Journal of Pharmacy and Alternative Medicine www.iiste.org
ISSN 2222-4807 (online) ISSN 2222-5668 (Paper) An International Peer-reviewed Journal
Vol.10, 2016

Review: Potential of Stem Cells as Regenerative Medicines

Muhammad Shahid Javaid[1]* Usman Ali Ashfaq[2] Muhammad Shareef Masoud[2]
1.Centre of Excellence in Molecular Biology, University of the Punjab, Lahore, Pakistan
2. Department of Bioinformatics & Biotechnology, Government College University Faisalabad, 38000 Faisalabad, Pakistan

Abstract
Regenerative medicines are used to restore the normal function of the damaged organs and tissues to repair them or replace them with functional ones by using a complex surgical process. Limited number of the organ donors as well as the complex surgical procedure turned this field to use an alternative way. The best alternative way is to use the stem cells. Stem cells are the cells that have self renewal capacity as well as have capability to differentiate into specialized and specific cell lineages to repair or replace the damaged tissue or organ. So, the problems that are faced during transplantation are overcome by using stem cells. There are a number of sources of stem cells and their differentiation abilities are vary according to their sources such as some cells give rise to all cell types while some are not. Sources of stem cells are embryo, adipose tissues, amniotic fluid, bone marrow etc. and cell type specific stem cells such as dental pulp stem cells etc. Stem cells have proved their importance and potential as regenerative medicines form fatal diseases such as damaging of heart, kidney, lung and liver to less fatal diseases such as osteoporosis and damaging of teeth. Stem cells also used in the enhancement of aesthetic value of a person by plastic or reconstructive surgery. Paracrine factors and the surrounding environment also have impact on the working of stem cells.
Keywords: Regenerative medicines, stem cells,differentiation

1. Introduction

Stem cells are defined as the cells that have the greater ability of self renewal which means that they have tendency to undergo a number of cycles of cell divisions to produce daughter cells and they also have capability to differentiate into specialized cell types [1, 2]. These stem cells are divided and differentiated into different cells that are appropriate for the tissues in which they are found. Stem cells are described as: **(1)** *Totipotent*: these stem cells are differentiated into all the cell types of an organism including extraembryonic tissues of embryo. **(2)** *Pluripotent*: these stem cells are differentiated into all cells types except extraembryonic tissues. **(3)** *Multipotent*: these stem cells are differentiated into all the cells types of a specific tissue. **(4)** *Unipotenet* : these stem cells are differentiated into only one specific lineage of cells of a specific tissue [3].

The types and sources of stem cells are: **(1)** Embryo: embryonic stem cells of human are pluripotent and source is blastocysts [4, 5]. **(2)** Adult stem cells: adult stem cells are multipotent and differentiate into cells that are specific to the organs where they are found [6, 7] and are derived from Bone Marrow , Dental pulp, Adipose Tissues, Amniotic fluid, skin, skeletal muscle and Cord Blood [6, 8, 9]. **(3)** Induced pluripotent stem cells: these cells are produced by reprogramming of adult somatic cells or from the cells of patient that have a specific disease [10-16].

Regenerative medicine is a multi-disciplinary field that holds the promise of repairing and replacement of the damaged organs or tissues as well as the restoration of the normal function of a damaged organ or tissue. It is done by the consistent and effectual therapies that are composed by living cells [17]. Regenerative medicines based on transplantation of the organs and cell therapies by hematopoietic cell transplantation has been practiced from many years for example transplantation of bone marrow [18]. Regenerative medicines hold the huge opportunity as there is increasing ageing population with illness. So for gene therapy, cultured and stem cells can be used and these cells can also be used to study the process of a specific disease or for drug development, in laboratory experiments [19].

The basic aim of the regenerative medicines is to restore the normal function of the organ that have damaged due to chemical, physical defect or genetic or infectious disease [20]. The patient with damaged organs or tissues have need to replace their organs with functional one by organ transplantation. Very low number of the organ donors for the organ transplantation has been triggered the regenerative medicine to research on stem cells as an alternative and potential source for the organ or tissue development and replacement. The discovery of the methods for the generation and isolation of stem cells from different sources holds the promise as an alternative for the cell based therapy. [21].

Stem cells play a significant role in the regeneration of the defective tissues. Among clinical therapies immense hope was showed by intraoperative cell based therapy [22]. For regenerative therapies stem cells have enormous applications because they are the fundamental units and they show potential for that purpose but they are not solo actors because stem cells respond to the extrinsic or molecular signals that subsequently direct their behavior [23]. By the expression of some combined transcription factors the adult somatic cells are converted into

stem cells called induced pluripotent stem cells (iPSCs) that are used for the treatment of numerous disorders and diseases of the organs/tissues [24]. Besides these, the embryonic, amniotic, dental pulp, cord blood and adipose derived stem cells are used as a regenerative medicines to treat different diseases or failure of organs.

2. Stem cells as regenerative medicines in dentistry

In dentistry, the regenerative therapy was used to replace or restore the function of defective teeth by using explants from autologous cells. It has been examined by using the biology of stem cell. Stem cells from the dental tissues that can only differentiate into in the lineages of the dental cells were identified and these cells have been used for the regeneration of the dental tissues. For the replacement of the whole tooth, production of bioengineered teeth was done by cell clamp and scaffold methods. *In vivo* development of tooth in the oral environment of adult was also reported [25].

It was identified that the pulps of the impacted, deciduous and human permanent teeth have stem cells that have the ability to differentiate into odontoblast [26-28]. Cells of the dental pulp of the human teeth and stem cells of the periodontal tissues that were isolated from the erupted human teeth, involved in the regeneration of the periodontal tissues by cellular transplantation into the teeth of adult [29, 30]. Multipotent stem cells of impacted teeth of human were identified to differentiate into the cells lineages of neurons and hepatocytes [31]. For the generation of the whole tooth, the stem cells of the somatic dental tissue were identified as valuable candidates and adult bone marrow was also identified as a source of beneficial cells [32]. It was examined that mesenchymal stem cells have ability to rapidly increase their number and thus have given an assurance that stem cells have positive influence in dentistry. Stem cells derived from adipose tissues have some prime factors such as strong capability of the secretion of growth factor as well as the high rate of the differentiation of cell. Adipose tissues have abundant number of stem cells and these cells were isolated easily from adipose tissues. Stem cell based regenerative medicines have some prime factors such as low number of unhealthy effects, have high duplication rate and a greater level of safety regarding both; the collection and the grafting of cells [33].

Dental pulp was identified as a source of mesenchymal stem cells. Dental pulp stem cells were shown multipotency as they have the ability to differentiate into different cell lineages such as adipocytes, osteoblast, chondrocytes, neural lineages and odontoblast. They possessed high duplication rate and accessed easily and have a role in teeth tissue regeneration [34]. Dental stem cells were played role in the development of whole human tooth and defected teeth were replaced with bioengineered human teeth in regenerative dentistry [35].

3. Stem cells as regenerative medicines for lung

The potential of the stem cells that were present inside the lung was investigated to study their potential to repair the injured or defective lung. Stem cells that were not taken from lung were also studied to analyze their efficiency potential in the repair mechanism of lung [36]. It was determined that the progenitor and the stem cells taken from the lung, played a role in epithelial conservation and in the restoration of the function of injured lung [37].

Mesenchymal stem cells (MSCs) were identified as promising candidates to repair the defects of lung based on immune system and inflammation response. Almost 50 studies were published to treat these disorders in animal models [38]. MSCs were also played role to reduce the inflammation of lung as well as deposition of collagen. It was thought that MSCs were produced an antagonist receptor of interleukin-1α of anti-inflammatory nature to repair the defects due to inflammation [39].

Adipose derived stem cells were proved helpful in the protection against sepsis and for the reduction of inflammation of lung. Mesenchymal stem cells were subjected and their role were determined for appropriate functioning of lung that was damaged by sepsis [40, 41].

4. Stem cells as regenerative medicines for Kidney

Kidney is one of the most complicated organs of the body. Kidney transplantation was performed to replace the damaged kidney but limited number of donor were posed a problem. Regenerative medicines based on stem cells was a new hope to overcome this problem [42].

With the help of different factors, embryonic stem cells were speciated into renal cells and thus played a role to form embryonic tubule epithelia when cultured with the addition of bone morphogenetic protein 4 [43].

Mesenchymal stem cells were differentiated into many types of renal cells such as into peritubular capillary of renal [44], into epithelium of renal [45], into stem cells of renal to cure the acute kidney disease in mouse model [46], into padocytes of glomerular as well as tubular cells [47] and into the mesangial cells of glomerular [48].

Stem cells derived from amniotic fluid were used to regenerate the kidney because they were divided at organogenesis stage of kidney [49]. Induced pluripotent stem cells were taken as the future of stem cells based regenerative medicines for kidney [50].

5. Stem cells as regenerative medicines for Heart

Mammals have no ability to regenerate the damaged tissues instead they were formed a scar tissue to heal and protect the further damaging of the tissue but function of organ was deteriorated. It was determined that stem cells combining with immune response were played a role for regeneration [51].

It was reported that resident stem cells of cardiac are able to replace the injured myocardium [52]. Embryonic stem cells were differentiated into cardiac muscle cells. Laboratory experiments were showed that these cardiomyoctes were contracted involuntary and have capacity to generate many cardiac phenotypes including organization of myofibrillar and cardiac protein. These cells were used to replace the damaged cardiomyocytes [53].

In vivo derived cardiac muscle cells from embryonic stem cells were used as pacemakers in those models of heart that were blocked atrioventriculary [54]. Laboratory experiments were showed that mysenchymal stem cells differentiated into sarcomeres and into cardiac muscle cells with involuntary action when treated with 5-Azacytidine [55]. By three dimensional compositions, human mysenchymal stem cells were produced cardiac protein in laboratory experiments [56].

The early experiments were done for the regeneration of the myocardial by directly injecting the undifferentiated embryonic stem cells into damaged heart. Reprogramming of somatic cells to produce induced pluripotent stem cells has been used to eliminate the need of embryonic stem cells [57, 58]. Improvements into myocardial function were showed by this but there are some associated risks such as these undifferentiated cells were formed teratomas in the heart's wall [59, 60]. One solution to overcome this problem is the differentiation of these cells into more ratios committed cells before transplantation [61].

It was demonstrated that mouse induced pluripotent stem cells were differentiated into all of the three cell types of cardiovascular by sharing pathway with embryonic stem cells for development [62, 63]. Human induced pluripotent stem cells were also showed the same ability [64]. In laboratory, beating activity was recorded by cardiac muscle cells that were derived from induced pluripotent stem cells without the use of Myc reprogramming factor [65].

It was examined in animal models that transplantation of cardiomyocytes, derived from induced pluripotent stem cells, boosted up the function of left ventricular. The subsequent treatment were examined to bring back the contractile performance, electric stability and thickness of the ventricular wall by on site differentiation of heart muscle, endothelial tissues and smooth muscle [66].

Coronary artery disease (CAD) was wide spread disease and stem cells especially mysenchymal stem cells were showed high potential as a regenerative medicine to cure CAD because of their high regenerative and plasticity capability. Stem cells that were present in adventitia of large vessels have activity of blood vessels formation with no safety risks and played a healing role in CAD [67]. Stroma of heart has niches of stem cells and these cardiac cells were phenotypically distinguished as Sca-1+, + MDR-1+, c-kit+ etc [68]. In mouse models, these cardiac stem cells were regenerated and differentiated into vessels but these cardiac cells were bounded by some limitations [68-70].

Mostly heart failure and the mortality of cardiovascular was done by the myocardial infarction [71] and early clinical studies were showed that stem cell therapy enhanced the function of heart [72, 73]. Repair mechanism by stem cell therapy was done by the release of paracrine factors from stem cells in the damaged myocardial tissues that lead to the formation of functional microvascular networks with red blood cell perfusion, cardiac remodeling and myocardial protection [74].

6. Stem cells as regenerative medicines for Liver

Exocrine as well as endocrine functions are carried by a gland called Liver [75]. Liver is responsible to carry out many essential functions that are involved in the homeostasis of human body. Damaged liver was unable to performe these functions and only potential cure for this was the liver transplantation that have limitation of donor. To overcome this limitation, bioartificial liver devices were developed by using human embryonic stem cells (hESCs) with tissue engineering technique. hESCs derived hepatic endoderm was used in regenerative medicine for liver [76]. Hepatic endoderm was developed from hESCs by using different signaling physiology [77-90].

Different therapies were developed to cure liver diseases. Therapies with hepatocytes required 100 to 150 million hepatic cells and immunosuppression and provide relief for several years. Mesenchymal stem cells were produced hepatic parenchymal cells by immune-modulation and paracrine signaling and provide relief from months to years [91].

For end stage liver disease, transplantation of hepatocytes was used as an effective treatment besides liver transplantation but problem was the shortage of the suitable cell source for that purpose. Different methods were developed to differentiate the adult and embryonic stem cells into hepatocytes and application of these heaptocytes in regenerative medicine [92].

It was reported that the pluripotent stem cells extracted from bone marrow were successfully transplanted into mouse model to regenerate the liver [93]. Experimental verification of a report was received when Y

chromosome positive hepatocytes were detected into the livers of the recipients of female mouse models that were subject to bone marrow transplantation from male donors [94-97].

A number of studies were also confirmed the differentiation of embryonic stem cells of human into hepatocytes [82, 88, 98, 99]. It was also reported that when embryoid body was formed then embryonic stem cells of human automatically developed into hepatocytes [82, 88, 89] or developed by following the steps of a sequential process. It was identified that hepatocytes like cells, derived from embryonic stem cells, could be induced to sodium butyrate medium directly [86, 87, 99] then the rearrangement of chromatin with the enhancement of liver function occurred and hepatocytes became immortalized [100, 101].

It was examined that pluripotent stem cells produced from fibroblast of human could be used to produced induced pluripotent stem cells. If enough quantity of induced pluripotent stem cells that have enough supplementation of endoderm and mesoderm was obtained then for a second generation regenerative therapy with embryonic stem cells could be developed [15].

7. Stem cells as regenerative medicines for Parkinson's disease

Parkinson's is a neurodegenerative disease that damaged the dopamine DA neurons [102] and regenerative medicine based on the stem cells holds the promise to stop, slowing down and reverse this disease by using mesenchymal, adult, induced pluripotent and embryonic stem cells. Recently it was discovered that in the stem cells that were transplanted to cure parkinson's disease, the dopamine (DA) expression was controlled by internal cellular mechanism and environmental effects [103].

A method was reported by cho et al to differentiate the neurons that were derived from human embryonic stem cells into mature tyrosine hydroxylase positive (TH+) neurons to cure this disease. Derivation of DA neurons with high efficacy was played a role in the efficient therapy as well as in the prevention of tumor formation by residual stem cells [104].

It was reported that when transplantation of DA neurons, derived from human embryonic stem cells, occurred into the patients that have severe parkinson's disease the improvements were seen as transplanted cells were able to survive.Its clinical consequences were reported in younger patients as compared to older ones [105]. In laboratory experiments, astrocytes, neurons and oligodendrocytes were produced from neuronal stem cells (NSCs) that were extracted from ventral mesencephalon (VM) [106].

Transduction method by retroviruses was reported to differentiate the induced pluripotent stem cells of mouse into DA neurons. These stem cells were gone to different parts of the brain and formed neurons s as well as ganglia when introduced into ventricles of embryonic cerebral [107]. Viruses were posed a risk that they introduced the cells randomly in genome and can changed the induced pluripotent differentiation [108].

Mesenchymal stem cells (MSCs) have ability to produced neuronal cells [109] as they have the ability to produce the dopaminergic neurons [110]. It was also reported that MSCs were able to produce some specific neuronal transcriptional factors (NTFs) along with the markers of neurons [111]. Enhancement in the neurons survival by these NTFs was also examined as these NTFs were involved in regeneration of nerve fiber and endogenous cell proliferation [112]. Immunoregulatory actions were also proved by MSCs [113]. MSCs produced some soluble factors for their immune suppressive activity [114]. So, neuroprotection activity was expected from MSCs and improvements were reported by using MSCs [115, 116].

8. Stem cells as regenerative medicines for Osteoporosis

Osteoporosis is the disorder of the bone and characterized by loss of bone mass due to resorption of bone by osteoclast. Stem cells based regenerative therapies to cure this disease were based on the application of adult stem cells, embryonic stem cells and induced pluripotent stem cells. Stem cells that were derived from adipocytes and from dental pulp were also used for bone repair [117].

Osteoporosis has severe effects on older people due to loss in the function of osteoclast with age and the reduction of mesenchymal stem cells (MSCs) in bone marrow. So, MSCs based regenerative therapy was used to treat this [118]. A little work was done on the regenerative therapy of osteoporosis based on stem cells [119]. First regenerative therapy that was reported to cure osteoporosis was based on MSCs application [120]. MSCs were played vital role in the treatment of osteoporosis by inhibiting the adipogenesis and increasing the ratio of osteogenesis by increasing the potential of osteobalst [121].

It was reported that integrins produced by the osteoproginetors were target by peptidomimetic ligands to treat the osteoporosis [122]. A synthetic peptidomimetic ligand named LLP2A-Ale for integrin $\alpha 4\beta 1$was used to direct the MSCs for the formation of new bone as well as to increase the strength of bone [123, 124].

9. Stem cells as regenerative medicines to cure the injury of Spinal cord

Injury of spinal cord was resulted in the loss of glia and neurons as well as loss in their function. Stem cells derived from human exfoliated deciduous teeth (SHEDs) and dental pulp stem cells of human (DPSCs) were reported in the prevention of apoptosis of neurons, glia and dendrocytes along with the regeneration of axons and myelin

sheath protection. Mostly dental pulp stem cells were examined in the functional recovery after spinal cord injury [125].

It was reported that function was recovered after spinal cord injury by intracerebral introduction of SHEDs along with the conditioned media that was also derived from SHEDs and involved in anti inflammatory activity [126].

Extension of co-cultured neurons with glia was reported by the production of neurotropic factors that was released from SHEDs and DPSCs [127, 128]. The prevention of myelin sheath and filaments of neurons that were present in the surrounding of lesion's epicenter was reported by the implementation of SHEDs which inhibited the neuron and dendrocytes apoptosis [127, 129]. SHEDs were also reported in the prevention of apoptosis of astrocytes [128]. Neurospheres formation was reported in laboratory experiments by using the undifferentiated stem cells of human and rat dental pulp [130, 131]. It was examined that DPSCs were differentiated into active neuron in a laboratory experiment and into neuron like cells in an *in vivo* experiment [132].

10. Stem cells as regenerative medicines in plastic and reconstructive surgery

First published study of reconstructive surgery was on the repair of severe calvarial defect by the application of autologous adipose derived stem cells [133].

Adipose derived stem cells (ADSCs) were reported to hold promise in the plastic surgery of breasts leading to their reconstruction and augmentation. These cells has also been reported in the augmentation of soft tissue, to improve the mark of misshapenness due to trauma and to improve the anomalies of congenital and abrasion due to cancer [134]. It was examined that ADSCs were involved in the formation of new blood vessels as well as to heal the skin that was damaged due to wound or skin ulcer [135]. It was reported that when skin flap was subjected to ADSCs then its survival rate was enhanced directly by the differentiation of ADSCs into cells of endothelia and indirectly by the releasing of growth factors for the formation of new blood vessels [136, 137]. For differentiation of ADSCs, cell assisted lipotransfer technique was used to improve the hemifacial degeneration, augmentation and reconstruction of breasts [138, 139].

Mesenchymal stem cells and ADSCs were proved beneficial to reduce the complications due to radiations [140].

11. Stem cells as regenerative medicines in the generation of beta cells

Diabetes is a disorder that is characterized by a state of hyperglycemia due to improper functioning and production of insulin. Human embryonic stem cells (HESCs) and human induced pluripotent stem cells (HIPSCs) were proved as potential candidates in the regeneration of pancreatic cells with high efficacy. These produced cells were non-functional and called first transition population. Second transition populations of functional pancreatic cells were produced by human pluripotent stem cells (HPSCs) [141]. Different methods were developed to produce beta cells in laboratory by using HPSCs [142-146].

It was reported that exocrine pancreatic cells as well as endocrine pancreatic cells were produced from progenitor cells that were already present in the epithelium of pancreas [147-150]. These progenitors of pancreas were identified on the basis of four transcription factors namely nkx6.1, ptf1a, pdx1 and sox9 [147, 148, 151-153]. Role of ptf1a was identified in exocrine lineage while the role of nkx6.1 and pdx1 was identified in the whole process of the development and maturation of beta cells [154].

In an *in vivo* experiment it was identified that in an immunocompromised mouse model the functional beta cells could be produced [155]. In laboratory experiments D'Amour and colleagues were produced pancreatic cells very first time to produce the pancreatic hormone [156]. Method of D'Amour and colleagues was modified by a number of groups to produce the pancreatic cells by HIPSCs and HESCs [157-168].

12. Stem cells as regenerative medicine for craniofacial

Craniofacial problems are cleft palate and cleft lip, microtia of ear, periodontal diseases, microsomia and cancer of neck etc. although these are not common but create severe troublesome in the field of medical and surgery. Therapies based on stem cells especially on the mesenchymal stem cells that were derived from bone marrow have potential as regenerative medicine to treat these problems [169].

13. Stem cells as regenerative medicine for Craniomaxillofacial Reconstruction

Look of a human, its social interaction and processes that supportive for life as well as the senses delivery depends upon the correct structure and function of craniomaxillofacial. Loss in the tissues of craniomaxillofacial is due to inflammatory responses. Pluripotent stem cells were proved as valuable candidates for regeneration and reconstruction [170].

It was examined that mesenchymal stem cells were helpful to treat the defects of skull [171, 172] and stem cells derived from adipose tissues were novel for reconstruction of maxillary [173]. For the reconstruction of mandibular, mesenchymal stem cells and stem cells derived from adipose tissues were promising candidates [174,

175].

14. Conclusion

It is concluded that stem cells are potential sources that are used as regenerative medicines to cure the injuries and to regenerate the damaged organs and tissues with high efficacy to bring back the normal function of the organs that support life. Among all stem cells, adipose derived stem cells and mesenchymal stem cells have wide applications in regenerative medicines. Induced pluripotnet stem cells eliminate the need of embryonic stem cells. Some tissues and organs also have niches of stem cells that are proved vital in the repairing of that specific organ or tissue. Successful work has been reported to cure the all above mentioned injuries and diseases and in some categories further experimentation is required. It is confirmed that the future of regenerative medicines based on stem cells to cure the fatal diseases is very bright.

References

Preynat-Seauve, O. and K.H. Krause, *Stem cell sources for regenerative medicine: the immunological point of view.* Semin Immunopathol, 2011. 33(6): p. 519-24.

Kolios, G. and Y. Moodley, *Introduction to stem cells and regenerative medicine.* Respiration, 2012. 85(1): p. 3-10.

Watt, F.M. and R.R. Driskell, *The therapeutic potential of stem cells.* Philos Trans R Soc Lond B Biol Sci, 2010. 365(1537): p. 155-63.

Bush, G.W., *Executive Order 13435: Expanding approved stem cell lines in ethically responsible ways.* Federal Register, 2007. 72(120): p. 13435.

Thomson, J.A., et al., *Embryonic stem cell lines derived from human blastocysts.* science, 1998. 282(5391): p. 1145-1147.

Spradling, A., D. Drummond-Barbosa, and T. Kai, *Stem cells find their niche.* Nature, 2001. 414(6859): p. 98-104.

Alison, M. and S. Islam, *Attributes of adult stem cells.* The Journal of pathology, 2009. 217(2): p. 144-160.

Presnell, S.C., B. Petersen, and M. Heidaran. *Stem cells in adult tissues*. in *Seminars in cell & developmental biology*. 2002. Elsevier.

Jiang, Y., et al., *Multipotent progenitor cells can be isolated from postnatal murine bone marrow, muscle, and brain.* Experimental hematology, 2002. 30(8): p. 896-904.

Aasen, T., et al., *Efficient and rapid generation of induced pluripotent stem cells from human keratinocytes.* Nature biotechnology, 2008. 26(11): p. 1276-1284.

Aoi, T., et al., *Generation of pluripotent stem cells from adult mouse liver and stomach cells.* science, 2008. 321(5889): p. 699-702.

Dimos, J.T., et al., *Induced pluripotent stem cells generated from patients with ALS can be differentiated into motor neurons.* science, 2008. 321(5893): p. 1218-1221.

Park, I.-H., et al., *Disease-specific induced pluripotent stem cells.* cell, 2008. 134(5): p. 877-886.

Park, I.-H., et al., *Reprogramming of human somatic cells to pluripotency with defined factors.* nature, 2007. 451(7175): p. 141-146.

Takahashi, K., et al., *Induction of pluripotent stem cells from adult human fibroblasts by defined factors.* cell, 2007. 131(5): p. 861-872.

Yu, J., et al., *Induced pluripotent stem cell lines derived from human somatic cells.* Science, 2007. 318(5858): p. 1917-1920.

Vacanti, J.P. and R. Langer, *Tissue engineering: the design and fabrication of living replacement devices for surgical reconstruction and transplantation.* The Lancet, 1999. 354: p. S32-S34.

Appelbaum, F.R., *Hematopoietic-cell transplantation at 50.* New England Journal of Medicine, 2007. 357(15): p. 1472-1475.

Polak, D.J., *Regenerative medicine. Opportunities and challenges: a brief overview.* J R Soc Interface, 2010. 7 Suppl 6: p. S777-81.

Gardner, R.L., *Stem cells and regenerative medicine: principles, prospects and problems.* C R Biol, 2007. 330(6-7): p. 465-73.

Hipp, J. and A. Atala, *Sources of stem cells for regenerative medicine.* Stem Cell Rev, 2008. 4(1): p. 3-11.

Coelho, M.B., J.M. Cabral, and J.M. Karp, *Intraoperative stem cell therapy.* Annu Rev Biomed Eng, 2012. 14: p. 325-49.

Wagers, A.J., *The stem cell niche in regenerative medicine.* Cell Stem Cell, 2012. 10(4): p. 362-9.

Wu, S.M. and K. Hochedlinger, *Harnessing the potential of induced pluripotent stem cells for regenerative medicine.* Nat Cell Biol, 2011. 13(5): p. 497-505.

Nakao, K. and T. Tsuji, *Dental regenerative therapy: Stem cell transplantation and bioengineered tooth replacement.* Japanese Dental Science Review, 2008. 44(1): p. 70-75.

Gronthos, S., et al., *Postnatal human dental pulp stem cells (DPSCs) in vitro and in vivo.* Proc Natl Acad Sci U S

A, 2000. 97(25): p. 13625-30.
Miura, M., et al., *SHED: stem cells from human exfoliated deciduous teeth.* Proceedings of the National Academy of Sciences, 2003. 100(10): p. 5807-5812.
Sonoyama, W., et al., *Mesenchymal stem cell-mediated functional tooth regeneration in swine.* PloS one, 2006. 1(1): p. e79.
Iohara, K., et al., *Side Population Cells Isolated from Porcine Dental Pulp Tissue with Self‐Renewal and Multipotency for Dentinogenesis, Chondrogenesis, Adipogenesis, and Neurogenesis.* Stem cells, 2006. 24(11): p. 2493-2503.
Seo, B.-M., et al., *Investigation of multipotent postnatal stem cells from human periodontal ligament.* The Lancet, 2004. 364(9429): p. 149-155.
Ikeda, E., et al., *Multipotent cells from the human third molar: feasibility of cell‐based therapy for liver disease.* Differentiation, 2008. 76(5): p. 495-505.
Ohazama, A., et al., *Stem-cell-based tissue engineering of murine teeth.* Journal of dental research, 2004. 83(7): p. 518-522.
Tobita, M., *Adipose-derived stem cells in dentistry.* Journal of Oral Biosciences, 2013. 55(3): p. 122-126.
Casagrande, L., et al., *Dental pulp stem cells in regenerative dentistry.* Odontology, 2011. 99(1): p. 1-7.
Nakahara, T., *Potential feasibility of dental stem cells for regenerative therapies: stem cell transplantation and whole-tooth engineering.* Odontology, 2011. 99(2): p. 105-111.
Lau, A.N., et al., *Stem cells and regenerative medicine in lung biology and diseases.* Mol Ther, 2012. 20(6): p. 1116-30.
Weiss, D.J., et al., *Stem cells and cell therapies in lung biology and lung diseases.* Proceedings of the American Thoracic Society, 2011. 8(3): p. 223-272.
Ortiz, L.A., et al., *Mesenchymal stem cell engraftment in lung is enhanced in response to bleomycin exposure and ameliorates its fibrotic effects.* Proceedings of the National Academy of Sciences, 2003. 100(14): p. 8407-8411.
Ortiz, L.A., et al., *Interleukin 1 receptor antagonist mediates the antiinflammatory and antifibrotic effect of mesenchymal stem cells during lung injury.* Proceedings of the National Academy of Sciences, 2007. 104(26): p. 11002-11007.
Gonzalez-Rey, E., et al., *Human adult stem cells derived from adipose tissue protect against experimental colitis and sepsis.* Gut, 2009.
Mei, S.H., et al., *Mesenchymal stem cells reduce inflammation while enhancing bacterial clearance and improving survival in sepsis.* American journal of respiratory and critical care medicine, 2010. 182(8): p. 1047-1057.
Nowacki, M., et al., *Is regenerative medicine a new hope for kidney replacement?* J Artif Organs, 2014. 17(2): p. 123-34.
Bruce, S.J., et al., *< i> In vitro</i> differentiation of murine embryonic stem cells toward a renal lineage.* Differentiation, 2007. 75(5): p. 337-349.
Li, J., et al., *The Contribution of Bone Marrow‐Derived Cells to the Development of Renal Interstitial Fibrosis.* Stem Cells, 2007. 25(3): p. 697-706.
Imasawa, T., et al., *The potential of bone marrow-derived cells to differentiate to glomerular mesangial cells.* Journal of the American Society of Nephrology, 2001. 12(7): p. 1401-1409.
Jia, X., et al., *Bone marrow-derived cells can acquire renal stem cells properties and ameliorate ischemia-reperfusion induced acute renal injury.* BMC nephrology, 2012. 13(1): p. 105.
Singaravelu, K. and B.J. Padanilam, *In vitro differentiation of MSC into cells with a renal tubular epithelial-like phenotype.* Renal failure, 2009. 31(6): p. 492-502.
Poulsom, R., et al., *Bone marrow contributes to renal parenchymal turnover and regeneration.* The Journal of pathology, 2001. 195(2): p. 229-235.
Perin, L., et al., *Renal differentiation of amniotic fluid stem cells.* Cell proliferation, 2007. 40(6): p. 936-948.
Lensch, M.W. and M. Rao, *Induced pluripotent stem cells: opportunities and challenges.* Regenerative medicine, 2010. 5(4): p. 483-484.
Santini, M.P. and N. Rosenthal, *Myocardial regenerative properties of macrophage populations and stem cells.* J Cardiovasc Transl Res, 2012. 5(5): p. 700-12.
Hsieh, P.C., et al., *Evidence from a genetic fate-mapping study that stem cells refresh adult mammalian cardiomyocytes after injury.* Nature medicine, 2007. 13(8): p. 970-974.
He, J.-Q., et al., *Human embryonic stem cells develop into multiple types of cardiac myocytes action potential characterization.* Circulation research, 2003. 93(1): p. 32-39.
Kehat, I., et al., *Electromechanical integration of cardiomyocytes derived from human embryonic stem cells.* Nature biotechnology, 2004. 22(10): p. 1282-1289.
Makino, S., et al., *Cardiomyocytes can be generated from marrow stromal cells in vitro.* The Journal of clinical investigation, 1999. 103(5): p. 697-705.

Potapova, I.A., et al., *Culturing of human mesenchymal stem cells as three-dimensional aggregates induces functional expression of CXCR4 that regulates adhesion to endothelial cells.* Journal of Biological Chemistry, 2008. 283(19): p. 13100-13107.

Min, J.-Y., et al., *Long-term improvement of cardiac function in rats after infarction by transplantation of embryonic stem cells.* The Journal of thoracic and cardiovascular surgery, 2003. 125(2): p. 361-369.

Singla, D.K., et al., *Transplantation of embryonic stem cells into the infarcted mouse heart: formation of multiple cell types.* Journal of molecular and cellular cardiology, 2006. 40(1): p. 195-200.

Nussbaum, J., et al., *Transplantation of undifferentiated murine embryonic stem cells in the heart: teratoma formation and immune response.* The FASEB Journal, 2007. 21(7): p. 1345-1357.

Behfar, A., et al., *Cardiopoietic programming of embryonic stem cells for tumor-free heart repair.* The Journal of experimental medicine, 2007. 204(2): p. 405-420.

Caspi, O., et al., *Transplantation of human embryonic stem cell-derived cardiomyocytes improves myocardial performance in infarcted rat hearts.* Journal of the American College of Cardiology, 2007. 50(19): p. 1884-1893.

Narazaki, G., et al., *Directed and systematic differentiation of cardiovascular cells from mouse induced pluripotent stem cells.* Circulation, 2008. 118(5): p. 498-506.

Schenke‐Layland, K., et al., *Reprogrammed mouse fibroblasts differentiate into cells of the cardiovascular and hematopoietic lineages.* Stem Cells, 2008. 26(6): p. 1537-1546.

Nsair, A. and W.R. MacLellan, *Induced pluripotent stem cells for regenerative cardiovascular therapies and biomedical discovery.* Adv Drug Deliv Rev, 2011. 63(4-5): p. 324-30.

Martinez-Fernandez, A., et al., *iPS programmed without c-MYC yield proficient cardiogenesis for functional heart chimerism.* Circulation research, 2009. 105(7): p. 648-656.

Nelson, T.J., et al., *Repair of acute myocardial infarction by human stemness factors induced pluripotent stem cells.* Circulation, 2009. 120(5): p. 408-416.

Vono, R., et al., *What's new in regenerative medicine: split up of the mesenchymal stem cell family promises new hope for cardiovascular repair.* J Cardiovasc Transl Res, 2012. 5(5): p. 689-99.

Barile, L., et al., *Endogenous cardiac stem cells.* Progress in cardiovascular diseases, 2007. 50(1): p. 31-48.

Anversa, P. and J. Kajstura, *Ventricular myocytes are not terminally differentiated in the adult mammalian heart.* Circulation research, 1998. 83(1): p. 1-14.

Urbanek, K., et al., *Stem cell niches in the adult mouse heart.* Proceedings of the National Academy of Sciences, 2006. 103(24): p. 9226-9231.

Lloyd-Jones, D., et al., *Heart disease and stroke statistics—2010 update A report from the American Heart Association.* Circulation, 2010. 121(7): p. e46-e215.

Melo, L.G., et al., *Molecular and cell-based therapies for protection, rescue, and repair of ischemic myocardium reasons for cautious optimism.* Circulation, 2004. 109(20): p. 2386-2393.

Laflamme, M.A. and C.E. Murry, *Regenerating the heart.* Nature biotechnology, 2005. 23(7): p. 845-856.

Mirotsou, M., et al., *Paracrine mechanisms of stem cell reparative and regenerative actions in the heart.* J Mol Cell Cardiol, 2011. 50(2): p. 280-9.

Ramadori, G., et al., *Physiology and pathophysiology of liver inflammation, damage and repair.* J Physiol pharmacol, 2008. 59(Suppl 1): p. 107-117.

Sharma, R., et al., *Three-dimensional culture of human embryonic stem cell derived hepatic endoderm and its role in bioartificial liver construction.* J Biomed Biotechnol, 2010. 2010: p. 236147.

Itskovitz-Eldor, J., et al., *Differentiation of human embryonic stem cells into embryoid bodies compromising the three embryonic germ layers.* Molecular Medicine, 2000. 6(2): p. 88.

Lavon, N. and N. Benvenisty, *Study of hepatocyte differentiation using embryonic stem cells.* Journal of cellular biochemistry, 2005. 96(6): p. 1193-1202.

Imamura, T., et al., *Embryonic stem cell-derived embryoid bodies in three-dimensional culture system form hepatocyte-like cells in vitro and in vivo.* Tissue engineering, 2004. 10(11-12): p. 1716-1724.

Baharvand, H., et al., *Differentiation of human embryonic stem cells into hepatocytes in 2D and 3D culture systems in vitro.* International Journal of Developmental Biology, 2006. 50(7): p. 645.

Dalgetty, D.M., et al., *Progress and future challenges in stem cell-derived liver technologies.* American Journal of Physiology-Gastrointestinal and Liver Physiology, 2009. 297(2): p. G241-G248.

Duan, Y., et al., *Differentiation and Enrichment of Hepatocyte‐Like Cells from Human Embryonic Stem Cells In Vitro and In Vivo.* Stem Cells, 2007. 25(12): p. 3058-3068.

Agarwal, S., K.L. Holton, and R. Lanza, *Efficient differentiation of functional hepatocytes from human embryonic stem cells.* Stem Cells, 2008. 26(5): p. 1117-1127.

Fletcher, J., et al., *The inhibitory role of stromal cell mesenchyme on human embryonic stem cell hepatocyte differentiation is overcome by Wnt3a treatment.* Cloning and stem cells, 2008. 10(3): p. 331-340.

Hay, D.C., et al., *Highly efficient differentiation of hESCs to functional hepatic endoderm requires ActivinA and*

Wnt3a signaling. Proceedings of the National Academy of Sciences, 2008. 105(34): p. 12301-12306.
Hay, D.C., et al., *Efficient differentiation of hepatocytes from human embryonic stem cells exhibiting markers recapitulating liver development in vivo.* Stem cells, 2008. 26(4): p. 894-902.
Hay, D.C., et al., *Direct differentiation of human embryonic stem cells to hepatocyte-like cells exhibiting functional activities.* Cloning and stem cells, 2007. 9(1): p. 51-62.
Lavon, N., O. Yanuka, and N. Benvenisty, *Differentiation and isolation of hepatic-like cells from human embryonic stem cells.* Differentiation, 2004. 72(5): p. 230-238.
Rambhatla, L., et al., *Generation of hepatocyte-like cells from human embryonic stem cells.* Cell transplantation, 2003. 12(1): p. 1-11.
Basma, H., et al., *Differentiation and transplantation of human embryonic stem cell–derived hepatocytes.* Gastroenterology, 2009. 136(3): p. 990-999. e4.
Lanzoni, G., et al., *Concise review: clinical programs of stem cell therapies for liver and pancreas.* Stem Cells, 2013. 31(10): p. 2047-60.
Ogawa, S. and S. Miyagawa, *Potentials of regenerative medicine for liver disease.* Surgery Today, 2009. 39(12): p. 1019-1025.
Petersen, B., et al., *Bone marrow as a potential source of hepatic oval cells.* Science, 1999. 284(5417): p. 1168-1170.
Theise, N.D., et al., *Liver from bone marrow in humans.* Hepatology, 2000. 32(1): p. 11-16.
Körbling, M., et al., *Hepatocytes and epithelial cells of donor origin in recipients of peripheral-blood stem cells.* New England Journal of Medicine, 2002. 346(10): p. 738-746.
Alison, M.R., et al., *Cell differentiation: hepatocytes from non-hepatic adult stem cells.* Nature, 2000. 406: p. 257.
Idilman, R., et al., *The fate of recipient‐derived hepatocytes in sex‐mismatched liver allograft following liver transplantation.* Clinical transplantation, 2007. 21(2): p. 202-206.
Schwartz, R.E., et al., *Defined conditions for development of functional hepatic cells from human embryonic stem cells.* Stem cells and development, 2005. 14(6): p. 643-655.
Cai, J., et al., *Directed differentiation of human embryonic stem cells into functional hepatic cells.* Hepatology, 2007. 45(5): p. 1229-1239.
Saito, H., et al., *Differentiating effect of sodium butyrate on human hepatoma cell lines PLC/PRF/5, HCC‐M and HCC‐T.* International journal of cancer, 1991. 48(2): p. 291-296.
Yoon, J., et al., *Development of a non-transformed human liver cell line with differentiated-hepatocyte and urea-synthetic functions: applicable for bioartificial liver.* The International journal of artificial organs, 1999. 22(11): p. 769-777.
Raichur, A., S. Vali, and F. Gorin, *Dynamic modeling of alpha-synuclein aggregation for the sporadic and genetic forms of Parkinson's disease.* Neuroscience, 2006. 142(3): p. 859-870.
El-Sadik, A.O., *Potential sources of stem cells as a regenerative therapy for Parkinson's disease.* Stem Cells Cloning, 2010. 3: p. 183-91.
Cho, M.S., et al., *Highly efficient and large-scale generation of functional dopamine neurons from human embryonic stem cells.* Proceedings of the National Academy of Sciences, 2008. 105(9): p. 3392-3397.
Freed, C.R., et al., *Transplantation of embryonic dopamine neurons for severe Parkinson's disease.* New England Journal of Medicine, 2001. 344(10): p. 710-719.
Gage, F.H., *Mammalian neural stem cells.* Science, 2000. 287(5457): p. 1433-1438.
Wernig, M., et al., *Neurons derived from reprogrammed fibroblasts functionally integrate into the fetal brain and improve symptoms of rats with Parkinson's disease.* Proceedings of the National Academy of Sciences, 2008. 105(15): p. 5856-5861.
Markoulaki, S., et al., *Transgenic mice with defined combinations of drug-inducible reprogramming factors.* Nature biotechnology, 2009. 27(2): p. 169-171.
Jiang, C., *Stem cell research: from molecular physiology to therapeutic applications.* Science in China Series C: Life Sciences, 2009. 52(7): p. 597-598.
Woodbury, D., et al., *Adult rat and human bone marrow stromal cells differentiate into neurons.* Journal of neuroscience research, 2000. 61(4): p. 364-370.
Blondheim, N.R., et al., *Human mesenchymal stem cells express neural genes, suggesting a neural predisposition.* Stem Cells and Development, 2006. 15(2): p. 141-164.
Mahmood, A., D. Lu, and M. Chopp, *Marrow stromal cell transplantation after traumatic brain injury promotes cellular proliferation within the brain.* Neurosurgery, 2004. 55(5): p. 1185-1193.
Lee, P.H. and H.J. Park, *Bone marrow-derived mesenchymal stem cell therapy as a candidate disease-modifying strategy in Parkinson's disease and multiple system atrophy.* Journal of Clinical Neurology, 2009. 5(1): p. 1-10.
Karussis, D., et al., *Immunomodulation and neuroprotection with mesenchymal bone marrow stem cells (MSCs): a proposed treatment for multiple sclerosis and other neuroimmunological/neurodegenerative diseases.*

Journal of the neurological sciences, 2008. 265(1): p. 131-135.
Li, Y., et al., *Human marrow stromal cell therapy for stroke in rat Neurotrophins and functional recovery.* Neurology, 2002. 59(4): p. 514-523.
Zhang, J., et al., *Human bone marrow stromal cell treatment improves neurological functional recovery in EAE mice.* Experimental neurology, 2005. 195(1): p. 16-26.
Mikami, Y., et al., *Current status of drug therapies for osteoporosis and the search for stem cells adapted for bone regenerative medicine.* Anat Sci Int, 2014. 89(1): p. 1-10.
Ito, H., *Clinical considerations of regenerative medicine in osteoporosis.* Curr Osteoporos Rep, 2014. 12(2): p. 230-4.
Liu, Y., et al., *Therapeutic application of mesenchymal stem cells in bone and joint diseases.* Clinical and experimental medicine, 2014. 14(1): p. 13-24.
Bruder, S.P., D.J. Fink, and A.I. Caplan, *Mesenchymal stem cells in bone development, bone repair, and skeletal regenaration therapy.* Journal of cellular biochemistry, 1994. 56(3): p. 283-294.
Nuttall, M.E., et al., *Human trabecular bone cells are able to express both osteoblastic and adipocytic phenotype: implications for osteopenic disorders.* Journal of Bone and Mineral Research, 1998. 13(3): p. 371-382.
Marie, P.J., *Targeting integrins to promote bone formation and repair.* Nature Reviews Endocrinology, 2013. 9(5): p. 288-295.
Yao, W., et al., *Reversing bone loss by directing mesenchymal stem cells to bone.* Stem Cells, 2013. 31(9): p. 2003-2014.
Guan, M., et al., *Directing mesenchymal stem cells to bone to augment bone formation and increase bone mass.* Nature medicine, 2012. 18(3): p. 456-462.
Yamamoto, A., et al., *Multifaceted neuro-regenerative activities of human dental pulp stem cells for functional recovery after spinal cord injury.* Neurosci Res, 2014. 78: p. 16-20.
Yamagata, M., et al., *Human dental pulp-derived stem cells protect against hypoxic-ischemic brain injury in neonatal mice.* Stroke, 2013. 44(2): p. 551-554.
de Almeida, F.M., et al., *Human dental pulp cells: a new source of cell therapy in a mouse model of compressive spinal cord injury.* Journal of neurotrauma, 2011. 28(9): p. 1939-1949.
Sakai, K., et al., *Human dental pulp-derived stem cells promote locomotor recovery after complete transection of the rat spinal cord by multiple neuro-regenerative mechanisms.* The Journal of clinical investigation, 2012. 122(122 (1)): p. 80-90.
Nosrat, I.V., et al., *Dental Pulp Cells Produce Neurotrophic Factors, Interact with Trigeminal Neurons in Vitro, and Rescue Motoneurons after Spinal Cord Injury.* Developmental biology, 2001. 238(1): p. 120-132.
Sasaki, R., et al., *Neurosphere generation from dental pulp of adult rat incisor.* European Journal of Neuroscience, 2008. 27(3): p. 538-548.
Wang, J., et al., *Stem cells from human-exfoliated deciduous teeth can differentiate into dopaminergic neuron-like cells.* Stem cells and development, 2010. 19(9): p. 1375-1383.
Arthur, A., et al., *Adult Human Dental Pulp Stem Cells Differentiate Toward Functionally Active Neurons Under Appropriate Environmental Cues.* STEM CELLS, 2008. 26(7): p. 1787-1795.
Lendeckel, S., et al., *Autologous stem cells (adipose) and fibrin glue used to treat widespread traumatic calvarial defects: case report.* Journal of Cranio-Maxillofacial Surgery, 2004. 32(6): p. 370-373.
Mizuno, H., *Adipose-derived stem cells for regenerative medicine in the field of plastic and reconstructive surgery.* Journal of Oral Biosciences, 2013. 55(3): p. 132-136.
Ho Jeong, J., *Adipose stem cells and skin repair.* Current stem cell research & therapy, 2010. 5(2): p. 137-140.
Lu, F., et al., *Improved viability of random pattern skin flaps through the use of adipose-derived stem cells.* Plastic and reconstructive surgery, 2008. 121(1): p. 50-58.
Uysal, A.C., et al., *The effect of adipose-derived stem cells on ischemia-reperfusion injury: immunohistochemical and ultrastructural evaluation.* Plastic and reconstructive surgery, 2009. 124(3): p. 804-815.
Yoshimura, K., et al., *Cell-assisted lipotransfer for cosmetic breast augmentation: supportive use of adipose-derived stem/stromal cells.* Aesthetic plastic surgery, 2008. 32(1): p. 48-55.
Yoshimura, K., et al., *Cell‐Assisted Lipotransfer for Facial Lipoatrophy: Efficacy of Clinical Use of Adipose‐Derived Stem Cells.* Dermatologic Surgery, 2008. 34(9): p. 1178-1185.
Akita, S., et al., *Mesenchymal stem cell therapy for cutaneous radiation syndrome.* Health physics, 2010. 98(6): p. 858-862.
Nostro, M.C. and G. Keller, *Generation of beta cells from human pluripotent stem cells: Potential for regenerative medicine.* Semin Cell Dev Biol, 2012. 23(6): p. 701-10.
Baiu, D., F. Merriam, and J. Odorico, *Potential pathways to restore β-cell mass: pluripotent stem cells, reprogramming, and endogenous regeneration.* Current diabetes reports, 2011. 11(5): p. 392-401.
Sumi, S., *Regenerative medicine for insulin deficiency: creation of pancreatic islets and bioartificial pancreas.* Journal of hepato-biliary-pancreatic sciences, 2011. 18(1): p. 6-12.

Chung, C.-H. and F. Levine, *Adult pancreatic alpha-cells: a new source of cells for beta-cell regeneration.* The review of diabetic studies: RDS, 2010. 7(2): p. 124.
Collombat, P., et al. *Pancreatic beta-cells: from generation to regeneration*. in *Seminars in cell & developmental biology*. 2010. Elsevier.
Yechoor, V. and L. Chan, *Minireview: β-cell replacement therapy for diabetes in the 21st century: manipulation of cell fate by directed differentiation.* Molecular Endocrinology, 2010. 24(8): p. 1501-1511.
Gu, G., J. Dubauskaite, and D.A. Melton, *Direct evidence for the pancreatic lineage: NGN3+ cells are islet progenitors and are distinct from duct progenitors.* Development, 2002. 129(10): p. 2447-2457.
Kawaguchi, Y., et al., *The role of the transcriptional regulator Ptf1a in converting intestinal to pancreatic progenitors.* Nature genetics, 2002. 32(1): p. 128-134.
Kim, S.K. and R.J. MacDonald, *Signaling and transcriptional control of pancreatic organogenesis.* Current opinion in genetics & development, 2002. 12(5): p. 540-547.
Gu, G., J.R. Brown, and D.A. Melton, *Direct lineage tracing reveals the ontogeny of pancreatic cell fates during mouse embryogenesis.* Mechanisms of development, 2003. 120(1): p. 35-43.
Seymour, P.A., et al., *SOX9 is required for maintenance of the pancreatic progenitor cell pool.* Proceedings of the National Academy of Sciences, 2007. 104(6): p. 1865-1870.
Zhou, Q., et al., *A multipotent progenitor domain guides pancreatic organogenesis.* Developmental cell, 2007. 13(1): p. 103-114.
Hald, J., et al., *Generation and characterization of Ptf1a antiserum and localization of Ptf1a in relation to Nkx6. 1 and Pdx1 during the earliest stages of mouse pancreas development.* Journal of Histochemistry & Cytochemistry, 2008. 56(6): p. 587-595.
Jørgensen, M.C., et al., *An illustrated review of early pancreas development in the mouse.* Endocrine reviews, 2007. 28(6): p. 685-705.
Kroon, E., et al., *Pancreatic endoderm derived from human embryonic stem cells generates glucose-responsive insulin-secreting cells in vivo.* Nature biotechnology, 2008. 26(4): p. 443-452.
D'Amour, K.A., et al., *Production of pancreatic hormone–expressing endocrine cells from human embryonic stem cells.* Nature biotechnology, 2006. 24(11): p. 1392-1401.
Jiang, J., et al., *Generation of Insulin‐Producing Islet‐Like Clusters from Human Embryonic Stem Cells.* Stem cells, 2007. 25(8): p. 1940-1953.
Jiang, W., et al., *In vitro derivation of functional insulin-producing cells from human embryonic stem cells.* Cell research, 2007. 17(4): p. 333-344.
Johannesson, M., et al., *FGF4 and retinoic acid direct differentiation of hESCs into PDX1-expressing foregut endoderm in a time-and concentration-dependent manner.* PloS one, 2009. 4(3): p. e4794.
Zhang, D., et al., *Highly efficient differentiation of human ES cells and iPS cells into mature pancreatic insulin-producing cells.* Cell research, 2009. 19(4): p. 429-438.
Ameri, J., et al., *FGF2 specifies hESC‐derived definitive endoderm into foregut/midgut cell lineages in a concentration‐dependent manner.* Stem Cells, 2010. 28(1): p. 45-56.
Cai, J., et al., *Generation of homogeneous PDX1+ pancreatic progenitors from human ES cell-derived endoderm cells.* Journal of molecular cell biology, 2010. 2(1): p. 50-60.
Mfopou, J.K., et al., *Noggin, retinoids, and fibroblast growth factor regulate hepatic or pancreatic fate of human embryonic stem cells.* Gastroenterology, 2010. 138(7): p. 2233-2245. e14.
Nostro, M.C., et al., *Stage-specific signaling through TGFβ family members and WNT regulates patterning and pancreatic specification of human pluripotent stem cells.* Development, 2011. 138(5): p. 861-871.
Rezania, A., et al., *Production of functional glucagon-secreting α-cells from human embryonic stem cells.* Diabetes, 2011. 60(1): p. 239-247.
Xu, X., V.L. Browning, and J.S. Odorico, *Activin, BMP and FGF pathways cooperate to promote endoderm and pancreatic lineage cell differentiation from human embryonic stem cells.* Mechanisms of development, 2011. 128(7): p. 412-427.
Kunisada, Y., et al., *Small molecules induce efficient differentiation into insulin-producing cells from human induced pluripotent stem cells.* Stem cell research, 2012. 8(2): p. 274-284.
Micallef, S., et al., *INS GFP/w human embryonic stem cells facilitate isolation of in vitro derived insulin-producing cells.* Diabetologia, 2012. 55(3): p. 694-706.
Sanchez-Lara, P.A. and D. Warburton, *Impact of stem cells in craniofacial regenerative medicine.* Front Physiol, 2012. 3: p. 188.
Jalali, M., et al., *Human stem cells for craniomaxillofacial reconstruction.* Stem Cells Dev, 2014. 23(13): p. 1437-51.
Thesleff, T., et al., *Cranioplasty with adipose-derived stem cells and biomaterial: a novel method for cranial reconstruction.* Neurosurgery, 2011. 68(6): p. 1535-1540.
He, X., et al., *BMP2 genetically engineered MSCs and EPCs promote vascularized bone regeneration in rat*

critical-sized calvarial bone defects. PloS one, 2013. 8(4): p. e60473.

Mesimäki, K., et al., *Novel maxillary reconstruction with ectopic bone formation by GMP adipose stem cells.* International journal of oral and maxillofacial surgery, 2009. 38(3): p. 201-209.

Warnke, P.H., et al., *Man as living bioreactor: fate of an exogenously prepared customized tissue-engineered mandible.* Biomaterials, 2006. 27(17): p. 3163-3167.

Sándor, G.K., et al., *Adipose Stem Cell Tissue–Engineered Construct Used to Treat Large Anterior Mandibular Defect: A Case Report and Review of the Clinical Application of Good Manufacturing Practice–Level Adipose Stem Cells for Bone Regeneration.* Journal of Oral and Maxillofacial Surgery, 2013. 71(5): p. 938-950.

Figures

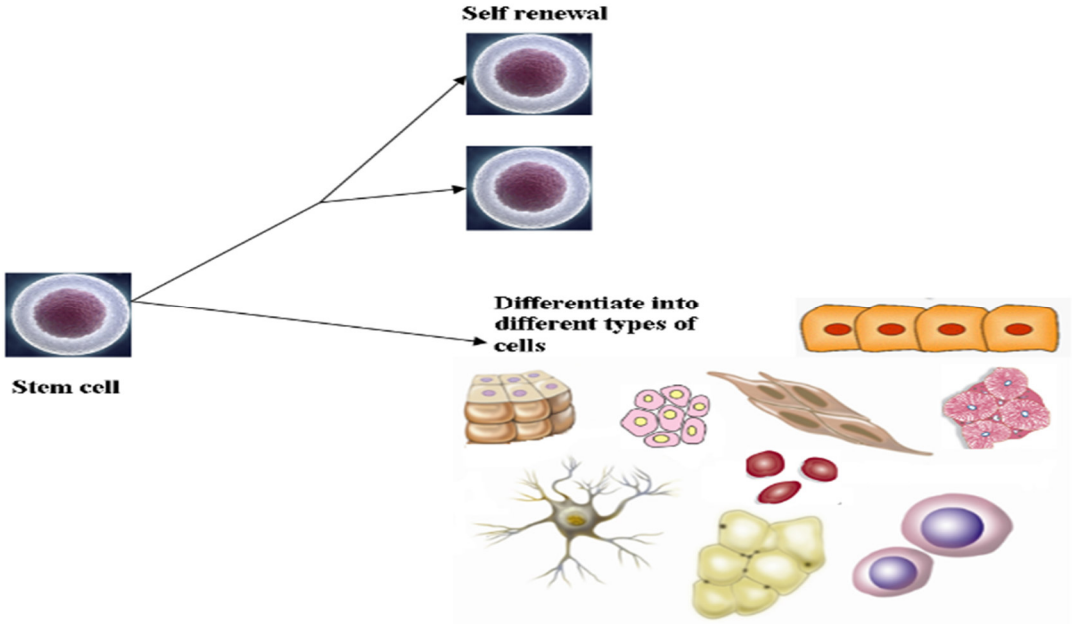

Figure 1: Figure 1 describing what is stem cells

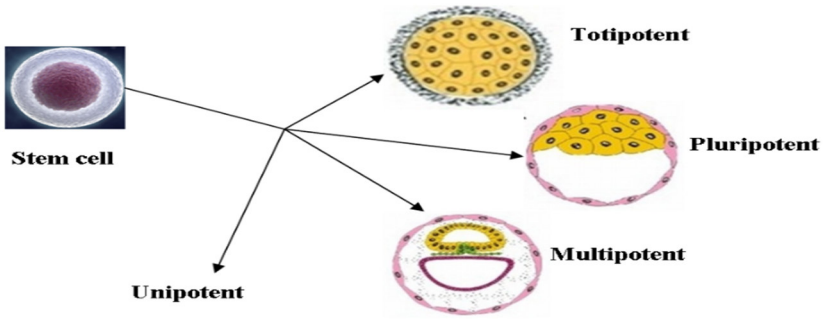

Figure 2: Types of stem cells on the basis of their differentiation ability

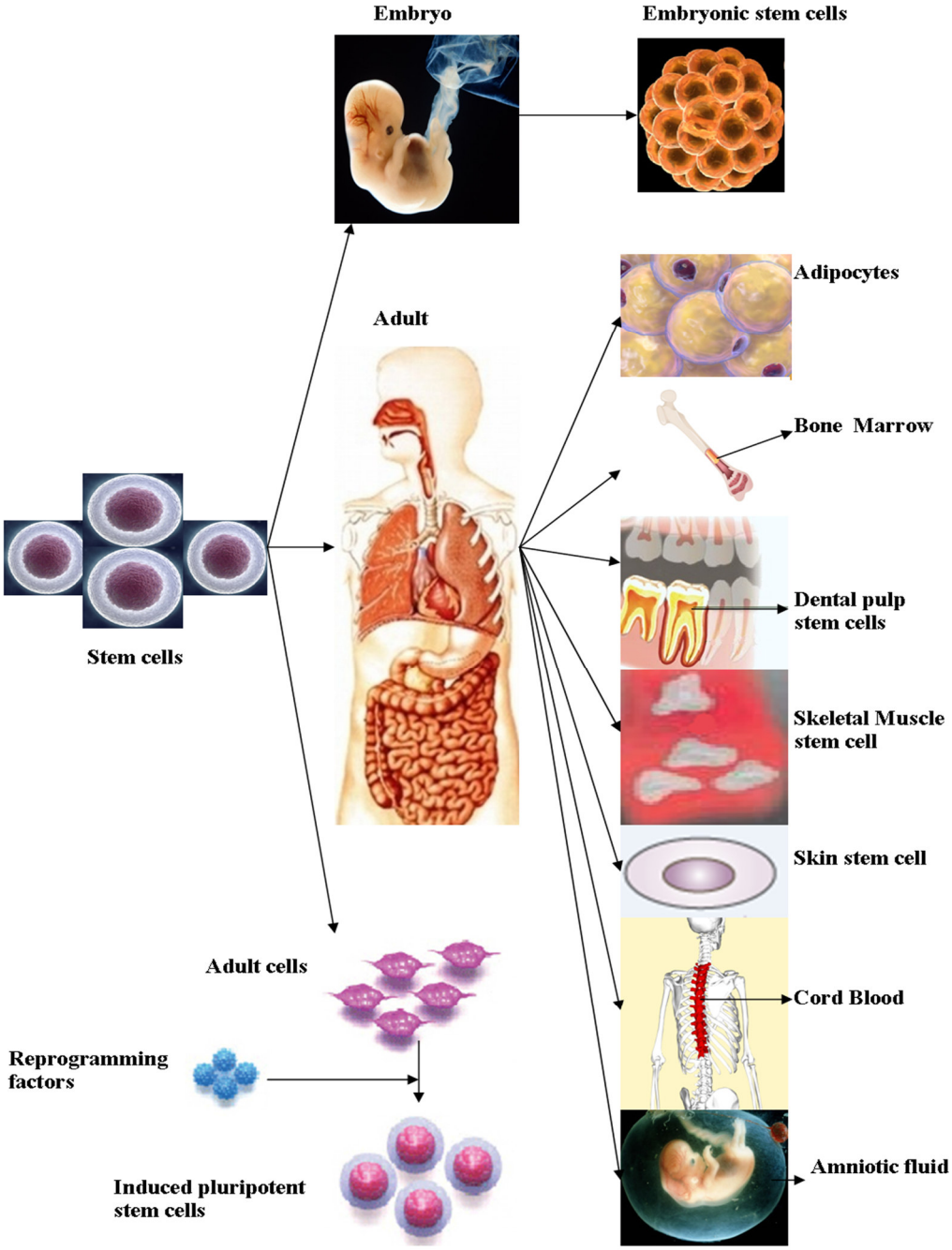

Figure 3: Stem cells, their sources and their types according to sources

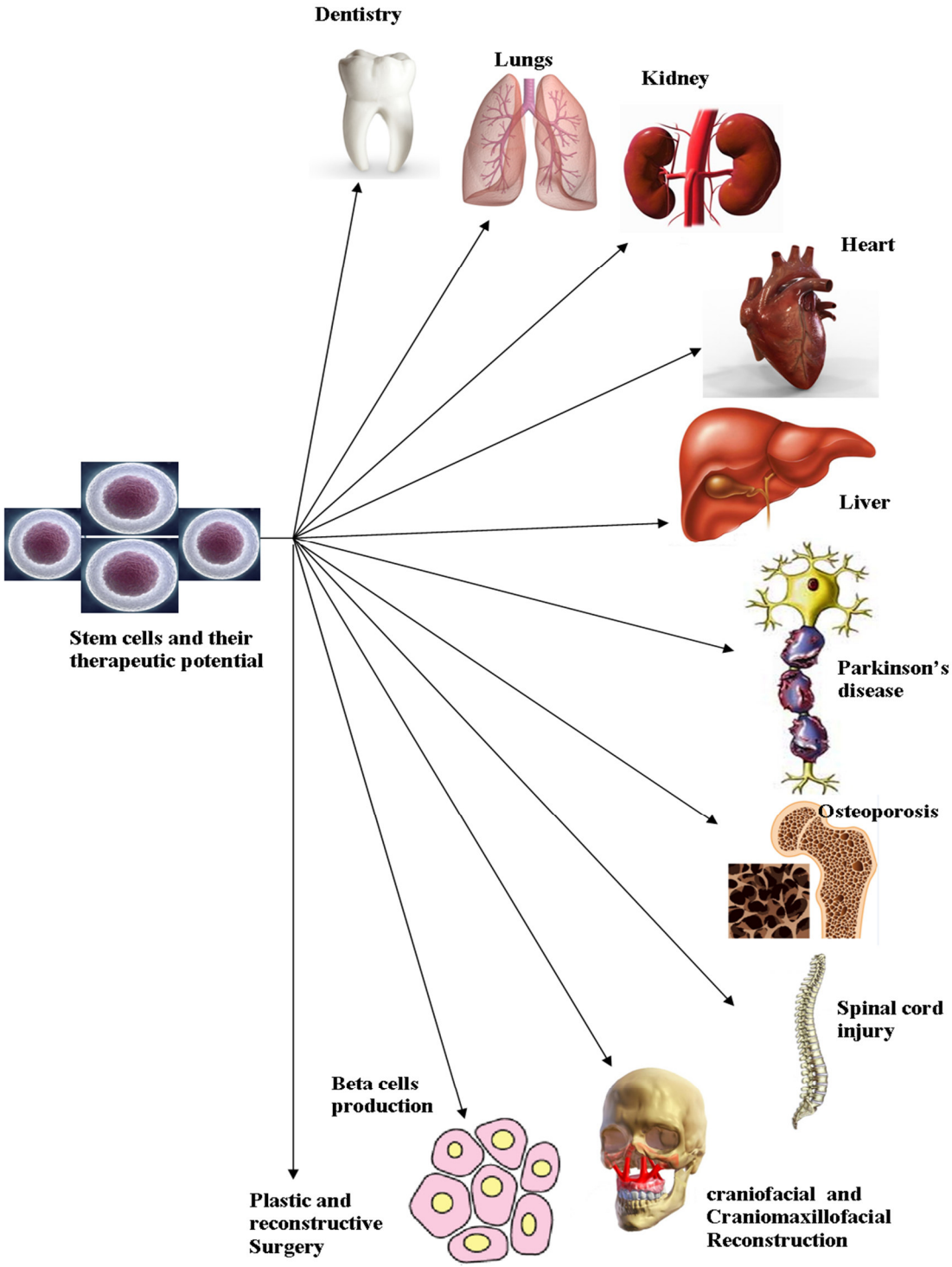

Figure 4: Regenerative potential of stem cells