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# Pluripotent and Multipotent Stem Cells and Current Therapeutic Applications: Review

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**Abstract:** There is numerous evidence for the presence of stem cells, which is important for the treatment of a wide variety of disease conditions. Stem cells have a great therapeutic effect on different degenerative diseases through the development of specialized cells. Embryonic stem (ES) cells are derived from preimplantation embryos, which have a natural karyotype. This cell has the capacity of proliferation indefinitely and undifferentiated. Stem cells are very crucial for the treatment of different chronic and degenerative diseases. For instance, stem cell clinical trials have been done for ischemic heart disease. Also, the olfactory cells for spinal cord lesions and human fetal pancreatic cells for diabetes mellitus are the other clinical importance of stem cell therapy. Extracellular matrix (ECM) and other environmental factors influence the fate and activity of stem cells.

**Keywords:** stem cell, embryonic stem cell, adult stem cell, stem cell therapy

## Introduction

Stem cells have excellent tissue regeneration and repair capacity, which is used in the production of drugs and regenerative medicine depends on the discovery of viable sources of multipotent and pluripotent cells.<sup>1</sup> For clinical applications pathogen-free human embryonic stem cells (ESC) and successful differentiation techniques are important.<sup>1,2</sup> The therapeutic potential of embryonic stem cells in the development of specialized cells to replace damaged tissue in patients with variable degenerative diseases.<sup>3</sup> However, the signaling pathways for the adoption of different cellular phenotypes involved in lineage restriction of ESC are still not clear.<sup>3</sup> Besides, as ESC-based therapies advance towards clinical applications, an appropriate culture environment must be established to create a genetically stable homogeneous cell population through the prevention of adverse effects of transplantation.<sup>3,4</sup> Until differentiating into the more advanced cells, which gives specialized tissues, embryonic stem cells are present in the embryo.<sup>5</sup>

## Embryonic Stem Cell

Embryonic stem cells are derived from preimplantation embryos, which are capable of indefinite and undifferentiated proliferation. Besides, primate ES cells retain their ability to distinguish between trophoblast and embryonic endoderm, mesoderm, and ectoderm derivatives.<sup>6</sup> Since these cells have the differentiation capacity to almost all cells or tissue, they have a good advantage to cure several diseases, including diabetes mellitus, Alzheimer's, anemia and spinal cord injuries.<sup>7</sup> Embryonic stem cells can be obtained from the embryo via processes called reproductive cloning.

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The main problem with reproductive cloning is the induction of the immune system as it is not genetically similar to the donor cells.<sup>8</sup> As a result of scientific advancement in the area of stem cell research, more genetically compatible cells will be produced.<sup>9</sup> These features make ESC an attractive regenerative medicine cell source, which is used to restore damaged tissue and cells lost due to disease.<sup>9,10</sup> In animal models, various ESC-based therapies have shown promise and some of them are now in clinical trials in humans.<sup>9,11</sup> However, in terms of processing, packaging, quality control and protection, the generation of ESC lines and their derivatives for cellular therapies pose specific challenges. In culture, they may be extended while maintaining the functional properties of early embryo cells that are pluripotent.<sup>6,9,12</sup>

This has stimulated interest in the isolation of human origin analogous cells.<sup>6</sup> These human pluripotent stem cells may be a renewable source of more differentiated cells that could be used for cellular transplantation.<sup>13,14</sup> The number of available human ES cell lines for study may also be inadequate to assess their therapeutic potential.<sup>14</sup> However, recent molecular and cellular developments in mouse ES cells represent the active use of these cells in therapeutics.<sup>14,15</sup> In developed nations since the funding for human embryonic stem cells is limited, many scientists use the animal model. Murine and embryonic cells can regenerate themselves and split into a cell of all forms.<sup>16,17</sup>

## Induced Pluripotent Stem Cell

Induced pluripotent stem (iPS) cells are derived from adult somatic cells, which are genetically reprogrammed by forced gene expression to an embryonic stem and are essential for preserving the defining properties of ES cells.<sup>18</sup> Reprogrammed induced pluripotent cell enables the development of an unlimited source of cells.<sup>19,20</sup> IPS cells are identical to ES cells that have similar cell marker expression features.<sup>21</sup>

## Adult Stem Cell

Stem cell clinical trials are performed for ischemic heart disease and to assist with bone non-union.<sup>22</sup> The olfactory cells for spinal cord lesions and human fetal pancreatic cells for type 1 diabetes are other adult stem cells applied in clinical trials.<sup>22,23</sup> These cells are limited in their ability to give various types of cells and are thus multipotent types of cells, while scientists are seeking a way to overcome this benefit. The multipotent cell of the brain

derivate is very crucial for the treatment of Parkinson's disease.<sup>24,25</sup> It is clearly stated that there is an abundance of bone marrow-derived stem cells, which are used for different therapeutic purposes.<sup>26,27</sup> Furthermore, stem cells are used for the treatment of the heart problem, which can become cardiac myocytes and neuro-progenitor cells have been identified within the brain, which was previously thought to be devoid of stem cells.<sup>28</sup>

## Fate of Pluripotent and Multipotent Cells

Adult stem cells are responsible for replacing differentiated cells in continuously regenerating tissues, like in the liver, skin and blood system.<sup>29,30</sup> A broad range of environmental factors related to the overall regulation of stem cell development.<sup>31</sup> In particular, new data continue to focus on the effect of the extracellular matrix (ECM) on stem cell fates through physical interactions with cells.<sup>31</sup> Another study reported that stem cell fate can be affected by extracellular matrices.<sup>31</sup> In addition to physical shape modulation, certain subsets of these effects arise from altered adhesive interactions between the cell and the substrate.<sup>31,32</sup> Many extrinsic and intrinsic factors interact to affect cell structure, including long-term interactions with the microenvironment of cells, as well as changes due to physical factors like mechanical or osmotic stress.<sup>31-33</sup>

Several studies have recently revealed that the geometric microenvironment plays an important role in stem cell fate regulation. Aside from the mechanical properties of scaffolds, pore sizes, porosity, surface stiffness, and mechanical stimulation may also influence stem cell fate.<sup>34</sup> Chemical factors such as cell-adhesive ligands and exogenous growth factors will also control the fate of stem cells.<sup>34</sup> To have a more complex and regulated scaffold cell, it is very crucial to have a good understanding of the physical and chemical signals that affect the fate of stem cell.<sup>34,35</sup> Generally, multipotent stem cells stay quiet while keeping their place in the stem cell pool without differentiating.<sup>17</sup> The formation of two daughter cells from cell division,<sup>36,37</sup> the division into two cells,<sup>17,37,38</sup> or separation of a stem cell from the parent cell to produce two daughters are the potential fate of stem cell differentiation.<sup>39</sup> Until differentiating into more advanced progenitor cells, it produces multiple folds of cells in a systematic way.<sup>40,41</sup>

## Stem Cell Differentiation

Differentiation of stem cells entails transforming a cell into a more specific type of cell, which involves changes in cellular structure, signal reactivity, and other factors.<sup>42</sup> The ability of stem cells to divide and differentiate is greatly affected by changes in their signaling pathways and gene expression.<sup>43,44</sup>

There are different types of stem cells based on their ability to differentiate: totipotent, pluripotent, and multipotent cells. Besides, Oligopotent differentiates into a few different types of cells, whereas Unipotent differentiates only one type of cell.<sup>16</sup> Generally, the cell aggregates and aggregated cells spontaneously divide when stem cells are cultured without an adherent surface, feeder cells.<sup>45</sup>

## Embryonic Stem Cell Differentiation

Embryonic stem cells are originated from blastocyst-stage embryos' inner cell mass.<sup>46</sup> They can be preserved and expanded in culture as pure populations of undifferentiated cells for prolonged periods.<sup>16</sup> In contrast to transformed tumor cell lines, ES cells preserve normal karyotypes after extensive passage in culture.<sup>1</sup> The ability to differentiate embryonic stem cells into different types of cells opens the door to new mammalian growth models and regenerative medicine cell sources.<sup>3</sup> It is critical to control ESC differentiation to realize this potential and guide the production of these cells along specific pathways.<sup>47,48</sup>

## Adult Stem Cell Differentiation

In a different type of adult tissue, stem cells produce new cells continuously or in response to injury.<sup>30</sup> However, some distinct populations of multipotent cells can develop additional cell types under certain conditions.<sup>49,50</sup> Differentiation of stem cells is triggered by both physical and chemical signals.<sup>17</sup> Stem cells may be guided to neuronal, myogenic, or osteogenic lineages through the adjustment of the stiffness of the substrate.<sup>17</sup> Since cells can be mature in both physical and chemical environments, a combination of the two would likely be sufficient for optimal stem cell differentiation.<sup>17,51</sup> Efficient and structured protocols must be developed before stem cells can be used therapeutically, ensuring that cells are a well-controlled and well-defined entity.<sup>52</sup>

## Stem Cell Therapy

For almost half a century the successful application of hematopoietic stem cells in hematopoietic transplants has

prompted attempts to employ stem cells in treating many other clinical issues, including weakened myocardium after heart infarction, brain after stroke and spinal cord after mechanical injury.<sup>22,23,53</sup> As stem cells can give additional potential cells, which have tremendous potential for tissue regeneration and reconstruction for medical application. The most and commonly used stem cell treatment is the transplant of blood stem cells to treat diseases and disorders of the blood and immune system.<sup>54</sup> The United States' national marrow donor program has a long list of diseases that can be treated with blood stem cell transplantation. The transplantation of healthy, active, and propagating cells to restore the function of deficient tissues is referred to as cell therapy. Self-renewal and the ability to distinguish differentiated cells are two characteristics of stem cells.<sup>22,55</sup>

## Embryonic Stem Cell

The potential of ES for self-renewal and differentiation has opened up the prospect of widespread use in regenerative research and medicine.<sup>5</sup> If these cells are rendered immune-compliant with the recipient, they can solve the problems of donor tissue shortages and implant rejection.<sup>5,56</sup> Cell therapy is an increasingly appealing notion in modern transplantation medicine.<sup>5</sup> For several clinical problems, the replacement of missing cells would be the ideal cure.<sup>5</sup> These include progressive cell loss diseases associated with age (various types of congestive heart failure, degenerative brain diseases, and sarcopenia), traumatic tissue loss and death of iatrogenic cells.<sup>53</sup>

## Adult Stem Cells

Currently, there is more advanced progress in the use of bone marrow derivatives to treat different pathological problems.<sup>57</sup> Many other disorders and health conditions are expected to benefit from multipotent cell therapy in the upcoming future. Stem cells extracted from bone marrow are in clinical trials to remedy heart ailments.<sup>17</sup>

## Induced Pluripotent Stem Cells

Induced pluripotent stem cells (iPSCs) are commonly used in disease modeling, regenerative medicine and drug development.<sup>58</sup> Induced pluripotent stem cells have a wide range of uses in gene therapy, disease modeling and drug development.<sup>59</sup> Despite the need for further research, researchers are concentrate on the potential usefulness of iPSCs as a method for drug discovery, disease modeling and transplantation medicine.<sup>59</sup> The idea that

a patient's tissues could have a plentiful supply of immune-matched pluripotent cells has piqued the interest of researchers and clinicians all over the world. Furthermore, ethical concerns about ESC processing do not extend to iPSCs, which provide a non-controversial way to produce patient-specific stem cell lines.<sup>60</sup>

## Conclusion

There are many expectations for stem cell treatment of human diseases, but many problems still need to be addressed. In the beginning, more advanced work should be done on embryonic and adult human stem cells, since there is a great biological difference between these laboratory mice and human cells. The other important issue that should be considered is that the shared characteristics and features of the uncontrolled division of cancer and stem cells, which may be very crucial to prevent many problems that are associated with extensive stem cell division. Besides, unique protocols must be developed to improve the growth, survival and integration of transplanted cells. Finally, clinical trials must be conducted to ensure the safety and efficacy of stem cell therapy. When it comes to stem cells, understanding they exist is a long way from using them therapeutically.

## Disclosure

The author reports no conflict of interest in this work.

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