

Selected Publications on Therapy Using Stem Cells from Teeth

This list of peer-reviewed publications illustrates research using Dental Pulp Stem Cells (DPSC) in Animals/ Humans (*in vivo*) and in a dish (*in vitro*). *In vivo* studies are those in which the DPSC are evaluated in living organism using animal models or humans in a clinical trial. *In vitro* studies are those in which DPSC are evaluated with cells in a laboratory. This document is intended to illustrate the current work (since 2007) being completed for each disease/disorder, it is NOT comprehensive. There are thousands of publication papers available regarding stem cells from teeth.

Dental Injury/Disease

Stem cells from dental pulp may one day be used to engineer whole, implantable teeth to replace teeth that are lost due to injury or disease. Pulp regeneration, periodontitis, and root canal formation are some of the active areas of research with dental pulp stem cells.

In vivo

Mobilized dental pulp stem cells for pulp regeneration: initiation of clinical trial.

Nakashima M, Iohara K. "Mobilized dental pulp stem cells for pulp regeneration: initiation of clinical trial." J Endod (2014) Apr; 40; PMID:24698690

<http://www.ncbi.nlm.nih.gov/pubmed/24698690>

**The efficacy and safety of pulp stem cell transplantation was evaluated before initiation of a clinical trial. Quality of dental pulp stem cells was assured by lack of abnormalities/aberrations in karyotype and lack of tumor formation after transplantation in mice. This study helped establish preclinical safety, feasibility, and efficacy of pulp regeneration by mobilized dental pulp stem cells in a dog model.

Allogeneic Stem Cells From Deciduous Teeth Mediated Treatment for Periodontitis in Miniature Swine.

Fu X, Jin L, Ma P, Fan Z, Wang S. "Allogeneic Stem Cells From Deciduous Teeth Mediated Treatment for Periodontitis in Miniature Swine." J Periodontol (2014) Jun 85; PMID:24001042

<http://www.ncbi.nlm.nih.gov/pubmed/24001042>

**Regeneration of lost periodontium in periodontitis is a challenge because bone, cementum and periodontal ligament need to be regenerated. Significant restoration in a periodontitis miniature swine model was observed after treatment with stem cells isolated from mini pig deciduous teeth or periodontal ligament stem cells. Periodontal ligament connective tissue regeneration was observed with both stem cells groups as compared to controls.

Immunohistochemical and histochemical analysis of newly formed tissues in root canal space transplanted with dental pulp stem cells plus platelet rich plasma.

Zhu X, Wang Y, Liu Y, Huang GT, Zhang C. "Immunohistochemical and histochemical analysis of newly formed tissues in root canal space transplanted with dental pulp stem cells plus platelet rich plasma." J Endod (2014) Oct; 40; PMID:25260728

<http://www.ncbi.nlm.nih.gov/pubmed/25260728>

**Tissue regeneration in root canals after pulpectomy can be achieved by transplantation of autologous dental pulp stem cells and/or platelet-rich plasma. Molars were extracted in dogs and then dental pulp stem cells alone or mixed with autologous platelet-rich plasma was implanted into each root canal. The tissue formed in the dog mature root canals after regenerative endodontic procedures are not pulp tissues but rather periodontal tissues.

Dental pulp tissue engineering in full-length human root canals.

Rosa V, Zhang Z, Grande RH, Nor JE. "Dental pulp tissue engineering in full-length human root canals." J Dent Res. (2013). Nov;92(11):970-5. PMID:24056227

<http://www.ncbi.nlm.nih.gov/pubmed/24056227>

**This study investigated whether stem cells from exfoliated deciduous teeth can generate a functional dental pulp when injected into full length root canals. Roots of human premolars were injected with scaffolds containing SHED and implanted into immune-deficient mice. It was found that scaffold containing SHED had similar cellularity and vascularization as compared to control human dental pulps.

Preliminary study on dental pulp stem cell-mediated pulp regeneration in canine immature permanent teeth.

Wang Y, Zhao Y, Jia W, Yang J, Ge L. "Preliminary study on dental pulp stem cell-mediated pulp regeneration in canine immature permanent teeth." J Endod. (2013) Feb;39(2):195-201. PMID:23321230

<http://www.ncbi.nlm.nih.gov/pubmed/23321230>

**The potential of using autologous dental pulp stem cells for pulp regeneration in a canine pulpless animal model was investigated. Dental pulp stem cells were found to generate pulp-like tissues containing blood vessels and dentin-like tissues. The study illustrates the possibility of using stem cell mediated tissue engineering for pulp regeneration in immature teeth.

Autologous Dental Pulp Stem Cells in Regeneration of Defect Created in Canine Periodontal Tissue.

Mohamadreza BE, Khorsand A, Arabsolghar M, Paknejad M, Ghaedi B, Rohn AR, Moslemi N, Nazarian H, Jahangir S. "Autologous Dental Pulp Stem Cells in Regeneration of Defect Created in Canine Periodontal Tissue." J Oral Implantol (2012) Aug 1; PMID:22852766

<http://www.ncbi.nlm.nih.gov/pubmed/22852766>

**This study investigated the effects of dental pulp stem cells on regeneration of the defect experimentally created in periodontium of canine model. It was observed that a combination of dental pulp stem cells and Bio-Oss scaffold led to regeneration of bone, cementum and periodontal ligament. The use of a scaffold with dental pulp stem cells can be a promising tool in regeneration of periodontal tissues.

Dental Stem Cell Therapy with Calcium Hydroxide in Dental Pulp Capping.

Ji YM, Jeon SH, Park JY, Chung JH, Choung YH, Choung PH. "Dental Stem Cell Therapy with Calcium Hydroxide in Dental Pulp Capping." Tissue Eng Part A. (2010) Feb 17. PMID: 20055661

<http://www.ncbi.nlm.nih.gov/pubmed/20055661>

**Calcium hydroxide is used for direct pulp capping and is known to induce hard tissue repair. The relationship between calcium hydroxide and recruitment, proliferation, and mineralization of postnatal dental stem cells obtained from immature dental tissue of beagle dogs was examined. It was found that calcium hydroxide increases recruitment, migration, proliferation, and mineralization of the DPSCs and periodontal ligament stem cells.

Dental pulp tissue engineering with stem cells from exfoliated deciduous teeth.

Cordeiro MM, Dong Z, Kaneko T, Zhang Z, Miyazawa M, Shi S, Smith AJ, Nör JE. "Dental pulp tissue engineering with stem cells from exfoliated deciduous teeth." J Endod. (2008) Aug;34(8):962-9. PMID: 18634928

<http://www.ncbi.nlm.nih.gov/pubmed/18634928>

**The morphologic characteristics of tissue formed when SHED seeded in biodegradable scaffold within human tooth slices were transplanted into immune-deficient mice in this study. It was found that the new tissue had similar cellularity and architecture as physiological dental pulp.

Diabetes (Type 1)

Type I diabetes results from destruction of insulin producing cells in the pancreas. Stem cells from teeth have been shown to differentiate into insulin secreting cells. Drugs that suppress the immune response are typically used to prevent the rejection of the stem cells that are transplanted into preclinical models. Immunosuppression drugs can potentially cause an increase in infections and possible cancer. Cells from teeth have been shown to reverse type 1 diabetes in mice without the need for drugs that suppress the immune response.

In vitro

A feasibility study of an in vitro differentiation potential toward insulin-producing cells by dental tissue-derived mesenchymal stem cells.

Sawangmake C, Nowwarote N, Pavasant P, Chansiripornchai P, Osathanon T. "A feasibility study of an in vitro differentiation potential toward insulin-producing cells by dental tissue-derived mesenchymal stem cells." Biochem Biophys Res Commun. (2014) Sep;26(452):581-7. PMID: 25181343

<http://www.ncbi.nlm.nih.gov/pubmed/25181343>

**In this study it was found that human dental pulp stem cells derived insulin producing cells expressed pro-insulin and release of c-peptide upon glucose stimulation to a better extent than human periodontal ligament stem cells. Overall human DPSC had better differentiation potential towards insulin producing cells as compared to human PDLSC.

In vitro differentiation into insulin-producing β -cells of stem cells isolated from human amniotic fluid and dental pulp.

Carnevale G, Riccio M, Pisciotta A, Beretti F, Maraldi T, Zavatti M, Cavallini GM, La Sala GB, Ferrari A, De Pol A. "In vitro differentiation into insulin-producing β -cells of stem cells isolated from human amniotic fluid and dental pulp." Dig Liver Dis. (2013) Aug;45(8):669-76. PMID: 23643565

<http://www.ncbi.nlm.nih.gov/pubmed/23643565>

**Human amniotic fluid stem cells and human dental pulp stem cells were induced to differentiate into pancreatic β -cells. By day 21 islet-like structures derived from both human amniotic fluid stem cells and human dental pulp stem cells released insulin in a glucose dependent manner.

Differentiation of Dental Pulp Stem Cells Into Islet Like Aggregates.

Govindasamy V, Ronald VS, Abdullah AN, Ganesan Nathan KR, Ab Aziz ZA, Abdullah M, Musa S, Abu Kasim NH, Bhonde RR. "Differentiation of Dental Pulp Stem Cells Into Islet Like Aggregates." J Dent Res. (2011) Feb 18. PMID: 21335539

<http://www.ncbi.nlm.nih.gov/pubmed/21335539>

**DPSC differentiated into pancreatic cell lineage resembling islet-like cell aggregates was investigated. It was confirmed that islet-like cell aggregates were obtained from DPSC via biomarker staining/expression and insulin C-peptide-glucose release. This is the first report demonstrating that DPSC could differentiate into pancreatic cell lineage and offer an unconventional and non-controversial source of human tissue that could be used for autologous stem cell therapy in diabetes.

In vivo

Transplantation of Stem Cells Obtained from Murine Dental Pulp Improves Pancreatic Damage, Renal Function and Painful Diabetic Neuropathy in Diabetic Type 1 Mouse Model.

Guimarães, ET, Cruz Gda S, Almeida TF, Souza BS, Kaneto CM, Vasconcelos JF, Santos WL, Santos RR, Villareal CF, Soares MB. "Transplantation of Stem Cells Obtained from Murine Dental Pulp Improves Pancreatic Damage, Renal Function and Painful Diabetic Neuropathy in Diabetic Type 1 Mouse Model." Cell Transplantation (2013). 22(12);2345-54. PMID:23068779

<http://www.ncbi.nlm.nih.gov/pubmed/23068779>

**A diabetic mouse model was used to investigate dental pulp stem cells treatment. Results indicate that DPSC may contribute to pancreatic B-cell renewal, prevention of renal damage, and production of powerful/long-lasting effect on behavioral neuropathic pain. Stem cell therapy can be option of the control of diabetes complications such as intractable diabetic neuropathic pain.

Transplantation of islet-like cell clusters derived from human dental pulp stem cells restores normoglycemia in diabetic mice.

Kanafi MM, Rajeshwari YB, Gupta S, Dadheech N, Nair PD, Gupta PK, Bhonde RR. "Transplantation of islet-like cell clusters derived from human dental pulp stem cells restores normoglycemia in diabetic mice." Cytotherapy. (2013) Oct;15(10):1228-36. PMID: 23845187

<http://www.ncbi.nlm.nih.gov/pubmed/23845187>

**It has been shown that stem cells from human exfoliated deciduous teeth were superior to dental pulp stem cells form permanent teeth in terms of treatment of hyperglycemic mice. Diabetic mice that were restored to normoglycemia within 3-4 weeks of treatment persisted for over 60 days. This is the first report in which islet-like cell clusters derived from SHED reversed diabetes in mice without immunosuppression and offer an autologous and non-controversial source of MSC for stem cell therapy in diabetes.

Ischemia/Angiogenesis/Vasculogenesis

Dental pulp stem cells can be used to create new blood vessels. They have been used in the treatment of heart damage from heart attack, and to grow blood vessels to give blood a route to regenerated tissue or tissue that has lost its blood supply in animal models. There is proof that transplanted dental pulp cells can increase blood flow by forming high density capillaries in rodent models.

In vitro

Pro-Angiogenic impact of dental stem cells *in vitro* and *in vivo*.

Hilkens P, Fanton Y, Martens P, Gervois T, Struys T, Politis C, Lambrichts I, Bronchaers A. "Pro-Angiogenic impact of dental stem cells *in vitro* and *in vivo*." Stem Cell Research. (2014)

<http://www.sciencedirect.com/science/article/pii/S187350611400035X>

**Dental stem cells had activation of several important components of the angiogenic cascade. This data shows the pro-angiogenic influence of DPSC and SCAPS *in vitro/ in vivo* in comparison to human fibroblast cells.

Angiogenic Properties of Human Dental Pulp Stem Cells.

Bronckaers A, Hilkens P, Fanton Y, Struys T, Gervois P, Politis C, Martens W, Lambrichts I. "Angiogenic Properties of Human Dental Pulp Stem Cells." PLoS One. (2013) Aug;7. PMID:PMC3737205

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3737205/>

**Angiogenesis is the formation of capillaries from pre-existing blood vessels and is a key process in tissue engineering. This *in vitro* study showed that dental pulp stem cells had numerous pro and anti-angiogenic factors released. In addition it was found that human DPSC were able to significantly induce blood vessel formation. DPSC have the ability to induce angiogenesis which could apply for treatment of chronic wounds, stroke and myocardial infarctions.

In vivo

Human dental pulp-derived stem cells protect against hypoxic-ischemic brain injury in neonatal mice.

Yamagata M, Yamamoto A, Kako E, Kaneko N, Matsubara K, Sakai K, Sawamoto K, Ueda M. "Human dental pulp-derived stem cells protect against hypoxic-ischemic brain injury in neonatal mice." *Stroke* (2013) Feb;44(2):551-4. PMID:23238858

<http://www.ncbi.nlm.nih.gov/pubmed/23238858>

**Perinatal hypoxia-ischemia has high rates of neurological deficits and mortality. The therapeutic effects of human exfoliated deciduous teeth (SHED) in neonatal hypoxia-ischemia was investigated. It was found that transplanted SHED (not fibroblast) significantly reduced brain tissue loss and improved neurological function. SHED also improved the survival of the mice.

Stem cells from human exfoliated deciduous tooth-derived conditioned medium enhance recovery of focal cerebral ischemia in rats.

Inoue T, Sugiyama M, Hattori H, Wakita H, Wakabayashi T, Ueda M. "Stem cells from human exfoliated deciduous tooth-derived conditioned medium enhance recovery of focal cerebral ischemia in rats." *Tissue Eng Part A*, (2013) Jan;19(1-2):24-9. PMID:22839964.

<http://www.ncbi.nlm.nih.gov/pubmed/22839964>

**In this study they investigated the effect of SHED on permanent middle cerebral artery occlusion (MCAO). Adult rats with MCAO were nasally administered SHED cells. It was found that intranasally administered SHED may help in the recovery of acute stroke. Regenerative therapy using SHED is very safe with no associated problems, it should be considered as a potential candidate for the innovative treatment of cerebral ischemia.

A novel stem cell source for vasculogenesis in ischemia: subfraction of side population cells from dental pulp.

Iohara K, Zheng L, Wake H, Ito M, Nabekura J, Wakita H, Nakamura H, Into T, Matsushita K, Nakashima M. "A novel stem cell source for vasculogenesis in ischemia: subfraction of side population cells from dental pulp." *Stem Cells*. (2008) Sep;26(9):2408-18. Jun 26. PMID: 18583536

<http://www.ncbi.nlm.nih.gov/pubmed/18583536>

**A highly vasculogenic subfraction of side population was isolated from dental pulp cells. In a mouse model of hind limb ischemia local transplantation of the subfraction resulted in successful engraftment and an increase in blood flow including high density capillary formation.

Intraventricular injection of human dental pulp stem cells improves Hypoxic-Ischemic brain damage in neonatal rats.

Fang CZ, Yang YJ, Wang QH, Yao Y, Zhang XY, He XH. "Intraventricular injection of human dental pulp stem cells improves Hypoxic-Ischemic brain damage in neonatal rats." *PLoS One*. (2013) Jun 14;8(6). PMID: 23799131

<http://www.ncbi.nlm.nih.gov/pubmed/?term=23799131>

**Neonatal rats were injected intraventricularly with human dental pulp stem cells to assess hypoxic ischemic brain damage. The hypoxic-ischemic brain damaged group of rats showed improvement as compared to controls on all behavior test. DPSC were found in the injected region and the left cortex. Intraventricular injection of human DPSCs improves hypoxic-ischemia brain damage in neonatal rats.

Liver Disease

Dental pulp stem cells have recently been shown to differentiate into functional hepatocyte or liver cells. Stem cells from human exfoliated deciduous teeth (SHED) as well as stem cells from third molar or wisdom teeth have the capacity to differentiate into hepatocytes. They have been used in preclinical animal models to treat acute liver injury or secondary biliary cirrhosis. These cells were found to incorporate into the donor liver and restore liver function.

In vitro

Human dental pulp stem cells derived from cryopreserved dental pulp tissues of vital extracted teeth with disease demonstrate hepatic-like differentiation.

Chen YK, Huang AH, Chan AW, Lin LM "Human dental pulp stem cells derived from cryopreserved dental pulp tissues of vital extracted teeth with disease demonstrate hepatic-like differentiation." *J Tissue Eng Regen Med*.

(2013) Aug;16 PMID: 23950016

<http://www.ncbi.nlm.nih.gov/pubmed/23950016>

**It is shown that human dental pulp stem cells isolated from liquid nitrogen stored dental pulp tissues or freshly derived dental pulp tissues showed hepatic-like differentiation with morphological change and normal karyotype. Differentiated DPSC expressed hepatic function genes and liver specific genes as well as glycogen storage. It was shown that DPSC can differentiate into hepatic-like cells.

High-purity Hepatic Lineage Differentiated from Dental Pulp Stem Cells in Serum-free Medium

Ishkitiev N, Yaegaki K, Imai T, Tanaka T, Nakahara T, Ishikawa H, Mitev V, Haapasalo M. "High-purity Hepatic Lineage Differentiated from Dental Pulp Stem Cells in Serum-free Medium." *Journal of Endodontics* (2012). PMID: 22414832

<http://www.ncbi.nlm.nih.gov/pubmed/22414832>

**The capacity for and purity of hepatocyte-like differentiated dental pulp stem cells without serum was investigated. It was found that without serum both mesenchymal cells from human deciduous and extracted third molar pulp differentiated into high-purity hepatocyte-like cells.

In vivo

Novel management of acute or secondary biliary liver conditions using hepatically differentiated human dental pulp cells.

Ishkitiev N, Yaegaki K, Imai T, Tanaka T, Fushimi N, Mitev V, Okada M, Tominaga N, Ono S, Ishikawa H. "Novel management of acute or secondary biliary liver conditions using hepatically differentiated human dental pulp cells." *Tissue Eng Part A*. (2015) Feb;21.3-4. PMID: 25234861

<http://www.ncbi.nlm.nih.gov/pubmed/25234861>

**It was examined as to whether SHED could hepatically differentiate and be used to treat acute liver injury or secondary biliary cirrhosis. The test for liver function recovery confirmed presence of human hepatic markers in rat blood serum. It was shown that SHED engraft morphologically and functionally into livers of rats having acute injury or secondary biliary cirrhosis.

Multipotent cells from the human third molar: feasibility of cell-based therapy for liver disease.

Ikeda E, Yagi K, Kojima M, Yagyuu T, Ohshima A, Sobajima S, Tadokoro M, Katsube Y, Isoda K, Kondoh M, Kawase M, Go MJ, Adachi H, Yokota Y, Kirita T, Ohgushi H. "Multipotent cells from the human third molar: feasibility of cell-based therapy for liver disease." *Differentiation*. (2008) May; 76(5):495-505. PMID: 18093227

<http://www.ncbi.nlm.nih.gov/pubmed/18093227>

**Novel stem cells called tooth germ progenitor cells (TGPC) obtained from third molar or wisdom teeth as characterized. The TFPC was transplanted into liver injury rat model. It was found that TGPC prevented progression of liver fibrosis in the liver of treated rats and contributed to restoration of liver function. TGPC can be a candidate for cell-based therapy to treat liver diseases and offer opportunities for developing therapies in treating tissue repair and regeneration.

Muscle Diseases

Dental pulp stem cells have been shown to differentiate into myocytes – muscle cells. These stem cells are now being investigated for treatment of genetic conditions like muscular dystrophy in canine models.

In-vitro

Mesenchymal Progenitor Cells from Different Sources and their Potential to Differentiate In Vitro into Muscle Cells.

Ranjith Kumar Indarapu, Leela Krishna and Subhadra Dravida. "Mesenchymal Progenitor Cells from Different Sources and their Potential to Differentiate In Vitro into Muscle Cells." *Cell Dev Biol*. (2013) doi:10.4172/2168-9296.1000124

**Dental pulp derived mesenchymal stem cells showed more propensity towards myogenic transdifferentiation as compared to umbilical cord tissue stem cells and adipose tissue stem cells.

In-vivo

Early transplantation of human immature dental pulp stem cells from baby teeth to golden retriever muscular dystrophy (GRMD) dogs: Local or systemic?

Kerkis I, Ambrosio CE, Kerkis A, Martins DS, Zucconi E, Fonseca SA, Cabral RM, Maranduba CM, Gaiad TP, Morini AC, Vieira NM, Brolio MP, Sant'Anna OA, Miglino MA, Zatz M. "Early transplantation of human immature dental pulp stem cells from baby teeth to golden retriever muscular dystrophy (GRMD) dogs: Local or systemic?" *J Transl Med*. (2008) Jul 3;6:35. PMID: 18598348

<http://www.ncbi.nlm.nih.gov/pubmed/18598348>

**Golden retriever muscular dystrophy (GRMD) dogs represent the best available animal model for therapeutic trials aiming at the future treatment of human Duchenne muscular dystrophy. No signs of immune rejection were observed, and the human immature dental pulp stem cells had significant engraftment in the GRMD dog muscles. Better clinical condition were observed in the dog that received monthly arterial injection of DPSC and was still clinically stable at 25 months of age.

***In vivo* evaluation of human dental pulp stem cells differentiated towards multiple lineages.**

Zhang W, Walboomers XF, Van Kuppevelt TH, Daamen WF, Van Damme PA, Bian Z, Jansen JA. "In vivo evaluation of human dental pulp stem cells differentiated towards multiple lineages."

J Tissue Eng Regen Med. (2008) Mar-Apr;2(2-3):117-25. PMID: 18338838

<http://www.ncbi.nlm.nih.gov/pubmed/18338838>

**DPSC showed the ability to further differentiate along odontogenic, myogenic, and adipogenic pathways in vivo and were able to spontaneously differentiate along odontogenic and adipogenic directions in vivo. Stem cells derived from human dental pulp form a suitable source for tissue engineering and cell-mediated therapy.

Myocardial Infarction (Heart Attack)/ Cardiac Diseases

Heart attack often leads to injured/damaged cardiomyocytes or heart cells. Dental pulp stem cells could provide an alternative cell population for repair of damaged cardiac tissue due to heart attack. Pre-clinical animal models have been treated with human dental pulp stem cells for heart injury caused by a heart attack.

In vivo

Injured cardiomyocytes promote dental pulp mesenchymal stem cell homing.

Di Scipio F, Sprio AE, Folino A, Carere ME, Salamone P, Yang Z, Berrone M, Prat M, Losano G, Rastaldo R, Berta GN. "Injured cardiomyocytes promote dental pulp mesenchymal stem cell homing." *Biochim Biophys Acta*. (2014) Jul;1840(7):2152-61. PMID: 24631652

<http://www.ncbi.nlm.nih.gov/pubmed/24631652>

**A rat dental pulp stem cell line (MUR-1) was used to assess stem cell migration in an ex-vivo model of heart ischemia. It was shown that the cells could reach the injured cells/tissue and make contact with damaged cardiomyocytes. A similarity was reported between what happens during heart organogenesis and early migration of stem cells in ischemic models. Further understanding of the early phase of stem cell migration with a damaged organ will help with future stem cell mediated organ regeneration.

Human dental pulp stem cells improve left ventricular function, induce angiogenesis, and reduce infarct size in rats with acute myocardial infarction.

Gandia C, Armiñan A, García-Verdugo JM, Lledó E, Ruiz A, Miñana MD, Sanchez-Torrijos J, Payá R, Mirabet V, Carbonell-Uberos F, Llop M, Montero JA, Sepúlveda P. "Human dental pulp stem cells improve left ventricular function, induce angiogenesis, and reduce infarct size in rats with acute myocardial infarction." *Stem Cells*. (2008) Mar;26(3):638-45. PMID: 18079433

<http://www.ncbi.nlm.nih.gov/pubmed/18079433>

**In this study DPSC were used to treat rats that had undergone an induced heart attack. After 4 weeks it was found that cell treated rats had an improvement in cardiac function, anterior wall thickening, and that went along with reduction in infarct size. This data shows that DPSC could provide a novel alternative cell population for cardiac repair.

Neurological Disorders

Dental pulp stem cells have been shown to differentiate into functional neurons in animal models. Dental pulp stem cells have been used to investigate facial nerve defect regeneration, heat stroke, optic nerve injury, and spinal cord injury.

In vitro

Neurogenic potential of dental pulp stem cells isolated from murine incisors.

Ellis KM, O'Carroll DC, Lewis MD, Rychkov GY, Koblar SA. "Neurogenic potential of dental pulp stem cells isolated from murine incisors." *Stem Cell Res Ther*. (2014) Feb;27(1). PMID: 24572146

<http://www.ncbi.nlm.nih.gov/pubmed/24572146>

**Dental pulp stem cells developed a neuronal morphology and high expression of neural markers. In addition intracellular electrophysiological analysis revealed voltage gated channels in the majority of cells with neuronal morphology.

Midbrain cues dictate differentiation of human dental pulp stem cells towards functional dopaminergic neurons.

Kanafi M, Majumdar D, Bhonde R, Gupta P, Datta I. "Midbrain cues dictate differentiation of human dental pulp stem cells towards functional dopaminergic neurons."

J Cell Physiol (2014) Oct; 229(10): 1369-77. PMID: 24477667

<http://www.ncbi.nlm.nih.gov/pubmed/24477667>

** Dental pulp originating from the neural crest are considered a better source of postnatal stem cell-based therapies in neurodegenerative diseases. Functional studies showed that induced DPSC could secrete dopamine and the induced DPSC showed ATP simulated calcium channel exchange. This study clearly shows for the first time that DPSC in the presence of embryonic midbrain cues show a tendency towards a functional dopaminergic cell type.

Neurogenic differentiation of human dental stem cells.

Lee Joo-Hee, Um S, Song I, Kim H, Seo B. "Neurogenic differentiation of human dental stem cells."

J Korean Assoc Oral Maxillofac Surg. (2014) Aug;40(4):173-80. PMID: 25247147

<http://www.ncbi.nlm.nih.gov/pubmed/25247147>

**Human dental stem cells including human dental pulp stem cells (DPSC), periodontal ligament stem cells (PDLSC), and stem cells from apical papilla (SCAP) may have neurogenic differentiation capability *in vitro*. Human dental pulp stem cells are a possible alternative source of stem cells for therapeutic use in the treatment of neurological diseases.

Multifaceted neuro-regenerative activities of human dental pulp stem cells for functional recovery after spinal cord injury.

Yamamoto A, Kiyoshi Sakai, Kohki Matsubara, Fumiya Kano, Minoru Ueda. "Multifaceted neuro-regenerative activities of human dental pulp stem cells for functional recovery after spinal cord injury." *Neuroscience research*. (2013) Jan;78:16-20. PMID:24252618.

<http://www.ncbi.nlm.nih.gov/pubmed/24252618>

**Primary characteristics of human pulp stem cells and their therapeutic benefits for treating spinal cord injury are summarized. Experimental data from multiple preclinical studies suggest that pulp stem cells may promote functional recovery after stem cells injury through multifaceted neuro-regenerative activities.

In vivo

Electrophysiologic and functional evaluations of regenerated facial nerve defects with a tube containing dental pulp cells in rats.

Sasaki R, Matsumine H, Watanabe Y, Takeuchi Y, Yamato M, Okano T, Miyata M, Ando T. "Electrophysiologic and functional evaluations of regenerated facial nerve defects with a tube containing dental pulp cells in rats."

Plast Reconstr Surg. (2014) Nov;134(5):970-8. PMID: 25347632

<http://www.ncbi.nlm.nih.gov/pubmed/25347632>

**Nerve tubes with dental pulp cells (DPC) promoted facial nerve regeneration in rats. Dental pulp cells tubulation could recover facial nerve defects functionally and electrophysiologically, the recovery was found to be comparable to that of nerve autografting in Lewis rats. Dental pulp may be a source of easily obtainable cells for potential use in facial nerve regeneration. Further studies are necessary to investigate if nerve guide with DPC can bridge nerve gaps or how many DPC are required for regeneration of facial nerve gaps.

Transplantation of human dental pulp-derived stem cells protects against heat stroke in mice.

Tseng LS, Chen SH, Lin MT, Lin YC. "Transplantation of human dental pulp-derived stem cells protects against heat stroke in mice." *Cell Transplant* (2014) Mar 7. PMID:24612725

<http://www.ncbi.nlm.nih.gov/pubmed/24612725>

**The therapeutic effects of SHED for the treatment of multiple organs including brain or hypothalamus injury in heat stroke mice was investigated. Intravenous administration of SHED immediately after whole body heat (WBH) exposure to mice offered the following therapeutic benefits for recovery after heat stroke. 1) Inhibition of WBH induced neurologic and thermoregulatory deficits, 2) reduction of WBH induced ischemia, hypoxia, and oxidative damage to brain, among others. Treatment with SHED post WBH reduced induction of pro-inflammation, enhanced plasma induction, and improved lethality in mice.

Intravitreally transplanted dental pulp stem cells promote neuroprotection and axon regeneration of retinal ganglion cells after optic nerve injury.

Mead B, Logan A, Berry M, Leadbeater W, Scheven BA. "Intravitreally transplanted dental pulp stem cells promote neuroprotection and axon regeneration of retinal ganglion cells after optic nerve injury." *Invest Ophthalmol Vis Sci* (2013). PMID: 24150755

<http://www.ncbi.nlm.nih.gov/pubmed/24150755>

**Sprague Dawley rats with optic nerve damage were treated with dental pulp stem cells injected into the vitreous of the eye. It was found that dental pulp stem cells and to a lesser extent bone marrow stem cells had higher survival and neuritogenesis/axogenesis. Intravitreal transplant of DPSC promoted retinal ganglion cells survival and axon regeneration after optic nerve injury.

Human Adult Dental Pulp Stem Cells Enhance Poststroke Functional Recovery Through Non-Neural Replacement Mechanisms

Leong, Wai Khay, *et al.* "Human Adult Dental Pulp Stem Cells Enhance Poststroke Functional Recovery Through Non-Neural Replacement Mechanisms." *Stem Cells Translational Medicine* 1.3 (2012): 177-187.

<http://stemcellstm.alphamedpress.org/content/1/3/177.short>

**Human adult dental pulp stem cells have the capacity to differentiate into neurons *in vitro*. Intracerebral transplantation of human DPSC in a rodent model resulted in improvement of forelimb function 4 weeks after treatment. Neural replacement is the likely mechanism in which DPSC enhance recovery. This study provides preclinical evidence for the use of human DPSC to improve outcome for stroke patients.

Human dental pulp-derived stem cells promote locomotor recovery after complete transection of the rat spinal cord by multiple neuro-regenerative mechanisms.

Sakai, Kiyoshi, A. Yamamoto, K. Matsubara, S. Nakamura, M. Naruse, M. Yamagata *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* 122.1, (2012): 80. PMID: 22133879
<http://www.ncbi.nlm.nih.gov/pubmed/22133879>

**Transplantation of human dental pulp stem cells into completely transected adult rat spinal cord resulted in recovery of hind limb locomotor function. It was also found that transplantation of human bone marrow stromal cells or skin derived fibroblast had less recovery of locomotor function. Tooth derived stem cells can provide therapeutic benefits for treating spinal cord injury.

Human dental pulp cells: a new source of cell therapy in a mouse model of compressive spinal cord injury.

De Almeida FM, Marques SA, Ramalho Bdos S, Rodrigues RF, Cadilhe DV, Furtado D. et al. "Human dental pulp cells: a new source of cell therapy in a mouse model of compressive spinal cord injury." *J Neurotrauma*. May 25 (2011) PMID: 21609310

<http://www.ncbi.nlm.nih.gov/pubmed/21609310>

**In this study human dental pulp cells were transplanted into the epicenter of a mouse spinal cord lesion. It was shown that this strategy promoted better tissue organization, larger areas of white matter preservation, and a better functional outcome. Human dental pulp cells may be used for therapeutic intervention after spinal cord injury and in central nervous system disorders in human s.

Integration of neuronally predifferentiated human dental pulp stem cells into rat brain in vivo.

Király M, Kádár K, Horváthy DB, Nardai P, Rácz GZ, Lacza Z, Varga G, Gerber G. "Integration of neuronally predifferentiated human dental pulp stem cells into rat brain in vivo." *Neurochem Int.* (2011) Jan 8. PMID: 21219952

<http://www.ncbi.nlm.nih.gov/pubmed/21219952>

**Engrafted DPSC derived cells integrate into the host brain and have been shown to have neuronal properties including biomarker expression and functionally with voltage dependent sodium/potassium channels. Predifferentiated human dental pulp stem cells can be used as a source of neuronal replacement in vivo.

Implanted Adult Human Dental Pulp Stem Cells Induce Endogenous Axon Guidance.

Arthur A, Shi S, Zannettino AC, Fujii N, Gronthos S, Koblar SA. "Implanted Adult Human Dental Pulp Stem Cells Induce Endogenous Axon Guidance." *Stem Cells.* (2009) Sep;27(9):2229-37. PMID: 19544412

<http://www.ncbi.nlm.nih.gov/pubmed/19544412>

**An avian embryonic model system was used to investigate axon guidance *in vivo* after transplantation of adult human dental pulp stem cells. This is the first direct evidence that dental pulp stem cells may induce neuroplasticity within a receptive host nervous system.

Adult human dental pulp stem cells differentiate toward functionally active neurons under appropriate environmental cues.

Arthur A, Rychkov G, Shi S, Koblar SA, Gronthos S. "Adult human dental pulp stem cells differentiate toward functionally active neurons under appropriate environmental cues." *Stem Cells.* (2008) Jul;26(7):1787-95. PMID: 18499892

<http://www.ncbi.nlm.nih.gov/pubmed/18499892>

**In this study it is shown that human adult dental pulp stem cells respond to neuronal induction conditions both in vitro and in vivo. DPSC expressed neuronal markers and acquired a neuronal morphology following transplantation into the mesencephalon of embryonic chicken embryos.

Putative Dental Pulp Derived Stem/Stromal Cells Promote Proliferation and Differentiation of Endogenous Neural Cells in the Hippocampus of Mice.

Huang AH, Snyder BR, Cheng PH, Chan AW. "Putative Dental Pulp Derived Stem/Stromal Cells Promote Proliferation and Differentiation of Endogenous Neural Cells in the Hippocampus of Mice." *Stem Cells.* (2008) Aug 7. PMID: 18687995

<http://www.ncbi.nlm.nih.gov/pubmed/18687995>

**In this study undifferentiated untreated dental pulp stem cells were grafted into the hippocampus of immune suppressed mice. It was shown that grafting of DPSC promotes proliferation, cell recruitment, and maturation of endogenous stem/progenitor cells by changing local microenvironment. DPSC have a unique therapeutic potential because of the simulating/modulating effects expressed on the local repair response in the central nervous system.

Parkinson's Disease

Dental pulp stem cells can differentiate into functional neurons and have been used in animals to reduce the symptoms of Parkinson's Disease, a disease of the central nervous system.

Human dental pulp stem cells protect mouse dopaminergic neurons against MPP⁺ or rotenone.

Nesti C, Pardini C, Barachini S, D'Alessandro D, Siciliano G, Murri L, Petrini M, Vaglini F. "Human dental pulp stem cells protect mouse dopaminergic neurons against MPP(+) or rotenone." *Brain Res.* (2011) Jan 7;1367:94-102. Epub 2010 Sep 18. PMID: 20854799

<http://www.ncbi.nlm.nih.gov/pubmed/20854799>

**Co-culture with DPSCs significantly attenuated MPP⁺ or rotenone-induced toxicity in primary cultures of neurons. DPSC can be viewed as possible candidates for studies on cell-based therapy in neurodegenerative disorders.

Stem cells from human-exfoliated deciduous teeth can differentiate into dopaminergic neuron-like cells.

Wang J, Wang X, Sun Z, Wang X, Yang H, Shi S, Wang S. "Stem cells from human-exfoliated deciduous teeth can differentiate into dopaminergic neuron-like cells." *Stem Cells Dev* (2010) Sep; 19; PMID:20131979

<http://www.ncbi.nlm.nih.gov/pubmed/20131979>

**This study investigated the therapeutic efficacy of human exfoliated deciduous teeth (SHED) in alleviating Parkinson's disease in a rat model. Transplantation of SHED spheres into parkinsonian rats partially improved the behavioral disorders as compared to controls. SHED may be an optimal source of postnatal stem cells for Parkinson's disease treatment.

Ocular Disease/Injury

Stem cells can act as a new source of cells to replace damaged cells in the eye. Dental pulp stem cells have been used for corneal reconstructions and retina regeneration in animal models. In addition more investigations are now focusing on how dental pulp stem cells can overcome on age-related eye diseases and conditions.

In-vitro

Dental pulp stem cells, a paracrine mediated therapy for the retina.

Mead B, Logan A, Berry M, Leadbeater W, Scheven B. "Dental pulp stem cells, a paracrine mediated therapy for the retina." *Neural Regen Res.* (2014) Mar 15;9(6). PMID:4146241

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4146241/>

** A review summarizing the alternative of using dental pulp stem cells for neural protection and regeneration in the eye. DPSC have a neural crest origin and this makes them more suitable as compared to other MSC in the treatment of CNS injuries.

In-vivo

Dental pulp stem cells: a new cellular resource for corneal stromal regeneration.

Syed-P, Du Y, Lathrop KL, Mann MM, Funderburgh ML, Funderburgh JL. "Dental pulp stem cells: a new cellular resource for corneal stromal regeneration." *Stem Cells Transl Med.* (2015). PMID:25713466.

<http://www.ncbi.nlm.nih.gov/pubmed/25713466>

** DPSC can differentiate into keratocytes which are cells from the corneal stroma. After implantation into mice the DPSC produced corneal stromal matrix and did not affect corneal transparency or induce any immune reactions. DPSC have the potential for clinical use for corneal stromal blindness.

Corneal reconstruction with tissue-engineered cell sheets composed of human immature dental pulp stem cells.

Gomes JA, Geraldine Monteiro B, Melo GB, Smith RL, Cavenaghi Pereira da Silva M, Lizier NF, Kerkis A, Cerruti H, Kerkis I. "Corneal reconstruction with tissue-engineered cell sheets composed of human immature dental pulp stem cells." *Invest Ophthalmol Vis Sci.* (2010) Mar;51(3):1408-14. Epub 2009 Nov 5. PMID: 19892864

<http://www.ncbi.nlm.nih.gov/pubmed/19892864>

** A tissue engineered cell sheet composed of human dental pulp stem cells was used for ocular surface reconstruction in a rabbit animal model. It was shown that the transplantation of the DPSC sheet was successful for the reconstruction of corneal epithelium in the animal model.

Skeletal Disease/Injury

Stem cells from dental pulp have been shown to have the ability to differentiate into osteoblasts. Studies have shown that dental pulp stem cells are a promising tool for bone generation. Stem cells from teeth have been expanded, differentiated, and implanted into animal models and have repaired bone defects. Stem cells from dental pulp may one day be used to treat human bone disorders, like osteoporosis, bone injury, and bone deformation.

In-vivo

Transplantation of stem cells from human exfoliated deciduous teeth for bone regeneration in the dog mandibular defect.

Behnia A, Haghghat A, Talebi A, Nourbakhsh N, Heidari F. "Transplantation of stem cells from human exfoliated deciduous teeth for bone regeneration in the dog mandibular defect." *World J Stem cells* (2014). PMID:25258673
<http://www.ncbi.nlm.nih.gov/pubmed/25258673>

**Human exfoliated deciduous teeth which had been isolated and characterized 5 years before were capable of proliferation and osteogenesis and no immune response was observed after 3 months of implantation.

Transplantation of SHED prevents bone loss in the early phase of ovariectomy-induced osteoporosis.

Liu Y, Wang L, Liu S, Liu D, Chen C, Xu X, Chen X, Shi S. "Transplantation of SHED prevents bone loss in the early phase of ovariectomy-induced osteoporosis." *J Dent Res* (2014). PMID:25252877
<http://www.ncbi.nlm.nih.gov/pubmed/25252877>

**Systemic infusion of SHED improves the osteoporotic phenotype in ovariectomized mice by rescuing the bone marrow mesenchymal stem cell deficiency and inhibiting osteoclastogenesis. The immunomodulating properties of SHED are able to overcome osteopenia and are described in detail.

Micro-CT and PET analysis of bone regeneration induced by biodegradable scaffolds as carriers for dental pulp stem cells in a rat model of calvarial "critical size" defect: Preliminary data.

Annibali S., Bellavia D, Ottolengi L, Cicconetti A, Cristalli MP, Quaranta R, Pilloni A. "Micro-CT and PET analysis of bone regeneration induced by biodegradable scaffolds as carriers for dental pulp stem cells in a rat model of calvarial "critical size" defect: Preliminary data." *J Biomed Mater Res Part B* (2013). PMID: 24142538
<http://www.ncbi.nlm.nih.gov/pubmed/24142538>

**Addition of dental pulp stem cells to scaffolds has the potential to improve bone regeneration process in rats although the optimal conditions require further investigation.

Three years after transplants in human mandibles, histological and in-line holotomography revealed that stem cells regenerated a compact rather than a spongy bone: biological and clinical implications.

Giuliani A, Manescu A, Langer M, Rustichelli F, Desiderio V, Paino F, De Rosa A, Laino L, d'Aquino R, Tirino V, Papaccio G. "Three years after transplants in human mandibles, histological and in-line holotomography revealed that stem cells regenerate a compact rather than a spongy bone: biological and clinical implications." *Stem Cells Transl Med* (2013). PMID: 23502599
<http://www.ncbi.nlm.nih.gov/pubmed/23502599>

**Regenerated tissue composed of seeded DPSC's from the graft sites was composed of a fully compact bone with a higher matrix density than control human alveolar spongy bone from the same patient. It creates steadier mandibles, may well increase implant stability, and, additionally, may improve resistance to mechanical, physical, chemical, and pharmacological agents.

Transplantation of human dental pulp stem cells: enhance bone consolidation in mandibular distraction osteogenesis.

Alkai A, Ismail AR, Mutum SS, Rifin Ahmad ZA, Masudi S, Razak NH. "Transplantation of human dental pulp stem cells: enhance bone consolidation in mandibular distraction osteogenesis." *J Oral Maxillofac Surg* (2013). PMID: 24040948
<http://www.ncbi.nlm.nih.gov/pubmed/24040948>

**SHED can serve as an additional cell resource for distraction osteogenesis enhancement in rabbits and might be a promising model for the reconstruction of large mandibular defects in human oral maxillofacial surgery.

Fibroin Scaffold Repairs Critical-Size Bone Defects *In Vivo* Supported by Human Amniotic Fluid and Dental Pulp Stem Cells.

Riccio, Massimo, et al. "Fibroin Scaffold Repairs Critical-Size Bone Defects *In Vivo* Supported by Human Amniotic Fluid and Dental Pulp Stem Cells." *Tissue Engineering Part A* 18.9-10 (2012): 1006-1013.
<http://online.liebertpub.com/doi/abs/10.1089/ten.tea.2011.0542>

**Strong potential of stem cells/fibroin bioengineered constructs for correcting large cranial defects in animal model and is likely a promising approach for the reconstruction of human large skeletal defects in craniofacial surgery.

Osteogenic potential of effective bone engineering using dental pulp stem cells, bone marrow stem cells, and periosteal cells for osseointegration of dental implants.

Ito K, Yamada Y, Nakamura S, Ueda M. "Osteogenic potential of effective bone engineering using dental pulp stem cells, bone marrow stem cells, and periosteal cells for osseointegration of dental implants." *Int J Oral Maxillofac Implants* (2011). PMID: 22010075
<http://www.ncbi.nlm.nih.gov/pubmed/22010075>

**Aim of this study is to investigate cell-based effective bone engineering and osseointegration of dental implants and tissue-engineering bone using DPSC, BMSC, and periosteal cells. DPSC showed the highest osteogenic potential and may be a useful cell source for tissue-engineered bone around dental implants.

Promising cell-based therapy for bone regeneration using stem cells from deciduous teeth, dental pulp, and bone marrow.

Yamada Y, Ito K, Nakamura S, Ueda M, Nagasaka T. “Promising cell-based therapy for bone regeneration using stem cells from deciduous teeth, dental pulp, and bone marrow” *Cell Transplant* (2011). PMID: 21054950
<http://www.ncbi.nlm.nih.gov/pubmed/21054950>

** These results demonstrate that stem cells from deciduous teeth, dental pulp, and bone marrow with PRP have the ability to form bone, and bone formation with DPSCs might have the potential to generate a graft between a child and parent.

A feasibility of useful cell-based therapy by bone regeneration with deciduous tooth stem cells, dental pulp stem cells, or bone-marrow derived mesenchymal stem cells for clinical study using tissue engineering technology.

Yamada Y, Nakamura S, Ito K, Sugito T, Yoshimi R, Nagasaka T, Ueda M. “A feasibility of useful cell-based therapy by bone regeneration with deciduous tooth stem cells, dental pulp stem cells, or bone-marrow derived mesenchymal stem cells for clinical study using tissue engineering technology.” *Tissue Eng Part A* (2010). PMID: 20067397
<http://www.ncbi.nlm.nih.gov/pubmed/20067397>

** Demonstrated that dental pulp stem cells (DPSCs) and deciduous tooth stem cells (DTSCs) with platelet-rich plasma have the ability to form bone and vascularization, and this bone formation activity might be useful for osseointegrated hydroxyapatite-coated dental implants with good levels of bone-implant contact.

Human mandible bone defect repair by the grafting of dental pulp stem/progenitor cells and collagen sponge biocomplexes.

d'Aquino R, De Rosa A, Lanza V, Tirino V, Laino L, Graziano A, Desiderio V, Laino G, Papaccio G. “Human mandible bone defect repair by the grafting of dental pulp stem/progenitor cells and collagen sponge biocomplexes.” *Eur Cell Mater.* (2009) Nov 12;18:75-83. PMID: 19908196
<http://www.ncbi.nlm.nih.gov/pubmed/19908196>

** This clinical study demonstrates that a DPC/collagen sponge biocomplex can completely restore human mandible bone defects and indicates that this cell population could be used for the repair and/or regeneration of tissues and organs.

Stem cells from deciduous tooth repair mandibular defect in swine.

Zheng Y, Liu Y, Zhang CM, Zhang HY, Li WH, Shi S, Le AD, Wang SL. “Stem cells from deciduous tooth repair mandibular defect in swine.” *J Dent Res.* (2009) Mar;88(3):249-54. PMID: 19329459
<http://www.ncbi.nlm.nih.gov/pubmed/19329459>

** Stem cells from miniature pig deciduous teeth, an autologous and easily accessible stem cell source, were able to engraft and regenerate bone to repair critical-size mandibular defects at 6 months post-surgical reconstruction.

SHED repair critical-size calvarial defects in mice.

Seo BM, Sonoyama W, Yamaza T, Coppe C, Kikuri T, Akiyama K, Lee JS, Shi S. “SHED repair critical-size calvarial defects in mice.” *Oral Dis.* (2008) Jul;14(5):428-34. PMID: 18938268
<http://www.ncbi.nlm.nih.gov/pubmed/18938268>

**There is a great demand for regeneration of orofacial defects caused by trauma, tumor, genetic malformation, and periodontal diseases. SHED were able to repair generated calvarial defects in mice with substantial bone formation. The novel discovery of SHED-mediated bone formation provides a promising stem cell resource for orofacial bone regeneration.

Dental pulp stem cells: a promising tool for bone regeneration.

d'Aquino R, Papaccio G, Laino G, Graziano A. “Dental pulp stem cells: a promising tool for bone regeneration.” *Stem Cell Rev.* (2008) Spring;4(1):21-6. PMID: 18300003
<http://www.ncbi.nlm.nih.gov/pubmed/18300003>

**Overview of DPSCs and why they are a promising tool for bone regeneration.

In vivo evaluation of human dental pulp stem cells differentiated towards multiple lineages.

Zhang W, Walboomers XF, Van Kuppevelt TH, Daamen WF, Van Damme PA, Bian Z, Jansen JA. “In vivo evaluation of human dental pulp stem cells differentiated towards multiple lineages.” *J Tissue Eng Regen Med.* (2008) Mar-Apr;2(2-3):117-25. PMID: 18338838
<http://www.ncbi.nlm.nih.gov/pubmed/18338838>

**DPSC showed the ability to further differentiate along odontogenic, myogenic, and adipogenic pathways in vivo and were able to spontaneously differentiate along odontogenic and adipogenic directions in vivo. Stem cells derived from human dental pulp form a suitable source for tissue engineering and cell-mediated therapy.

Reconstruction of large cranial defects in nonimmunosuppressed experimental design with human dental pulp stem cells.

de Mendonça Costa A, Bueno DF, Martins MT, Kerkis I, Kerkis A, Fanganiello RD, Cerruti H, Alonso N, Passos-Bueno MR. ‘Reconstruction of large cranial defects in nonimmunosuppressed experimental design with human dental pulp stem cells.’ J Craniofac Surg. (2008) Jan;19(1):204-10. PMID: 18216690

<http://www.ncbi.nlm.nih.gov/pubmed/18216690>

**Bone formation was present in a cranial bone defect rat model after 1 month. The use of hDPSC in nonimmunosuppressed rats did not cause any graft rejection. hDPSC is a cell resource for correcting large cranial defects in rats and constitutes a promising model for reconstruction of human large cranial defects in craniofacial surgery.

Mesenchymal progenitor cells in adult human dental pulp and their ability to form bone when transplanted into immunocompromised mice.

Otaki S, Ueshima S, Shiraishi K, Sugiyama K, Hamada S, Yorimoto M, Matsuo O. ‘Mesenchymal progenitor cells in adult human dental pulp and their ability to form bone when transplanted into immunocompromised mice.’

Cell Biol Int. (2007) Oct;31(10):1191-7. Epub 2007 Apr 14. PMID: 17524678

<http://www.ncbi.nlm.nih.gov/pubmed/17524678>

**It was shown that DPSC produce bone instead of dentin when they are implanted into immunocompromised mice with a powder based carrier. Evidence shows that DPSC are the common progenitors of odontoblast and osteoblasts. Dental pulp stem cells are useful cell source for tissue engineering and contain the potential of new therapeutic approaches for the restoration of damaged or diseased tissue.

Wound Healing

Wound healing requires a complex bimolecular process including cell movement, cell growth, angiogenesis-or new blood vessel formation, and extracellular remodeling. Angiogenesis or new blood vessel formation is one of the most important aspects of early wound healing. Dental pulp stem cells are being investigated for their wound healing ability in pre-clinical animal models.

In-vivo

Human deciduous teeth dental pulp cells with basic fibroblast growth factor enhance wound healing of skin defect.

Nishino Y, Ebisawa K, Yamada Y, Okabe K, Kamei Y, Ueda M. ‘Human deciduous teeth dental pulp cells with basic fibroblast growth factor enhance wound healing of skin defect.’ J Craniofac Surg (2011). PMID: 21403563

<http://www.ncbi.nlm.nih.gov/pubmed/21403563>

**A combination of hDPC and bFGF was used on a skin defect mouse model. It was shown that hDPC accelerated wound healing and that hDPC enhanced wound healing more in the presence of bFGF. It is important to note that rodent skin is very different than human skin in terms of wound healing and the results are presented as a first step to evaluate wound healing effects of hDPCs.

Stem cells from human exfoliated deciduous teeth (SHED) enhance wound healing and the possibility of novel cell therapy.

Nishino Y, Yamada Y, Ebisawa K, Nakamura S, Okabe K, Umemura E, Ueda M. ‘Stem cells from human exfoliated deciduous teeth (SHED) enhance wound healing and the possibility of novel cell therapy.’ Cytotherapy (2011). PMID:21341975.

<http://www.ncbi.nlm.nih.gov/pubmed/21341975>

**SHED might offer a unique stem cell resource and the possibility of novel cell therapies for wound healing.

The purpose of this document is to educate the reader on recent advances in the field of cell research and application.

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