

# Concept of Stem Cells and Its Importance in Dentistry - A Review

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## Abstract

Scientists have tried for decades to understand cancer development in the context of therapeutic strategies. The realization that cancers may rely on “cancer stem cell” that share the self-renewal feature of normal stem cells has changed the perspective with regard to new approaches for treating the disease. Given their unique regenerative abilities, stem cells offer new potentials for treating diseases such as diabetes, heart diseases etc. Dental stem cell (DSCs) are considered suitable candidates for cell-based treatment strategies and tissue engineering applications. However, much work remains to be done in the laboratory and the clinic to understand how to use these cells for cell-based therapies to treat disease which is also referred to as regenerative or reparative medicine.

**Keywords:** Cancer stem cell, Dental Pulp Stem Cells, Dental Follicle Stem Cell, Periodontal ligament stem cells, Dental Follicle Stem Cells, Totipotent cells

## Introduction

Stem cells are primitive cells present in all organisms that can divide and give rise to more stem cells, or switch to become more specialised cells, such as those of the brain, heart, muscle and kidney<sup>1</sup>. Stem cells have the remarkable potential to develop in to many different cell types in the body during early life and growth. In addition, in many tissues they serve as a sort of internal repair system dividing essentially without limit to replenish other cells as long as the person or animal is still alive. When a stem cell divides, each new cell has the potential either to remain a stem cell or become another type of cell with a more specialized function, such as a muscle cell, a red blood cell, or a brain cell<sup>2</sup>.

### Historical perspectives:

The history of stem cell research had a benign, embryonic beginning in the mid 1800s with the discovery that some cells could generate other cells. In the early 1900s the first real stem cells were discovered. The term “stem cells” was proposed for scientific use by the Russian histologists Alexander Maksimov in 1908. Haemopoietic stem cells were discovered in human cord blood in 1978. Scientists at Newcastle university in England create the first ever artificial liver cells using umbilical cord blood stem cells in oct 2006. It is suggested that these stem cells have the ability to

differentiate in to more cell types than adult stem cells, opening up greater possibilities for cell-based therapies. For the first time human embryonic stem cells have been cultured under chemically controlled conditions without the use of animal substances which is essential for future clinical uses in 2010<sup>3</sup>.

### Types and Properties:

The most primitive type of stem cell is the fertilized egg and its first few divisions early in development produce cells that retain the ability to generate all the different types of cells of the adult body. they are described as “totipotent cells”. As the embryonic development proceeds, these totipotent cells become directed towards differentiation into the many distant tissue types of the adult individual (stem cells for blood, bones, mucosa, etc.).As they do so they lose some of their developmental potential and become either “pluripotent”, that is restricted to forming only a few types of tissues, or “unipotent” restricted to generating only a single tissue.

The general property that characterizes adult (somatic) stem cells is that they can be divided indefinitely, normally producing one cell that remains a stem cell and one cell that differentiates itself into a functional tissue cell. This normal “asymmetrical”

division pattern is important as it results in the maintenance of the same number of stem cells while also providing another cell for tissue function. And also stem cells can be divided “symmetrically” to form two stem cells and thus increase their number <sup>4</sup>.

Differences between cancer and normal stem cell:

Cancer stem cells (CSCs) are present in various solid tumors, including OSCC. It represent a small subpopulation of tumor cells, they are characterized by several features that confers high tumorigenic potential associated with elevated self-renewal and differentiation capacity. Various proteins have been tested as biomarkers of CSCs including podoplanin (PDPN),

adenosine triphosphate –binding cassette transporter 2 (ABCG2), aldehyde dehydrogenase (ALDH), CD133, MII, leucine-rich repeat-containing G- protein coupled receptor5 (LGR5), and LGR4<sup>5</sup>.

Cancer stem cells are now thought to be responsible for cancer initiation, progression, metastasis, recurrence and drug resistance. There are some similarities and differences between CSCs and healthy stem cell<sup>6</sup>.One of the major differences is their degree of dependence on the stem cell niche, a specialized microenvironment in which stem cell reside.it plays an essential role in maintaining stem cells or preventing tumorigenesis by providing primary inhibitory signals for both proliferation and differentiation. Niche also provides transient signals for stem cell division to support ongoing tissue regeneration<sup>7</sup>.

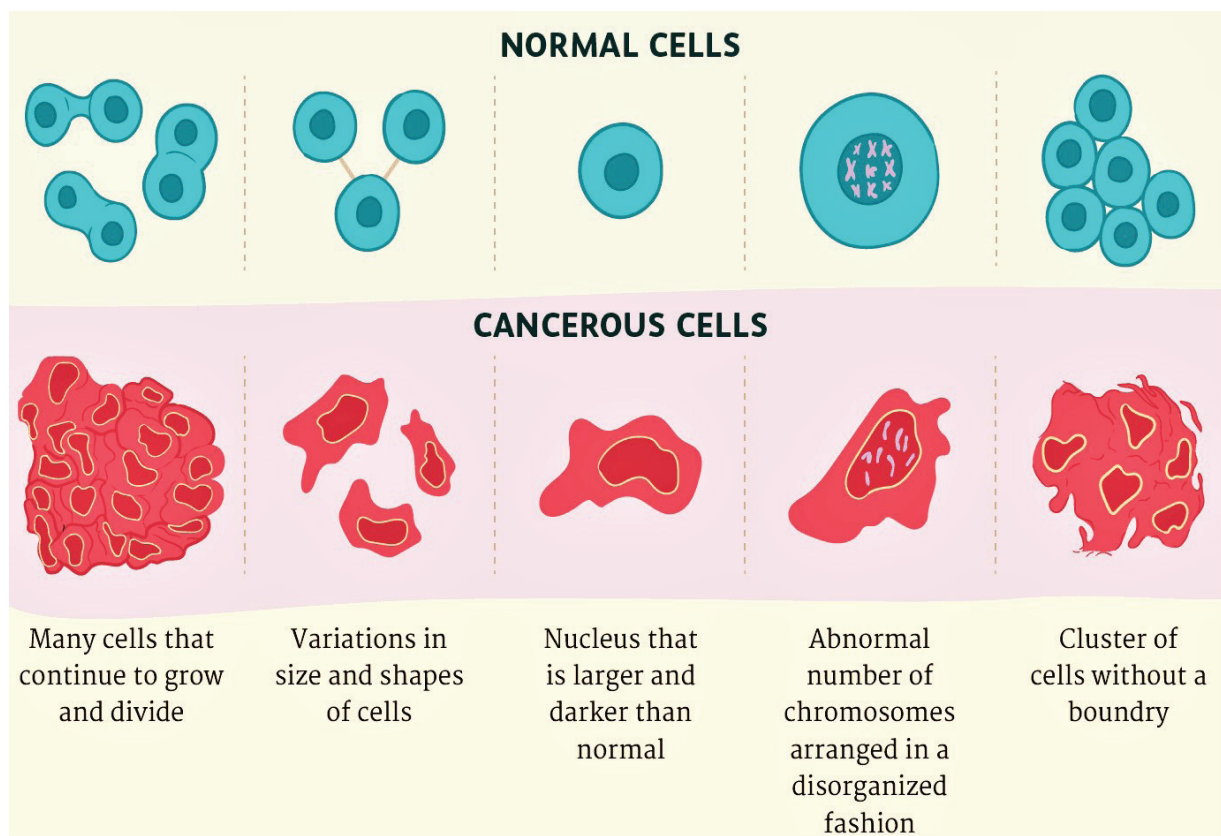


Figure 1: Normal cell vs Cancer cell

Courtesy:

<https://www.google.co.in/url?sa=i&source=images&cd=&ved=2ahUKEwjYh8mO1IznAhUYXSsKHaFkC2IQjRx6BAgBEAQ&url=https%3A%2F%2Fwww.verywellhealth.com%2F%2Fcancer-cells-vs-normal-cells->

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Normal stem cell properties versus CSCs properties<sup>6</sup>

<b>Extensive but limited self-renewal capacity</b>	<b>Extensive and in definitive self- renewal capacity</b>
Organogenic capacity	Tumorigenic capacity
Highly regulated self -renewal and differentiation	Highly dysregulated self-renewal and differentiation
Rare in normal adult tissue	Infrequent or rare within tumours
Can be identified based on surface markers	Similar types of surface markers as ordinary stem cells in the same tissues
Normal karyotype	Abnormal karyotype
Quiescent most of the time	Less mitotically active than other cancer cells
Capacity to generate normal progeny with limited proliferative potential	Phenotypically diverse progeny

### **Common features found in normal and cancer stem cells**

Capacity for asymmetric divisions that produce a quiescent stem cell and a dedicated progenitor and plays important role towards emerging a dangerous cell mass
Regulation of self –renewability by similar signalling pathways
Capacity to arrange a hierarchy of cellular derivatives that includes progenitors and differentiating cells
Expression of similar surface receptors and predilection for growth factor independence through the secretion of growth factors and cytokines
Stimulation of angiogenesis through secretion of angiopoietic factors
Extended telomeres and telomerase activity that increases the cellular life span

### **Cancer stem cell markers:**

Specific markers have been investigated in the hope of developing a deeper understanding of role of cancer stem cells in oral cancer pathogenesis.

**CD44 :** It is the most familiar CSC marker that has previously been identified in various solid malignancies such as breast, CNS, colon, pancreas. It is involved in cell adhesion, migration and metastasis. CD44 subpopulation demonstrated its tumorigenic potential, tumor sphere formation, and chemo-resistance in both cell lines and primary tissues of OSCC<sup>8</sup>.

**CD133 :** It is a cell surface marker also known as prominin-1. It was discovered as a marker of normal haematopoietic stem cells. In OSCC, CD133+ cells displayed increase in colonogenicity.

**Aldehyde dehydrogenase (ALDH):** It comprises a family of intracellular cytosolic enzymes that are mostly found in the liver. Their functions include the

conversion of retinol to retinoic acid in early stem cell differentiation. In OSCC increased level of ALDH correlated with disease staging, radio-resistance and negative correlation prognosis.

**Growth factor (HGF):** It also called as tyrosine kinase receptor. Normally only stem cells and progenitor cells express Met, however, CSCs seize this ability which is from the normal stem cells expressing with tumour invasion and metastasis, leading to decreased survival and angiogenesis in various neoplasms.

**Side population:** Defined as sub group of cells that behave differently than the main population when analysed with a specific marker. Cell multi drug transporters efflux of vital dyes has been investigated as a potential marker for cancer stem cells. The cells ability to actively pumps the dye Hoechst 33342 by the ATP binding cassette transporter can be used to identify cells with increased longevity, and this concept is applied to cancer stem cells with remain in a quiescent state<sup>9</sup>.

**Potential applications in medicine and dentistry:**

Stem cells are being explored for a variety of chronic debilitating diseases that have so far escaped remodel measures from traditional allopathic approaches with a hope that cell therapy would repair, repopulate, replace and rewire tissues and organs under conditions like Parkinson's disease, spinal cord injury, heart failure, haematological disease, cancer, arthritis, diabetes, and peripheral vascular diseases<sup>10</sup>. The regenerative potential of adult stem cell obtained from various sources including dental tissues has been of interest for clinicians over the past years

In 2000, Gronthos et al. were the first to describe a heterogeneous, clonogenic, and highly proliferative cell population within the dental pulp, namely dental pulp stem cells (DPSCs). In addition to DPSCs and stem cells from human exfoliated deciduous teeth (SHEDs), a number of other distinct stem cell populations have been reported to reside within the human tooth and its surrounding tissues. For example, stem cell from apical papilla (SCAPs) can be found in the loosely attached soft connective tissue at the apex of developing permanent teeth. Dental follicle stem cells (FSCs), on the other hand, are isolated from the dental follicle. Within the periodontal ligament another population of stem cells found namely, periodontal ligament stem cells (PDLSCs). According to the minimal criteria defined by the International Society for Cellular Therapy, DPSCs, SHEDs, FSCs, and PDLSCs (collectively referred to as dental stem cells (DSCs)) are considered to be mesenchymal stem cells. In general, SCAPs and FSCs are considered to be more immature, given their origin from developing dental tissues, and thus more potent in comparison to DPSCs. SCAPs have already been reported to have high proliferative rate, a more distinct doubling capacity, and enhanced migratory properties in comparison with DPSCs<sup>11</sup>.

Stem cell research is presently focused on the treatment of certain oral mucosal lesions also these are:

- Ulcerative lesions: Like oral ulcers and wounds, oral mucositis, pemphigus vulgaris
- Premalignant disorders: Oral submucous fibrosis, oral lichen planus
- Malignant lesions: Like oral carcinomas

Role of stem cell therapy in oral lesions is primarily aimed at neoangiogenesis, tissue regeneration,

modulation of collagen gene expression, and immunomodulation, thereby making it noninterventive and innovative treatment modality<sup>12</sup>.

**Limitations of stem cell therapy**

Cell therapy is not a solution to all existing health problems. Each person reacts differently; the main purpose of these procedure is to give tools to the body and create ideal conditions to generate damaged tissue by itself. There are two important limitations to cell therapy

If stem cell production in the bone marrow is low, then the amount of cell harvested is limited causing a poor transfusion with a low number of cells. Even though cells have the chemical capacity to detect damaged tissue, there might be a physical obstruction like a blocked artery that will not allow stem cells to travel to damaged areas. If the cause of obstruction is not eradicated there will be poor, slow, or no tissue regeneration. Second obstacle is related to lack of medical knowledge in regards to cancer. Adding progenitor cells could have a possible negative effect in the body through an acceleration of tumor growth. Therefore, cell therapy for cancer conditions, nowadays requires greater knowledge and studies. Quality of stem cell is extremely important. Older patient have less capability for stem cell production in bone marrow than younger patients<sup>13</sup>.

**Conclusion**

The spectacular progress in the field of stem cells research represent great scope of stem cells regenerative therapeutics. It can estimated in near future we will be able to produce wide array of tissue, organoid, and organs from adult stem cells. and there might be new pharmaceutical compounds those can activate tissue specific stem cells, promote stem cells to migrate to the side of tissue injury, and promote their differentiation to tissue specific cells. It is expected that stem cell therapies will bring considerable benefits to the patients suffering from wide range of injuries and disease. For advancement of translational application of stem cells there is a need of clinical trials, which needs funding rejoinder from both public and private organizations in India. The government should bring about regulatory guidelines with respect to stem cell research and monitor the institutions which are actively involved in research. The critical evaluation of regulatory guidelines at each phase of clinical trial is a must to comprehend the success and efficiency in time frame.

**Conflicts of Interest:** There are no conflicts of interest

**Source of Funding:** Not Required

**Ethical Clearance:** Not Required

### References

1. Passier R, Mummery C. Origin and use of embryonic and adult stem cells in differentiation and tissue repair. *Cardiovascular research*. 2003 May 1;58(2):324-35.
2. Kolios G, Moodley Y. Introduction to stem cells and regenerative medicine. *Respiration*. 2013;85(1):3-10.
3. Kalra K, Tomar P. Stem cell: basics, classification and applications. *American Journal of Phytomedicine and Clinical Therapeutics*. 2014 Jul 31;2(7):919-30.
4. Rodini CO, Lopes NM, Lara VS, Mackenzie IC. Oral cancer stem cells-properties and consequences. *Journal of Applied Oral Science*. 2017 Dec;25(6):708-15.
5. Nikitakis NG, Pentenero M, Georgaki M, Edwards P, Fred C, Lingen M, Sauk JJ. Molecular markers associated with development and progression of potentially premalignant oral epithelial lesions.
6. Rahman M, Jamil HM, Akhtar N, Rahman KM, Islam R, Asaduzzaman SM. Stem cell and cancer stem cell: a tale of two cells. *Progress in Stem Cell*. 2016 Jun 24;3(02):97-108.
7. Linbeng L et al. *Cancer Res* 2006;06(15):4553-4556.
8. Patel SS, Shah KA, Shah MJ, Kothari KC, Rawal RM. Cancer stem cells and stemness markers in oral squamous cell carcinomas. *Asian Pac J Cancer Prev*. 2014 Jan 1;15(20):8549-56.
9. Patel SS, Shah KA, Shah MJ, Kothari KC, Rawal RM. Cancer stem cells and stemness markers in oral squamous cell carcinomas. *Asian Pac J Cancer Prev*. 2014 Jan 1;15(20):8549-56.
10. Nadig RR. Stem cell therapy—Hype or hope? A review. *Journal of conservative dentistry: JCD*. 2009 Oct;12(4):131.
11. Ratajczak J, Bronckaers A, Dillen Y, Gervois P, Vangansewinkel T, Driesen RB, Wolfs E, Lambrichts I, Hilkens P. The neurovascular properties of dental stem cells and their importance in dental tissue engineering. *Stem cells international*. 2016; 2016.
12. G N Suma, Madhu Pranthi, Arora, Manisha Lakhanpal et al. *J Pharm Bioallied Sci*. 2015; Jan-Mar;7(1):2-8
13. Biehl JK, Russell B. Introduction to stem cell therapy. *The Journal of cardiovascular nursing*. 2009 Mar;24(2):98.