

General

Stem cells: a comprehensive review of origins and emerging clinical roles in medical practice

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Keywords: Stem cells, regenerative medicine, bone marrow, umbilical cord, placental tissue

<https://doi.org/10.52965/001c.37498>

Orthopedic Reviews

Vol. 14, Issue 3, 2022

Stem cells are types of cells that have unique ability to self-renew and to differentiate into more than one cell lineage. They are considered building blocks of tissues and organs. Over recent decades, they have been studied and utilized for repair and regenerative medicine. One way to classify these cells is based on their differentiation capacity. Totipotent stem cells can give rise to any cell of an embryo but also to extra-embryonic tissue as well. Pluripotent stem cells are limited to any of the three embryonic germ layers; however, they cannot differentiate into extra-embryonic tissue. Multipotent stem cells can only differentiate into one germ line tissue. Oligopotent and unipotent stem cells are seen in adult organ tissues that have committed to a cell lineage. Another way to differentiate these cells is based on their origins. Stem cells can be extracted from different sources, including bone marrow, amniotic cells, adipose tissue, umbilical cord, and placental tissue. Stem cells began their role in modern regenerative medicine in the 1950's with the first bone marrow transplantation occurring in 1956. Stem cell therapies are at present indicated for a range of clinical conditions beyond traditional origins to treat genetic blood diseases and have seen substantial success. In this regard, emerging use for stem cells is their potential to treat pain states and neurodegenerative diseases such as Parkinson's and Alzheimer's disease. Stem cells offer hope in neurodegeneration to replace neurons damaged during certain disease states. This review compares stem cells arising from these different sources of origin and include clinical roles for stem cells in modern medical practice.

I. INTRODUCTION

Stem cells are a unique population of cells present in all stages of life that possess the ability to self-renew and differentiate into multiple cell lineages. These cells are key mediators in the development of neonates and in restorative processes after injury or disease as they are the source from which specific cell types within differentiated tissues and organs are derived.¹ Within the neonate stage of life stem cells serve to differentiate and proliferate into the multitude of cell types and lineages required for continuing development, while in adults their primary role is regenerative and restorative in nature.² Stem cells have unique properties that set them apart from terminally differentiated cells allowing for their specific physiological roles.

The ability of stem cells to differentiate into multiple cell types is termed potency, and stem cells can be classified by their potential for differentiation as well as by their origin. Totipotent or omnipotent stem cells can form embryonic tissues and can differentiate into all cell lineages required for an adult. Pluripotent stem cells can differentiate into all three germ layers while multipotent stem cells may only differentiate into one kind of germ line tissue. Oligopotent and unipotent stem cells are the type seen in adult organ tissues that have committed to a cell lineage and can only diversify into cell types within that lineage.¹ Embryonic stem cells are derived from the inner cell mass of a blastocysts and are totipotent. The range of their use is typically restricted due to legal and ethical factors and for this reason mesenchymal stem cells are typically preferred. Mesenchymal stem cells can be isolated from a variety of both

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neonate and adult tissues but still maintain the ability to differentiate into multiple cell types allowing for their clinical and research utilization without the ethical issues associated with embryonic stem cells.³

Another key feature of stem cells is their ability to self-renew and proliferate providing a continuous supply of progeny to replace aging or damaged cells. During the developmental phase this proliferation allows for the growth necessary to mature into an adult. After the developmental phase has concluded, this continued proliferation allows for healing and restoration on a cellular level after tissue or organ injury has taken place.² These physiological and developmental characteristics make stem cells an integral part in the field of regenerative medicine due to their ability to generate entire tissues and organs from just a handful of progenitor cells.

Stem cells began their role in modern regenerative medicine in the 1950's with the first bone marrow transplantation occurring in 1956. This breakthrough shed light on the potential treatments possible in the future with further development and refinement of clinical techniques and paved the way for the stem cell therapies that are now available.^{4,5} Stem cell therapies are now indicated for a range of clinical conditions beyond traditional origins to treat genetic blood diseases and have seen substantial success where other treatments have fallen short. One emerging use for stem cells is their potential to treat pain states and neurodegenerative diseases such as Parkinson's and Alzheimer's disease. Stem cells offer the hope in the setting of neurodegeneration to replace the neurons damaged during the pathogenesis of certain diseases, a goal not achievable utilizing current technologies and methods.⁶

Organ bioengineering is yet another rapidly developing and exciting new application for stem cells with both clinical and research implications.⁷ Immunosuppression free organ transplants are now a possibility with the advancement organ manufacturing utilizing the patient's own cells.⁸ This along with the potential for eliminating organ donor waiting lists is an enticing prospect, but many technological developments are necessary before this technology can be implemented in clinical settings on a wide scale. Research has already benefitted greatly from this field because organ like tissues can be grown in lab settings to model disease progression. This offers the potential to develop new treatments while determining their efficacy on a cellular level without risk to patients.^{9,10}

Currently one of the most prolific clinical uses of stem cells in the field of regenerative medicine is to treat inherited blood diseases. Within these diseases a genetic defect or defects prevents the proper function of cells derived from the hematopoietic stem cell lineage. Treatment includes implantation of genetically normal cells from a healthy donor to serve as a lifelong self-renewing source of normally functioning blood cells. However these treatments are limited by the availability of suitable donors.¹¹

Stem cells can be derived from multiple sources including adult tissues or neonatal tissues such as the umbilical cord or placenta. Embryonic stem cells have been utilized in the past for research, but ethical concerns have led to them

being replaced largely by stem cells derived from other origins.¹² Common tissues from which adult oligopotent and unipotent stem cells are isolated include bone marrow, adipose tissue, and trabecular bone.¹³ Bone marrow has traditionally been the most common site from which to extract non neonatal derived stem cells but involves an invasive and painful procedure. Peripheral blood progenitor cells have been utilized to avoid harvesting cells from bone marrow. However, this technique has issues and risks of its own and was initially a less potent source of stem cells. It is also now known that stem cells differ in their proliferative and differentiation potential based on their origin. Cells sourced from umbilical Wharton's jelly and adipose tissue were found to proliferate significantly more quickly than cells sourced from bone marrow and placental sources.^{14,15}

A rapidly advancing source of stem cells known as induced pluripotent stem cells (iPSC's) are now being utilized clinically as well. These iPSC's are derived from somatic cells that have been reprogrammed back to a pluripotent state utilizing reprogramming factors and require less invasive techniques to harvest in comparison to traditional sources.^{16,17} Once returned to a pluripotent state, the cells then undergo a process called directed differentiation in which they are converted into desired cell types. Directed differentiation is achieved by mimicking microenvironments and extracellular signals in vitro in a manner that produces predictable cell types.¹⁸ In the future, this technique could provide a novel form of personalized gene therapy in which oligopotent or unipotent cells are procured from tissue, reprogrammed back to a less differentiated state, and then reintroduced into a different location within the patient. Work is also being done to combine this technique with modern gene editing methods to provide an entirely new subset of therapies.¹⁹ This method of transplantation would greatly reduce the chance for rejection and does not require a suitable donor, as the cells are sourced from the patient being treated.^{20,21}

II. BONE MARROW AS A SOURCE FOR STEM CELLS

Stem cells are required by self-renewing tissues to replace damaged and aging cells because of normal biological processes. Both myeloid and lymphoid lineage cells derived from hematopoietic stem cells are relatively short-lived cell types and require a continuous source of newly differentiated replacement cells.²² Hematopoietic stem cells (HSC's) are those that reside within the bone marrow and provide a source for the multiple types of blood cells required for normal physiological and immunological functions. These cells inhabit a physiological niche which allows them to undergo the process of asymmetric division. When stem cells divide asymmetrically the progeny of the division includes one identical daughter cell but also results in the production of a differentiated daughter cell. Differentiation of these daughter cell into specialized cell types is guided by certain microenvironments, extrinsic cues, and growth factors that the cell comes in contact with.^{23,24} This mechanism allows for bone marrow stem cell numbers to stay relatively con-

stant despite sustained proliferation and differentiation of progeny taking place.^{22,25,26}

HSC's are the most studied class of adult tissue derived stem cells and their clinical potential was recognized early in the history of regenerative medicine. At the beginning of the 1960's, HSC's were isolated from bone marrow and therapeutic models in mice induced with leukemia were developed in order to show the efficacy of bone marrow derived stem cell treatments. Success in these experiments led to further refinement of techniques and by the 1970's and 80's clinical stem cell transplants were a regular occurrence and began to make the impact on blood diseases that we continue to see today.^{27,28}

Bone marrow has historically been the predominant harvesting site for stem cell collection due to its accessibility, early identification as a source, and lengthy research history. Isolating stem cell from bone marrow involves an invasive and painful surgical procedure and does come with a risk hospitalization or other complications. Patients also report increased post procedural pain and pre-procedural anxiety when compared with other harvesting techniques.^{29,30} Bone marrow however has proved to be a denser source of cells than other harvesting methods yielding 18 times more cells than peripheral blood progenitor cell harvesting techniques initially. As technology and methods improved however, it was found that treating patients with a cytokine treatment prior to peripheral blood progenitor cell harvesting mobilized many of the desired cells into the blood stream and drastically increased the efficacy of this technique, making it clinically viable.³¹⁻³³ In a double blinded randomized study 40 patients underwent bone marrow and peripheral blood progenitor cell collections and the yield of useable harvested cells were compared. It was found that blood progenitor cell collection yielded significantly more useable stem cells and patients were able to undergo the collection procedure more frequently when compared to the bone marrow harvesting method.³² This, coupled with the invasiveness and risks associated with harvesting stem cells from bone marrow have increased peripheral blood progenitor cell collections popularity.

Overall, bone marrow as a reservoir of stem cells continues to be a clinical and research necessity related to its well understood and documented history as a source of viable stem cells and track record of efficacy. According to the European Group for Blood and Marrow Transplantation, only one fatal event was recorded stemming from the first 27,770 hematopoietic stem cell transplants sourced from bone marrow during the period of 1993-2005.³⁴ This undeniable track record of safety coupled with clinicians' experience performing bone marrow transplant procedures guarantees the continued use of bone marrow as a source of HSC's for the near future.

III. AMNIOTIC CELLS AS A SOURCE FOR STEM CELLS

Historically, the two most common types of pluripotent stem cells include embryonic stem cells (ESCs) and induced

pluripotent stem cells (iPSCs).³⁵ However, despite the many research efforts to improve ESC and iPSC technologies, there are still enormous clinical challenges.³⁵ Two significant issues posed by ESC and iPSC technologies include low survival rate of transplanted cells and tumorigenicity.³⁵ Recently, researchers have isolated pluripotent stem cells from gestational tissues such as amniotic fluid and the placental membrane.³⁵ Human amnion-derived stem cells (hADSCs), including amniotic epithelial cells and amniotic mesenchymal cells, are a relatively new stem cell source that have been found to have several advantageous characteristics.^{35,36}

For background, human amniotic stem cells begin emerging during the second week of gestation when a small cavity forms within the blastocyst and primordial cells lining this cavity are differentiated into amnioblasts.³⁶ Human amniotic epithelial stem cells (hAESC) are formed when epiblasts differentiate into amnioblasts, whereas human amniotic mesenchymal stem cells (hAMSCs) are formed when hypoblasts differentiate into amnioblasts.^{35,36} This differentiation occurs prior to gastrulation, so amnioblasts do not belong to one of the 3 germ layers, making them theoretically pluripotent.³⁵⁻³⁷

Previously, pluripotency and immunomodulation are qualities that have been thought to be mutually exclusive, as pluripotency has traditionally been regarded as a characteristic limited to embryonic stem cells whereas immunomodulation has been a recognized property of mesenchymal stem cells.³⁶ However, many recent studies have found that these two qualities coexist in hADSCs.^{35,36}

In recent years, hADSCs, including human amniotic epithelial stem cells (hAESC) and human amniotic mesenchymal stem cells (hAMSCs) have been attractive cell sources for clinical trials and medical research, and have been shown to have advantages over other stem cell types.^{35,37} These advantages include low immunogenicity and high histocompatibility, no tumorigenicity, immunomodulatory effects, and significant paracrine effects.³⁵ Also, several studies have evaluated the proangiogenic ability of hADSCs.³⁵ Interestingly, they found that hAMSCs were shown to augment blood perfusion and capillary architecture when transplanted into ischemic limbs of mice, suggesting that hAMSCs stimulate neovascularization.^{35,38} Additionally, another advantage is that hADSCs are easier to obtain compared to other stem cell sources, such as bone marrow stem cells (BMSCs).³⁵

Regarding the low immunogenicity, hADSCs have been shown to have a low expression of major histocompatibility class I antigen (*HLA-ABC*), and no expression of major histocompatibility class II antigen (*HLA-DR*), β 2 microglobulin, and *HLA-ABC* costimulatory molecules, including CD40, CD80 and CD8635. Notably, there have been reports of transplantation of hAMSCs into patients with lysosomal diseases who had no obvious rejection.³⁵ Moreover, a recent study demonstrated no hemolysis, allergic reactions, or tumor formations in mice who received intravenous hAESC.^{35,39}

Additionally, studies have demonstrated that both hAESC and hAMSCs have great potential to play an impor-

tant role in regenerative medicine. They both have demonstrated that they can differentiate into several specialized cells, including adipocytes, bone cells, nerve cells, cardiomyocytes, skeletal muscle cells, hepatocytes, hematopoietic cells, endothelial cells, kidney cells, and retinal cells.³⁵

Multiple preclinical studies have revealed the potential for hADSCs to be used in the treatment of several diseases including premature ovarian failure, diabetes mellitus, inflammatory bowel disease, brain/spine diseases, and more.^{35,40,41} For example, one preclinical study investigated the effect of hAMSC-therapy on ovarian function in natural aging ovaries within mice.⁴⁰ They found that after the hAMSCs were transplanted into the mice, the hAMSCs significantly improved follicle proliferation and therefore ovarian function.⁴⁰ Another study investigated the effect of hAESC-therapy on outcomes after stroke in mice.⁴¹ They found that, administration of hAESCs after acute (within 1.5 hours) stroke in mice reduced brain infarct development, inflammation, and functional deficits.⁴¹ Additionally, they found that after late administration (1-3 days poststroke) of hAESCs, functional recovery in the mice was still improved.⁴¹ Overall, they concluded that administration of hAESCs following a stroke in mice showed a significant neuroprotective effect and facilitated repair and recovery of the brain.⁴¹

Although a number of preclinical studies, like the ones previously described, have shown considerable promise regarding the use of ADSC-therapy, more studies are needed. Future studies can continue to work toward determining if hADSCs are capable of being used for cell replacement and better elucidate the mechanisms by which hADSCs work.

IV. ADIPOSE TISSUE AS A SOURCE FOR STEM CELLS

Although the use of bone marrow stem cells (BMSCs) is now standard, dilemmas regarding harvesting techniques and the potential for low cell yields has driven researchers to search for other mesenchymal stem cell (MSCs) sources.⁴² One source that has been investigated is human adipose tissue.⁴²

After enzymatic digestion of adipose tissue, a heterogeneous group of adipocyte precursors are generated within a group of cells called the stromal vascular fraction (SVF).⁴² Adipose-derived stem cells (ADSCs) are found in the SVF.^{42,43} Studies have demonstrated that ADSCs possess properties typically associated with MSCs, and that they have been found to express several CD markers that MSCs characteristically express.⁴³ ADSCs are multipotent and have been shown to differentiate into other cells of mesodermal origin, including osteoblasts, chondroblasts, myocytes, tendocytes, and more, upon *in vitro* induction.⁴²⁻⁴⁵ Additionally, ADSCs have demonstrated *in vitro* capacity for multi-lineage differentiation into specialized cells, like insulin-secreting cells.^{43,46}

A significant advantage of ADSCs over BMSCs is how easy they are to harvest.^{43,45} White adipose tissue (WAT) contains an abundance of ADSCs.⁴³ The main stores of WAT

in humans are subcutaneous stores in the buttocks, thighs, abdomen and visceral depots.⁴³ Due to this, ADSCs can be harvested relatively easily by liposuction procedures from these areas of the body.^{43,45} Moreover, ADSCs make up as much as 1-2% of the SVF within WAT, sometimes even nearing 30% in some tissues.^{43,45} This is a significant difference from the .0001-.0002% stem cells present in bone marrow.⁴³ Given this difference in stem cell concentration between the sources, there will be more ADSCs per sample of WAT compared to stem cells per bone marrow sample, further demonstrating an easier acquisition of stem cells when using adipose tissue.

Another advantage of ADSCs is their immune privilege status due to a lack of major histocompatibility complex II (MHC II) and costimulatory molecules.^{42,43,45,47} Some studies have even demonstrated a higher immunosuppression capacity in ADSCs compared to BMSCs as ADSCs expressed lower levels of human antigen class I (HLA I) antigen.⁴⁷ They also have a unique secretome and can produce immunomodulatory, anti-apoptotic, hematopoietic, and angiogenic factors that can help with repair of tissues – characteristics that may support successful transplantations without the need for immunosuppression.⁴²⁻⁴⁵ Moreover, ADSCs have the ability to be reprogrammed to induced pluripotent stem (iPS) cells.⁴³

The number of ADSC clinical trials has risen over the past decade, and some have shown significant promise. They have demonstrated abilities to differentiate into multiple cell lines in a reproducible manner and be safe for both autogenetic and allogeneic transplantations.⁴⁵ Several recent studies have demonstrated that ADSC-therapy may potentially be useful in the treatment of several conditions, including diabetes mellitus, Crohn's disease, multiple sclerosis, fistulas, arthritis, ischemic pathologies, cardiac injury, spinal injury, bone injuries and more.⁴⁴⁻⁴⁸

One clinical trial conducted in 2013 investigated the therapeutic effect of co-infusion of autologous adipose-derived differentiated insulin-secreting stem cells and hematopoietic stem cells (HSCs) on patients with insulin-dependent diabetes mellitus.⁴⁶ Ten patients were followed over an average of about thirty-two months, and they found that all the patients had improvement in C-peptide, HbA1c, blood sugar status, and exogenous insulin requirement.⁴⁶ Notably, there were no unpleasant side effects of the treatment and all ten patients had rehabilitated to a normal, unrestricted diet and lifestyle.⁴⁶

In another 4-patient clinical trial in which ADSCs were used to heal fistulas in patients with Crohn's disease, full healing occurred in 6 out of the 8 fistulas with partial healing in the remaining two.⁴⁴ No complications were observed in the patients 12 months following the trial.⁴⁴ Although these results are promising, the mechanism by which the healing took place remains unclear. When considering the properties of ADSCs, there are a number of factors that could have played a role in the healing, such as the result of paracrine expression of angiogenic and/or anti-apoptotic factors, stem cell differentiation, and/or local immunosuppression.⁴⁴

Other exciting studies have demonstrated a use of ADSCs in the treatment of osteoarthritis (OA). One meta-analysis compared the use of ADSCs and BMSCs in the treatment of osteoarthritis.⁴⁷ This meta-analysis included 14 studies comprising 461 original patient records.⁴⁷ Overall, the comparison between treatment of OA didn't show a significant difference in the disease severity score change rate between patients treated with ADSCs and those treated with BMSCs.⁴⁷ However, there was significantly more variability in the outcomes of those treated with BMSCs with the highest change rate being 79.65% in one study and the lowest being 22.57% in another study.⁴⁷ Given this, ADSCs may represent a more stable cell source for the treatment of OA.⁴⁷ Although this study is specific to OA treatment, it is worth acknowledging the possibility that ADSCs may also represent a more stable cell source for treatment of other diseases as well.

Though recent ADSC research, as described above, has been promising, unfortunately reproducible *in vivo* studies are still lacking in both quality and quantity.⁴² Therefore, further studies are necessary prior to progression to routine patient administration.⁴²

V. UMBILICAL CORD AS A SOURCE FOR STEM CELLS

Umbilical Cord stem cells can be drawn from a variety of locations including umbilical cord blood, umbilical cord perivascular cells, umbilical vein endothelial cells, umbilical lining, chorion, and amnion. Umbilical cord blood can be drawn with minimal risk to the donor, and it has been used since 1988 as a source for hematopoietic stem cells.⁴⁹ When compared to stem cells obtained from bone marrow, umbilical cord derived stem cells are much more readily available. With a birth rate of more than a 100 million people per year globally, there is a lot of opportunity to use umbilical cord blood as a source for stem cells.

The process of extracting the blood is very simple and involves a venipuncture followed by drainage into a sterile anti-coagulant-filled blood bag. It is then cryopreserved and stored in liquid nitrogen. There are quite a few benefits to utilizing umbilical cord stem cells rather than stem cells drawn from adults. One of the biggest benefits is that the cells are more immature which means that there is a lower chance of rejection after implantation in a host and would lead to decreased rates of graft-versus-host disease. They also can differentiate into a very wide variety of tissues. For example, when compared with bone marrow stem cells or mobilized peripheral blood, umbilical cord blood stem cells have a greater repopulating ability.⁵⁰ Cord blood derived CD34+ cells have very potent hematopoietic abilities, and this is attributed to the immaturity of the stem cells relative to adult derived cells. Studies have been done that analyze long term survival of children with hematologic disorders who were transplanted with umbilical cord blood from a sibling donor. These studies revealed the same or better survival in the children that received the umbilical cord blood relative to those that got transplantation from bone marrow cells. Furthermore, rates of relapse were the

same for both umbilical cord blood and bone marrow transplant.⁵¹

One of the unique features of stem cells taken from umbilical cord blood is the potential to differentiate into a wide variety of cell types. There are three different kinds of stem cells that can be found in the umbilical cord blood which include hematopoietic, mesenchymal, and embryonic-like stem cells. Not only can these cell types all renew themselves, but they can differentiate into many different mature cell types through a complex number of signaling pathways. This means that these cells could give rise to not only hematopoietic cells but bone, neural and endothelial cells. There are studies taking place currently to see if umbilical cord blood derived stem cells can be utilized for cardiomyogenic purposes. Several studies have showed the ability to transform umbilical cord blood mesenchymal stem cells into cells of cardiomyogenic lineage utilizing activations of Wnt signaling pathways.⁵² Studies are also being conducted on the potential of neurological applications. If successful, this could help diseases such as cerebral palsy, stroke, spinal cord injury and neurodegenerative diseases. Given these cell's ability to differentiate into tissues from the mesoderm, endoderm and ectoderm, they could be utilized for neurological issues in place of embryonic stem cells that are currently extremely controversial.⁵³ There are currently studies involving *in vitro* work, pre-clinical animal studies, and patient clinical trials, all for the application of stem cells in neurological applications. There is big potential for the use of umbilical blood stem cells in the future of regenerative medicine.

VI. PLACENTAL TISSUE AS A SOURCE FOR STEM CELLS

Placental tissue contains both stem cells and epithelial cells that can differentiate into a wide variety of tissue types which include adipogenic, myogenic, hepatogenic, osteogenic, cardiac, endothelial, pancreatic, pulmonary, and neurological. Placental cells can differentiate into all these different kinds of tissues due to lineages originating from different parts of the placenta such as the hematopoietic cells that come from the chorion, allantois, and yolk sac while the mesenchymal lineages come from the chorion and the amnion.⁵⁴ It can be helpful to think of human fetal placental cells as being divided into four different groups: amniotic epithelial cells, amniotic mesenchymal stromal cells, chorionic mesenchymal stromal cells and chorionic trophoblast cells.⁵⁴

Human amniotic epithelial cells (hAECs) can be obtained from the amnion membrane where they are then enzymatically digested to be separated from the chorion. When cultured under certain settings hAECs have been found to be able to produce neuronal cells that synthesize acetylcholine, norepinephrine as well as dopamine.^{55,56} This ability would mean they have potential for regenerative purposes in diseases such as Parkinson's Disease, multiple sclerosis, and spinal cord injury. There is also research being done to utilize hAECs for ophthalmological purposes, lung fibrosis, liver disease, metabolic diseases, and familial

hypercholesterolemia. Once cultured, hAECs have been shown to produce both albumin and alpha-fetoprotein as well as showing ability to store glycogen. Furthermore, they have been found to metabolize ammonia and testosterone. In more recent studies conducted in mouse models, these cells have been found to have therapeutic efficacy after transplantation for cirrhosis.⁵⁷

Mesenchymal stem cells are in many different tissues such as the bone marrow, umbilical cord blood, adipose tissue, Wharton's jelly, amniotic fluid, lungs, muscle and the placenta. Placental mesenchymal stromal cells specifically originate from the extraembryonic mesoderm. Human amniotic mesenchymal stromal cells (hAMSCs) and chorionic mesenchymal stromal cells (hCMSCs) have both been found to have very low levels of HLA-A,B,C. This means that they have immune privileged profiles for potential transplantation.^{58,59} Placental derived mesenchymal stem cells have been shown to have expression of CD29, CD44, CD105 and CD166 which is the same as adipose derived mesenchymal stem cells. These markers have been shown to have osteogenic differentiating abilities.⁵⁷ An interesting element of placental mesenchymal stem cells is that their properties differ depending on the gestational age of the placenta. When cells are harvested at lower gestational ages, they show faster generation doubling times, better proliferative abilities, wider differentiation potential and more phenotypic stability than cells harvested from placental tissue that is considered to be at term.⁶⁰ Furthermore, they have great potential to be used clinically. Placental mesenchymal stromal cells have been studied for use in treating acute graft-versus-host disease that was refractory to steroid treatment. Studies have shown that the 1-year survival rates in patients treated with placenta derived stromal cells were 73% while retrospective control only showed 6% sur-

vival.⁶¹ Placenta derived MSCs have also been found to aid in wound healing and could potentially be used to aid with certain inherited skin conditions such as epidermolysis bullosa.⁶²

CONCLUSION

Stem cells are diverse in their differentiation capacity as well as their source of origin. As we can see from this review, there are similarities and differences when these cells are extracted from different sources. Research has shown initial promise in neurodegenerative diseases such as Alzheimer's and Parkinson's Disease. It has also shown to be beneficial in the areas of musculoskeletal regenerative medicine and other pain states. Organ bioengineering for transplantation is another potential benefit that stem cells may offer. For these reasons, extensive research is still needed in this area of medicine to pave the way for new developing therapy modalities.

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DEDICATIONS

This review is dedicated to Dr. Justine C. Goldberg MD

CONFLICT OF INTEREST OF EACH AUTHOR

none

FUNDING

none

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