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# Stem Cells in the Umbilical Cord

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## Abstract

Stem cells are the next frontier in medicine. Stem cells are thought to have great therapeutic and biotechnological potential. This will not only to replace damaged or dysfunctional cells, but also rescue them and/or deliver therapeutic proteins after they have been engineered to do so. Currently, ethical and scientific issues surround both embryonic and fetal stem cells and hinder their widespread implementation. In contrast, stem cells recovered postnatally from the umbilical cord, including the umbilical cord blood cells, amnion/placenta, umbilical cord vein, or umbilical cord matrix cells, are a readily available and inexpensive source of cells that are capable of forming many different cell types (i.e., they are "multipotent"). This review will focus on the umbilical cord-derived stem cells and compare those cells with adult bone marrow-derived mesenchymal stem cells.

### Index Entries

Umbilical cord matrix cells; Wharton's Jelly; mesenchymal stem cells; umbilical cord blood cells

## Introduction

### Stem Cells Defined

Stem cells are defined simply as cells meeting three basic criteria (illustrated in Fig. 1. First, stem cells renew themselves throughout life, i.e., the cells divide to produce identical daughter cells and thereby maintain the stem cell population. Second, stem cells have the capacity to undergo differentiation to become specialized progeny cells (1). When stem cells differentiate, they may divide asymmetrically to yield an identical cell and a daughter cell that acquires properties of a particular cell type, for example, specific morphology, phenotype, and physiological properties that categorize it as a cell belonging to a particular tissue (2). Stem cells that may differentiate into tissues derived from all three germ layers, for example, ectoderm, endoderm, and mesoderm, are called "pluripotent." The best example of pluripotent stem cells are the embryonic stem cells (ESCs) derived from the inner cell mass of early embryos. In contrast with ESCs, most stem cells that have been well characterized are multipotent, i.e., they may differentiate into derivatives of two of the three germ layers. The third property of stem cells is that they may renew the tissues that they populate. All tissue compartments contain cells that satisfy the definition of "stem cells" (3), and the rate at which stem cells contribute to replacement cells varies throughout the body. For example, blood-forming stem cells, gut epithelium stem cells, and skin-forming stem cells must be constantly replaced for normal health. In contrast, the stem cells in the nervous

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system that replace neurons are relatively quiescent and do not participate in tissue renewal or replace neurons lost to injury or disease.

In the body, stem cells live in specialized "niches," microenvironments included stem cell support cells and extracellular matrix. The niche microenvironment regulates the growth and differentiation of stem cells (4–6). Understanding the role of the various "support" cells and the environment of the niche is helpful for in vitro manipulation and maintenance of stem cell populations. For example, a normal atmospheric oxygen concentration of 21% is relatively toxic to stem cells, and growth in "hyoxic" conditions of 2–3% oxygen is preferred (7). Other components of the niche, such as the extracellular matrix and growth and angiogenic factors, play a role in stem cell regulation. Understanding the stem cell microenviornment is rapidly unfolding and is an important topic which, however, is beyond the scope of this article.

## When are Stem Cells Found?

Stem cells have been isolated from virtually all of life's stages. That is, stem cells have been isolated from the inner cell mass of 5-d-old embryos as well as collected from the olfactory epithelium of senior citizens. Human embryo-derived stem cells and stem cells derived from human fetal tissues have raised moral/ethical concerns that have yet to be adequately discussed and addressed by our society. These society level concerns impact the research effort directly by way of the federally mandated support limitations, blue ribbon panel inquiries, ethical debates, lawsuits, and political posturing. The bottom line is that the United States lacks clear, consistent research goals and unified leadership regarding embryonic stem cell research; this is reflected in the state-to-state differences in legislation and support for embryonic stem cell research. These issues are huge and require serious work. They are beyond the scope of this review.

Importantly, ESCs are the *de facto* pluripotent cells for biomedical research. Proponents state that ESCs will enable cell-based therapeutics and biopharmaceutical testing/manufacturing. In contrast, biomedical research conducted using postnatally collected tissues and stem cells has generated less controversy and enjoyed more therapeutic applications to date. This is likely owing to the fact that blood and bone marrow stem cells were found to rescue patients with bone marrow deficiencies about 40 yr ago (8,9). The result of this work produced the national bone marrow registry, which was established in the United States in 1986.

Use of adult bone marrow-derived stem cells brought to the forefront, the limitations that these types of cells are thought to have. Specifically, scientific dogma states that adult-type stem cells have limited capacity to expand in vitro. Initial work indicated that bone marrow-derived mesenchymal stem cells (bmMSCs) become senescent (cease to divide in vitro) by passage 6–10. Furthermore, bone marrow-derived stem cells are reported to be more difficult to extract from the marrow cavity in normal aging because the red marrow space changes to a yellow marrow (fat-filled) as a consequence of aging. Optimal stem cell aspirates from the marrow are found in young donors (e.g., 18–19 yr of age; 9a). One would think that the fat-derived MSCs would be a useful alternative to the marrow-derived MSCs for autologous grafting in aged individuals. We do not know whether this will be the case. It is known that fat-derived MSCs are more rare than bmMSCs. Therefore, extraction and expansion may be required prior to therapeutic use. It is generally thought that stem cells derived from "younger" tissues, for example, tissues derived from the early embryo or fetus, would have longer telomeres and have the capacity for extended expansion in culture prior to becoming senescent. There are some data to support this contention (10).

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## Sources of Stem Cells for Therapeutic Use

In the last 10 yr, umbilical cord blood has been shown to be therapeutically useful for rescuing patients with bone marrow-related deficits and inborn errors of metabolism. Umbilical cord blood offers advantages over bone marrow because cord blood does not require perfect human leukocyte antigen (HLA) tissue matching, has less incidence of graft vs host disease, and may be used allogenically (11,12). In addition, cord blood may be banked, and thus is available for use "off-the-shelf." Last year, a federally supported program was established to expand the national umbilical cord blood banks to include a wide sample of HLA types. By 2004, there were more than 6000 cord blood stem cell units banked. As of January 2006, it is estimated that there are about 300,000 units in public and private banks in the United States.

Next to hematopoeitic stem cells, the most widely studied stem cells in bone marrow are marrow-derived MSCs, also known as marrow stromal cells. In the adult, MSCs are found in highest concentration in the marrow cavity. MSCs are found at lower density in blood and in peripheral, adipose, and other tissues. MSC-like cells can be isolated from umbilical cord blood, placenta, perivascular areas, amniotic fluid, and from the tissue surrounding the umbilical cord vessels, i.e., Wharton's jelly. The collection of MSC-like cells from tissues that are discarded at birth is easier and less expensive than collecting MSCs from a bone marrow aspirate. During the collection of these tissues, there is no health impact on either the mother or the newborn. At least in theory, these cells may be stored frozen and then thawed to provide stem cells for therapeutic use decades after cryogenic storage.

As shown in Table 1, at least five different laboratories have extracted MSC-like cells from umbilical cord tissues. Some differences in the ease with which MSC-like cells are isolated from the various tissues are reported. Importantly, the methods for isolating MSC-like cells are robust, i.e., labs throughout the world independently isolate MSC-like cells from these tissues. This opens the door for independent verification, scalable production, and a large-team approach.

In contrast, although there are several reports of pluripotent cells being isolated from adults (13–17), this work is in need of independent verification. Such verification is important because an alternative source of pluripotent cells, cells derived from adults, offers the best of both worlds: pluripotent cells for therapeutics and cells that are collected with consent from adults (no controversy there). Two such cell types are discussed briefly later.

The work from Dr. Verfaillie's lab on the multipotent adult progenitor cell (MAPC) has received much attention (15,16,18–22). Their findings indicate that the MAPC is pluripotential and slightly enigmatic, as it appears after extensive passage in cell culture. Similarly, in umbilical cord blood, Kogler et al. (17,23) identified a cell that they call the universal somatic stem cell (USSC). The USSC is another rare cell (average of 16 cells in initial isolate; able to isolate USSC in 50% of the cords attempted). The USSC, like the MAPC, offers much promise as an embryo-safe pluripotent cell. Widespread acceptance of these two cells will come when the methods for their isolation become robust such that any laboratory can isolate them and contribute to the field.

## Characterization of Umbilical Cord-Derived MSCs

Recently the minimal defining characteristics of MSCs was the subject of a blue ribbon panel of scientists (24). This panel ascribed three defining characteristics to MSCs. First, MSCs are plastic-adherent when maintained in standard culture conditions. Second, MSCs express the cell surface markers CD105, CD73, and CD90 and lack expression of CD45, CD34, CD14 or CD11b, CD79 or CD19, and HLA-DR. Third, MSCs differentiate to

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osteoblasts, adipocytes, and chondroblasts in vitro. As shown in Table 1, mesenchymal-like cells collected from the umbilical cord, placenta, and from umbilical cord blood, perivascular space, and placenta all share a relatively consistent set of surface markers, which is apparently consistent with the hypothesis that they are MSC-like.

Our work has focused on human umbilical cord matrix (UCM) cells. There are cells isolated in large numbers from the Wharton's jelly of human cords (25–28). Two other research labs have published on the isolation and characterization of cells from the Wharton's jelly: Dr. Davies' lab at the University of Toronto (29) and Dr. Y. S. Fu at the National Yang-Ming University, Taipei (30–32). All three groups reported that UCM cells are MSC-like cells and are robust. These cells can be isolated easily, frozen/thawed, clonally expanded, engineered to express exogenous proteins, and extensively expanded in culture. Human UCM cells express a marker of neural precursors, nestin, without exposure to differentiation signals (26,28,30). In response to differentiation signals, human UCM cells can differentiate to catecholaminergic neurons, expressing tyrosine hydroxylase TH (28,30,31). Human UCM cells meet the basic criteria established for MSCs described previously (29,32). Similarly, MSC-like cells are derived from other umbilical cord tissues, e.g., umbilical vein sub-endothelium, umbilical cord blood, amnion, placenta, and amniotic fluid (Table 1).

Whether UCM cells are MSC-like or fit into a unique niche is currently not clear. For example, when the vital stain Hoechst 33342 was used in the dye exclusion test, about 20% of UCM cells were found to exclude dye (28). About 85% of the UCM cells expressed CD 44, the hyaluronate receptor marker found on several stem cell populations, and about 85% of the cells expressed ABCG2, the receptor thought to mediate dye exclusion. Attempts to enrich the Hoechst-dim cells were partially successful, with maximal enrichment at about 32%. It is assumed that culture conditions are the limiting factor for further enrichment of what is assumed to be the most primitive populations.

A literature review revealed a question about the stability of umbilical cord cells in culture. Two groups found that the cell surface marker expression shifted over passage (28,29). Sarugaser's (29) work indicated that HLA-1 was lost as a result of cryopreservation. Whereas, umbilical cord perivascular cells lost cell surface staining for HLA-1 with freeze–thaw, HLA-1 surface staining was consistent out to passage 5 for cells maintained in culture. In contrast, Weiss et al. (28) reported a decrease in the percentage of cells expressing CD49e and CD105 when human UCM cells were maintained in culture for passage 4–8 and no significant changes in HLA-1 expression. This question about the stability of surface marker expression may indicate that epigenetic phenomena associated with cell culture are influencing the cord MSC-like cells. Further characterization of the cord MSC-like cells is needed to understand the mechanisms of these changes.

The gene expression analysis and reverse-transcription polymerase chain reaction (RT-PCR) of MSCs from the umbilical cord was reported by one lab using the National Institutes on Aging (NIA) human 15k gene array (28). That work indicated that human UCM cells express genes found in cells derived from all three germ layers to some extent. At least one report indicates that UCM cells express the pluripotency gene markers *Oct-4, nanog*, and *Sox-2* at low levels relative to ESCs (33). One interpretation of these findings is that cord matrix stem cells are pleiotropic and express a relatively large number of genes in relatively low abundance. On the other hand, it may serve as evidence that the cord matrix cell population has a subset of primitive stem cells. Because gene array is not a sensitive method by which to examine low copy number message, we suggest that massively parallel signature sequencing (MPSS) is a more appropriate method of assessing matrix cell gene expression. RT-PCR alone is not useful for characterizing cord matrix stem cells:

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quantitative RT-PCR is needed to make meaningful statements about gene expression and to compare gene expression between experimental conditions.

## Properties of Umbilical Cord Matrix Stem Cells

Several groups have isolated MSC-like cells from the umbilical cord tissues or blood and have reported that those cells may express neural markers when differentiated (26,32), and differentiate into neural cells upon transplantation into rat brain. This is not too surprising, because adult bone marrow-derived MSCs injected into fetal rat brain engrafted, differentiated along neural-like lineages, and survived into the postnatal period (34). Similarly, Jiang et al. (19) demonstrated convincingly that bone marrow-derived MAPCs could be differentiated in vitro to become cells with electrophysiological properties of neurons. Increasingly, reports are indicating that bone marrow-derived cells may differentiate, first to neurospheres and then to neurons with proper neuronal electrophysiological characteristics (35,36).

In 2003, we reported that UCM cells can be induced in vitro to become cells with morphological and biochemical characteristics of neurons (26). These findings have been extended by others, for example, neurons (30–32), cardiac muscle, bone, and cartilage (29,32). Using two in vitro differentiation methods, Wang et al. (32) found that umbilical cord matrix stem (UCMS) cells could be induced to exhibit cardiomyocyte morphology and synthesize cardiac muscle proteins such as *N*-cadherin and cardiac troponin I. The cells responded to five azacytidine or culture in cardiomyocyte-conditioned media. Fu et al. (30) used media conditioned by primary rat brain neurons to induce human UCMS cells to synthesize NeuN neurofilament. Furthermore, they could invoke an inward current in UCM cells with glutamate. In that report, exposure to neural-conditioned media also increased the proportion of cells synthesizing the astroglial protein glial fibrillary acidic protein (GFAP) from 94% initially to 5% after 9 d, although the percentage had declined to about 2% by day 12. The multilineage potential of UCMS cells was also verified by Wang and colleagues (32), who showed that they could be induced in vitro into chondrogenic, osteogenic, and adipogenic lineages.

MSC-like cells derived from Wharton’s jelly adjacent to umbilical vessels (termed human umbilical cord perivascular cells) cultured in nonosteogenic media nevertheless contained a subpopulation that demonstrated a functional osteogenic phenotype with the elaboration of bone nodules (29); addition of osteogenic supplements further enhanced this population. These findings suggest that cord matrix stem cells, like bmMSCs, are multipotent: capable of making ectoderm- and mesoderm-derived cells.

We have shown that porcine UCM stem cells can be xeno-transplanted into nonimmune-suppressed rats, where they engrafted, proliferated in a controlled fashion, and exhibited TH expression in some cells (27). Most recently, our lab (28), and others (31) have reported that UCM cells ameliorate behavioral deficits in the hemi-parkinsonian rat, and UCM cell transplantation resulted in significantly more dopaminergic neurons in the substantia nigra compared with lesioned, nontransplanted rats that responded to the transplant (28). In contrast with our work, in which UCM cells were transplanted without prior differentiation, Fu et al. (31) subjected UCM cells to an in vitro induction protocol utilizing neuronconditioned media, sonic hedgehog, and fibroblast growth factor (FGF)-8 to increase the number of tyrosine hydroxylasepositive cells. After transplantation of these predifferentiated human UCMS cells into hemi-parkinsonian rats, Dr. Fu’s lab reported that they prevented the progressive degeneration/ deterioration in their Parkinson’s disease model.

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From these findings, it is suggested that UCM cells offer advantages over stem cells as a source of therapeutic cells. First, UCM cells are derived from a noncontroversial, inexhaustible source, and can be harvested noninvasively at low cost. Second, unlike human ESCs, UCM cells did not induce teratomas or death after $1 \times 10^6$ to $6 \times 10^6$ human UCM cells were transplanted either intravenously or subcutaneously into severe combined immunodeficient beige mice (Rachakatla, Medicetty, Burton, Troyer, and Weiss, unpublished observations). Third, UCM cells are easy to start and do not require feeder layers or medium containing high serum concentrations to be maintained. Fourth, they are not acutely rejected when transplanted as xenografts in nonimmune-suppressed rats. For example, we demonstrated that pig UCM cells undergo a moderated expansion following transplantation into rat brain without obvious untoward behavioral effects or host immune response (25).

## Immune Suppression

MSCs are reported to have immune-suppressive effects. To comment human fetal and adult MSCs are not inherently immunostimulatory in vitro and fail to induce proliferation of allogeneic lymphocytes (37–39; for review, *see* ref. 40). In one human case, fully mismatched allogeneic fetal liver-derived MSCs were transplanted into an immunocompetent fetus with osteogenesis imperfecta in the third trimester of gestation (41). No immunoreactivity was observed when patient lymphocytes were re-exposed to the graft in vitro, indicating that MSCs can be tolerated when transplanted across MHC barriers in humans. Similarly, after intrauterine transplantation of human MSCs into sheep, the cells persisted long-term and differentiated along multiple mesenchymal lineages (42). Instead, the cells are immunosuppressive and reduce lymphocyte proliferation and the formation of cytotoxic T-cells and natural killer cells when present in mixed lymphocyte cultures. The mechanism whereby MSCs suppress lymphocyte proliferation is still largely unknown but appears to, at least in part, be mediated by a soluble factor. Several factors, including MSC-produced prostaglandin E2, indoleamine 2,3-dioxygenase-mediated tryptophan depletion, transforming growth factor-β1, and hepatocyte growth factor have been proposed to mediate the suppression, but the data remain controversial.

There is indirect support for an immune-suppressive effect of the MSC-like cells derived from umbilical cord: two labs have transplanted UCM cells xenogenically in nonimmune-suppressed hosts without observation of frank immune rejection (25,27,28,31). In preliminary work, we have found that human UCM cells suppress the proliferation of rat splenocytes exposed to the mitogen ConA, and that a diffusible factor is likely involved (Anderson, Medicetty, and Weiss, unpublished observations). These data would support the hypothesis that UCM cells, like MSCs, may have immunosuppressive effects. We speculate that these effects may facilitate the engraftment of other therapeutic cells, that has been reported recently for co-grafts of MSC with hematopoietic cells (43).

## Homing

In addition to their immune-suppressive properties, MSCs appear to exhibit a tropism for damaged or rapidly growing tissues. For example, following injection into the brain, MSCs migrate along known pathways when injected into the corpus striatum (44). MSCs migrated throughout forebrain and cerebellum, integrated into central nervous system cytoarchitecture, and expressed markers typical of mature astrocytes and neurons after injection into the lateral ventricle of neonatal mice (45). MSCs injected into injured spinal cord were found to form guiding “cord,” ushering in regenerating fibers (46). MSCs may assist with regeneration in stroke (47–51) or myocardial ischemia (52–55) by release of

trophic factors such as brain-derived neurotrophic factor, glial cell line-derived neurotrophic factor, or angiogenic factors (56–61).

The tissue infiltration response of MSCs is seen in experimental stroke (62) and myocardial ischemia (63), in addition to the infiltration in injured nervous system tissue listed previously.

There is now compelling evidence that MSCs, guided by chemokines and other cues emanating from areas of pathology such as tumors, will "home" specifically to those areas. The supporting connective tissue stroma of a tumor is formed in a manner similar to wound healing and scar formation (64), and tumors generate signals to recruit stromal cells from contiguous regions as well as from bone marrow to sustain themselves (65,66). Because UCM stem cells are very closely related to MSCs (28), it would not be surprising to find that they also will home to tumors, and in fact such a phenomenon has been observed in preliminary experiments in our laboratory (unpublished observations). The exact signals that recruit transplanted or endogenous cells to regions of inflammation or neoplasia remain obscure. However, stromal cell-derived factor-1α plays a crucial role in recruitment of bone marrow-derived cells to the heart after myocardial infarction (67). Matrigel invasion assays have implicated such molecules as platelet-derived growth factor-BB, epidermal growth factor, and stromal cell-derived factor-1α as chemokines for MSCs; however, neither basic FGF (bFGF) nor vascular endothelial growth factor (VEGF) had an affect (68). In any event, the directed trafficking of umbilical and other mesenchymal stem cells to tumors opens the enticing prospect that they may be a platform for targeted delivery of high local levels of protein. Often, such proteins have a short half-life and/or cause major side effects when given systematically.

## MSCs Support Expansion of Other Stem Cells

Mesenchymal cells have been reported to act as supporting cells that promote the expansion of other stem cell types. For example, MSCs and MSC-like cells support ex vivo expansion of hematopoietic stem cells (28,69–71). When co-grafted, MSCs and MSC-like cells support in vivo engraftment of hematopoietic stem cells, too (23,43,72). This work suggests that MSCs from a variety of sources, including umbilical cord, may facilitate engraftment of hematopoietic stem cells. This addresses two significant problems found in umbilical cord blood transplantation: (1) getting enough cells to engraft an adult and (2) increasing the speed of engraftment (12,73). Theoretically, cografting or ex vivo expansion may enable transplantation of cord blood units into larger patients and speed the engraftment in other patients.

In addition to hematopoietic cells, Mesenchymal cells derived from Wharton's jelly are useful as feeder layers for the propagation of other stem cell types. For example, equine embryonic stem cell-like cells derived from the inner cell mass were propagated successfully for more than 350 divisions on a feeder layer derived from stem cells isolated from Wharton's jelly of equine umbilical cords (74). The equine ES-like cells could be maintained without leukemia inhibitory factor (LIF) as long as they were on the cord matrix cells.

## UCM Cells for Tissue Engineering

A major potential application of stem cells in medicine is for "tissue engineering," in which the ultimate goal is to provide off-the-shelf tissues and organs. UCM cells demonstrate excellent cell growth properties on bioabsorbable polymer constructs (75). UCM cells were used to seed blood vessel conduits fashioned from rapidly bioabsorbable polymers and grown in vitro in a pulse duplicator bioreactor (76). Recently, living patches engineered



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from UCMS cells and cord-derived endothelial precursor cells have been described for potential use in human pediatric cardiovascular tissue engineering (77,78).

## Summary

MSCs and MSC-like cells are useful multipotent stem cells that are found in many tissues. While MSCs can be isolated from adults via peripheral blood, adipose tissue, or bone marrow apiration, MSCs derived from the discarded umbilical cord offer a low-cost, pain-free collection method of MSCs that may be cryogenically stored (banked) along with the umbilical cord blood sample. From the umbilical cord, isolation of cells from the Wharton's jelly has the greatest potential for banking, presently, because the most cells can be isolated consistently. The challenge for the future is to define industrial-grade procedures for isolation and cryopreservation of umbilical cord-derived MSCs and to generate Food and Drug Administration (FDA)-approved standard operating procedures (SOPs) to enable translation of laboratory protocols into clinical trials. This represents a paradigm shift from what has been done with umbilical cord blood banking because the cord blood cells do not require much in the way of processing for cryopreservation or for transplantation (relatively). For such a challenge to be met, researchers in the field of umbilical cord-derived MSC need to organize and reach consensus on the characterization, freezing/ thawing, and expansion of clinical-grade cells for therapies and tissue engineering. Thus, more and more umbilical cord stem cells can be diverted from the biohazardous waste bag and into the clinic, where their lifesaving potential can be realized.

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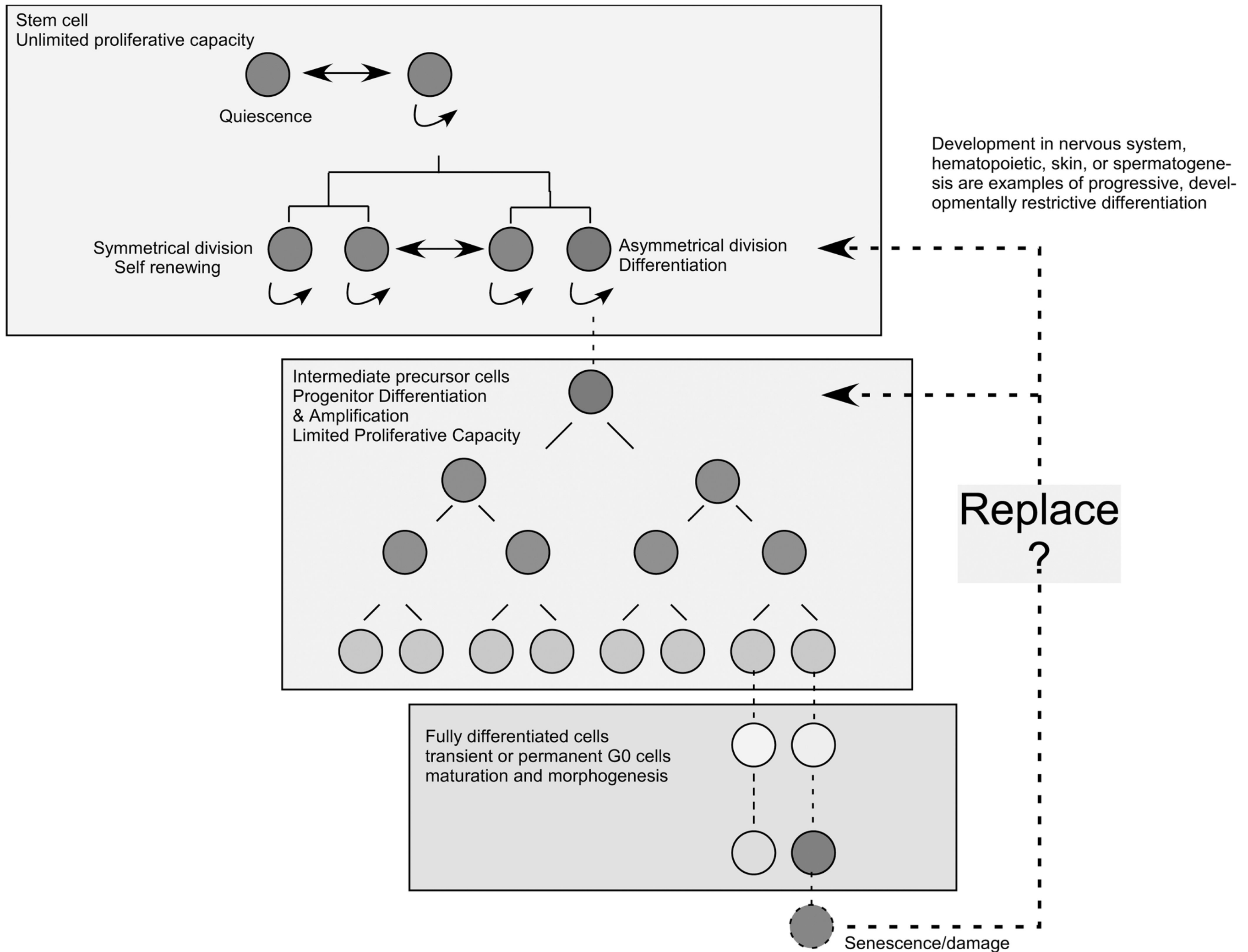


**Fig. 1.**

Generalized stem cell lineage concept. The lineage is characterized by a self-maintaining “parent” true stem cell population that resides within a specialized niche microenvironment, which aids the regulation of stem cell division or quiescence (nondividing). Derivative cells (called progeny or daughter cells) are of two types: symmetric division produces two identical daughter cells to expand or maintain the stem cell population; asymmetric division produces an identical daughter and a specialized cell (a differentiated cell). The differentiated cell is an intermediate type of precursor cell, termed the transient dividing population. The number of divisions of the intermediate precursor is fairly tightly regulated by microenvironment and inborn regulation factors. The intermediate precursors are thought to have a limited proliferative capacity. Further tissue-specific specialization continues form the intermediate precursors, producing specialized populations with a commitment to a progressively more specialized (differentiated) fate. The end points are fully differentiated cells that are nondividing and that live for various, tissue-specific periods prior to senescence or damage that leads to cell death. In some tissues, the naturally occurring cell loss produces various feedback signals that trigger normal cell replacement via amplification/differentiation of either stem cells or the intermediate precursors.

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**Table 1**

Cell Surface Markers of MSC-Like Cells

| | Cell type (see footnotes) | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **UCM** | **UCM** | **UCPV cells** | **USSC** | **USSC** | **CBMSC** | **CBMSC** | **CBMSC** | **CBMSC** | **UVMSC** | **UVMSC** | **placenta MSC** | **placenta MSC** | **placenta MSC** | **fetal marro MSC** | **fetal marro MSC** |
| **FACS Antibody** | **reference 1** | **reference 2** | **reference 3** | **reference 4** | **reference 5** | **reference 6** | **reference 7** | **reference 8** | **reference 9** | **reference 10** | **reference 11** | **reference 12** | **reference 13** | **reference 14,15** | **reference 16** | **reference 17** |
| CD9 | | | | ND | | | | | | | | pos | | | | |
| CD10 | 35% | | | | low | | | | | | | | | | | |
| CD13 | 98% | | | low | pos | | | | | | 88% | pos | | | | |
| CD14 | N/D | | | N/D | N/D | | immunodepleted | | low | N/D | N/D | N/D | | N/D | N/D | |
| CD16 | | | | pos | N/D | | | | | | | | | | | |
| CD19 | | | | N/D | N/D | | immunodepleted | | N/D | | | | | | | |
| CD29 | 98% | pos | | | pos | | pos | pos | pos | | 80% | pos | pos | pos | pos | 99% |
| CD31 | N/D | | | | N/D | | N/D | | low-N/D | N/D | N/D | | N/D | N/D | N/D | |
| CD33 | N/D | | | | N/D | | N/D | | N/D | | | | | | N/D | |
| CD34 | N/D | N/D | N/D | | N/D | N/D | N/D | N/D | N/D | | | N/D | | N/D | N/D | |
| CD44 | 96% | pos | pos | | pos | pos | pos | | pos | | 57% | pos | pos | pos | pos | 96% |
| CD45 | N/D | N/D | N/D | | N/D | N/D | N/D | | N/D | N/D | 0.70% | N/D | N/D | N/D | N/D | |
| CD49b | | | | N/D | pos/neg? | | pos | | pos | | | | | | | 91% |
| CD49c | pos | | | | N/D | | | | | | | | | | | 86% |
| CD49d | | | | | N/D | | pos (low) | | pos (low) | | 3.60% | | | | | 58% |
| CD49e | 83->16% | | | N/D | pos, rt-pcr | | pos | | pos | | 63% | | | | | 92% |
| CD50 | | | | N/D | N/D | | | | | | | | | | | |
| CD51/61 | 57% | pos | | N/D | pos | | pos | | pos | | 8% | | | | | 82% |
| CD54 | | | | N/D | | | | | pos | Ioderately staine | 44% | | pos | | | |
| CD56 | N/D | | | N/D | N/D | | | | | | | | | | | 47% |
| CD58 | | | | | pos | | pos | | pos | | | | | | | |
| CD62-p | | | | pos | N/D | | N/D | | N/D | | | | | | | |
| CD62-L | | | | | N/D | | N/D | | N/D | | | | | | | |
| CD71 | | | | | low | pos | | pos | | | | | | | | |
| CD73, SH3 | pos | pos | pos | | | | pos | | pos | | | pos | | pos | | |
| CD90 thyl | 81->67% | | pos | N/D | pos | pos | N/D | | Low or N/D | | 95% | pos | | | | |
| CD105 SH-2 | 86->24% | pos | pos | | pos | pos | pos | | pos | | | | | pos | low | |
| CD106 | | | N/D | | low? | | | | low | pos | 0.30% | | | | pos | |
| CD117 | N/D | | 15% | pos | low? | | N/D | | N/D | | | N/D | | | | |

| | Cell type (see footnotes) | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **UCM** | **UCM** | **UCPV cells** | **USSC** | **USSC** | **CBMSC** | **CBMSC** | **CBMSC** | **CBMSC** | **UVMSC** | **UVMSC** | **placenta MSC** | **placenta MSC** | **placenta MSC** | **fetal marro MSC** | **fetal marro MSC** |
| **FACS Antibody** | **reference 1** | **reference 2** | **reference 3** | **reference 4** | **reference 5** | **reference 6** | **reference 7** | **reference 8** | **reference 9** | **reference 10** | **reference 11** | **reference 12** | **reference 13** | **reference 14,15** | **reference 16** | **reference 17** |
| CD133/AC133 | N/D | | | | N/D | | N/D | | N/D | | | N/D | N/D | | | |
| CD135 | | | | | N/D | | N/D | | N/D | | | | | | | |
| HLA-ABC MHC I | 58% | | 75% | pos | pos | | pos | | pos | | 42% | pos | | pos | | |
| HLA-DR, DP, DQ MHC II | N/D | | N/D | N/D | N/D | | N/D | | N/D | | 0.30% | N/D | | N/D | N/D | 0% |
| HLA-G | weak | | N/D | | | | | | | | | N/D | | | | |
| Prolyl-4-hydroxylase | | | | pos | | | | | | | | | | | pos | |
| vimentin | + | | pos | pos | pos | | | | | | | pos | | pos | pos | |
| alpha smooth muscle action | + | | pos | N/D | | | | | | pos | pos | | | N/D | low | |
| type I collagen | | | | pos | | | | | | pos | pos | | | | N/D | |
| vWF von Willebrand factor | | | | | N/D | | | | low | N/D | N/D | N/D | | | N/D | |
| SSEA4 | | | N/D | pos | low | | | | | | | pos | | | | |
| Alkaline phosphatase | | | pos | | | | | | | pos | | | | | | |



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