Review / Derleme

Stem Cell Studies of Professor Doctor Sureyya Tahsin Aygun
Profesör Doktor Süreyya Tahsin Aygün'ün Kök Hücre Çalışmaları

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Abstract: Stem cells are unspecialized cells in the human body. They can differentiate into any cell of the organism and have the ability to renew themselves. Thus, they contribute to the formation of all mature cells in the body and form the basis of every cell, tissue and organ. A stem cell can ensure both self-renewal and differentiation. Süreyya Tahsin Aygün (1895-1981) received his Ph.D. from the Berlin School of Veterinary Medicine in 1926. He focused on cell culture and conducted studies on cardiac stem cells. He observed the regenerative and proliferative capacity of cardiac stem cells. Aygün concluded that young, immature, homogeneous human cells have an unexpected medical effect because animal cells are suitable for animal organism and human cells are suitable for human organism. Aygün's treatment with human cell cultures can be used for many diseases such as heart, kidney, liver and circulatory diseases, stroke, tumors, schizophrenia and multiple sclerosis. Even prolongation of physiological age and life expectancy combined with visible rejuvenation has come into the realm of possibility as pathophysiologically aging cells regress and are replaced by young, viable human cultured cells. Süreyya Tahsin Aygün is the first Turkish scientist to work on stem cells. Süreyya Tahsin Aygün's studies in Germany and Turkey demonstrate his contribution to stem cell and regenerative medicine. Looking at Aygün's other studies, one better understands the importance of joint research between veterinary medicine and medicine. Ord. prof. Aygün's work "Die Human-Zellkultur-Therapie, Neue erfolgreiche Möglichkeiten zur Therapie des Mongolismus und anderer Krankheiten" and other works should be reissued in view of their contribution to today's medical developments.
Anahtar Kelimeler: Stem cell, cell culture, Süreyya Tahsin Aygün, Cell culture history, Stem-cell history

Özet: Kök hücreler insan vücudundaki özelleşmemiş hücrelerdir. Organizmanın herhangi bir hücresine farklılaşabilirler ve kendilerini yenileme yeteneğine sahiptirler. Böylece vücuttaki tüm olgun hücrelerin oluşumuna katkıda bulunurlar ve her hücre, doku ve organın temelini oluştururlar. Bir kök hücre hem kendini yenilemeyi hem de farklılaşmayı sağlayabilir. Süreyya Tahsin Aygün (1895-1981), doktorasını 1926 yılında Berlin Veteriner Fakültesi'nden aldı. Hücre kültürü üzerine yoğunlaştı ve kalp kök hücreleri üzerine çalışmalar yaptı. Kalp kök hücrelerinin rejeneratif ve proliferatif kapasitesini gözlemledi. Aygün, genç, olgunlaşmamış, homojen insan hücrelerinin beklenmedik bir tıbbi etkiye sahip olduğu sonucuna vardı çünkü hayvan hücreleri hayvan organizması için, insan hücreleri ise insan organizması için uygundu. Aygün'ün insan hücre kültürleri ile tedavisi kalp, böbrek, karaciğer ve dolaşım hastalıkları, felç, tümörler, şizofreni ve multipl skleroz gibi birçok hastalık için kullanılabilir. Patofizyolojik olarak yaşlanan hücreler gerileyip yerlerini genç, canlı insan kültür hücrelerine bıraktıkça, fizyolojik yaşın ve yaşam süresinin uzatılması ve gözle görülür bir gençleşme bile mümkün hale gelmiştir. Süreyya Tahsin Aygün, kök hücreler üzerinde çalışan ilk Türk bilim insanıdır. Süreyya Tahsin Aygün'ün Almanya ve Türkiye'de yaptığı çalışmalar, kök hücre ve rejeneratif tıbba yaptığı katkıları ortaya koymaktadır. Aygün'ün diğer çalışmalarına bakıldığında veteriner hekimlik ile tıp arasındaki ortak araştırmaların önemi daha iyi anlaşılıyor. Ord. prof. Aygün'ün "Die Human-Zellkultur-Therapie, Neue erfolgreiche Möglichkeiten zur Therapie des Mongolismus und anderer Krankheiten" adlı eseri ve diğer eserleri günümüz tıbbındaki gelişmelere katkıları açısından yeniden yayınlanmalıdır.
Keywords: Kök hücre, hücre kültürü, Süreyya Tahsin Aygün, hücre kültürü tarihi, kök hücre kültürü tarihi

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1. Introduction

1.1 Stem Cells

Stem cells are cells that have not yet developed their structures or proteins and have not differentiated into the characteristics of a particular cell or tissue type. Therefore, they contribute to the formation of all mature cells in the human body and form the basis of every cell, tissue, and organ. A stem cell can ensure both self-renewal and differentiation. The way to do this is through asymmetric division. However, cell division can be both symmetric and asymmetric. Symmetric division results in identical cells (cloning of cells). Asymmetric division is specific to stem cells and therefore gives rise to cells for differentiation (different from the stem cell), but still associated with cells of the same origin (i.e., still stem cells). In this way, self-renewal is also ensured, and over time a lineage of differentiated cells is generated, which in turn are transferred to the affected tissue or organ (1).

Stem cells are unspecialized cells of the human body. They can differentiate into any cell of an organism and are capable of self-renewal. Stem cells are found in both embryos and adult cells. There are several stages of specialization. The developmental potential decreases with each stage, which means that a unipotent stem cell cannot differentiate into as many cell types as a pluripotent stem cell (2).

In recent decades, several categories of stem cells have been studied in detail: ESCs, fetal stem cells, and somatic/adult stem cells. However, the derivation of pluripotent ESCs, which involves the destruction of a developing embryo, and the use of fetal stem cells from aborted/viable fetal tissue are associated with several ethical and legal problems. In addition, these pluripotent ESCs and possibly fetal stem cells, which have oncogenic properties similar to cancer stem cells, pose a major safety risk because they can undergo unwanted differentiation and carry the risk of malignant transformation after transplantation. For example, teratomas form in vivo when inoculated into mice with severe combined immunodeficiency. The human placenta is a transient but vital organ in reaching stem cells. Pregnancy is an alternative source of stem cells. Not only does the uterus play an important role in determining the optimal growth path of the fetus, but it also provides a rich source of stem cells that may offer additional advantages in proliferation and plasticity compared to adult stem cells. The placenta and umbilical cord have traditionally been considered only biological waste and are usually discarded after birth. This helps to reduce the ethical concerns associated with ESCs. Unlike stem cells from other sources such as bone marrow, adipose tissue, and endometrium, placental and umbilical cord tissue are available in large quantities, and stem cell derivatives can be readily obtained without donors having to undergo invasive surgery (3).

Stem cells are divided into five categories depending on the source from which they are obtained (derived):

Embryonic stem cells

Embryonic cell lines are derived from the epiblast tissue of the blastocyst structure, which is aligned with the inner wall of the blastocyst. The blastocyst is a structure that forms in the early stages of embryonic development, approximately between the 4th and 5th day after fertilization in humans. The blastocyst consists of 50-150 ESCs. It is pluripotent and pluripotent stem cells can form all cell types of each of the three main germ layers of the body (endoderm, mesoderm and ectoderm). Given sufficient and necessary stimulation of a particular cell type, ESCs can differentiate into more than 200 cell types found in the adult body. ESC has the potential to divide in vitro after administration of appropriate stimulants for differentiation, with each daughter cell also remaining pluripotent. Because of their unique unlimited expansion capacity, ESCs are considered a hypothetical cell source for regenerative medicine and a basis for tissue replacement in various diseases.

Fetal stem cells

Fetal stem cells (FSCs) can be isolated from fetal hematopoietic stem cells, fetal mesenchymal stem cells and neural crest stem cells. FSCs have been shown to have higher pluripotency potential and lower immunogenicity compared to adult stem cells (ASCs).

Stem cells from infants

Stem cells from infants can be obtained from perinatal stem cells. These are tissues such as amniotic fluid, umbilical cord and placental membranes. These tissues are composed of several stem cell types that have characteristics of both ESCs and ASCs. Amniotic fluid stem cells, umbilical cord stem cells (UCSCs), and placenta-derived stem cells can be easily obtained at the end of pregnancy. These stromal cells are considered the best candidates for stem cell therapy because they are the richest source of hematopoietic stem cells (HSCs) and mesenchymal stem cells (MSCs).

Adult stem cells

ASCs or somatic stem cells are undifferentiated cells found in postnatal adult tissues and can be unipotent or multipotent. However, due to their lower capacity for cellular differentiation, ASCs are sometimes referred to as progenitor cells. These cells are usually epidermal stem cells (EDSCs), neural stem cells (NSCs), MSCs and HSCs.

Induced pluripotent stem cells

Induced pluripotent stem cells (iPSCs) are generated from somatic stem cells that have been reprogrammed into an ESC -like state. iPSCs have the characteristics of ESCs and can differentiate into three main germ layers. These cells have the advantage of being derived from autologous cells of several patients and have a lower risk of rejection (4).

Origin, aggregation process and plasticity of stem cells: After in vitro fertilization of the native oocyte or in vitro, pluripotent embryonic stem cells form as an inner cell mass in a blastocyst. Stem cells show that their potential spectrum is large and that cells in one tissue can be reprogrammed under experimental conditions and with appropriate culture cells to become mature cells in another tissue from which they are derived. In other words, they can act as multipliers. This is called plasticity and is the basis of cell therapy. Fetal stem cells are found in the organs of the fetus. This source belongs to embryonic body tissue (which can be obtained after spontaneous abortion due to disease, etc.) and then, with proper culture, to reprogrammed cells that act as multipotent cells. The plasticity of stem cells is the ability to give rise to different cell types. The potency of stem cells decreases through differentiation as they develop from early embryogenesis into mature, specialized cells. In this study, stem cell research and the contribution of Süreyya Tahsin Aygün to stem cell research are discussed.

The History of Stem Cell Research

The term stem cell was first used in 1868 by the famous German biologist Ernst Haeckel to describe the property of the fertilized egg cell to form all the cells of the organism. The history of stem cell therapy began in 1888, when German scientist and Darwinist Ernst Haeckel combined the concepts of phylogenesis and ontogenesis to define a stem cell. The stem cell, an evolutionary concept for a primitive cell that decays into all cells and multicellular organisms, is often given as Haeckel's argument from his observations of embryonic development and the distinction between fertilized and unfertilized eggs. When stem cells were first defined by two German zoologists, Theodor Heinrich Boveri and Valentin Haecker, they set out to identify a population of different cells in the embryo that could differentiate into further specifications. When the term stem cells were used by other histo-embryologists such as Theodor Boveri and Valentin Haecker to describe the hereditary properties of germ cells (spermatogonia and oocytes), they officially entered the scientific field and led to the development of the term pluripotency. They precisely determined the self-renewal and differentiation properties of adult cells and a stem cell into somatic (adult) cells (5).

Stem cells have also attracted the attention of researchers working in fields other than

embryology. For example, Artur Pappenheim, working with amphibians at Virchow's Pathological Institute in Berlin on the formation of erythrocytes, referred to the precursors of erythrocytes and leukocytes as "stem cells" Pappenheim knew "stem cells" or "mother cells" as well as their egg or follicle cells, spermatoblasts or spermatogonia, sensory cells or sensory support cells, and noted that they differentiate into ganglion cells or neuroglia and various connective tissue cells. In his later studies with various types of leukemia, Pappenheim found that myelocytes and lymphocytes arise from the same "lymphomyeloblastic multipotent stem cells" (6).

Studies by Franz Ernst Christian Neumann and Alexander Alexandrovich Maximov, histologists who worked on bone marrow research in 1902, have revealed that the first stem cell transplant for treatment purposes was performed by French oncologist George Mathe in 1958. Six nuclear researchers who were accidentally exposed to radioactive material were implanted with stem cells through a bone marrow transplant. Another study by George Mathe in 1963 enlightened the scientific community when he successfully performed a bone marrow transplant on a patient with leukemia. The first allogeneic hematopoietic stem cell transplant (HSCT) was initiated in 1957 by Dr. E. Donnall Thomas, who pioneered it. In this first attempt, all six patients died. in 1969, Dr. E. Donnall Thomas performed the first bone marrow transplant in the United States, but the success of allogeneic therapy remained secret. In 1972, the year cyclosporine (an immunosuppressant) was discovered, the first successes of allogeneic transplantation for aplastic anemia and acute myeloid leukemia in a 16-year-old girl were reported. In the 1960s to 1970s, Friendenstein and colleagues demonstrated the relationship between osteogenic differentiation and a small subpopulation of bone marrow-derived cells in a series of studies on bone marrow aspirates. These cells were then able to differentiate from the hematopoietic population as adherent cells in tissue culture dishes and proliferate rapidly. Another important breakthrough for Friendenstein's team is the discovery that these cells can form the colony-forming unit when bone tissue is formed. Bone marrow was cultured as a suspension culture and then differentiated into osteoblasts, adipocytes and chondrocytes, giving these cells the ability to proliferate and differentiate into different cell types. The discovery of human embryonic stem cells (hESCs) by Caplan in 1991 coined the term "mesenchymal" stem cells, which had previously been called stromal stem cells or "osteogenic" stem cells and is still in common use today. The path of stem cell therapy prior to the 1960s, which began with bone marrow transplantation and evolved into a new therapeutic tool in advanced years, is regenerative medicine for the treatment of numerous incurable diseases, including neurological disorders, pulmonary dysfunction, metabolic/endocrine disorders, reproductive disorders, skin burns, and cardiovascular disease (7).

1.2 Prof. Dr. Süreyya T. Aygün and Stem Cell Studies

Süreyya Tahsin Aygün (1895-1981) entered the Military Veterinary School in Haydarpaşa in 1910. After completing his studies in 1920, which he had to interrupt due to the outbreak of World War I, he joined the army as a first lieutenant of veterinary medicine. During the War of Independence, he worked as a specialist and manager at the Serum and Vaccine Institute in Ankara. He continued his studies at the Faculty of Veterinary Medicine, which he began in Ankara in 1923, and was appointed associate professor on December 22, 1934. Aygün passed the examination opened on September 10, 1924, and completed his specialization in "Bacteriology, Virology and Infectious Diseases" at the Reich Health Office in Berlin. On May 20, 1926, he received his doctorate from the Higher Veterinary School in Berlin. To expand his knowledge, he worked at the Pasteur Institute in France, at the Experimental Therapy in Frankfurt, at the Robert Koch Institutes in Berlin and at the Mödling Serum Vaccine Institute. Aygün returned to his homeland on October 22, 1927, and continued his studies at the Faculty of Veterinary Medicine, which began teaching in Ankara as the faculty of the Higher Institute

of Agriculture, opened in 1933 by decisions of the Ministry of National Defense and the Council of Ministers, and became an associate professor on December 22, 1934. He was promoted to professor on July 24, 1937, and to full professor on October 9, 1944. He was retired on July 13, 1965, in accordance with the College Act. He is the first Turkish scientist to begin work on stem cells. In addition to vaccine research, he conducted studies on cardiac stem cells, focusing on cell cultures. He observed the regenerative and proliferative abilities of cardiac stem cells. Aygün gradually concluded that young immature homogeneous human cells have unexpected medicinal power, just as animal cells are suitable for animal organism and human cells are suitable for human organism. The human cell culture preparations that Aygün produced in his laboratory using his special methods were administered by his colleagues to humans by intravenous or intramuscular injections, where they reached homologous or related cell areas, showed rapid reproductive activity, and restored the structure of the diseased organ and took over functions that were impaired or, better, were shown to be unable to perform. One of Aygün's greatest contributions to our country was to prevent the importation of the drug thalidomide, which was manufactured to treat morning sickness and vomiting in pregnant women. The side effects and damage (babies with missing limbs and handicapped births) of this drug, produced in the 1950s to treat morning sickness and vomiting in pregnant women, were discovered in 1961-1962 and went down in history as the "thalidomide disaster". It is thanks to his initiative that almost no one in our country was affected by this disaster (8).

Prof. Süreyya Aygün continued his studies, which he had started with the aim of growing viruses on tissue culture media, for many years and brought the techniques and developments into the scientific life with his researchs and publications for the first time in our country. The tissue culture medium that Aygün used in this research was his own formula. In addition to this originality, it is of great importance that he introduced an economical technique to laboratory research, which is used instead of the experimental animal (live sheep), which is expensive and cumbersome and always brings the possibility of contamination. Aygün prepared an average of 400 tissue cultures from one sheep embryo by using skin and lung tissues from sheep embryos and the corioallentoic membrane from chicken embryos, obtaining a material that can replace 400 experimental animals. With this research, Aygün introduced the in vitro titration method in parallel with in vivo titrations of sheep pox virus in sheep and achieved success in applying the neutralization assay, which is the basis for virus studies and diagnosis, to tissue cultures. The smallpox vaccine produced by detecting viruses in tissue cultures was successfully used in thousands of animals in Ankara and Konya (9).

Aygün published an article in 1937 entitled "Filterable virus species, cultivation and immunity experiments carried out with them, in the field of artificially cultured living cells (10).

Dr. Aygün taught in graduate seminars the methods of "growing tissue cultures and reproduce viruses on cultures," which he supplemented with his own knowledge during his studies at the Virus Research Institute of Cornel College, to which he was sent for a year in the United States between 1953 and 1954. As a result of his work here, he grew and produced seven different viruses in tissue culture (9).

Süreyya Aygün emphasized with his study and publications that cell material is the best test material for studying the effects of drugs, vaccines, sera and various pathogens on cells and organs, both in our country and internationally. This research method has proven to be useful in comparison with experiments on live animals and is also a method that leads to a meaningful result. These studies brought Aygün into contact with the "Europäischen Unuion gegen den Missbrauch der Tiere" (European Union against the Abuse of Animals) and "Internationalen Vereinigung gegen qualvolle Tierversuche "(International Association against Torturous Animal Experiments)." Through these channels he held scientific conferences in many cities in Europe. In this

way, he made the results of his uninterrupted work known to the scientific world outside the college, where he retired in 1965. Aygün concluded that young, immature, homogeneous human cells have an unexpected medical effect, as animal cells are suitable for animal organism and human cells are suitable for human organism. Süreyya Tahsin Aygün is one of the scientists who have pioneered the field of stem cells worldwide. He has conducted research using fetal transplants from animals and umbilical cord blood transplants to find cures for diseases (9).

According to Dr. Med. Karl Otto Heede, Aygün succeeded in demonstrating through detailed scientific research that human cell culture preparations injected intravenously or intramuscularly reach homologous organs or related cell regions. It was observed that these undifferentiated fetal cells, in the course of rapid proliferation, could rebuild the diseased organ and take over its impaired or weakened function. In this way, it was thought, injection implantation could successfully replace organ transplantation, which is unsuccessful in most cases. Aygün achieved the most sensational success in treating mongoloid children by injecting fetal human cells. A few days after the injection, the cell culture selected according to the type of disease began to develop, resulting in complete normalization with continued cell division in the dysfunctional brain centers (9).

The methods of cell culture injection prepared by Aygün in the laboratory and applied by his colleagues were used in about 2000 mongoloid children and patients with nodular bovine exanthema (Lumpy Skin Disease, LSD) in the "Aygun Institute" founded on his behalf in Germany (8).

The treatment with human cell cultures developed by Aygün can be used not only for all diseases of the central nervous system such as schizophrenia or multiple sclerosis, but also for heart, kidney, liver and circulatory diseases, paralysis and tumors. In this way, unimaginable healing possibilities arise for diseases that were considered incurable with the previously known treatment options. Even the extension of physiological age and life expectancy in conjunction with visible rejuvenation have moved into the realm of possibility, as pathophysiologically aging cells regress and are replaced by young, vital human cultured cells (10).

In the last half of the twentieth century, Dr. Aygün added a new international collaboration between physicians and veterinarians that provided unforgettable examples in the history of medicine in tuberculosis, tetanus and cancer (9). Aygün summarized all his researches in his work entitled "**Die Human-Zellkultur-Therapie**, Neue erfolgreiche Möglichkeiten zur Therapie des Mongolismus und anderer Krankheiten", which we could find only in Germany. In this article, only his studies on stem cells were discussed (Figure 1).

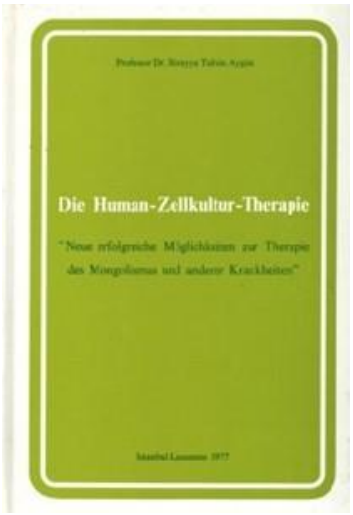

Figure 1. Süreyya Tahsin Aygün's book on cell culture.

2. Discussion and Conclusion

Süreyya Tahsin Aygun, whose rightful place in the history of stem cells is not yet sufficiently known, should definitely be made known to young researchers. Murat Avcı in his article "*Stem Cell; Definition and General Properties, Uses, History, Surface Markers*" describes the history of stem cells chronologically from the discovery of the cell to the present in 1967, while Prof. Dr. Süreyya Tahsin Aygün was among the first scientists to perform stem cell therapy with his studies. In his article, he highlights that Dr. Aygün's studies on the proliferation of embryonic carcinoma cells in a culture medium were one of the first important steps in this field and that he explored the treatment of various diseases with grafts from fetal and umbilical cord blood in animals (11). The manuscript "*Stem Cell Mediated Cardiovascular Repair*" by Serkan Durdu and colleagues states that in the organism injected with Aygün's heart cell culture, the cells settled in the heart and regeneration of the diseased area was observed within 35-45 days after a propagation period of 2-7 months (12).

Thousands of similar works by Aygün are used day by day with advanced technological capabilities. In a clinical study by Theresa R. Cassino et al, significant improvement was observed by transferring stem cells to the area of myocardial infarction (13).

The work of Mohammad T. Alrefai et al, titled *Cardiac Tissue Engineering and Regeneration Using Cell-Based Therapy*, is considered to be at the forefront of stem cell therapy and tissue engineering, the current research for the treatment of heart disease. These technologies are being used to make advances in the irreversible treatment of chronic heart failure and acute ischemic myocardial injury. Current clinical management in the treatment of cardiac ischemia addresses restoration of blood flow to the heart. Discusses allogeneic and autologous stem cell trials, including the use of embryonic, bone marrow, adipose tissue, and adult and cardiac stem cells (14).

The study by Fisher SA et al, entitled Stem cell treatment for acute myocardial infarction (Review), collected data from patients in whom autologous bone marrow-derived cells were used in patients diagnosed with AMI. Studies with a total of 2732 participants (1564 cell treatments, 1168 controls) were scanned: Data from the Cochrane Central Register of Controlled Trials (CENTRAL 2015, Issue 2), MEDLINE (1950-March 2015), EMBASE (1974-March 2015), CINAHL (1982- March 2015), and Transfusion Evidence Library (1980- March 2015) were searched. In addition, several international and ongoing databases and relevant conference proceedings through January 2011 were searched in March 2015. The results of this

review suggest that there is insufficient evidence to support meaningful cell therapy for AMI patients. However, most of the evidence comes from small studies that do not differ in clinically relevant outcomes. More studies are needed that are sufficiently powered, and until then, approval of this app is not proven (15).

The study by Keelin O'Donoghue & Nicholas M. Fisk, *Fetal stem cells*, states that central nervous system (CNS) stem cells have been characterized for the first time and derived from fetal rat or mouse brains. Their differentiation potential is more limited than that of pluripotent embryonic stem cells, but they can still be used to derive the three major CNS cell types: Neurons, astrocytes, and oligodendrocytes. Neural stem cells have also been isolated from the adult human CNS, although they appear to have a more limited fate. One of the most important cell sources for replacement therapy of the injured nervous system is neural tissue from fetuses. Transplantation of fetal neural cells has been used in various models of brain injury, and fetal cortical grafts survive and function in the injured rat brain. There is existing experience with the transfer of human fetal neural tissue in neurodegenerative diseases. Fetal mesencephalic progenitor cells have been transplanted into the striatum of many patients with Parkinson's disease. While these grafts result in symptom improvement, they also have unacceptable side effects. These problems and the limited supply of fetal tissue (up to six fetal stem cells are needed to treat one patient) have led to a search for alternatives (16).

Amniotic fluid and placenta, which Aygün dealt with for many years, are still being studied today. The review article "Amniotic fluid and placental stem cells" by Dario Fauza summarizes this topic: Amniotic fluid and placenta may provide the least invasive access to various stem cell populations, including mesenchymal and possibly embryonic stem cells. Mesenchymal stem cells are much more abundant and easier to isolate. However, embryonic-like stem cells cannot always be isolated using current methods and account for less than 1% of cells found in amniotic fluid or placental samples. To date, the potential for several cell lineages has been demonstrated in mesenchymal amniocytes, promiogenic progenitor cells, fibroblasts, adipocytes, and osteocytes. Amniocytes and placental cells expressing markers also found in embryonic stem cells have already been distinguished. Myogenic, adipogenic, osteogenic, nephrogenic, neural, and endothelial cells, but not necessarily from a uniform population of undifferentiated cells. However, recent experimental studies have revealed a number of promising new therapeutic approaches using these cells for tissue engineering, cell transplantation, gene therapy, and other purposes (17).

The importance of this issue is highlighted in the study titled "Stem Cells: A Historical Review about Biological, Religious, and Ethical Issues" by Ioannis Alexandros Charitos et al. In this review, the authors highlight that stem cell research can be used in hematology (e.g., bone marrow transplantation), ophthalmology (e.g., age-related macular degeneration), and endocrinology (diabetes) for drug discovery and development. In the experimental study by Firdevs Gurer (2009) entitled "Therapeutic use of cloning: Osmangazi Turk Identical Embryonic Stem Cells and Embryonic Stem Cell Transfer To Diabetic Mice", diabetic mice were treated with mouse dental pulp embryonic stem cells (18).

Stem cell-based therapy is an important branch of regenerative medicine with the goal of improving the body's repair mechanisms by stimulating, modulating, and regulating the body's stem cell population and/or renewing the cell pool for tissue homeostasis and regeneration. Since the definition of stem cells with their unique self-renewal and differentiation properties is well established, they have been the subject of numerous basic research and clinical studies and have been identified as potential therapeutics. Since the main concern of regenerative medicine is tissue regeneration and cell replacement, different types of stem cells have been used to achieve these goals, including human pluripotent stem cells (hPSCs), multipotent stem cells, and progenitor cells. Concerns remain among the public about the safety of stem cell therapy, as its efficacy has not been

fully proven and research and treatment are ongoing. As regenerative medicine continues to evolve, stem cell therapy is a new technique that utilizes the unique properties of stem cells, including self-renewal and differentiation, to regenerate damaged cells and tissues in the human body or replace these cells with new, healthy, and fully functional cells by administering exogenous cells. therapeutic approach. Süreyya Tahsin Aygün's studies in Germany and Turkey show his contributions to stem cell and regenerative medicine. When Dr. Aygün is considered along with his other studies, one better understands the importance of joint research between veterinary medicine and medicine. Prof. Aygün's work "**Die Human-Zellkultur-Therapie,** Neue erfolgreiche Möglichkeiten zur Therapie des Mongolismus und anderer Krankheiten" and other works should be reprinted given their contribution to today's medical developments.

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