Chapter 16
Role of Stem Cells in Cancer Therapeutics

Madhu Rani
Jamia Millia Islamia, New Delhi, India

Sumit Kumar
National Institute of Pathology, New Delhi, India

M. Moshahid Alam Rizvi
Department of Biosciences, Jamia Millia Islamia, New Delhi, India

ABSTRACT

Stem cells are pluripotent cells having capacity of self-renewal and produce various types of mature cells. Cancer stem cells are known to be responsible for drug resistance and tumor relapse, yet stem cells offer multiple avenues to treat same. Stem cells have been employed for treating of blood and immune systems damaged during chemotherapy and radiotherapy. Stem cell transplantation is emerged as critical therapy in cancer treatment, yet other potential applications of stem cells in cancer treatment are largely unexplored or underutilized. Recently, stem cells reengineered express different cytotoxic agents. It has shown to cause tumor regression and enhance the animal survival in preclinical studies. Stem cell therapy can be also employed for targeted drug delivery, gene delivery, and even used as virus to target cancer cell. In recent years, research is devoted on stem cells worldwide for new and newer application. Although the field of stem cells is nascent and raises many ethical concerns, scientific responsibilities, and future challenges, scientific community are still hopeful and filled with optimism. Currently, stem cell therapy represents the beginning of the new era in cancer treatment and giving a ray of hope to clinicians and also patients who are suffering from untreatable diseases and desperately looking for new therapies. In the present chapter, the authors mainly shed light on potential applications of stem cells to treat cancer. At the end, they also discussed the factor influencing stem cell therapies and current challenges in stem cell therapy.

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INTRODUCTION

Stem cells are defined as cells that have clonogenic and self-renewing capacities which differentiate into multiple cell lineages and also potency to produce replacement cells for a wide range of tissue and organs like heart, liver, pancreas and nervous system.(Law, Hunt, & Qu, 2019; Sachin & Singh, 2006). Stem cells are present from the early stages of human development until life ends.

The discovery of stem cells in the past became open to the new medicine era in the treatment of many diseases which led to extensive attention and research on stem cells. In 1981, Evans et al have isolated stem cells from mouse embryos(Evans & Kaufman, 1981). Further studies on mouse embryo led the discovery of isolation of stem cells from a human embryo which opens the door for use of stem cells in the treatment of diseases. Improvement in advance technology helped a lot to understand the potency and efficacy of stem cells especially the discovery of the oct3/4, sox2, klf-4 and myc which have capacity to turn any normal cell into stem cell. Table 1 shows the progression of stem cell research worldwide.

Table 1. Summary of the History of Stem Cell Research, adopted with permission from Hawsawi et al. (2018)

Year	Research Performed	References
1878	The first report of endeavors to fertilize mammalian eggs outside the body is published.	Caplan (2017)
1959	The first report on animals produced through IVF is published.	Caplan (2017)
1960	Studies of teratocarcinoma in the testes of several inbred strains of mice indicate that the teratocarcinoma originated from embryonic germ cells.	Stevens (1960)
1968	The first human egg in vitro fertilization is performed.	Hawsawi et al. (2018)
1970	Cultured stem cells are explored as models of embryonic development, although their complement of chromosomes is abnormal.	Hawsawi et al. (2018)
1978	Louise Brown, the first IVF baby, is born.	Johnson and Elder (2015)
1980	Australia's first IVF baby, Candace Reed, is born in Melbourne.	Verhoeven (2006)
1981	Evans and colleagues derive mouse cells (ESCs) from the inner cell mass of blastocysts and develop culture conditions for growing pluripotent mouse ESCs in vitro; they find that infusing the ESCs into mice induced the formation of teratomas. The first IVF baby in the United States, Elizabeth Carr, is born.	Evans and Kaufman (1981); Martin (1981)
1984-1988	Andrews and coworkers develop pluripotent cells (ECCs) from the Tera-2 human testicular teratocarcinoma cell line. Thus, the teratoma cells exposed to retinoic acid differentiate into neuron-like cells and other cell types	Andrews (1988); S. Thompson et al. (1984)
1989	Pera and coworkers isolate and characterize multipotent clones of human embryonal carcinoma cells, which yield tissues of all 3 primary germ layers.	Pera, Cooper, Mills, and Parrington (1989)
1994	Human blastocysts are established for reproductive purposes using IVF and are donated by patients for research. The inner cell mass is isolated and cultured.	Bongso, Fong, Ng, and Ratnam (1994)
1995-96	Nonhuman primate ESCs are derived and maintained in vitro; these cells were first isolated from the inner cell mass of rhesus monkeys and then from that of marmosets. The primate ESCs resemble human ECCs, indicating that it should be possible to derive and maintain human ESCs in vitro.	Hawsawi et al. (2018)
1998	Thompson and coworkers acquire and maintain human ESCs from the inner cell mass of human blastocysts that were produced through in vitro fertilization and were donated for research purposes. Gearhart and colleagues derived human embryonic germ (EG) cells from the gonadal ridge and mesenchymal tissue of fetal material originating from abortions at 5 to 9 weeks of gestation.	B. Thompson et al. (1998)
2000	Scientists in Singapore and Australia derive human ES cells from the inner cell mass of blastocysts donated by couples undergoing treatment for infertility. The ES cells proliferate for extended periods in vitro, maintain normal karyotypes, differentiate into somatic cell lineages derived from all 3 primary germ layers, and form teratomas when injected into immunodeficient mice.	Lohar (2019)
2001	Human ES cell lines are shared and new lines are derived in vitro. Many methods are aimed at generating human tissues for transplantation purposes.	Lohar (2019)