Stem Cell Differentiate Research Literatures

Mark Herbert, PhD

World Development Institute
39-06 Main Street, Flushing, Queens, New York 11354, USA, ma8080@gmail.com

Abstract: Stem cells are derived from embryonic and non-embryonic tissues. Most stem cell studies are for animal stem cells and plants have also stem cell. Stem cells were discovered in 1981 from early mouse embryos. Stem cells have the potential to develop into all different cell types in the living body. Stem cell is a body repair system. When a stem cell divides it can be still a stem cell or become adult cell, such as a brain cell. Stem cells are unspecialized cells and can renew themselves by cell division, and stem cells can also differentiate to adult cells with special functions. Stem cells replace the old cells and repair the damaged tissues. Embryonic stem cells can become all cell types of the body because they are pluripotent. Adult stem cells are thought to be limited to differentiating into different cell types of their tissue of origin. This article introduces recent research reports as references in the related studies.
[Mark H. **Stem Cell Differentiate Research Literatures.** *Stem Cell* 2018;9(4):135-140]. ISSN: 1945-4570 (print); ISSN: 1945-4732 (online). http://www.sciencepub.net/stem. 7. doi:10.7537/marsscj090418.07.

Key words: stem cell; differentiate; life; research; literature

Introduction

The stem cell is the origin of an organism's life that has the potential to develop into many different types of cells in life bodies. In many tissues stem cells serve as a sort of internal repair system, dividing essentially without limit to replenish other cells as long as the person or animal is still alive. When a stem cell divides, each new cell has the potential either to remain a stem cell or become another type of cell with a more specialized function, such as a red blood cell or a brain cell. This article introduces recent research reports as references in the related studies.

The following introduces recent reports as references in the related studies.

Borhani-Haghighi, M., et al. (2015). "Wharton's Jelly-derived Mesenchymal Stem Cells can Differentiate into Hepatocyte-like Cells by HepG2 Cell Line Extract." Iran J Med Sci **40**(2): 143-151.

BACKGROUND: Wharton's jelly is an unlimited source of stem cells that can be used in cell therapy and tissue engineering without any ethical concern. It has been revealed the cell-free extract could be effective to induce cell differentiation. The objective of this study was to induce Wharton's jelly-derived mesenchymal stem cells (MSCs) into hepatocyte-like cells by premeabilization of the cells in the presence of HepG2 cell line extract. METHODS: MSCs were isolated from the umbilical cord, CD marker profile and their differentiation potential into adipogenic and osteogenic lineages were determined. The cells were then, permeabilized by streptolysin O in the presence of HepG cell extract. The treated cells were cultured for 17 days. The cell phenotype was evaluated and the hepatocyte specific markers were detected by immunofluorescence and immunocytochemistry. The Periodic Acid Schiff (PAS) reaction and the cellular uptake of indocyanine green were performed to evaluate the functional behavior of the differentiated cells. RESULTS: The phenotype of extract-treated MSCs changed into a round or polygonal cells with few short processes and they could express high level of albumin, cytokeratin 18 and 19. The MSCs also could store glycogen and uptake and release indocyanine green. CONCLUSION: We demonstrated for the first time that Wharton's jelly-derived MSCs could differentiate into hepatocyte-like cells by premeabilization of them in the presence of HepG2 cell extract. This study suggests a feasible method to differentiate MSCs into functional hepatocyte-like cells.

Brachvogel, B., et al. (2005). "Perivascular cells expressing annexin A5 define a novel mesenchymal stem cell-like population with the capacity to differentiate into multiple mesenchymal lineages." Development **132**(11): 2657-2668.

The annexin A5 gene (Anxa5) was recently found to be expressed in the developing and adult vascular system as well as the skeletal system. In this paper, the expression of an Anxa5-lacZ fusion gene was used to define the onset of expression in the vasculature and to characterize these Anxa5-lacZ-expressing vasculature-associated cells. After blastocyst implantation, Anxa5-lacZ-positive cells were first detected in extra-embryonic tissues and in angioblast progenitors forming the primary vascular plexus. Later, expression is highly restricted to perivascular cells in most blood vessels resembling pericytes or vascular smooth muscle cells. Viable

Anxa5-lacZ+ perivascular cells were isolated from embryos as well as adult brain meninges by specific staining with fluorescent X-gal substrates and cell-sorting. These purified lacZ+ cells specifically express known markers of pericytes, but also markers characteristic for stem cell populations. In vitro and in vivo differentiation experiments show that this cell pool expresses early markers of chondrogenesis, is capable of forming a calcified matrix and differentiates into adipocytes. Hence, Anxa5 expression in perivascular cells from mouse defines a novel population of cells with a distinct developmental potential.

Carbone, A., et al. (2016). "Adipose-derived mesenchymal stromal (stem) cells differentiate to osteoblast and chondroblast lineages upon incubation with conditioned media from dental pulp stem cell-derived osteoblasts and auricle cartilage chondrocytes." J Biol Regul Homeost Agents **30**(1): 111-122.

The potential of adipose-derived mesenchymal stromal (stem) cells (ADSCs) to differentiate into either osteoblasts or chondrocytes is controversial. In this study we investigated the multicapacity potential of ADSCs to differentiate towards adipocyte, osteoblast, and chondrocyte lineages when cells are seeded onto plastic in comparison with incubation with conditioned media (CM) obtained from differentiated cell types. ADSCs, obtained from liposuctions, were characterized for mesenchymal and hematopoietic markers by cytofluorimetry. Their differentiation capacity towards adipocytes, osteoblasts, and chondrocytes was investigated by histochemistry methods (Oil-Red-O staining, Safranin O and Alizarin Red staining, respectively). Dental pulp stem cells (DPSCs) and dedifferentiated auricle derived-chondrocytes were differentiated towards osteoblastic and chondrocytic lineages respectively, and the CM obtained from these cultures was used to induce differentiation of ADSCs. ADSCs were positive for mesenchymal markers (CD29, CD105, CD73, CD44), but not for hematopoietic lineage markers (CD14, CD34, CD45) and this behavior was conserved from the isolation up to the fifth passage. While ADSCs were readily differentiated in adipocytes, they were not towards chondrocytes and osteoblastic lineages, a behavior different from that of bone marrow-derived MSCs that differentiated into the three lineages at two weeks post-induction. Only ADSCs treated with CM from cultured chondrocytes and DPSCs, produced glycosaminoglycans and mineralized matrix. These results indicate that ADSCs need growth/morphogenic factor supplementation from the tissue environment to be appropriately differentiated to mesodermic lineages.

Floren, M., et al. (2016). "Human mesenchymal stem cells cultured on silk hydrogels with variable stiffness and growth factor differentiate into mature smooth muscle cell phenotype." Acta Biomater **31**: 156-166.

UNLABELLED: Cell-matrix and cell-biomolecule interactions play critical roles in a diversity of biological events including cell adhesion, growth, differentiation, and apoptosis. Evidence suggests that a concise crosstalk of these environmental factors may be required to direct stem cell differentiation toward matured cell type and function. However, the culmination of these complex interactions to direct stem cells into highly specific phenotypes in vitro is still widely unknown, particularly in the context of implantable biomaterials. In this study, we utilized tunable hydrogels based on a simple high pressure CO2 method and silk fibroin (SF) the structural protein of Bombyx mori silk fibers. Modification of SF protein starting water solution concentration results in hydrogels of variable stiffness while retaining key structural parameters such as matrix pore size and beta-sheet crystallinity. To further resolve the complex crosstalk of chemical signals with matrix properties, we chose to investigate the role of 3D hydrogel stiffness and transforming growth factor (TGF-beta1), with the aim of correlating the effects on the vascular commitment of human mesenchymal stem cells. Our data revealed the potential to upregulate matured vascular smooth muscle cell phenotype (myosin heavy chain expression) of hMSCs by employing appropriate matrix stiffness and growth factor (within 72h). Overall, our observations suggest that chemical and physical stimuli within the cellular microenvironment are tightly coupled systems involved in the fate decisions of hMSCs. The production of tunable scaffold materials that are biocompatible and further specialized to mimic tissue-specific niche environments will be of considerable value to future tissue engineering platforms. STATEMENT OF SIGNIFICANCE: This article investigates the role of silk fibroin hydrogel stiffness and transforming growth factor (TGF-beta1), with the aim of correlating the effects on the vascular commitment of human mesenchymal stem cells. Specifically, we demonstrate the upregulation of mature vascular smooth muscle cell phenotype (myosin heavy chain expression) of hMSCs by employing appropriate matrix stiffness and growth factor (within 72h). Moreover, we demonstrate the potential to direct specialized hMSC differentiation by modulating stiffness and growth factor using silk fibroin, a well-tolerated and -defined biomaterial with an impressive portfolio of tissue engineering applications. Altogether, our study reinforce the fact that complex differentiation protocols may be

simplified by engineering the cellular microenvironment on multiple scales, i.e. matrix stiffness with growth factor.

Han, N. R., et al. (2013). "Generation of priming mesenchymal stem cells with enhanced potential to differentiate into specific cell lineages using extracellular matrix proteins." Biochem Biophys Res Commun **436**(3): 413-417.

Poor understanding of the differentiation of mesenchymal stem cells (MSCs) has resulted in a low differentiation yield, and has hindered their application in medicine. As a solution, priming MSCs sensitive to signaling, thus stimulating differentiation into a specific cell lineage, may improve the differentiation yield. To demonstrate this, priming MSCs were produced by using a gelatin matrix for the isolation of primary MSCs from bone-marrow-derived primary cells. Subsequently, cellular characteristics and sensitivity to specific differentiation signals were analyzed at passage five. Compared to non-priming MSCs, priming MSCs showed no significant differences in cellular characteristics, but demonstrated a significant increase in sensitivity to neurogenic differentiation signals. These results demonstrate that generation of priming MSCs by specific extracellular signaling increases the rate of differentiation into a cell-specific lineage.

Hill, A. J., et al. (2009). "Human umbilical cord blood-derived mesenchymal stem cells do not differentiate into neural cell types or integrate into the retina after intravitreal grafting in neonatal rats." Stem Cells Dev **18**(3): 399-409.

This study investigated the ability of mesenchymal stem cells (MSCs) derived from full-term human umbilical cord blood to survive, integrate and differentiate after intravitreal grafting to the degenerating neonatal rat retina following intracranial optic tract lesion. MSCs survived for 1 week in the absence of immunosuppression. When host animals were treated with cyclosporin A and dexamethasone to suppress inflammatory and immune responses, donor cells survived for at least 3 weeks, and were able to spread and cover the entire vitreal surface of the host retina. However, MSCs did not significantly integrate into or migrate through the retina. They also maintained their human antigenicity, and no indication of neural differentiation was observed in retinas where retinal ganglion cells either underwent severe degeneration or were lost. These results have provided the first in vivo evidence that MSCs derived from human umbilical cord blood can survive for a significant period of time when the host rat response is suppressed even for a short period. These results, together with the observation of a lack of neuronal differentiation and integration of MSCs after intravitreal grafting, has raised an important question as to the potential use of MSCs for neural repair through the replacement of lost neurons in the mammalian retina and central nervous system.

Jung, N., et al. (2016). "Tonsil-Derived Mesenchymal Stem Cells Differentiate into a Schwann Cell Phenotype and Promote Peripheral Nerve Regeneration." Int J Mol Sci **17**(11).

Schwann cells (SCs), which produce neurotropic factors and adhesive molecules, have been reported previously to contribute to structural support and guidance during axonal regeneration; therefore, they are potentially a crucial target in the restoration of injured nervous tissues. Autologous SC transplantation has been performed and has shown promising clinical results for treating nerve injuries and donor site morbidity, and insufficient production of the cells have been considered as a major issue. Here, we performed differentiation of tonsil-derived mesenchymal stem cells (T-MSCs) into SC-like cells (T-MSC-SCs), to evaluate T-MSC-SCs as an alternative to SCs. Using SC markers such as CAD19, GFAP, MBP, NGFR, S100B, and KROX20 during quantitative real-time PCR we detected the upregulation of NGFR, S100B, and KROX20 and the downregulation of CAD19 and MBP at the fully differentiated stage. Furthermore, we found myelination of axons when differentiated SCs were cocultured with mouse dorsal root ganglion neurons. The application of T-MSC-SCs to a mouse model of sciatic nerve injury produced marked improvements in gait and promoted regeneration of damaged nerves. Thus, the transplantation of human T-MSCs might be suitable for assisting in peripheral nerve regeneration.

Peng, J., et al. (2011). "Human umbilical cord Wharton's jelly-derived mesenchymal stem cells differentiate into a Schwann-cell phenotype and promote neurite outgrowth in vitro." Brain Res Bull **84**(3): 235-243.

Cell-based therapy has achieved promising functional recovery for peripheral nerve repair. Although Schwann cells (SCs) and bone marrow derived mesenchymal stromal cells (BM-MSCs) are the main cell source for nerve tissue engineering, the clinical application is limited because of donor site morbidity, the invasive procedure, and the decreased number of SCs and BM-MSCs. Wharton's jelly-derived mesenchymal stem cells (WJMSCs) could be a promising cell source for nerve tissue engineering because they are easily accessible and their use has no ethical issues. We investigated the phenotypic, molecular and functional characteristics of WJMSCs differentiated along a Schwann-cell lineage. Cultured

WJMSCs were isolated from human umbilical cord, and the undifferentiated WJMSCs were confirmed by the detection of MSC-specific cell-surface markers. WJMSCs treated with a mixture of glial growth factors (basic fibroblast growth factor, platelet-derived growth factor and forskolin) adopted a spindle-like morphology similar to SCs. Immunocytochemical staining, RT-PCR analysis, and Western blot analysis revealed that the treated cells expressed the glial markers glial fibrillary acidic protein, p75, S100 and P0 and indicative of differentiation. On co-culture with dorsal root ganglia neurons, the differentiated WJMSCs enhanced the number of sprouting neurites and neurite length in dorsal root ganglia neurons. Furthermore, using enzyme-linked immunosorbent assay and RT-PCR methodology, we found differentiated WJMSCs secrete and express neurotrophic factors, including brain-derived neurotrophic factor (BDNF), nerve growth factor (NGF), and neurotrophin-3 (NT-3). Quantification of neurite outgrowth from PC12 cells grown in differentiated WJMSCs-conditioned media demonstrates that the neurite length is significantly more than control medium and undifferentiated WJMSCs group. WJMSCs can be differentiated into cells that are Schwann-like in terms of morphologic features, phenotype, and function and could be suitable Schwann-cell substitutes for nerve repair in clinical applications.

Pulavendran, S., et al. (2010). "Hepatocyte growth factor incorporated chitosan nanoparticles differentiate murine bone marrow mesenchymal stem cell into hepatocytes in vitro." IET Nanobiotechnol **4**(3): 51-60.

Delivery of growth factor for the differentiation of stem cells into lineage specific cells holds great potential in regenerative medicine. Stem cell differentiation is governed by cytokines and growth factors secreted upon the organelle injury and, however, their short half-life necessitates exogenous supply. Development of suitable nanodevices using biodegradable polymers to deliver therapeutic proteins to the targeted site in a sustainable manner attracts scientists and clinicians. Here, for the first time, hepatocyte growth factor (HGF) was incorporated into chitosan nanoparticles (CNP) by ionotrophic gelation method. An average size of nanoparticles prepared was 100 nm, showing sustainable release of HGF. Cytotoxicity study did not reveal any adverse effect on bone marrow mesenchymal stem cells (MSC) up to 4 mg CNP/ml culture medium. To evaluate the effect of HGF incorporated CNP (HGF-CNP) on hepatic differentiation in in vitro, MSC were incubated with HGF-CNP and other supplements. After 21 days, fibroblast-like morphology of MSC became round-shape, a typical characteristic of hepatocyte cell. Immunofluorescence study for albumin expression confirmed the hepatic differentiation. In conclusion, HGF released from the HGF-CNP can differentiate MSC into hepatocytes, and this novel technique could also be extended to deliver therapeutic proteins for a variety of tissue regeneration.

Shi, C., et al. (2008). "HRMAS 1H-NMR measured changes of the metabolite profile as mesenchymal stem cells differentiate to targeted fat cells in vitro: implications for non-invasive monitoring of stem cell differentiation in vivo." J Tissue Eng Regen Med **2**(8): 482-490.

Mesenchymal stem cells (MSCs) have shown a great potential for clinical applications in regenerative medicine. However, it remains challenging to follow the transplanted cell grafts in vivo. Nuclear magnetic resonance spectroscopy (NMR or MRS) is capable of determining and quantifying the cellular metabolites in tissue and organs non-invasively, therefore it is an attractive method for monitoring and evaluating the differentiation and functions of transplanted stem cells in vivo. In this study, metabolic changes of MSCs undergoing adipogenic differentiation to targeted fat cells were investigated in vitro, using solid-state high-resolution magic angle spinning (1)H nuclear magnetic resonance spectroscopy. Quantification of metabolite concentrations before and after differentiation of MSCs showed decreased levels of intracellular metabolites, including choline, creatine, glutamate and myo-inositol, and a substantially increased level of fatty acids, when mesenchymal stem cells were differentiated preferentially to fat cells. Intracellular creatine, myo-inositol and choline reduced from 10.4 +/- 0.72, 16.2 +/- 1.2 and 8.22 +/- 0.51 mM to 3.27 +/- 0.34, 6.1 +/- 0.46 and 3.11 +/- 0.32 mM, respectively, while fatty acids increased from 32.6 +/- 1.5 to 91.2 +/- 3.2 mM after undergoing 3 weeks of differentiation. The increase of the fatty acid concentration measured by NMR is confirmed by the observation of 80% fat cells in differentiated cells by cell counting assay, suggesting resonances from fatty acids may be used as metabolite markers for monitoring MSC differentiation to fat cells in vivo, using the magnetic resonance spectroscopic technique readily available on MRI scanners.

Wang, T., et al. (2006). "Cell-to-cell contact induces mesenchymal stem cell to differentiate into cardiomyocyte and smooth muscle cell." Int J Cardiol **109**(1): 74-81.

BACKGROUND: Recent evidences have suggested that stem cell can differentiate into cardiomyocyte and smooth muscle cell (SMC) in vivo or in vitro. But the mechanism on how stem cell

differentiates is still unknown. We investigated whether intercellular interaction or soluble chemical factors would induce mesenchymal stem cells (MSCs) to acquire the phenotypical characteristics of cardiomyocytes or SMC. METHODS: MSCs were isolated from rat bone marrow with density gradient centrifugation and amplified in vitro. Flow cytometry was used to monitor the expression of surface antigen profile. After labeled by GFP (green fluorescent protein) transfection, rat MSCs were used to culture with adult rat cardiomyocytes and rat aortic SMCs in direct co-culture, indirect co-culture and conditioned culture, respectively. One week later, immunofluorescence staining against alpha-actin, desmin, and cardiac troponin T (cTnT) for cardiomyocyte, smooth muscle calponin and SM-alpha-actin for SMC were performed. RESULTS: Immunofluorescence staining was positive against alpha-actin, desmin, and cTnT on MSCs in co-culture group with adult cardiomyocytes, positive against smooth muscle calponin and SM-alpha-actin on MSCs in co-culture group with SMCs. In contrast, no alpha-actin, desmin, and cTnT expression was observed in the indirect co-culture group and conditioned culture group; no smooth muscle calponin and SM-alpha-actin in the indirect co-culture group and conditioned culture group. CONCLUSIONS: Direct cell-to-cell contact between MSC and adult cardiomyocyte or SMC, but not the soluble signaling molecules is obligatory in the differentiation of MSC into cardiomyocytes or SMC.

Wang, Y. C. and Y. Zhang (2008). "[Proliferative capacity of mesenchymal stem cells from human fetal bone marrow and their ability to differentiate into the derivative cell types of three embryonic germ layers]." Sheng Li Xue Bao **60**(3): 425-430.

Strong proliferative capacity and the ability to differentiate into the derivative cell types of three embryonic germ layers are the two important characteristics of embryonic stem cells. To study whether the mesenchymal stem cells from human fetal bone marrow (hfBM-MSCs) possess these embryonic stem cell-like biological characteristics, hfBM-MSCs were isolated from bone barrows and further purified according to the different adherence of different kinds of cells to the wall of culture flask. The cell cycle of hfBM-MSCs and MSC-specific surface markers such as CD29, CD44, etc were identified using flow cytometry. The expressions of human telomerase reverse transcriptase (hTERT), the embryonic stem cell-specific antigens, such as Oct4 and SSEA-4 were detected with immunocytochemistry at the protein level and were also tested by RT-PCR at the mRNA level. Then, hfBM-MSCs were induced to differentiate toward neuron cells, adipose cells, and islet B cells under certain conditions. It was found that 92.3% passage-4 hfBM-MSCs and 96.1% passage-5 hfBM-MSCs were at G (0)/G (1) phase respectively. hfBM-MSCs expressed CD44, CD106 and adhesion molecule CD29, but not antigens of hematopoietic cells CD34 and CD45, and almost not antigens related to graft-versus-host disease (GVHD), such as HLA-DR, CD40 and CD80. hfBM-MSCs expressed the embryonic stem cell-specific antigens such as Oct4, SSEA-4, and also hTERT. Exposure of these cells to various inductive agents resulted in morphological changes towards neuron-like cells, adipose-like cells, and islet B-like cells and they were tested to be positive for related characteristic markers. These results suggest that there are plenty of MSCs in human fetal bone marrow, and hfBM-MSCs possess the embryonic stem cell-like biological characteristics, moreover, they have a lower immunogenic nature. Thus, hfBM-MSCs provide an ideal source for tissue engineering and cellular therapeutics.

The above contents are the collected information from Internet and public resources to offer to the people for the convenient reading and information disseminating and sharing.

References

1. Baidu. http://www.baidu.com. 2019.
2. Borhani-Haghighi, M., et al. (2015). "Wharton's Jelly-derived Mesenchymal Stem Cells can Differentiate into Hepatocyte-like Cells by HepG2 Cell Line Extract." Iran J Med Sci 40(2): 143-151.
3. Brachvogel, B., et al. (2005). "Perivascular cells expressing annexin A5 define a novel mesenchymal stem cell-like population with the capacity to differentiate into multiple mesenchymal lineages." Development 132(11): 2657-2668.
4. Cancer Biology. http://www.cancerbio.net. 2019.
5. Carbone, A., et al. (2016). "Adipose-derived mesenchymal stromal (stem) cells differentiate to osteoblast and chondroblast lineages upon incubation with conditioned media from dental pulp stem cell-derived osteoblasts and auricle cartilage chondrocytes." J Biol Regul Homeost Agents 30(1): 111-122.
6. Floren, M., et al. (2016). "Human mesenchymal stem cells cultured on silk hydrogels with variable stiffness and growth factor differentiate into mature smooth muscle cell phenotype." Acta Biomater 31: 156-166.
7. Google. http://www.google.com. 2019.
8. Han, N. R., et al. (2013). "Generation of priming mesenchymal stem cells with enhanced potential to differentiate into specific cell lineages using

extracellular matrix proteins." Biochem Biophys Res Commun 436(3): 413-417.
9. Hill, A. J., et al. (2009). "Human umbilical cord blood-derived mesenchymal stem cells do not differentiate into neural cell types or integrate into the retina after intravitreal grafting in neonatal rats." Stem Cells Dev 18(3): 399-409.
10. Journal of American Science. http://www.jofamericanscience.org. 2019.
11. Jung, N., et al. (2016). "Tonsil-Derived Mesenchymal Stem Cells Differentiate into a Schwann Cell Phenotype and Promote Peripheral Nerve Regeneration." Int J Mol Sci 17(11).
12. Life Science Journal. http://www.lifesciencesite.com. 2019.
13. Ma H, Chen G. Stem cell. The Journal of American Science 2005;1(2):90-92. doi:10.7537/marsjas010205.14. http://www.jofamericanscience.org/journals/am-sci/0102/14-mahongbao.pdf.
14. Ma H, Cherng S. Eternal Life and Stem Cell. Nature and Science. 2007;5(1):81-96. doi:10.7537/marsnsj050107.10. http://www.sciencepub.net/nature/0501/10-0247-mahongbao-eternal-ns.pdf.
15. Ma H, Cherng S. Nature of Life. Life Science Journal 2005;2(1):7-15. doi:10.7537/marslsj020105.03. http://www.lifesciencesite.com/lsj/life0201/life-0201-03.pdf.
16. Ma H, Yang Y. Turritopsis nutricula. Nature and Science 2010;8(2):15-20. doi:10.7537/marsnsj080210.03. http://www.sciencepub.net/nature/ns0802/03_1279_hongbao_turritopsis_ns0802_15_20.pdf.
17. Ma H. The Nature of Time and Space. Nature and science 2003;1(1):1-11. doi:10.7537/marsnsj010103.01. http://www.sciencepub.net/nature/0101/01-ma.pdf.
18. Marsland Press. http://www.sciencepub.net. 2019; http://www.sciencepub.org. 2019.
19. National Center for Biotechnology Information, U.S. National Library of Medicine. http://www.ncbi.nlm.nih.gov/pubmed. 2019.
20. Nature and Science. http://www.sciencepub.net/nature. 2019.
21. Peng, J., et al. (2011). "Human umbilical cord Wharton's jelly-derived mesenchymal stem cells differentiate into a Schwann-cell phenotype and promote neurite outgrowth in vitro." Brain Res Bull 84(3): 235-243.
22. Pulavendran, S., et al. (2010). "Hepatocyte growth factor incorporated chitosan nanoparticles differentiate murine bone marrow mesenchymal stem cell into hepatocytes in vitro." IET Nanobiotechnol 4(3): 51-60.
23. Shi, C., et al. (2008). "HRMAS 1H-NMR measured changes of the metabolite profile as mesenchymal stem cells differentiate to targeted fat cells in vitro: implications for non-invasive monitoring of stem cell differentiation in vivo." J Tissue Eng Regen Med 2(8): 482-490.
24. Stem Cell. http://www.sciencepub.net/stem. 2019.
25. Wang, T., et al. (2006). "Cell-to-cell contact induces mesenchymal stem cell to differentiate into cardiomyocyte and smooth muscle cell." Int J Cardiol 109(1): 74-81.
26. Wang, Y. C. and Y. Zhang (2008). "[Proliferative capacity of mesenchymal stem cells from human fetal bone marrow and their ability to differentiate into the derivative cell types of three embryonic germ layers]." Sheng Li Xue Bao 60(3): 425-430.
27. Wikipedia. The free encyclopedia. http://en.wikipedia.org. 2019.

12/25/2018