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Popular Article

Transformative role of stem cells in drug development

Mamta Meena, Meemansha Sharma, S. Ilavarsan, Rakesh Karwa, Poorba Sen, Sunita Kumawat, G. Ravi Prakash and T. U. Singh
Division of Pharmacology and Toxicology, ICAR-IVRI, Izatnagar, Bareilly
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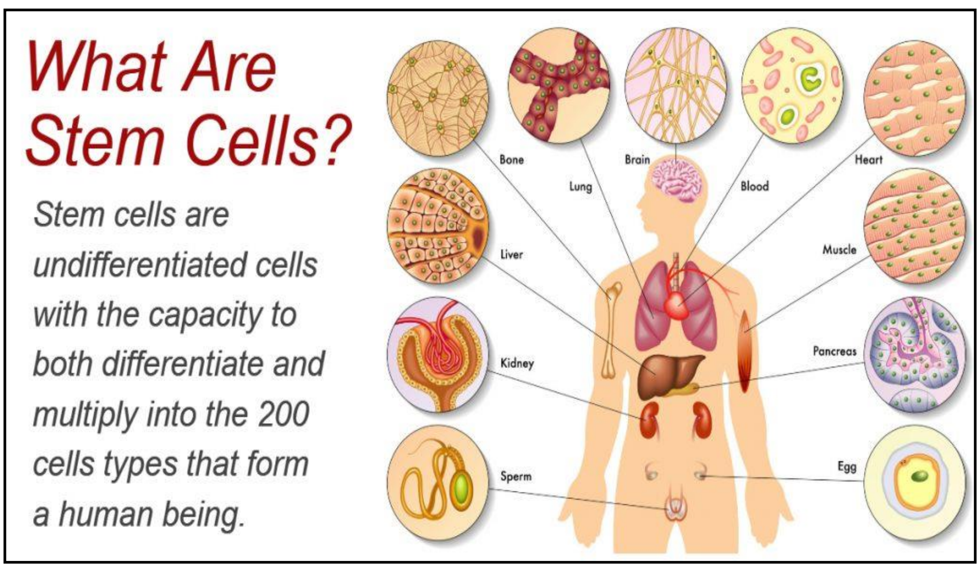
Introduction

Biopharmaceutical research relies on animal cells or immortalized human cell lines representing human system to test drug efficacy or toxicity. These functional cell models are robust and reproducible, they still fail to represent or mimic the human cellular system, posing an enormous challenge to precise and efficient drug discovery for human or animal disorders. Tissue culture system offers an alternative technique to isolate the cells of interest. However, the major limitation is that they dedifferentiate quickly and possess only limited cell divisions *in vitro.* It is therefore not surprising that the clinical outcome of pharmaceutical compound remains low as animal models may not truly representing or lack adequate similarities to the human cell system. To circumvent these problems, embryonic stem cells offer far



(Source: https://bioinformant.com/stem-cells) reaching implications, allowing us to generate a variety of fully differentiated cells, rendering an efficient and diverse tissue population for various pharmaceutical research purposes on the road to drug discovery. Stem cell-based therapy is a 21st century approach of therapeutic intervention which epitomizes a shift from conventional symptomatic treatment strategy to addressing the root cause of the disease process. This is especially a hope for the patients suffering from diseases such as Alzheimer, diabetes, ‘00b ./ 7+\]990-++/0-pplp[lyocardial infarction and other diseases which have always been considered as incurable. Moreover, stem cells provide excellent *in vitro* disease models for drug development. There are more than 100 different diseases that have been treated with stem cell transplantation. The first application of hematopoietic stem cells (HSCs) in 1950 showed that stem cells could be used as drugs to treat diseases.

Potency of stem cells

Stem cells have the remarkable potential to renew themselves. They can develop into many different cell types in the body during early life and growth. The capacity to differentiate into specialized cell types and be able to give rise to any mature cell type is referred to as potency. Potency of the stem cell specifies the differentiation potential i.e., the potential to differentiate into different cell types. Stem cells are classified on the basis of their potency in different types of cells-

Stem cell type	**Description**
Totipotent	Totipotent stem cells can differentiate into embryonic and extra-embryonic cell types. Such cells can construct a complete, viable organism. Totipotent stem cells give rise to somatic stem/progenitor cells and primitive germ-line stem cells.
Pluripotent	Pluripotent stem cells are the descendants of totipotent cells and can differentiate into nearly all cells, i.e. cells derived from any of the three germ layers. These pluripotent cells are characterized by self-renewal and a differentiation potential for all cell types of the adult organism. These are true stem cells, with the potential to make any differentiated cell in the body. Embryonic stem cells come under this category.
Multipotent	Multipotent stem cells can differentiate into a number of cells, but only those of a closely related family of cells. These are true stem cells but can only differentiate into a limited number of types. For example, the bone marrow contains multipotent stem cells that give rise to all the cells of the blood but not to other types of cells.
Oligopotent	Oligopotent stem cells can differentiate into only a few cells, such as lymphoid or myeloid stem cells. The corneal epithelium is a squamous epithelium that is constantly renewing and is oligopotent.
Unipotent	Unipotent cells can produce only one cell type, their own, but have the property of self-renewal, which distinguishes them from non-stem cells. Such unipotent cells include muscle stem cells. Most epithelial tissues self-renew throughout adult life due to the presence of unipotent progenitor cells.

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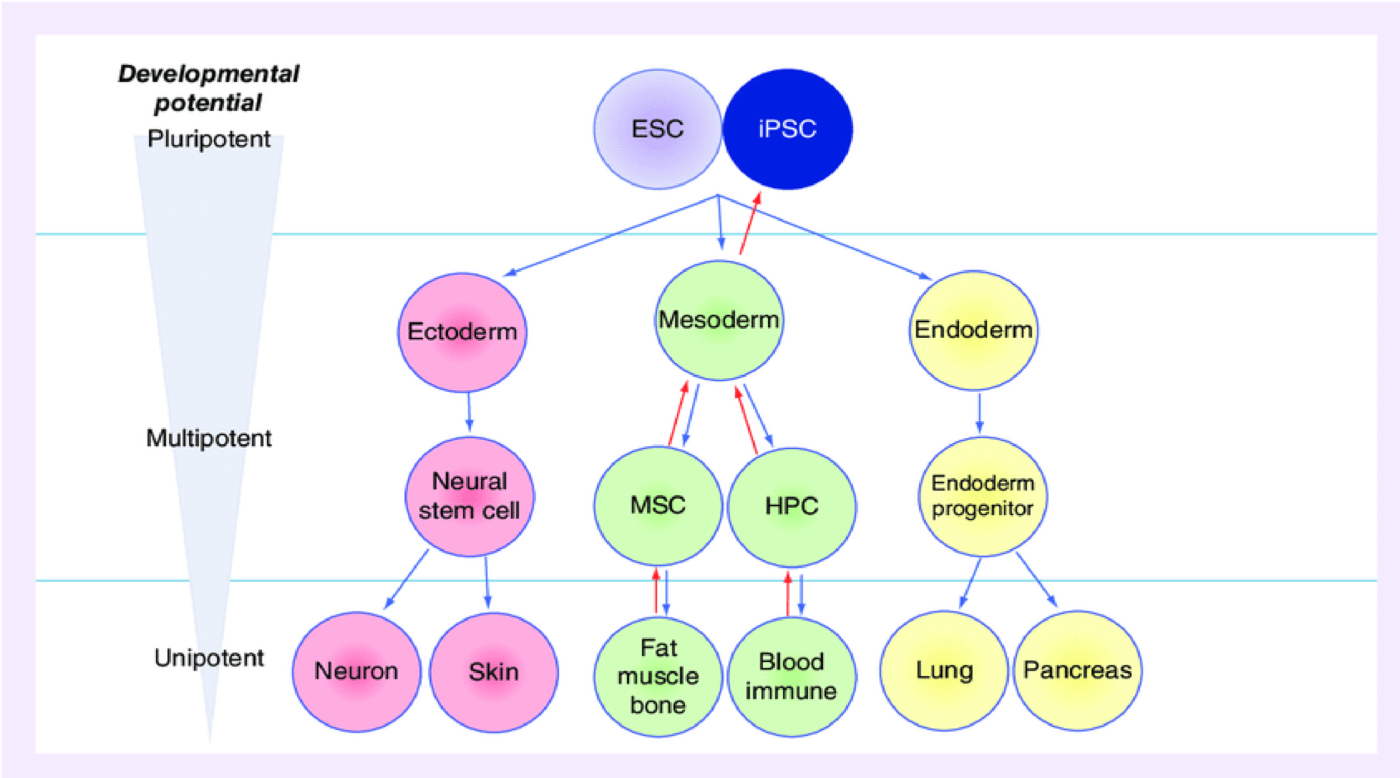

(Source: Karanu *et al.*, 2020)

There are also several other categories of stem cells: Embryonic stem cells, induced pluripotent stem cells, non-embryonic or somatic stem cells (commonly called "adult" stem cells). Adult stem cells are found in a tissue or organ and can differentiate to yield the specialized cell types of that tissue or organ.

Stem cells in drug development

1) Modeling disease in the lab

One of the most significant contributions of stem cells to drug development is their role in disease modeling. By coaxing stem cells to differentiate into specific cell types affected by various diseases, researchers can recreate pathological conditions in the laboratory. These stem cell-derived models provide invaluable insights into disease mechanisms, allowing scientists to study disease progression and test potential therapies in a controlled environment. From neurodegenerative disorders like Alzheimer's and Parkinson's to cardiovascular diseases and cancer, stem cell models offer a platform for exploring the intricacies of complex diseases.

2) Advancing drug screening techniques:

Traditional drug screening methods often rely on animal models or simplistic cell cultures that may not accurately reflect human/animal physiology. Stem cell-based assays offer a more sophisticated alternative, allowing for high-throughput screening of potential drug candidates in human-derived tissues. By exposing stem cell-derived tissues to different compounds, researchers can assess drug efficacy, toxicity, and safety profiles more accurately. This approach not only accelerates the drug discovery process but also reduces reliance on animal testing and enhances the translatability of preclinical findings to human patients.

3) Pioneering personalized medicine:

Stem cells have paved the way for personalized medicine by enabling the generation of patient-specific cell lines. By reprogramming somatic cells into induced pluripotent stem cells (iPSCs), scientists can create cell models that faithfully recapitulate an individual's genetic makeup and disease phenotype. These personalized cellular models open new avenues for tailoring treatments to the unique characteristics of each patient, ultimately improving therapeutic outcomes and minimizing adverse reactions. From predicting drug responses to identifying novel targets for intervention, personalized stem cell-based approaches hold immense promise for the future of healthcare.

4) Enhancing toxicity testing:

Assessing the safety of potential drug candidates is a critical step in the drug development process. Stem cell-derived tissues offer a valuable tool for evaluating drug toxicity in a human-relevant context. Stem cells can provide a valuable source of human cells for testing drugs or measuring the effects of toxins on normal tissues without risking the health of a single human volunteer. By subjecting these tissues to candidate compounds, researchers can assess their impact on cellular function, viability, and physiological responses. Early identification of potential toxicities can help prioritize safer drug candidates for further development, reducing the risk of adverse reactions and failures in clinical trials. To test carcinogenicity of various genotoxic as well as nongenotoxic carcinogens, the Syrian Hamster Embryo (SHE) cell transformation assay is the only available option which often yields imprecise toxicology outcomes.

5) Fostering regenerative therapies:

In addition to their role in drug discovery, stem cells hold tremendous potential for regenerative medicine. Stem cell-based therapies aim to harness the body's innate regenerative capacity to repair damaged tissues and organs. From treating neurodegenerative diseases and spinal cord injuries to regenerating cardiac tissue after heart attacks, stem cell therapies offer hope for patients with debilitating conditions. Ongoing research is exploring novel approaches to optimize the efficacy, safety, and scalability of stem cell-based regenerative treatments, bringing us closer to realizing the full potential of regenerative medicine.

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