic increase in extracellular collagen leads to interstitial fibrosis, and although this can be useful in limiting ventricular enlargement, it decreases the compliance of ventricular wall and affects heart function. MSCs transplantation improves cardiac function in part through regulation of cardiac fibroblasts proliferation and transcriptional down regulation of types I and III collagen syntheses. This may be one of the mechanisms through which they inhibit the ventricular remodeling.

Stem cells in tissue regeneration

Apart from long lasting replicative property of stem cells, stem cells from haemopoietic tissues seem to have 'extraordinary' abilities to generate or switch between haematopoietic and non-haematopoietic lineages, exhibiting an unexpected degree of developmental or differentiation potential. On theoretical grounds, this allows HSC to be used to regenerate any non-haematopoietic tissue.

Cancer stem cells

Cancer stem cells can be defined as cells in the tumour growth with a tumour initiating potential. Normal stem cells are characterised by three properties: 1 Capability of self-renewal; 2 strict controls on stem cell numbers; 3 Ability to divide and differentiate to generate all functional elements of that particular tissue

The cancer stem cells were also shown in the solid tumours such as breast cancer and brain tumours Compared to normal stem cells, the cancer stem cells are believed to have no control on the cell numbers. Cancer stem cells form very small numbers in whole tumour growth and they are said to be responsible for the growth of the tumour cells.

It has been well-known that in order to induce a tumour in an animal model, hundreds of thousands of cancer cells need to be injected. This has been explained to be due to limitations in the assay to support tumour growth, or due to tumour formation deficiency. With the recent concept of the cancer stem cells, it may be explained that higher numbers of cancer cells are needed to maximize the probability of injecting cancer stem cells in animal model. At present, the shrinkage in the size of a tumour is considered as a response to the treatment.

Origin of cancer stem cells

origin of the cancer stem cells, two important factors need to be considered; 1 a number of mutations are required for a cell

to be cancerous and a stem cell needs to overcome any genetic constraints on both self-renewal and proliferation capabilities

Implications for cancer treatment

The cancer treatment is targeted at its proliferation potential and its ability to metastasise.

For tumours in which the cancer stem cells play role, three possibilities exist. First, the mutation of normal stem cells or progenitor cells into cancer stem cells can lead to the development of the primary tumour. Second, during chemotherapy, most of the primary tumour cells may be destroyed but if cancer stem cells are not eradicated, they become refractory cancer stem cells and may lead to recurrence of tumour. Third, the cancer stem cells may migrate to distal sites from the primary tumour and cause metastasis.

4. Therapy

The conventional therapies may reduce the size of the tumour; by contrast, if the therapies are directed against the cancer stem cells, they are more effective in removal the tumour Also most effective methods are

- radiation therapy
- chemotherapy
- Surgery
- Targeted therapy

In which radiation therapy use of ionizing radiations to kill the cancer cells and decrease the tumor cells

In which chemotherapy using the cytotoxic (anti cancer drugs) to decrease the count of the cancer cells

Targeted therapy involved in the small peptides bound to the extracellular matrix surrounding the tumor and also photodynamic therapy most frequently used therapy in the targeted therapy.

These deregulated signalling pathways and gene expressions may have impact on response to cancer therapy.

5. Reports

The intestinal surface is rapidly regenerating tissue; this generation is carried by the stem cells. Damage of intestinal stem cells is considered as chemotherapy, leads to improper renewing of the intestine and severe illness.

When the hereditary mutations further promote the increase in the number of intestinal stem cells are associated with the uncontrolled organ regeneration and development of the colon cancer. Boundcontrol of the intestinal stem cells is require to allow for regeneration but to prevent the cancer cells.

Bacteria within the normal gut micro bio tacan seize the intestinal tissue and activate the enzyme stem cells that facilitate the stem cell growth and reduce the number of cancer cells.

The study of stem cells offers great promise for better understanding basic mechanisms of human development, as well as the hope of harnessing these cells to treat a wide range of diseases and conditions.²However, stem cell research—particularly human embryonic stem cell (hESC) research, which involves the destruction of days-old embryos has also been a source of ongoing ethical, religious, and political controversy [2].

6. Conclusion

Stem cells technologies are best/efficiency method for

treatment for cancer therapy. When stem cells are penetrate into cancer tumors and metastatic divisions, shows anti cancer activity on targeted sites. Stem cells act as the anti cancer agents on treatment of cancer. When using the conventional chemotherapeutic agents such as anti cancer drugs to reduce the shelf life period of cancer tumors. We establish the better research for determining the relationship between the normal stem cells and cancer stem cells. For the better understanding methods are to improve the stem cell-based regenerative medicines and developing the anti cancer treatment methods.

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