



## Stem Cell Research Literatures (1)

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**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.

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**Key words:** stem cell; 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.

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Alexanian, A. R. (2015). "Epigenetic modulators promote mesenchymal stem cell phenotype switches." *Int J Biochem Cell Biol* **64**: 190-194.

Discoveries in recent years have suggested that some tissue specific adult stem cells in mammals might have the ability to differentiate into cell types from different germ layers. This phenomenon has been referred to as stem cell transdifferentiation or plasticity. Despite controversy, the current consensus holds that transdifferentiation does occur in mammals, but only within a limited range. Understanding the mechanisms that underlie the switches in phenotype and development of the methods that will promote such type of conversions can open up endless possibilities for regenerative medicine. Epigenetic control contributes to various

processes that lead to cellular plasticity and DNA and histone covalent modifications play a key role in these processes. Recently, we have been able to convert human mesenchymal stem cells (hMSCs) into neural-like cells by exposing cells to epigenetic modifiers and neural inducing factors. The goal of this study was to investigate the stability and plasticity of these transdifferentiated cells. To this end, neurally induced MSCs (NI-hMSCs) were exposed to adipocyte inducing factors. Grown for 24-48 h in fat induction media NI-hMSCs reversed their morphology into fibroblast-like cells and regained their proliferative properties. After 3 weeks approximately 6% of hMSCs differentiated into multilocular or plurivacuolar adipocyte cells that demonstrated by Oil Red O staining. Re-exposure of these cultures or the purified adipocytes to neural induction medium induced the cells to re-differentiate into neuronal-like cells. These data suggest that cell plasticity can be manipulated by the combination of small molecule modulators of chromatin modifying enzymes and specific cell signaling pathways.

Chikhovskaya, J. V., et al. (2012). "Human testis-derived embryonic stem cell-like cells are not pluripotent, but possess potential of mesenchymal progenitors." *Hum Reprod* **27**(1): 210-221.

**BACKGROUND:** Spontaneous in vitro transition of undifferentiated spermatogonia into the pluripotent cell state has been achieved using neonatal and adult mouse testis tissue. In an effort to establish an analogous source of human patient-specific pluripotent stem cells, several research groups have described the derivation of embryonic stem cell-like cells from primary cultures of human testis. These cells are characterized in all studies as growing in compact colonies, expressing pluripotency-associated markers and possessing multilineage differentiation capabilities in vitro, but only one study claimed their ability to induce teratomas. This controversy initiated a debate about the pluripotent state and origin of human testis-derived ES-like cells (htES-like cells). **METHODS:** htES-like cell colonies were obtained from primary testicular cultures of three individuals and selectively expanded using culture conditions known to support the propagation of blastocyst-derived human embryonic stem cells (ESCs), mouse epiblast stem cells and 'naive' human ESCs. The stem cell properties of htES-like cells were subsequently assessed by testing the expression of ESC-specific markers, differentiation abilities in vitro and in vivo, and microarray profiling. **RESULTS:** The expression of pluripotency-associated markers in htES-like cells and their differentiation abilities differed significantly from those of ESCs. Gene expression microarray analysis revealed that htES-like cells possess a transcriptome distinct from human ESCs and fibroblasts, but closely resembling the transcriptome of mesenchymal stem cells (MSCs). The similarity to MSCs was confirmed by detection of SSEA4/CD146 expressing cells within htES-like colonies and efficient in vitro differentiation toward three mesodermal lineages (adipogenic, osteogenic, chondrogenic). **CONCLUSIONS:** Taken together, these results indicate that htES-like cells, in contrast to pluripotent stem cells derived from adult mouse testis, are not pluripotent and most likely not of germ cell but of mesenchymal origin.

Conde-Green, A., et al. (2010). "Influence of decantation, washing and centrifugation on adipocyte and mesenchymal stem cell content of aspirated adipose tissue: a comparative study." *J Plast Reconstr Aesthet Surg* **63**(8): 1375-1381.

**BACKGROUND:** In the last decade, controversy has arisen regarding the influence of fat harvesting, processing and injection techniques on adipose tissue graft. The aim of this study is to compare the influence of three widely used fat processing techniques in plastic surgery on the viability and number of adipocytes and mesenchymal stem cells (MSCs) of aspirated fat. **METHODS:** A prospective cross-sectional study was conducted in 20 adult healthy female patients in whom material obtained by liposuction of the lower abdomen was separated and processed by decantation, washing or centrifugation. The morphology and quantity of adipocytes were determined by histological analysis. The viability and number of MSCs in the middle layer of each lipoaspirate and the pellet derived from centrifuged samples were obtained by multi-colour flow cytometry. **RESULTS:** Cell count per high-powered field of intact nucleated adipocytes was significantly greater in decanted lipoaspirates, whereas centrifuged samples showed a greater majority of altered adipocytes. MSC concentration was significantly higher in washed lipoaspirates compared to decanted and centrifuged samples. However, the pellet collected at the bottom of the centrifuged samples showed the highest concentration of MSCs. **CONCLUSION:** Based on the theory of cell survival stating the importance of adipocytes' integrity for graft survival and the theory claiming the importance of regenerative MSCs in the maintenance and stabilisation of fat transplant, washing may turn out to be the best processing technique for adipose tissue graft take. While eliminating most contaminants during the process, it preserved and maintained the quantity, integrity and viability of the most important components of aspirated adipose tissue.

Dickhut, A., et al. (2005). "Mesenchymal stem cells obtained after bone marrow transplantation or peripheral blood stem cell transplantation originate from host tissue." *Ann Hematol* **84**(11): 722-727.

Mesenchymal stem cells (MSC) obtained from human bone marrow have been described as adult stem cells with the ability of extensive self-renewal and clonal expansion, as well as the capacity to differentiate into various tissue types and to modulate the immune system. Some data indicate that leukapheresis products may also

contain non-hematopoietic stem cells, as they occur in whole bone marrow transplantation (BMT). However, there is still controversy whether MSC expand in the host after transplantation like blood progenitor cells do. Therefore, we were interested in finding out if graft MSC can be detected in leukapheresis products and in bone marrow after BMT and peripheral blood stem cell transplantation (PBSCT). Every sample from total bone marrow transplants exhibited growth of MSC after in vitro culture, but not one of nine leukapheresis products did. In addition, bone marrow aspirates of 9 patients receiving BMT and of 18 patients after PBSCT were examined for origin of MSC. Almost all MSC samples exhibited a complete host profile, whereas peripheral blood cells were of donor origin. We conclude that even if trace amounts of MSC are co-transplanted during PBSCT or BMT, they do not expand significantly in the host bone marrow.

Kaplan, A., et al. (2017). "Impact of starting material (fresh versus cryopreserved marrow) on mesenchymal stem cell culture." *Transfusion* **57**(9): 2216-2219.

**BACKGROUND:** Mesenchymal stem cells (MSCs) continue to be investigated in multiple clinical trials as potential therapy for different disorders. There is ongoing controversy surrounding the clinical use of cryopreserved versus fresh MSCs. However, little is known about how cryopreservation affects marrow as starting material. The growth kinetics of MSC cultures derived from fresh versus cryopreserved marrow were compared. **STUDY DESIGN AND METHODS:** Data were reviewed on the growth kinetics of MSCs derived from fresh versus cryopreserved marrow of nine donors. Marrow harvested from each donor was separated into four aliquots (one fresh and three cryopreserved for culture). Data on the date of mononuclear cell cryopreservation/thaw, MSC counts at Passages 1 and 2, MSC doubling, MSC fold expansion, viability (of mononuclear cells and final MSCs), and on flow cytometry markers of mononuclear cells and final MSCs were analyzed for the fresh and cryopreserved marrow groups. **RESULTS:** In total, 21 MSC lots (seven fresh and 14 cryopreserved) were obtained. The average age of cryopreserved mononuclear cell product was 295 days (range, 18-1241 days). There were no significant differences between MSC numbers at Passage

1 ( $p = 0.1$ ), final MSC numbers ( $p = 0.5$ ), MSC doubling ( $p = 0.7$ ), or MSC fold expansion ( $p = 0.7$ ). A significant difference was observed in viability by flow cytometry for both mononuclear cells ( $p = 0.002$ ) and final MSCs ( $p = 0.009$ ), with higher viability in the fresh marrow group. **CONCLUSION:** This study demonstrates that MSCs derived from cryopreserved marrow have the same growth characteristics as fresh marrow-derived MSCs. Further studies are needed to explore potential differences in clinical efficacy.

Stolzing, A., et al. (2008). "Age-related changes in human bone marrow-derived mesenchymal stem cells: consequences for cell therapies." *Mech Ageing Dev* **129**(3): 163-173.

Human mesenchymal stem cells (hMSC) represent a promising cell-based therapy for a number of degenerative conditions. Understanding the effect of aging on hMSCs is crucial for autologous therapy development in older subject whom degenerative diseases typically afflict. Previous investigations into the effects of aging on hMSC have proved contradictory due to the relative narrow age ranges of subjects assessed and the exclusive reliance of in vitro assays. This study seeks to address this controversy by using a wider range of donor ages and by measuring indices of cellular aging as well as hMSC numbers ex vivo and proliferation rates. CFU-f analysis and flow cytometry analysis using a CD45(low)/D7fib(+ve)/LNGF(+ve) gating strategy were employed. In addition a variety of markers of cellular aging, oxidative damage and senescence measured. A reduction in CFU-f and CD45(low)/D7fib(+ve)/LNGF(+ve) cell numbers were noted in adulthood relative to childhood. Indices of aging including oxidative damage, ROS levels and p21 and p53 all increased suggesting a loss of MSC fitness with age. These data suggest that hMSC numbers obtained by marrow aspiration decline with age. Furthermore, there is an age-related decline in overall BM MSC "fitness" which might lead to problems when using autologous aged MSC for cell-based therapies.

Sung, W. J., et al. (2015). "Epithelial-mesenchymal transition in patients of pulmonary adenocarcinoma: correlation with cancer stem cell markers and prognosis." *Int J Clin Exp Pathol* **8**(8): 8997-9009.

Adenocarcinoma is the most common histologic type of non-small cell lung carcinomas. The existence of lung cancer stem cells (CSCs) and epithelial-mesenchymal transition (EMT) in human tissue is controversy. The aim of this study is to investigate the expression and clinical significance of CSCs and EMT markers and evaluate the correlation between the two in lung adenocarcinoma. A total of 97 cases comprise the tissue microarray from surgical resection for primary lung adenocarcinoma. Immunohistochemistry for ALDH1 and CD44 as CSC markers and E-cadherin, vimentin, fibronectin, SMA as EMT markers was performed. High ALDH1A1 expression was statistically associated with female gender (P=0.001), smoker (P=0.012), and high pT stages (P=0.046). High CD44 expression was statistically associated with female gender (P=0.008), non-smoker (P=0.000), and no pleural invasion (P=0.039). High expression of ALDH1 was associated with good overall survival (P=0.021). High expression of CD44 was correlated with both good overall survival (P=0.024) and disease-free survival (P=0.000). Vimentin expression was associated with pT stage (P=0.001) and pleural invasion (P=0.028). E-cadherin, fibronectin and SMA were not associated with clinicopathologic correlation and all EMT markers were not correlated with survival of lung adenocarcinoma. CSC markers expression was not related to EMT. Our results showed that the expression of CSCs was associated with a good prognosis in lung adenocarcinoma. The prognostic significance of EMT markers was skeptical in this study. There is a need for more research about CSC, EMT, and the relation between these two in human lung adenocarcinoma.

Torsvik, A., et al. (2012). "Comment to: "Spontaneous transformation of adult mesenchymal stem cells from cynomolgus macaques in vitro" by Z. Ren et al. *Exp. Cell Res.* 317 (2011) 2950-2957: spontaneous transformation of mesenchymal stem cells in culture: facts or fiction?" *Exp Cell Res* 318(5): 441-443.

There is at present a controversy in the literature whether MSCs are susceptible to spontaneous in vitro transformation or not. Several groups have reported spontaneous transformation of MSCs from various species. However, some of these reports were not true transformations and later proven to be due to cross-contaminating cancer cells. To date

there is no solid evidence that MSCs can undergo spontaneous transformation in culture. Only two groups used DNA fingerprinting to authenticate their transformed cells, and both groups later showed cross-contamination of cancer cells in their cultures. In this commentary, we address the paper "Spontaneous transformation of adult mesenchymal stem cells from cynomolgus macaques in vitro" by Z. Ren et al. *Exp. Cell Res.* 317 (2011) 2950-2957. In this article the authors characterize the transformed mesenchymal cells (TMCs) and claim to have verified their origin. We question the authentication of the TMCs made by the authors and we also believe it is in the interest of the scientific community, that a highly controversial finding, such as spontaneous transformation of MSCs, should be properly verified by stringent methods, preferably DNA fingerprinting, in order to validate if an actual transformation event has occurred.

Wagner, W. and A. D. Ho (2007). "Mesenchymal stem cell preparations--comparing apples and oranges." *Stem Cell Rev* 3(4): 239-248.

Mesenchymal stem cells (MSC) represent a type of adult stem cells that can easily be isolated from various tissues and expanded in vitro. Past reports on their pluripotency and possible clinical applications have raised hopes and interest in MSC. Multiple designations have been given to different MSC preparations. So far MSC are poorly defined by a combination of physical, phenotypical and functional properties. As MSC could be derived from different tissues as starting material, by diverse isolation protocols, cultured and expanded in different media and conditions, the MSC preparations from different laboratories are highly heterogeneous. All of these variables might have implications (1) on the selection of cell types and the composition of heterogeneous subpopulations; (2) they can selectively favor expansion of different cell populations with totally different potentials; or (3) they might alter the long term fate of adult stem cells upon in vitro culture. The recent controversy on the multilineage differentiation potentials of some specific MSC preparations might be attributed to this lack of common standards. More precise molecular and cellular markers to define subsets of MSC and to standardize the protocols for expansion of MSC are urgently needed.

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.

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