MEDULA ÓSSEA DE OSSOS TUBULARES NO PROCESSO ONCOLÓGICO

BONE MARROW OF TUBULAR BONES IN THE ONCOLOGICAL PROCESS

КОСТНЫЙ МОЗГ ТРУБЧАТЫХ КОСТЕЙ ПРИ ОНКОЛОГИЧЕСКОМ ПРОЦЕССЕ

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RESUMO

A causa do câncer em pacientes permanece um mistério. Várias teorias e suposições não dão confiança na compreensão do processo de câncer. Até que a etiologia do câncer seja estudada, não poderemos avançar apesar do desenvolvimento de tecnologias farmacêuticas e tratamentos inovadores. Para resolver esse problema, pretende-se usar todos os dados relacionados ao desenvolvimento do câncer, mesmo que eles não tenham um vínculo óbvio com a doença. Mesmo quando uma célula cancerígena aparece e começa a criar seu pool de células cancerígenas alteradas, não sabemos. Os médicos diagnosticam o câncer quando o tumor atinge certos tamanhos e afeta a função do órgão. O número de células cancerígenas aumenta muito rapidamente. Os fatores que aceleram essa reprodução das células cancerígenas são muitos, o que significa que ainda não vemos a verdadeira causa. A célula cancerígena mantém os recursos da célula original em graus variados, da semelhança pronunciada à perda quase completa de propriedades celulares saudáveis. Quanto mais a célula estranha é alterada, mais rápido ela cresce e o prognóstico para o paciente se deteriora. O mais preocupante é que a incidência de câncer está aumentando, o que significa que a causa não foi encontrada. As mortes por câncer continuam altas. Este artigo discute o caso de um paciente com um membro amputado por câncer (câncer de pele do pé). Durante um estudo de 10 anos da medula óssea do fêmur, pela primeira vez, a medula óssea foi obtida do fêmur de um paciente com câncer. As descobertas podem ajudar pesquisadores e médicos a entender melhor o processo do câncer e a encarar o problema de maneira diferente.

Palavras-chave: *medula óssea femoral, células-tronco, células-tronco hematopoiéticas, câncer de pele.*

ABSTRACT

The cause of cancer in patients remains a mystery. Various theories and assumptions do not give confidence in understanding the cancer process. Until the etiology of cancer is studied, we will not be able to move forward despite the development of pharmaceutical technologies and innovative treatments. To solve this problem, it is intended to use all data related to cancer development, even if they have no obvious link to the disease. Even when a cancer cell appears and starts creating its pool of altered cancer cells we don't know. Doctors diagnose cancer, when the tumor reaches certain sizes and disorders the function of the organ. The number of cancer cells increases very quickly. The factors that accelerate this reproduction of cancer cells are many, which means that we still do not see the true cause. The cancer cell retains the features of the original cell to varying degrees from pronounced similarity to almost complete loss of healthy cell properties. The more the foreign cell is altered, the faster it grows and the prognosis for the patient is deteriorated. The most worrying thing is that the incidence of cancer is increasing, which means the cause is not found. Cancer deaths remain high. This article discusses the case of a patient having a limb amputated for cancer (foot skin cancer). During a 10-year study of bone marrow from the femur, for the first time, bone marrow was obtained from the femur of a patient with cancer. The findings could help researchers and doctors better understand the cancer process and look at the problem differently.

Keywords: *femoral bone marrow, stem cells, hematopoietic stem cells, skin cancer.*

АННОТАЦИЯ

Причина возникновения рака у больных остается загадкой. Различные теории и предположения не

дают уверенности в понимании онкологического процесса. До тех пор, пока этиология рака не будет изучена, мы не сможем двигаться вперед, несмотря на развитие фармацевтических технологий и инновационных методов лечения. Для решения этой проблемы предполагается использовать все данные, связанные с развитием рака, даже если они не имеют очевидной связи с болезнью. Даже когда появляется раковая клетка и начинает создавать свой пул измененных раковых клеток, мы этого не знаем. Врачи диагностируют рак, когда опухоль достигает определенных размеров и нарушается функция органа. Количество раковых клеток увеличивается очень быстро. Факторов, ускоряющих такое размножение раковых клеток, очень много, а это значит, что мы до сих пор не видим истинной причины. Раковая клетка сохраняет черты исходной клетки в разной степени - от ярко выраженного сходства до почти полной потери свойств здоровой клетки. Чем больше чужеродная клетка изменяется, тем быстрее она растет и прогноз для пациента ухудшается. Самое тревожное заключается в том, что заболеваемость раком растет, а значит, причина не найдена. Смертность от рака остается высокой. В данной статье рассматривается случай пациента, которому ампутировали конечность по поводу рака (рак кожи стопы). Во время 10-летнего исследования костного мозга из бедренной кости впервые был получен костный мозг из бедренной кости больного раком. Полученные результаты могут помочь исследователям и врачам лучше понять процесс развития рака и взглянуть на проблему по-другому.

Ключевые слова: *костный мозг трубчатых костей, стволовые клетки, гемопоэтические стволовые клетки, рак кожи.*

1. INTRODUCTION:

Worldwide, the number of cancer patients is increasing. In overwhelming numbers, these are older people, regardless of gender. The importance of determining the cause of cancer and the overall understanding of the pathogenesis of the process is understood by doctors in all countries. But there is no consensus, most hold the hypothesis of immune system disruption, which stops determining cells are necessary for removal (Weaver, *et al.*, 2008).

The assumption of the cause of the cancer process as a result of the incorrect protective work of the immune system does not explain the whole variety of cancer transformations. The cancer process is based on two important details, cell growth, which can be different and loss of differentiation, the degree of which can differ greatly from the healthy cell of this tissue. In recent years, we have studied the cellular mechanisms of cancer development, the discovery of oncogenes and antioncogenes. So far, this is of interest, but will this data make a difference? By influencing the work of anti-oncogenes, the fight against cancer can be improved, but the problem remains problem (Hernández, 2015).

The most important thing is to understand the function and features of the cancer cell, without fine study of this cell there is no point in looking for a drug for treatment. For now, we're still losing cancer in the fight. In surgical practice, they are periodically forced to amputate the lower limb because it is impossible to preserve it (Nikolaeva *et al.*, 2017). High amputations lead to limited social adaptation of patients (Nikolaeva *et al.*, 2015), significantly reduce the life expectancy of

patients as a result of damage to the contralateral limb and the addition of various complications (Sisla *et al.*, 2011).

The lower limb that is removed during a forced amputation is an important bone marrow depot, where about 25% of the patient's total bone marrow is located in the femoral cavity. Currently, it is proved that the restoration of a damaged organ occurs not only due to the activation of organ regional stem cells, but also due to migration to the zone of damage of MMSCs from other organs, and primarily from the bone marrow (Nikolaeva 2015; Bruder *et al.*, 1994; Gu *et al.*, 2008).

The immediate goal of biomedical research in this area is to use innovative cell technologies (Paladino *et al.*, 2008; Weaver *et al.*, 2008; Krause, *et al.*, 2002). Most of the known technologies for taking bone marrow from living individuals for subsequent bone marrow transplantation (Nolan *et al.*, 2010; Zielins *et al.*, 2016; Rothrauff *et al.*, 2013). use of an isolated stem cell concentrate involves the use of invasive trepanobiopsy techniques (Vos *et al.*, 2006; Jamshidi *et al.*, 1971; Lu *et al.*, 2011). For the first time, mesenchymal stem cells were found in the bone marrow (Norgren *et al.*, 2007; Onodera *et al.*, 2010), but all bone marrow studies were conducted on the bone marrow of flat bones – the red bone marrow (sternal puncture or iliac crest (Hernández 2015; Eagle *et al.*, 2018; Wei *et al.*, 2013). Studies of the bone marrow of tubular bones were not performed due to the impossibility of obtaining it in vivo.

This study aimed a quantitative analysis of multipotent mesenchymal stromal (MMSC) and hematopoietic stem cells (HSCs) in bone marrow samples of amputated limbs in a patient with skin

cancer of the limb.

2. MATERIALS AND METHODS:

2.1. Characteristics of the patient

This case is presented by one patient who had a lower limb amputation after signing informed consent. The indication for amputation was: a trophic ulcer of the limb with signs of malignancy. Obtaining bone marrow samples: The test bone marrow sample was obtained in the operating room immediately after the amputation of the lower limb. Bone marrow was extracted from the lumen of the femur with a Volkmann spoon into a sterile test tube, which was transported to the laboratory.

The bone marrow was subjected to soft homogenization with the addition of a phosphate-salt buffer. The removal of adipose tissue was carried out by 10 minutes of settling the sample, while the fat of the bone marrow rises to the upper layer. Without affecting the upper layer, the lower phase of nucleated bone marrow cells was taken into a new tube and washed twice in a phosphate buffer, followed by centrifugation at 400g for 5 minutes. The cell sediment was resuspended in 300 µl of phosphate buffer, and their number was calculated in the Goryaev chamber. The cell suspension was diluted with a phosphate buffer to a concentration of 107 cells/ml.

2.2. Immunophenotyping of HSCs and MMSCs

The study of the HSC and MMSC phenotype was performed by flow cytometry using direct immunofluorescence. We used ready-made monoclonal antibodies from B.D. Biosciences (Becton Dickinson, USA) labeled with FITC (fluorescein isothiocyanate), P.E. or RD1 (phycoerythrin), PC5, 5 (phycoerythrin-cyanin 5.5), PC7 (phycoerythrin-cyanin 7), and APC (allophycocyanin). The cd90-PE/CD45-PC5,5/CD45RA-PC5,5/CD34-PC7/CD38-APC panel was used for phenotyping HSCs. The human MSC Analysis Kit (Becton Dickinson, USA) containing the CD90-FITC/CD45-PE/CD34-PE/CD11b-PE/CD19-PE/HLA-DR-PE/CD105-PC5, 5/CD73-APC panel was used for phenotyping MMSCs. The distribution of antibodies along the fluorescence channels was carried out in accordance with the principles of panel formation for multicolored cytofluorimetric studies (*Kudryavtsev et al.*, 2015). Sample preparation was performed using the standard method (*Sutherland et al.*, 2018). At least 50,000 cells were analyzed in each sample.

A total of 5 µl of antibodies were added to

a 50 µl bone marrow sample, incubated in the dark for 15 min., 500 µl of BD FACS Solution 1X (Becton Dickinson) lysing solution was added, incubated for 10 min. in the dark, then centrifuged at 1500 rpm for 5 min., the supernatant was drained, the precipitate was washed three times with BD FACS Flow (Becton Dickinson) solution, followed by centrifugation at 1500 rpm for 5 min. 300 µl of BD FACS flow solution was diluted and analyzed using a flow cytometer BD FACSCantoII (Becton Dickinson). For immunophenotyping, HSCs used antibodies to surface antigens of human cells on the recommendation of the manufacturer B.D. Biosciences (Becton Dickinson) PE-Cy7 CD34, PE CD90 and a mixture of negative control antibodies (APC CD38, PerCP-Su5. 5 CD45 and PerCP-Su5. 5 CD45RA). Immunophenotyping of MMSCs was performed using the Human MSC Analysis Kit (Becton Dickinson), which contains conjugated antibodies to MMSC markers (FITC CD90, PerCP-Su5.5 CD105, and APC CD73), and a mixture of negative control antibodies (PE CD45, PE CD34, PE CD11b, PE CD19, and PE HLA-DR).

2.3. Characteristics of the used markers

CD11b is non-covalently associated with $\beta 2$ integrin and is expressed on granulocytes, macrophages, dendritic cells, N.K. cells, and subsets of T and B cells. CD11b It participates in the transfusion of cells such as neutrophils and monocytes, increases the activity of neutrophils, causes granulocyte adhesion, increases the activity of neutrophils (<https://www.biolegend.com/en-us/products/fic-anti-human-cd11b-antibody-8299>).

CD19 is part of the superfamily of immunoglobulins expressed on B cells and follicular dendritic cells. CD19 is involved in the development, activation, and differentiation of B cells. CD34 is a monomeric sialomucin-like type I glycoprophosphoprotein, selectively expressed on most hematopoietic stem/progenitor cells, bone marrow stromal cells, capillary endothelial cells, embryonic fibroblasts, and some nerve tissues. CD34 mediates cell adhesion of lymphocytes by binding to L-selectin and E-selectin ligands.

CD38 is expressed on early hematopoietic progenitors and white blood cells, liver stellate cells, astrocytes, and epithelial cells. CD38 expression can be increased when cells are activated. CD38 catalyzes the production of ADP cyclic ribose. CD38 induces proinflammatory cytokine production and proliferation.

CD90, also known as Thy-1, a member of

the immunoglobulin superfamily, interacts with CD45 during signal transduction during lymphocyte proliferation and differentiation. CD90 is expressed on hematopoietic stem cells, neurons, thymocytes, peripheral T cells, fibroblasts, and stromal cells (Alexa Fluor®). CD45, a panleukocytic marker represented by a single-stranded I-type membrane glycoprotein. CD45 is a signaling molecule that regulates various cellular processes, including cell growth, differentiation, cell cycle, and oncogenic transformation.

CD45RA, a marker of young cells, a variant of the 4-exon compound of CD45 tyrosine phosphatase. The CD45RA isoform is expressed on resting T cells, medullary thymocytes, B cells, and monocytes. CD73 is expressed on mesenchymal stem cells, T and B cells and their derivatives (<https://www.biolegend.com/en-us/products/pe-anti-human-cd73-ecto-5-nucleotidase-antibody-6092>). CD73 performs t-cell costimulation and mediates lymphocyte adhesion to follicular dendritic cells and endothelial cells.

CD105, an integral membrane homodimeric type I protein found on vascular endothelial cells and placental syncytiotrophoblasts. CD105 is not expressed on fibroblasts, but is detected on macrophages and monocytes (<https://www.biolegend.com/en-us/products/pe-anti-human-cd105-antibody-3711>). CD105 expression is increased on activated endothelium in tissues undergoing angiogenesis, such as tumors, or in cases of wound healing or skin inflammation.

HLA-DR, a marker of activated cells, an antigen of the main histocompatibility complex of class II, is expressed on B cells, activated T cells, monocytes/macrophages, dendritic cells, and other non-professional antigen-presenting cells

3. RESULTS AND DISCUSSIONS:

It is known that the amount of bone marrow obtained depends on the level of amputation (Nikolaeva, 2015). The level of amputation in this study was determined individually. The volume of extracted bone marrow was determined by the level of amputation (upper, lower, or middle third of the thigh) and was equal from 10 to 100 ml the largest amount of bone marrow (up to 100 ml) was obtained when the limb was amputated at the level of the upper third of the thigh. Bone marrow is a ready-made drug with many important effects (Zielins *et al.*, 2016; Rothrauff and Tuan, 2013). In this case, the patient was amputated at the level

of the middle third of the thigh. The number of cells in the bone marrow depended on the amount of bone marrow obtained and was approximately 500 thousand to 3 million cells per sample.

On average, the content of MMSC and HSC in the bone marrow of amputated limbs is the same, with a small predominance of the number of MMSCs. This patient was diagnosed with skin cancer of the lower leg, MMSCs were completely absent, it was the only bone marrow that did not have mesenchymal stem cells.

Malignant neoplasms have their own stem tumor cells. This is a small subpopulation of the least specialized cancer cells that have the ability to self-renew and give rise to all cell populations present in the original tumor, including initiating neoangiogenesis and growth of the tumor stroma. In all normal organs and tissues, there are stem cells that are responsible for self-renewal-physiological or reparative regeneration, as well as more specialized and Mature cells that perform the main functions of the organ or tissue. The same is true for tumors. That is, the tumor resembles an organ in structure and, of course, should not differ from the General principle of building biological structures.

It should be noted that for a long time, there was a question of how much cancer stem cells are similar to normal stem cells. And which type of stem cells first begins to change in malignant neoplasm. It was assumed that the tumor begins with changes in completely undifferentiated stem cells, giving rise to all other cells capable of almost unlimited self-renewal. Cancer stem cells in leukemia, these important cells-self-replicating beginnings of tumors do not originate from undifferentiated stem cells, but from their offspring-partially committed non-self-renewing progenitor cells (short-lived cells that can give rise to several, but not all, types of blood cells).

The genetic program of fully developed leukemic stem cells is not the same as that of normal stem cells. This is a very important discovery, which is likely to be typical for most other types of tumors because the most important properties of stem cells are resistance to damaging factors and rare division. These properties do not allow stem cells to accumulate the mass of genetic changes that are necessary for the transformation of a normal cell into a cancer cell. But progenitor cells, on the contrary, actively proliferate, but less plastic than stem cells. They are committed, and the ways of their further development are predetermined by gene expression and limited. In the study of the femoral bone marrow, hematopoietic and mesenchymal

stem cells were determined in the resulting bone marrow. Usually, the number of cells did not exceed 3 million. In this patient with skin cancer, the total number of cells was 75 million, which is much higher than the cell content in comparison with other amputations (25 times). In addition to the absence of MMSCs, this patient had a higher hematopoietic stem cell content than other amputations of 0.025%.

The cause of cancer is not yet clear, and this is a big problem. There are many theories, each representing some aspect and revealing the mystery of the curtain of the origin of the disease. But there are also those who contradict each other, and the general answer to the question—where does cancer come from? "not yet. At the present stage, the immune theory prevails, because the immune system is being suppressed, it is the immune system that first begins to fight mutated cells and destroys them in the first stages.

The etiology is based on several factors: there is an influence both external and internal, on genes during cell division and during normal life. As a result, the cells' genetics break down, and they mutate, turning into cancer cells. After that, such tissues begin to divide and grow endlessly, absorbing, and damaging the nearest organs. The so-called oncogenes were found — these are genes that, under certain conditions and external factors, begin to regenerate any cell in the body into a cancer cell. Until this state, these genes are dormant. That is, a gene is that part of the program code in the body that begins to work only at a certain moment and under certain conditions. That is why the risk of getting sick in people whose parents had cancer is higher than in others. But we must remember that all mutated or damaged cells are fought by our immune system, which constantly scans the body for damage and destroys dangerous cells. If the immune system is lowered, the chance of getting sick in this case is greater.

Today, this theory is the main and most common, which is used by almost all oncologists and scientists. Since all other theories are mostly just a risk factor, whether it's viruses or hepatogenic, it has been observed that most oncocytes occur in an acidic environment. In such an environment, the immune system and all nearby tissues of the body are weakened. And if the environment is made alkaline, then everything will be the opposite, and cancer cells will simply not be able to survive in it, and the immune system will be normal. When the environment is acidic, the immune system is greatly reduced, and the body has a favorable environment for the emergence of

cancer cells. Proponents of the immune theory believe that cancer cells constantly occur in the course of life, but the immune system periodically destroys them. With any impact inside the body and during the regeneration process, our cells grow and repair all damage. And the whole process is controlled by the immune system.

But with the constant occurrence of damage and various disorders, mutation may occur, and control may stop. In the laboratory, under any conditions, no doctor or scientist in the world has been able to turn a normal cell into a cancer cell. They were affecting it with both chemical reagents and radiation. No one in the lab was able to initiate metastasis. The DNA of a cancer cell is 70% similar to that of protozoa. Healthy cells cannot turn into cancer, changing by 70%. They can't move around the body and metastasize, forming new tumors.

The basis of the pathogenesis of all neoplasms is the appearance and reproduction of genetically modified tumor cells with special properties in the body. Tumor cells are changed genetically in the sense that they are able to transmit their pathological properties to descendants: when a tumor cell divides, daughter cells are formed, at least some of which retain their tumor properties. This transfer of tumor properties by cells to descendants can occur in an infinite number of generations. In most cases, the division of tumor cells is the main way to grow primary tumor nodes.

Primary nodes of many types of human and animal tumors are clones, i.e., all cells of this node are descendants of one original tumor cell. The tumor tissue also retains specific antigens of the original tissue. Therefore, successful transplantation of tumors to animals of other species (heterotransplantation) is possible only if the recipient's immune responses are weakened or prevented. This can be achieved in several ways:

1. transplanting tumor cells into tissues where immune responses are weakly induced, such as the anterior chamber of the eye or the brain;
2. introducing immunosuppressive drugs to the recipient;
3. using animals with genetic defects in the immune response as recipients.

Against the background of a weakened immune system, human tumors have already been successfully transplanted to animals. The properties of a population of tumor cells can

change during the growth of primary and secondary tumor nodes, as well as during the passivation of the transplanted tumor. These changes seem to be a consequence of the fact that new genetic variants of tumor cells with properties different from those of most cells in the population may appear in the tumor tissue. If these cell variants have any "advantages" over most tumor node cells, then as a result of selection, these cells will accumulate in the tumor tissue.

Persistent irreversible changes in one or more properties of tumor tissues are called tumor progression. The progression of each tumor can be multi-stage: during the development and growth of this tumor, several different variants of tumor cells may consistently prevail in it. Under normal conditions, each subsequent stage of progression increases the difference between the tumor tissue and the original normal tissue. As a result of tumor growth, its individual cells can break off, get into other organs and tissues, and cause the growth of a secondary, daughter tumor there. This process is called metastasis, and the daughter tumor is called metastasis.

Only malignant neoplasms are prone to metastasis. In this case, the structure of metastases usually does not differ from the primary tumor. Very rarely, they have even lower differentiation, and therefore are more malignant. There are three main ways of metastasis: lymphogenic, hematogenic, and implantation.

- a. The lymphogenic pathway of metastasis is the most frequent. Depending on the ratio of metastases to the lymph flow pathway, antegrade and retrograde lymphogenic metastases are isolated.
- b. The hematogenic pathway of metastasis is associated with the entry of tumor cells into the blood capillaries and veins.
- c. The implantation pathway of metastasis is usually associated with the entry of malignant cells into the serous cavity (when all layers of the organ wall germinate) and from there - to neighboring organs. The fate of a malignant cell that has entered the circulatory or lymphatic system, as well as the serous cavity, is not completely predetermined: it can give rise to a daughter tumor, or it can be destroyed by macrophages.

Currently, there are no changes in the clinical and biochemical parameters of blood that are specific for oncological processes. However, recently, tumor markers (O.M.) have become

increasingly important in the diagnosis of malignant tumors. O.M. in most cases are complex proteins with a carbohydrate or lipid component, synthesized in tumor cells in high concentrations. These proteins can be associated with cellular structures and then they are detected in immunohistochemical studies.

A large group of O.M. is secreted by tumor cells and accumulates in the biological fluids of cancer patients. In this case, they can be used for serological diagnostics. The concentration of O.M. (primarily in the blood), to a certain extent, may correlate with the occurrence and dynamics of the malignant process. In recent years, there have been a number of trends in the epidemiological situation of cancer morbidity and mortality: first, there has been an increase in cancer morbidity and mortality in all countries of the world.

For many years, oncological diseases have confidently occupied the 2nd place in the structure of causes of death after cardiovascular pathology. Since there is now a tendency to reduce mortality from the latter, tumors have a clear chance of becoming a leader among the causes of death in the XXI century. Secondly, the increase in the incidence of tumors is registered in all age groups, but the largest number of cancer patients are people older than 50 years. Proto-oncogenes: these are normal cell genes that are usually inactive. Their activation and transformation into oncogenes that encode certain oncoproteins are accompanied by cell proliferation. Normally, this process takes place in embryogenesis, with age-related growth of organs and tissues, and regeneration. Antioncogenes: Genes that have the opposite effect. The most studied antioncogene p53. Pathological activation of oncogenes or suppression of antioncogenes can lead to tumor growth.

4. CONCLUSIONS:

The development of a pathological process of an oncological nature is affected by the state of the bone marrow. Perhaps this is the root cause of the etiological factor. If mesenchymal stem cells are completely absent, it can be assumed that the body's defenses are exhausted. (in this case, the patient died after four weeks). A significant number of hematopoietic stem cells show that the generalization process occurs through these stem cells.

Mesenchymal stem cells (MSCS) are the precursors of a number of human tissues and have a wide range of possible applications in medicine. The uniqueness of MSCS is that when cells are

grown outside the body, they multiply rapidly, but do not differentiate into anything specific until a unique stimulus is applied. The peculiarity of mesenchymal cells is their ability to give rise to many cells such as muscle cells, bone cells, fat cells, and even neurons, and hematopoietic stem cells only all blood cell lines (<https://www.differencebetween.com/difference-between-mesenchymal-and-hematopoietic-stem-cells/>).

Stem cells are undifferentiated or non-specialized cells present in our bodies. They are able to divide and give the same type of stem cells or differentiate into specialized cells in tissues that have specific functions. These features of stem cells make it possible to apply them in regenerative medicine. These two types of stem cells each perform certain functions. Presumably, hematopoietic stem cells are more differentiated than mesenchymal stem cells. Mesenchymal stem cells are a type of adult stem cells that are multipotent and can differentiate into several different specialized cell types, including cells of neurons, bones, cartilage, muscle, and adipose tissue. These cells are stromal cells or connective tissue cells. Mesenchymal stem cells are small in size with thin processes on the surface.

Pluripotent stem cells are also hematopoietic stem cells, which are especially abundant in the bone marrow of flat bones. Hematopoietic stem cells provide the hematopoietic system with all the necessary cells. Therefore, the process of differentiation of hematopoietic stem cells (hematopoiesis) mainly occurs in the bone marrow. Since hematopoietic stem cells can form any type of blood cell, they are also called blood stem cells. In addition to the bone marrow, there are few hematopoietic stem cells in the peripheral blood and cord blood.

Hematopoietic and mesenchymal stem cells of the bone marrow are multipotent. They can differentiate into different types of specialized cells. They are found in tissues throughout the body. They are also found in cord blood, cord tissue, and placental tissue. Both types of cells are used in the repair and regeneration of damaged tissue. The bone marrow contains both of these types of cells. Mesenchymal stem cells facilitate hematopoiesis.

Mesenchymal stem cells are multipotent stem cells that can differentiate into cells of neurons, bones, cartilage, muscle, and adipose tissue, whereas hematopoietic stem cells are multipotent stem cells that can differentiate into any type of blood cell. The main difference

between mesenchymal and hematopoietic cells is differentiation into different end cells.

Mesenchymal stem cells are now found in many tissues. Hematopoietic stem cells are found in the bone marrow and peripheral blood, especially in cord blood. Both types of cells are of great importance in the treatment of diseases. Mesenchymal stem cells are used in the treatment of diabetes, heart disease, liver disease, stroke injuries, spinal cord injuries, lung cancer, etc., while hematopoietic stem cells are used in the treatment of blood and bone diseases, including blood cancer, autoimmune disorders. And some genetic disorders, etc. So this is also the difference between mesenchymal and hematopoietic stem cells.

Hematopoietic and mesenchymal stem cells ensure the restoration of tissues and organs in case of damage, ensuring the functional state of the body as a whole. Each type of these cells ensures the constancy of the cellular composition of blood and tissues (<https://www.differencebetween.com/difference-between-mesenchymal-and-hematopoietic-stem-cells/>). Mesenchymal stem cells can differentiate into cells of neurons, bones, cartilage, muscle, and adipose tissue, while hematopoietic stem cells can differentiate into blood cells of any type. In addition, mesenchymal stem cells are present in bone marrow. Mesenchymal stem cells have a higher differentiation potential and create a greater variety of cells. In hematopoietic stem cells, it is much lower, they are responsible for the presence

First of all, a hematopoietic cell is a cell that gives rise to all blood cells. Over time, it differentiates and forms certain histogenetic series for white blood cells, red blood cells, and platelets. All these seemingly different cells came from a single cell. The hematopoietic cell is the least immature. The process of its maturation and hematopoiesis begins directly in the red bone marrow under the action of certain components such as macrophages, reticulocytes, cytokines, and growth factors. Stem hematopoietic cells, as well as mesenchymal cells, are used for transplantation, receiving them from the bone marrow and cord blood

By their nature, mesenchymal stem cells (MSCs) and hematopoietic cells share a common ancestor. However, in the process of differentiation, they have taken very different paths histogenesis. Thus, MSCs give rise to the connective tissue itself, the cells lining the vessels, and other mesenchyma derivatives.

Accordingly, getting it will be the same, but

the application will be different. Violation of the processes of regenerative regeneration of an organ, accompanied by a lack of its function, is characterized by growing and not compensated cell death. This is facilitated by violations of information intercellular interaction, regulated primarily by cells of the immune system, and deep inhibition of migration activity of stem and progenitor cells that provide structural replacement of differentiated dead cells. The bone marrow is the only organ in which two different types of stem cells coexist and interact functionally.

The main functions of bone marrow MSCs are 1. Formation of a hematopoietic microenvironment (GIM). 2. The formation of a stromal microenvironment. 3. Participation in morphogenesis. 4. Self-maintenance and recovery of the MSK pool. 5. Participation in homeostatic reactions of the body and in the processes of regeneration, repair, and adaptation of the mesenchymal cell system in normal and pathological conditions.

Mesenchymal stem cells play an important role in the capture of hematopoietic stem cells by the stroma (extracellular matrix and stromal cells), differentiation of hematopoietic cell precursors into Mature cells under the influence of various secretory factors. It is assumed that the study of mesenchymal stem cells of the bone marrow in various diseases of the hematopoietic system will help to detect the mechanisms of regulation and maintenance of normal hematopoiesis.

Along with the increased interest in mesenchymal stem cells, the vast majority of research is conducted with samples of mesenchymal stem cells from healthy subjects and removed from various areas. On the other hand, the presence of various pathologies of hematopoietic cells, such as leukemia, suggested the presence of possible compensatory adaptive changes in mesenchymal stem cells, which are components of the bone marrow microenvironment, the study of which will lead to a better understanding of the mechanism of the development of blood pathology.

5. ETHICS:

Permission was obtained from the Ethics Committee to conduct this study (Protocol No. 56/2014).

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