Stem Cell Introduction

Stem cell research offers unprecedented opportunities for developing new medical therapies for debilitating diseases and a new way to explore fundamental questions of biology.

Stem cells are unspecialized cells that can self-renew indefinitely and also differentiate into more mature cells with specialized functions at a single cell level (Figure 1). In mammals, there are broadly two broad types of stem cells: adult stem cells that are found in various postnatal tissues and embryonic stem cells, which are isolated from the inner cell mass of blastocysts and pluripotent (Figure 2). In a developing embryo, stem cells can differentiate into all the specialized cells—ectoderm, endoderm and mesoderm (Figure 2)—but also maintain the normal turnover of regenerative organs, such as blood, skin, or intestinal tissues. In adult organisms, stem cells and progenitor cells act as a repair system for the body, replenishing adult tissues.

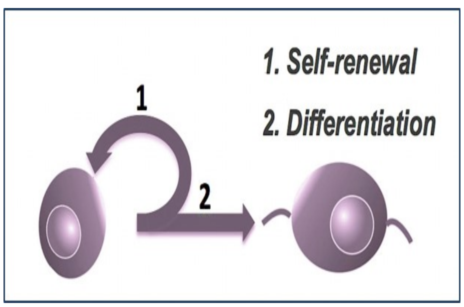

Figure 1. Cell self-renewal and differentiation

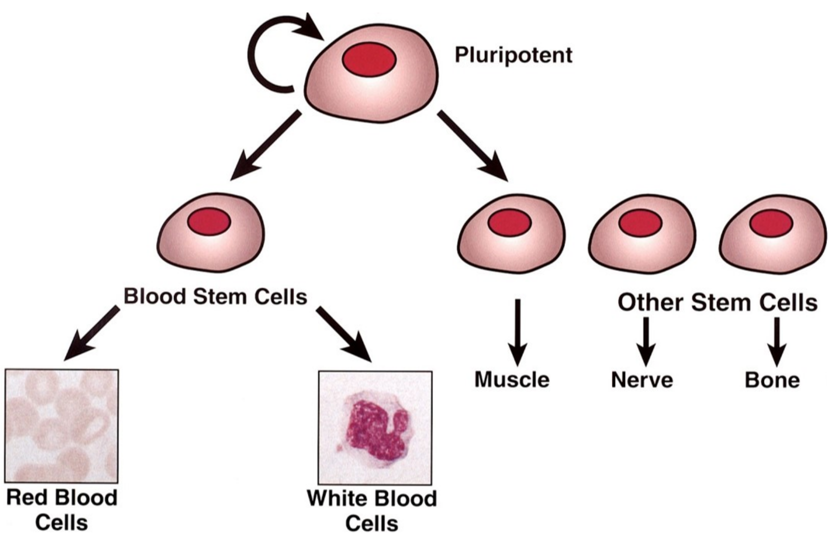

Figure 2. Stem cells are undifferentiated biological cells that can differentiate into specialized cells and can divide (through mitosis) to produce more stem cells. Embryonic stem cells are pluripotent, that is, they can differentiate into all derivatives of the three primary germ layers: ectoderm, endoderm, and mesoderm.

There are important biological differences between adult and embryonic stem cells (ESCs), and among adult stem cells found in different types of tissue. The implications of these biological differences for therapeutic uses are not yet clear, and additional data are needed on all stem cell types. Adult stem cells from bone marrow have so far provided most of the examples of successful therapies for replacement of diseased or destroyed cells. Despite the enthusiasm generated by recent reports, the potential of adult stem cells such as those from blood or skin) to differentiate fully into other cell types (such as brain, nerve, pancreas cells) is still poorly understood and remains to be clarified. In contrast, studies of human embryonic stem cells have shown that they can develop into multiple tissue types and exhibit long-term self-renewal in culture, features that have not yet been demonstrated with many human adult stem cells.

Since adult stem cells have limitations with their potency, unlike ESCs, they are not able to differentiate into cells from all three germ layers. However, reprogramming allows for the creation of pluripotent cells, induced pluripotent stem cells (iPSCs), from adult cells. It is important to note that these are not adult stem cells, but adult cells (e.g. epithelial cells) reprogrammed to give rise to cells with pluripotent capabilities. Using genetic reprogramming with protein transcription factors, pluripotent stem cells with ESC-like capabilities have been derived. The first demonstration of iPSCs was conducted by Shinya Yamanaka and his colleagues at Kyoto University, using the transcription factors Oct3/4, Sox2, c-Myc, and Klf4 to reprogram mouse fibroblast cells into pluripotent cells. Subsequent work used these factors to induce pluripotency in human fibroblast cells by the same group. Drs. Junying Yu, James Thomson, and their colleagues at the University of Wisconsin–Madison used a different set of factors, OCT4, SOX2, NANOG and LIN28, and carried out their experiments using cells from human foreskin. Since then, this group and many others have been able to generate human iPSCs from fibroblasts, blood mononuclear cells and nearly all types of proliferating cells in culture.

For more information, please refer to NIH website https://stemcells.nih.gov/info/basics.htm

Potential Applications

Research is underway to develop various sources from stem cells, and to apply stem cell treatments for neurodegenerative diseases and conditions, diabetes, heart disease, and other conditions. Research is also underway in generating organoids using stem cells, which would allow for further understanding of human development, organogenesis, and modeling of human diseases. Some potential applications are illustrated in the following figure:

Furthermore, induced pluripotent stem cells provide several therapeutic advantages. Like ESCs, they are pluripotent. They thus have great differentiation potential; theoretically, they could produce any cell within the human body (if reprogramming to pluripotency was "complete"). Moreover, unlike ESCs, they potentially could allow doctors to create a pluripotent stem cell line for each individual patient. In fact, frozen blood samples can be used as a source of induced pluripotent stem cells, opening a new avenue for obtaining the valued cells. Patient specific stem cells allow for the screening for side effects before drug treatment, as well as the reduced risk of transplantation rejection. Despite their current limited use therapeutically, iPSCs hold great potential for future use in medical treatment and research.

Nowadays, iPSCs have been used in multiple stages of drug development (Figure 3) to help scientists to detect potential drug toxicities early in the drug development process.

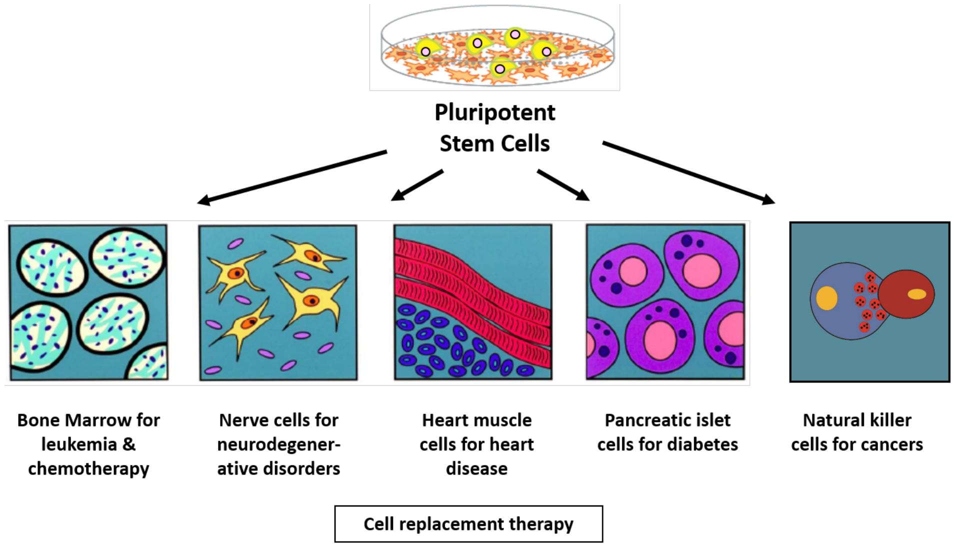

Figure 1. Stem cell holds great promise for regenerative medicine.

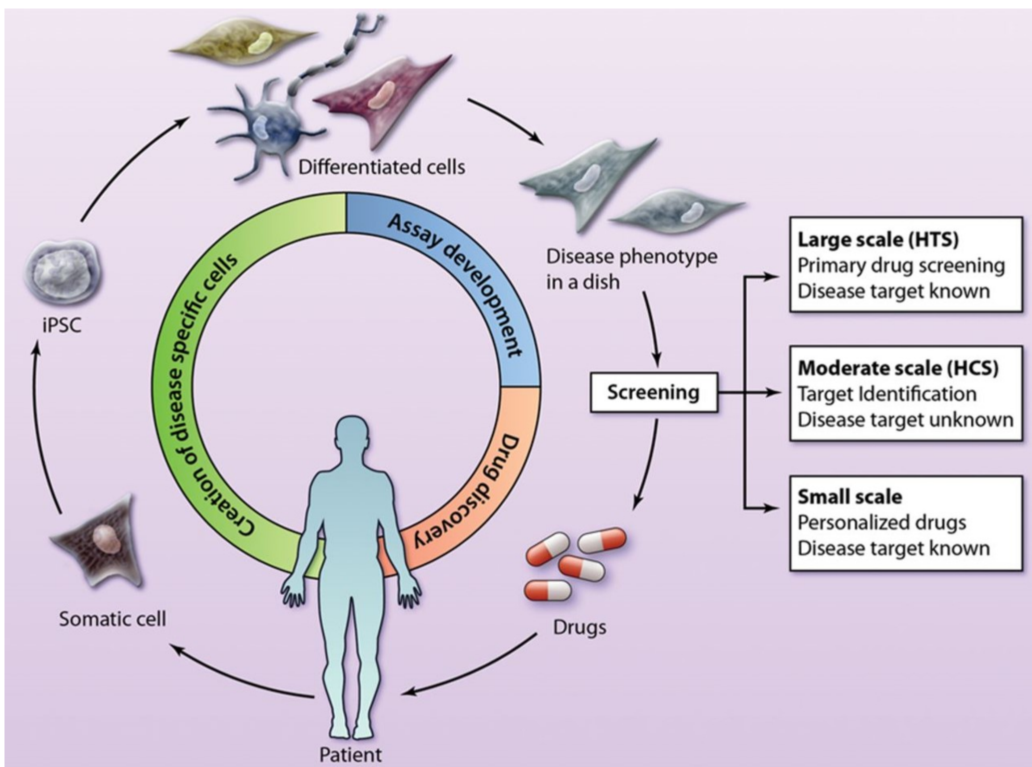

Figure 2. Stem cells derived from patient may be able to illuminate disease pathophysiology, identify novel drug targets and enhance the probability of clinical success of new drugs.

More information about potential applications of stem cells can be found at:
http://www.alzforum.org
https://www.alzheimers.org.uk/site/scripts/documents_info.php?documentID=1039
http://www.eurostemcell.org/alzheimers-disease-how-could-stem-cells-help