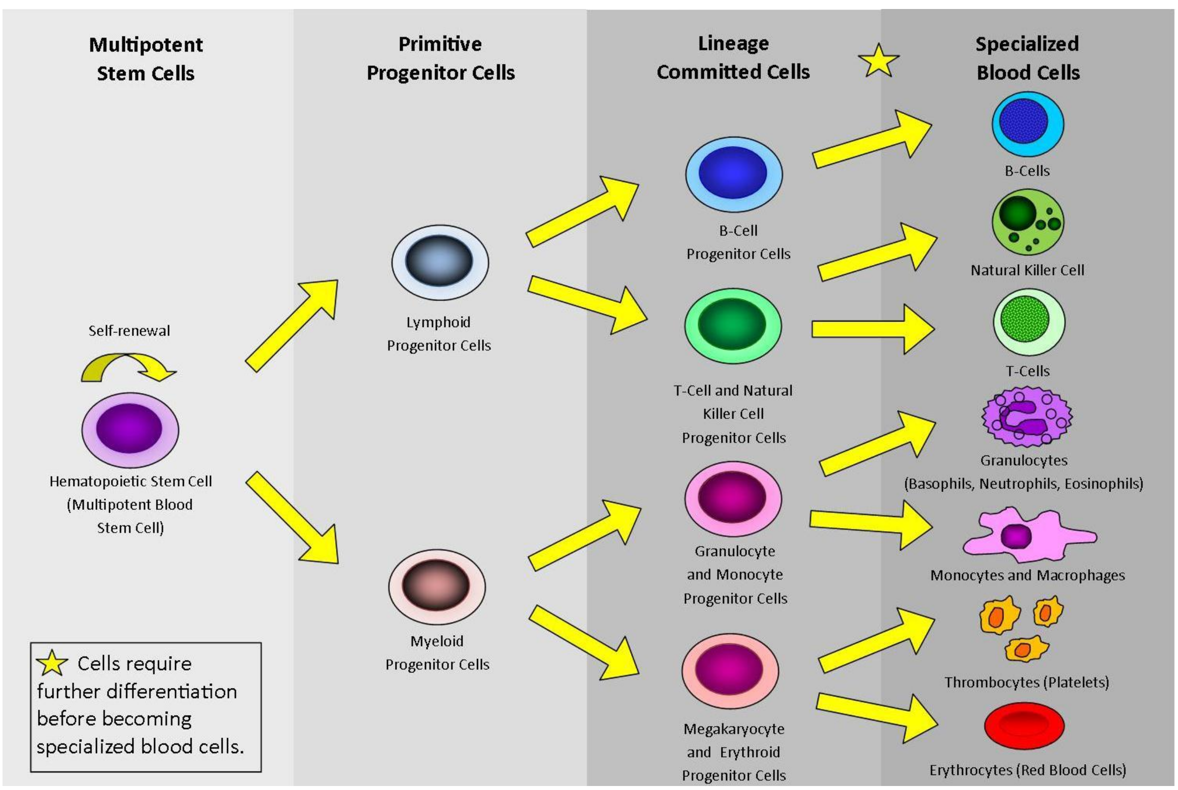
Stem Cells and Types of Stem Cells

What are Stem Cells?

Our bodies are made up of various specialized cell types that are organized into tissues, blood and organs. Examples of specialized cell types include hepatocytes (liver cells), erythrocytes (red blood cells) and cardiomyocytes (heart cells). Specialized cells express unique sets of genes, which allow them to perform specific cellular functions. For example, liver cells produce detoxifying enzymes, which metabolize the toxins that we ingest. All specialized cells come from populations of unspecialized cells known as stem cells. Although stem cells do not themselves perform specific cellular functions, they have the potential to become mature specialized cell types that orchestrate specific cellular functions of the body.

What properties define a stem cell?

Stem cells are defined by two characteristic properties: differentiation and self-renewal. Differentiation is the process where unspecialized cells acquire specific cellular traits, which convert them into specialized cell types. The ability for stem cells to differentiate into all of the specialized cell types of a specific cellular lineage is a key property of stem cells. For example, a blood stem cell is considered a stem cell because it has the ability to differentiate into all the specialized cell types of the blood cell lineage including red blood cells, white blood cells and platelets. To think of it in another way, all the specialized cells of the blood system arise (or 'stem') from a population of blood stem cells.



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The differentiation of stem cells into specialized cells is not an immediate process, but rather differentiation occurs in a series of stages in which cells become more restricted in the types of specialized cells they can give rise to at each stage. As stem cells differentiate, they are said to become committed, which means they can no longer differentiate into cell types outside of the specified lineage. The number of different specialized cell types that a stem cell can give rise to defines the potency of a stem cell. In this regard, stem cells can be broadly classified as totipotent, pluripotent or multipotent.

In addition to being able to differentiate, a stem cell must also self-renew. Self-renewal is the process where, through mitosis, a stem cell divides to produce at least one daughter cell that remains an undifferentiated stem cell. Through self-renewal a stem cell population can be expanded or maintained throughout the life of an organism. For example, when our bodies need more white blood cells to fight off an infection, our blood stem cells self-renew to make more blood stem cells that can then differentiate into specialized white blood cells.

What are the different types of stem cells?

Totipotent Stem Cells

Totipotent (toti = whole, potent = able to) stem cells can give rise to all cell types of an organism, including extraembryonic cells (i.e., cells that comprise supportive tissues of the embryo, such as the placenta). An example of a totipotent stem cell is the fertilized egg of the mammalian embryo (also called the zygote). This single stem cell undergoes a number of cell divisions to generate distinct embryonic tissues (embryo proper) and extraembryonic support tissues (the placenta and nutrient providing yolk sac). During the first few cell divisions of embryonic development, the cells of the embryo remain totipotent. If at this time the embryo splits, the totipotent cells can continue to develop normally to yield identical (or monozygotic) twins.

Pluripotent Stem Cells

Pluripotent (pluri = several, potent = able to) stem cells have the potential to differentiate into all cells of the embryo proper, but not cells of the extraembryonic support tissues (placenta and yolk sac). For this reason, pluripotent stem cells are distinct from totipotent stem cells, and thus cannot continue to develop into an entire organism *in utero*. However, compared to other stem cell populations, pluripotent stem cells are considered unrestricted in developmental potential. In other words, pluripotent stem cells maintain the potential to specialize into every cell type of the mature adult organism. During embryonic development pluripotent stem cells form the inner cell mass of the preimplantation embryo (also called the blastocyst). When inner cell mass cells are removed from the blastocyst and cultured in a dish, these cells can continuously divide and still maintain their potential to differentiate into all cell types of the body. These cells are known as embryonic stem cells (ESCs). In the embryo, cells of the inner cell mass differentiate into three germ layers: mesoderm, ectoderm and endoderm. These germ layers continue to develop into all cell types of the fetus and eventually the mature organism.

Pluripotent stem cells can be derived from two sources: the inner cell mass of the blastocyst (ESCs), or through cellular reprogramming of somatic cells (see section on induced pluripotent stem cells). Remarkably, pluripotent stem cells can be cultured in a dish, and under the appropriate conditions they can be directed to differentiate into various specialized cell types of the organism (i.e., erythrocytes and cardiomyocytes). For this reason, scientists use pluripotent stem cells as a tool to understand the process of cellular differentiation, and to hopefully use these stem cells as a renewable source of specialized cells for cellular therapies (see section on regenerative medicine).

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Multipotent or Tissue-resident Stem Cells

Stem cells also exist in various tissues of the body, such as the bone marrow, brain, skin and muscle. These stem cell populations exist in their host tissues for the lifetime of an organism and are referred to as tissue-resident stem cells (also called adult or somatic stem cells). Tissue-resident stem cells are considered multipotent (multi = many, potent = able to) because they can differentiate into many but not all specialized cell types of an organism. Tissue-resident stem cells are restricted in developmental potential since they can produce all the specialized cells of the resident tissue but not cells of another tissue type. For example, a blood stem cell (also called a hematopoietic stem cell) can differentiate into all cells of the blood system including the oxygen-carrying red blood cells, the white blood cells of the immune system and platelets, but not cells of the nervous system. Despite their limited developmental potential, tissue-resident stem cells have been used to treat human diseases. Blood stem cells extracted from the bone marrow have been used in the treatment of leukemia and other blood borne disorders through bone marrow transplants for over fifty years. Scientists are trying to harness the potential of other stem cell populations in the body to restore damaged tissues involved in degenerative diseases such as diabetes, osteoarthritis and multiple sclerosis.

Tissue-resident stem cells have an important function in the maintenance of tissues during the lifetime of an organism. During the normal ageing process, older cells gradually die; however, the tissue remains functional because tissue-resident stem cells replenish the dead cells with a new wave of specialized cells. Tissue-resident stem cells exist in low numbers in a specialized microenvironment known as a stem cell niche. Under most circumstances, tissue-resident stem cells are quiescent - they are not actively dividing. However, in conditions that require tissue regeneration or repair, factors in the stem cell niche promote self-renewal to expand the number of stem cells that are then able to differentiate into the specialized cell types. Because tissue-resident stem cells are rare and hidden deep within their resident tissues, they can be difficult to identify, isolate and culture. Additionally, because it is difficult to replicate the precise conditions required for stem cell survival, maintenance and growth in a dish, certain tissue-resident stem cell populations have been difficult to culture for long periods in the laboratory. Despite these challenges, scientists have been able to identify, isolate and culture tissue-resident stem cells derived from a number of tissues, including the brain, skin and bone marrow.

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