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Review

Hematopoietic Stem Cells

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ABSTRACT

Hematopoietic stem cells (HSCs) are cells that can differentiate into any type of blood cell and can keep on making blood for the rest of a person's life. There is a role of HSCs in blood production and in many cellular processes such as apoptosis, calcium balance, mitochondria, and reactive oxygen species production. Mutations originating in HSCs)underlie genetic blood diseases. Additionally, HSCs are subject to the effects of aging, impairing their ability to maintain cell polarity. In this chapter, we extensively examined the characteristics and implications of HSCs.

Keywords: Embryonic stem cells, hematopoietic stem cells, long-term hematopoietic stem cells, mesenchymal stem cells, short-term hematopoietic stem cells.

The term "stem cell (SC)"[1-3] was first used in a scientific publication in 1868 by the German biologist Ernst Haeckel. When referring to the single-celled organism's ancestor, Haeckel called it a "Stammzelle" (stem cell). In 1892, Valentin Hacker referred to SCs as cells that produce immature egg cells in sexual organs. In the 1960s, Stevens et al.[4] revealed that the embryonal carcinoma cells they studied were actually pluripotent stem cells (PSCs).[5] In the early 1980s, Gail Martins, Martin Evans, and Matthew Kaufman isolated stem cells from mouse embryos and coined the term "embryonic stem cells (ESCs)" in the literature.[6] Jamie Thompson first cultured human ESCs in 1999, following monkey ESCs.[5] Stem cells are valuable for organ formation during growth, helping a living thing's lifelong tissue function.[7] Stem cells are found in many adult tissues, including blood, umbilical cord blood (UCB), bone marrow (BM), the hematopoietic system, adipose tissue, gametes, the gut, the nervous system, the epidermis, the heart, skeletal muscles.[5,8-10]

Stem cells are one of the main sources of tissue development. In normal processes, SCs are dormant but are activated during certain life cycle processes or in cases of injury.[8] The proliferation and cell cycle differentiation of SCs replaces damaged and aging cells.[11] The ability to reproduce indefinitely is associated with telomerase enzyme activity. The end zone of the deoxyribonucleic acid (DNA) sequence, which regulates the proliferation of cells, has a chain of telomeres. This is slightly different in the SC telomere chain is longer, and telomerase enzyme activity is higher. As a result, SCs can replicate for a long time by self-replication.[12] Basic properties of SCs include self-renewal ability, differentiation (potency) into various cell lineages and tissue types, proliferation capacities, usually arising from a single cell (clonal), unlimited proliferation, and repairing tissue when given to a damaged cell.[5,6,9,13-17]

Stem cells have critical potential in regenerative medicine treatments since they can maintain homeostasis, obtain it easily, regenerate injured or damaged tissue, and can be transferred from the same body to transplanted (autologous) or to different recipients (allogenic) in inheritance within the same species.[5,9,17] Stem cells are called niches, the microenvironment that provides the necessary functions for their growth and change.[9,11] In 1970, the term "SC niche" was proposed for the human hematopoietic system.[11] The idea of being able to

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regenerate damaged tissue is based on the Titan god of fire Prometheus in ancient Greek mythology. Prometheus was condemned to eternal torment by the Greek god Zeus for stealing fire and giving it to humans. Prometheus is chained to a rock, and Zeus sends an eagle, the symbol of Zeus, to eat Prometheus' liver every day. Every night the liver regenerates and grows.[16,18] With the ability of SCs to self-replenish and repair damaged tissue offers hope for an entire future recovery from many diseases.[5] Stem cells are divided into five groups according to their differentiation power; totipotent, pluripotent, oligopotent, multipotent, and unipotent.[6,12,14,16,17]

Stem cells are divided into three groups by origin; ESCs, adult stem cells, and induced pluripotent stem cells (iPSCs), as shown in Figure 1.[16]

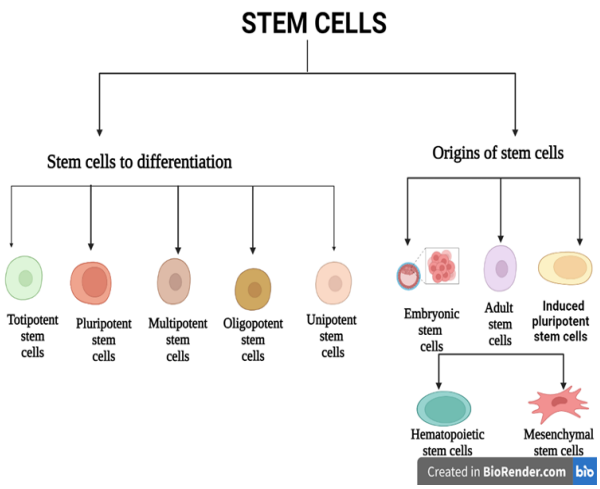

Figure 1: Stem cell diagram

Totipotent Stem Cells

The fertilized egg cell (zygote) is the first ESC that can change into all the cells in the creation of a living being. These cells are called "totipotent cells" (Totus: not fully divided, potential: power) that can do many things.[12,16,17] Totipotent stem cells, which can form embryonal structures, can change all of the cells required for adulthood.[5,12] Totipotent cells are pluripotent, multipotent, and unipotent stem cells that can give rise to embryonic structures such as the umbilical cord, amniotic sac, umbilical cord gel (Wharton's gel), and placenta.[6,12,16,17]

Pluripotent Stem Cells

Pluripotent stem cells are found in the blastocyst stage of the embryo.[12] They have the ability to differentiate into all embryonal structures, but they do not form a new living thing.[6,17] They can become an average of 200 cell types under mandatory cells.[12] Pluripotent stem cells can develop into all cell types from the three germ layers, ectoderm, endoderm, and mesoderm, from which all tissues and organs develop.[6,14,16,17] It can be derived from many adult tissues, such as BM.[6]

Multipotent Stem Cells

Multipotent stem cells can differentiate into a single type of germ layer and can be found in many tissues.[5,6,14,16,17] The bottom section of the hierarchical tree has multipotent stem cells.[5] They are cells from other stages of embryonic development.[12] It is isolated from BM, fat tissue, bone, UCB, amniotic sac, gel (Wharton gel) in the umbilical cord, and peripheral blood.[16] Under laboratory conditions, it can differentiate into a plethora of different cell types.[17]

Oligopotent Stem Cells

Oligopotent stem cells have the ability to self-renew. It can form two or more species in a given cell.[6,13,16] The oligopotent stem structure is made up of BM, adipose tissue, and trabecular bone at the ends of the spine's long bones.[14]

Unipotent Stem Cells

Unipotent stem cells have the ability to self-regenerate and have the ability to change to a limited type of cells.[6,14,16,17] As a result, they are known as stable progenitors since they can support extremely limited cell proliferation (proliferative).[5] It serves in the repair of cells, but PSCs are needed to repair large cell destructions.[17] Unipotent stem cells are derived from BM, fat tissue, and trabecular bone, which is located on the tip of long bones in the vertebrae.[14]

Induced Pluripotent Stem Cells

Induced pluripotent stem cells are derived from reprogrammed matured somatic cells.[14]

They are SCs that grow at speed, they are used in the clinic. Induced pluripotent stem cells are used in areas such as drug development, modeling of diseases, and renewed medicine.[16]

Embryonic Stem Cells

Embryonic stem cells are extracted from a blastocyst, which forms in the uterus 5-6 days after fertilization.[5,14,16,17] Embryonic stem cells have the ability to reproduce infinitely.[17] Embryonic stem cells are defined as pluripotent according to their differentiation power. The ectoderm, where all tissues

and organs develop, can be differentiated into three germ layers, the endoderm, and the mesoderm.[5,16,17] Due to legal and ethical rules, the use of ESCs is limited. For this reason, mesenchymal stem cells (MSCs) are used.[14,16]

Adult Stem Cells

Adult stem cells are derived from mature tissues.[16] Adult stem cells can replenish themselves asymmetrically by splitting.[17] They are the most studied multipotent, hematopoietic, and MSCs capable of multipotent from their group in adult stem cells.[17] Although the entire tissue of the three germ layers is isolated, differentiation capacity is limited. Adult stem cells are advantageous from an ethical standpoint. [16]

Mesenchymal Stem Cell

Mesenchymal stem cells[20-22] are derived from the mesoderm layer, neonatal and adult tissues.[14,17] Many types of cells are called MSCs since they can change and multiply under laboratory conditions. Bone marrow, adipose tissue, fatty tissue, and cord blood are all sources of MSC.[17] Today it is used in the treatment of many diseases; It is used in cartilage destruction, calcification (osteoarthritis), bone damage, osteoporosis, and degenerative diseases.[12]

HEMATOPOIETIC STEM CELLS

Hematopoietic stem cells (HSCs) are constantly self-renewing to protect against stem cell accumulation.[23-30] Hematopoietic stem cells are the only SCs that can differentiate into all types of blood cells capable of producing blood for life.[23,24,28,31-34]

Blood is the body fluid that provides the vital functions of a living being.[35,36] The soul was thought to be in the blood of ancient times.[35]

Hematopoiesis, the production of blood cells to keep the fetus alive, occurs in the yolk sac (vitellus sac) on day 27, the third week of the embryo.[29,37-39] The dorsal aorta is the main site where the first HSCs form.[38] Hematopoietic stem cells are stored in the aorta-gonad-mesonephros region, placenta, fetal liver, thymus gland, spleen, and finally BM.[29,40-43]

Hematopoietic stem cells from the aorta-gonad-mesonephros region and the placenta self-renew. Hematopoietic stem cells in the BM and fetal liver can differentiate into all types of blood cells.[29,40,44-46] Mature blood cells are produced by HSCs found in the BM, as shown in Figure 2.[20,25,27,29,35,47,48]

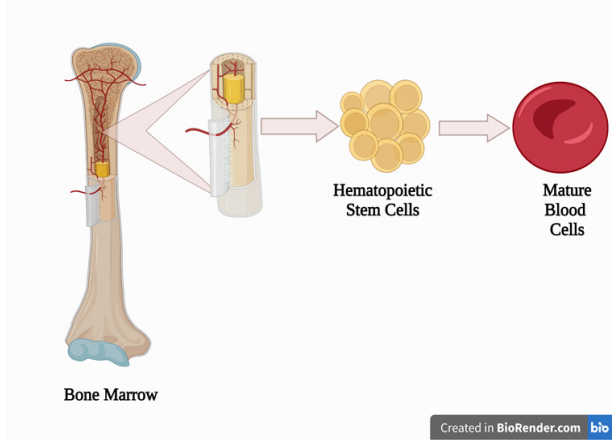

Figure 2: Derivation of mature blood cells from HSCs in the bone marrow.

According to the European Blood and Marrow Transplant Group, a single case of death was recorded from the first 27,770 HSC transplants isolated from the BM during the 1993-2005 period.[14] On a daily basis in an adult individual, HSC produces an average of 1011 blood cells.[23] The most commonly studied species of adult tissue-based stem cells are HSCs.[14] The first traces of HSCs II. It emerged as a result of the observation that blood production was negative as a result of exposure to high amounts of radiation as a result of the atomic bombing in World War II.[38] In the late 20th century, HSCs were isolated from BM. They began to be studied on mice with leukemia for use in treatment. With the successful results of these studies, clinical stem cell transplantation started in 1970 the 1980s and is still used in the treatment of blood diseases today.[14,22,25,49-51]

Many genetic blood disorders are caused by point mutations that affect HSCs and their types, resulting in hematopoiesis or cell type errors.[52,53] Hematopoietic stem cells are obtained from BM, peripheral blood, and cord blood.[17,24,25,50,54] They were realized clinical potential early in the history of renewed medicine.[14] In the emerging field of tissue engineering, HSCs are used in BM transplants, gene therapy, and the production of blood products.[55] It's used as a therapeutic cellular tool for treating blood diseases. The treatment method using hematopoietic stem cells is an HSC transplant (HSCT).[24,36]

There are HSCs in many cellular processes, such as apoptosis, calcium balance, mitochondria, and reactive oxygen species (ROS) production.[34,37,56-58]

In natural conditions and under stress, HSCs are rare (~3,000 to 10,000 per adult human) and are often

inactive, moving in motionless, quiet, and active states to meet the needs of the body.[26-30,59-61]

The very low oxygen level (hypoxic) SC niche is the most suitable environment for the long-term preservation and storage of HSCs, as the energy requirement will be low.[56] Bone morphogenetic protein (BMP), Notch, and Wnt signaling pathways are important for the production of HSCs.[36] Cytokines appear to influence HSC survival through transcriptional or translational regulation of molecules involved in apoptosis. It is not known which of the growth factors plays a crucial role in the survival and proliferation of HSCs. In laboratory studies, IL-3, SCF (ligand for c-kit), Flt-3 ligand, and GM-CSF were found to be valuable, but these results imply that cytokines are overworked. Recently, IL-3 has been found to be involved in the survival of HSCs in the region of the mid-gestational anogenital space (AGM).[37,41,62,63]

To date, many surface markers have been identified to obtain more HSCs. These; CD34, membrane glycoprotein Sca-1, tyrosine kinase receptor (CD117) c-Kit, CD150, and signaling lymphocyte activation molecule (SLAM) are still in use in laboratories today.[37,44,49,51,64] According to CD34 tokens, HSC is divided into two subgroups: 1. Long-term HSCs (LT-HSCs), 2.Short-term HSCs (ST-HSCs).[49]

Long-Term Hematopoietic Stem Cells

Long-term hematopoietic stem cells are uncommon and inactive in the BM.[29,39,49] Demonstrates ability to regenerate long term > six months and longer regenerates.[34,49,50] In the G0 cell cycle during blood production, the appropriate extracellular cannot replicate unless they are separated by signals, they have low mitochondria activity.[29,37] The LT-HSCs can be converted to all adult species.[29] It is known that recurrent infections and chronic inflammation reduce the self-renewal ability of LTR-HSCs, resulting in a decrease and extinction of HSC accumulation. [50]

Short-Term Hematopoietic Stem Cells

Short-term hematopoietic stem cells have limited ability to renew themselves.[29,34,50,59] Short Term<1 month is recreated.[39,49,50]

AGED HEMATOPOIETIC STEM CELLS

Hematopoietic stem cells are known to age. Studies have shown that HSCs obtained from older mice become weaker than HSCs obtained in young mice.[37] It is known that the density of the aged HSCs[65] HSCs in the BM increases with age and loses their function. Another feature of aged HSCs is the loss of cell polarity. The aging of HSCs results from permanent cell cycle arrest, apoptosis, or accumulative cells that cause senescence, and genomic destruction.[20] The senescence of HSCs indicated by defective signaling pathways, DNA damage, epigenetic differences, and high levels of ROS, as well as senescence-related differences in the structure of the BM niche, were thought to be the main cause of HSC senescence. The aged BM niche influences the functional senescence of young HSCs.[34,66] Since the density of HSCs with low levels of ROS decreases with age, ROS production is the hallmark of aging. Adequate ROS levels are important intermediaries of different signal transmission paths. Increased ROS levels affect the life, self-renewal, and change of HSCs. Reactive oxygen species, causing HSC aging and excessive ROS production stimulate apoptosis in HSCs.[67] The bone marrow is a space for cleaning aged HSCs.[20]

BONE MARROW NICHE

Bone marrow contains a stack of inert multipotent stem cells, the main source for the constant renewal of all blood cell types for life.[66,68] Bone marrow is where SCs that do not belong in the newborn are obtained.[6,14] Hematopoietic stem cells are located in the BM.[51,65,69,70] Inside the BM niche, there are personal HSC niches.[59,64,66] The complex vasculature of the BM consists of different small arteries, which are composed of the feeding artery that directs the blood to the extensive vein network.[66] Stem cell niches in 1970 situated special cells appanage chapters with specific is and at this place motionless by means of halt.[6,59] The niche is a special compartment in the BM that protects HSCs found in the extracellular matrix, blood, and synovial fluid.[6,21,24,30,59,71]

Hematopoietic stem cell niches are located around vessels in the spleen and BM. Endothelial cells and stromal cells secrete factors that support the maintenance and regulation of HSC niches.[72] Important features of HSC niches are cell adhesion, regulation of migration, proliferation, control of differentiation, and determination of cell shape.[71] It has an effect on the formation of many cell HSC niches such as osteoblasts, endothelial cells, CXCL12 abundant reticular (CAR) cells, mesenchymal progenitor cells, myelinated Schwann cells surrounding autonomic nerves, macrophages, megakaryocytes, osteoclasts.[24,72]

In conclusion, HSCs produce blood. In an adult person, HSC can produce an average of 1,011 blood cells. There are HSCs in many cellular processes; apoptosis, calcium balance, mitochondria, and ROS

production. The cause of hereditary blood diseases is mutations occurring in HSCs. And the way that these diseases are cured is by transplanting HSC. It is known that HSCs have a role in aging. There are many complex molecular mechanisms in the spatial process and aging of HSCs. Although it's used today to treat blood disorders, we think it's possible to use HSC for treating all diseases with advanced technology and molecular mechanisms illuminated every day.

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