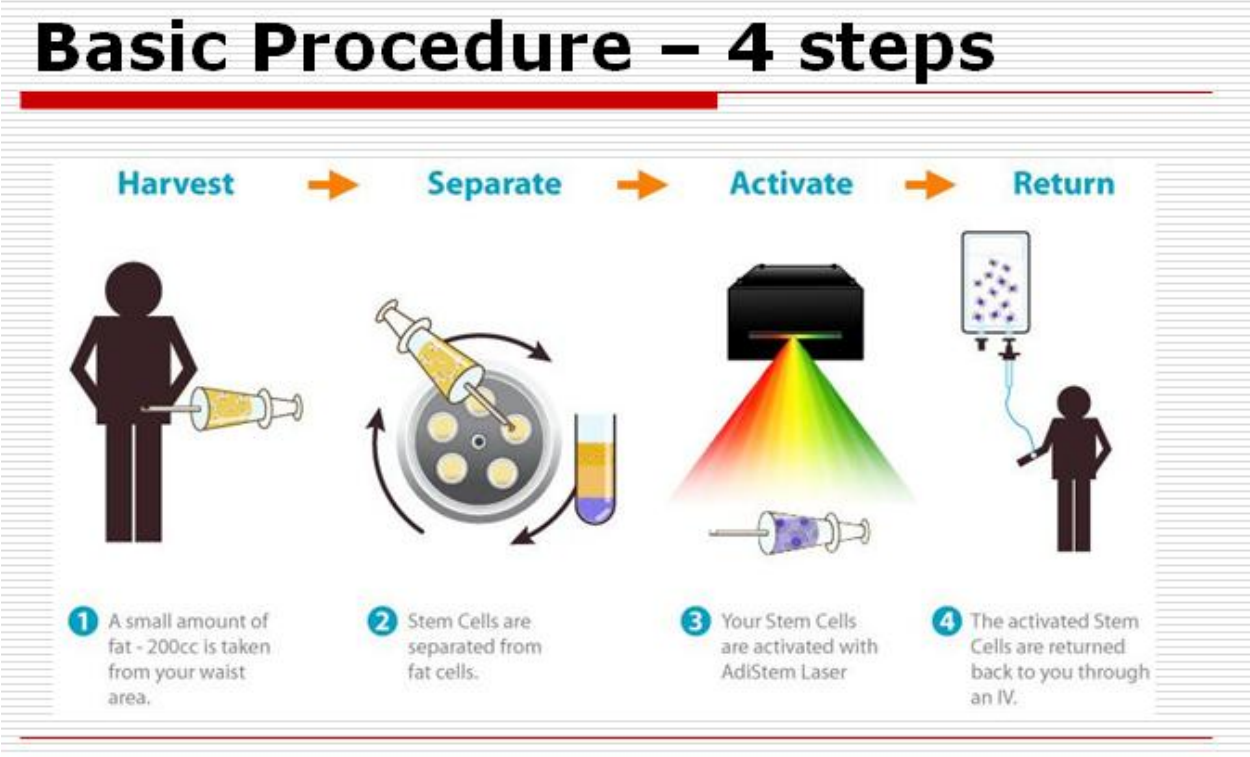
AdiStem™

Patient derived fat stem cells for Stroke Treatment



- Same day procedure – can “bank” or freeze extra cells for later treatments or doses, usually 3 doses.

The Adistem procedure has been performed on many patients with a variety of neurological and brain defects, including Stroke. The following scans clearly show “tagged” activated stem cells cross the blood brain barrier and home on the injured area of the brain. Our partner hospitals and clinics have treated stroke patients using our technology as an adjunct therapy to a complete rehabilitation program.

There are over 130 published clinical trials using Adult Stem Cells to treat Stroke and neurological conditions. Results, techniques, cellular implantation and protocols are still being developed and improved. (see below)

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338 Hennessy Road, Wanchai
Hong Kong

www.adistem.com

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Grace Draper – San Francisco Resident Stroke Survivor discusses her improvements after the Adistem Procedure.

Stroke

About This Video

Grace Draper Case

Video Descriptions:
Grace Draper was a victim of hemorrhagic stroke, and was paralysed as a result. This interview takes place after Grace was treated with AdiStem's stem cell IV therapy. This is what she has to say....

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http://www.adistem.com/application/stroke.htm

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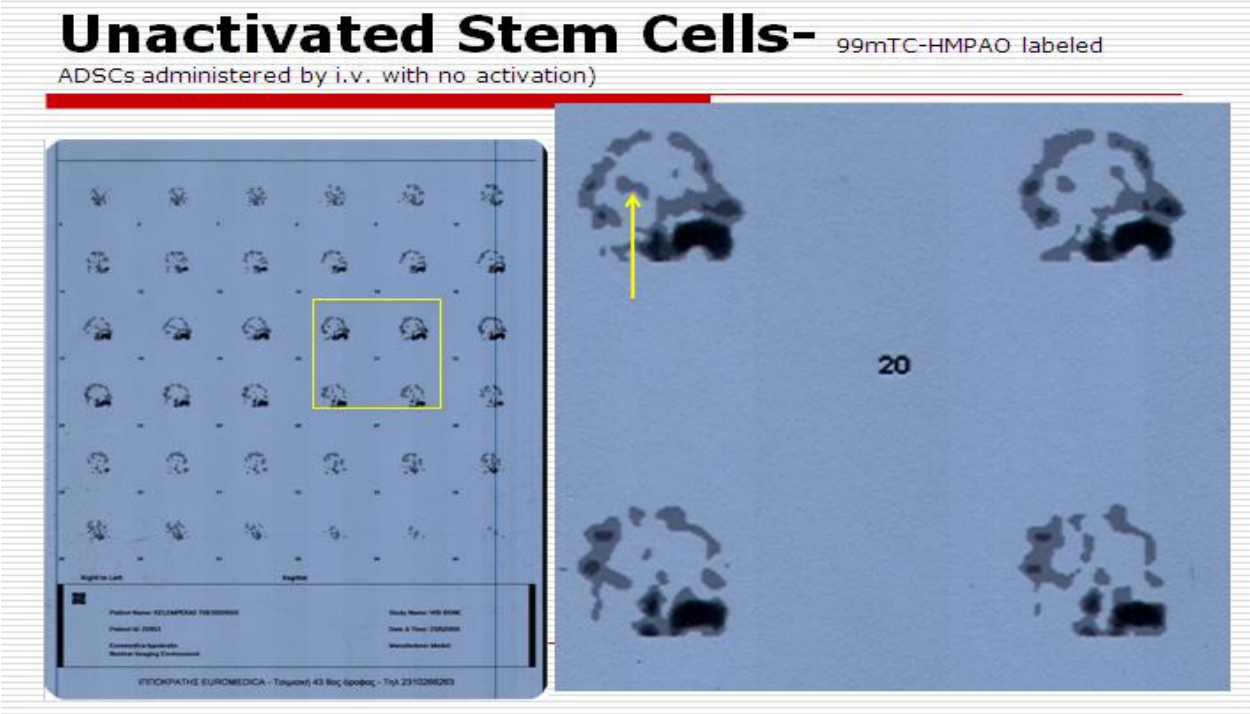
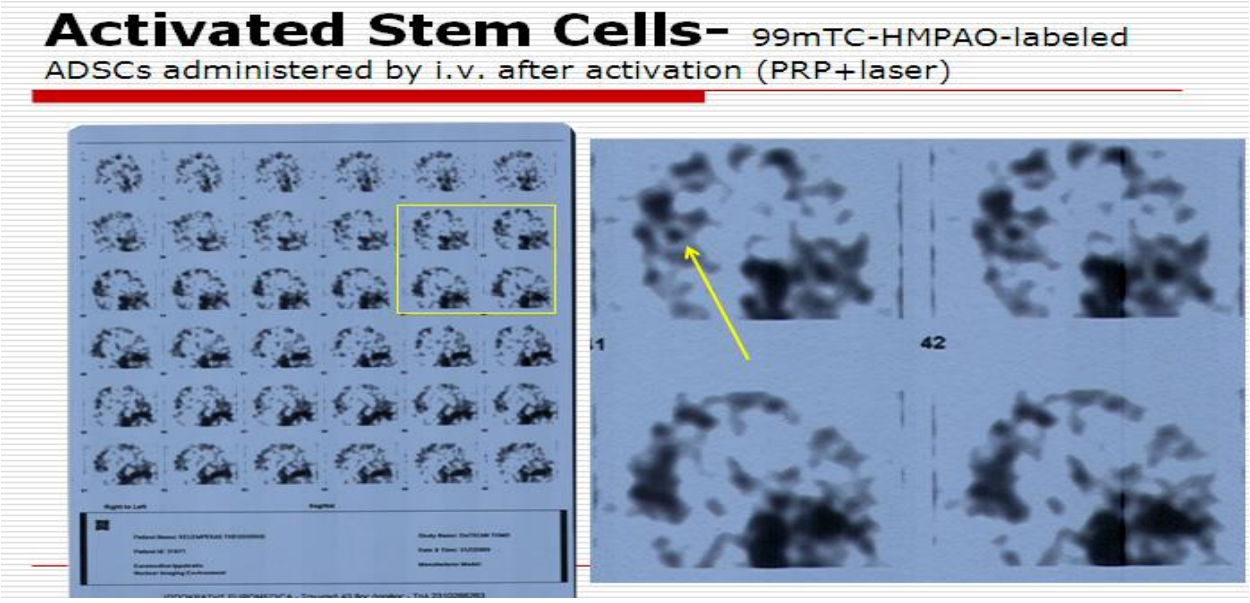
Example of radio tagging of the stem cells with brain injury

The stem cells were injected via IV drip **without activating the cells** with the Adistem technology. The **unactivated stem cells did not go** to the site of the injury.



The stem cells were injected via IV drip **after activating the cells** with the Adistem technology. The **activated stem cells go** to the site of the injury.



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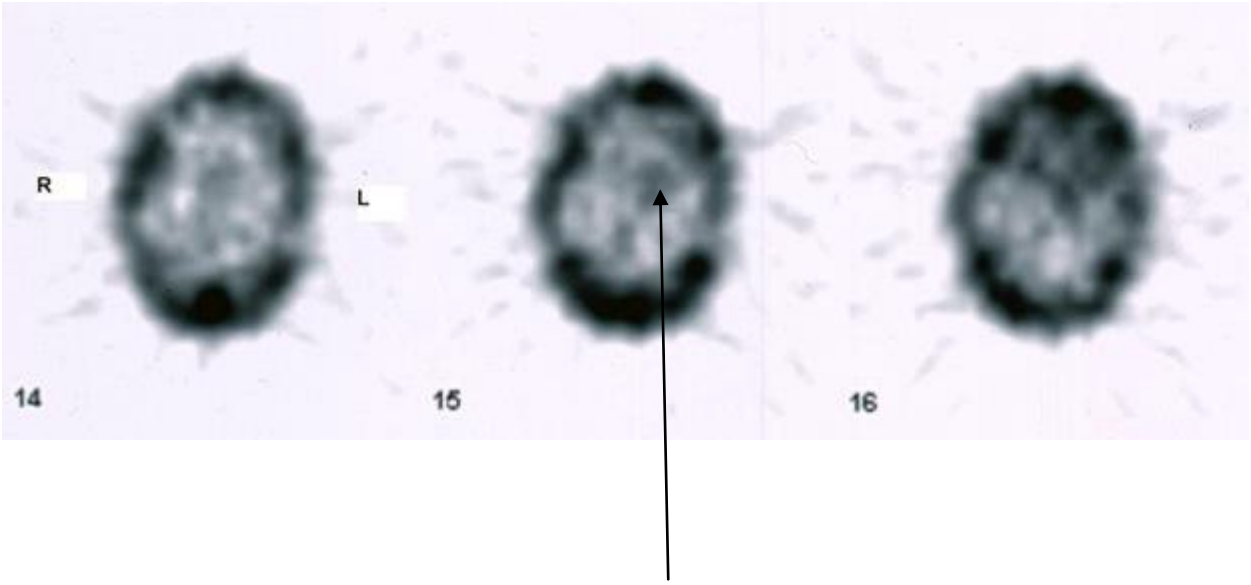
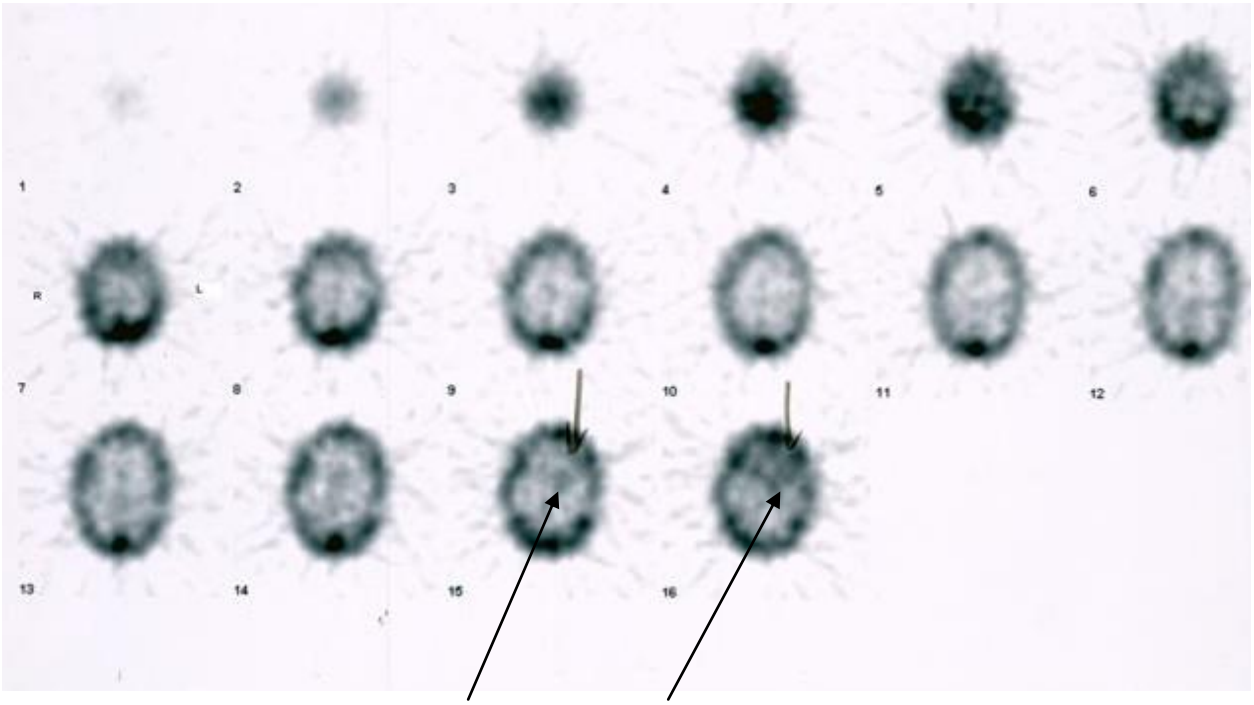
Indium brain scan - male, Australia



Note slide 15 (above)–indicates indium tagged stem cells implanted in brain



Dark spot are on slide 15 and 16 (above) indicates

indium tagged stem cells - see arrows

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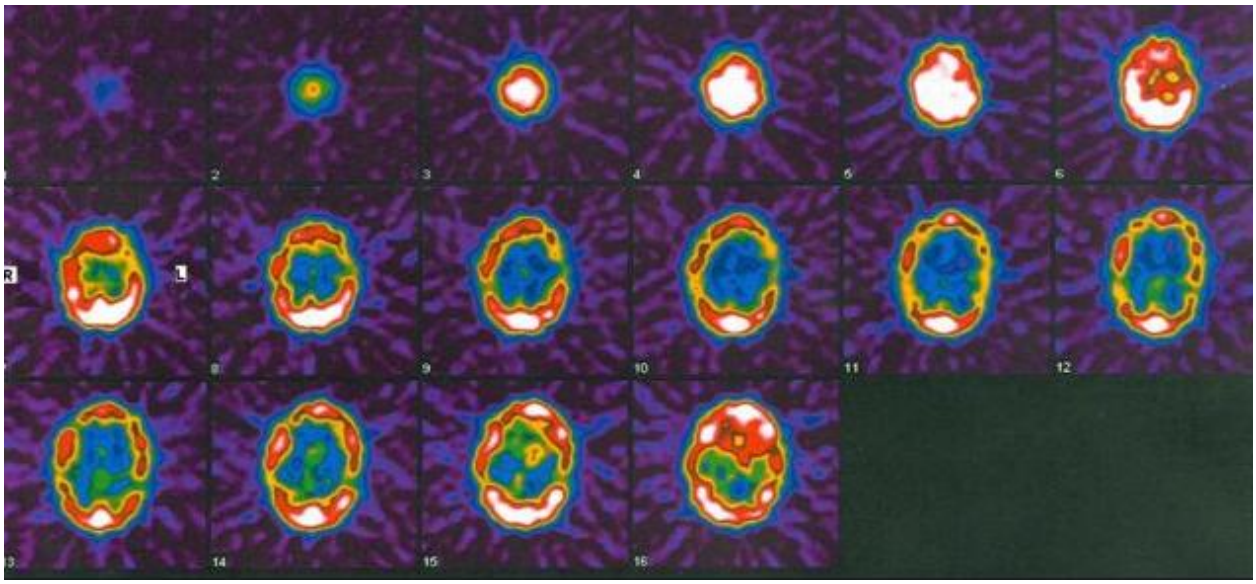
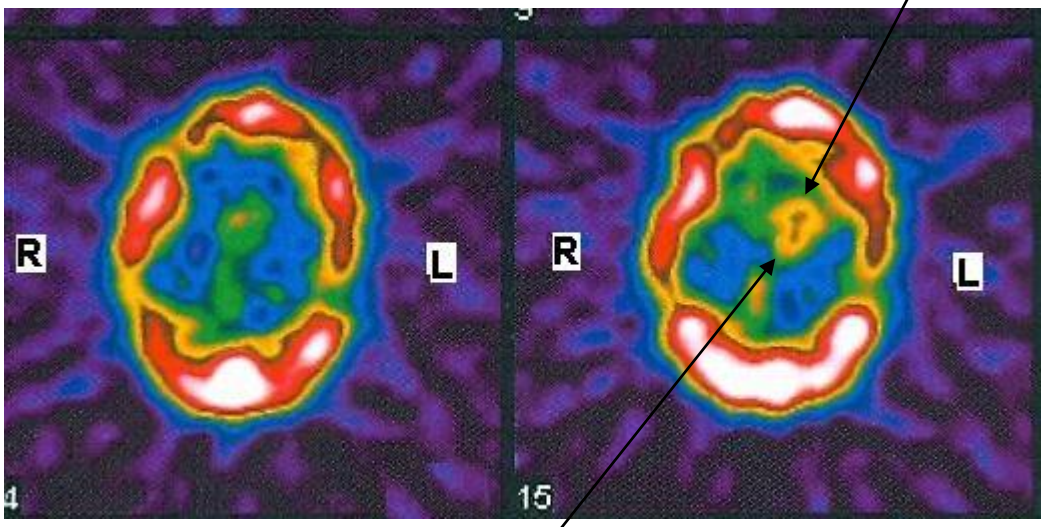
Color indium brain scan, male, Australia



See scan 15 (above) – yellow orange area indicates “hot spot” indium tagged stem cells



Scan 15 (above) – yellow orange indicates indium tagged stem cells have lodged in damaged brain tissue

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References – Adult (from the patient) Stem Cells for Stroke

PubMed – 130 Cited References and Studies

http://www.ncbi.nlm.nih.gov/sites/entrez?db=pubmed&cmd=link&linkname=pubmed_pubmed&uid=17370780

Results: 1 to 20 of 130

☐ Stem cell therapy in stroke: strategies in basic study and clinical application.

1. Liu DD, Shyu WC, Lin SZ.
Acta Neurochir Suppl. 2006;99:137-9.
PMID: 17370780 [PubMed - indexed for MEDLINE]
Related citations

☐ Homing genes, cell therapy and stroke.

2. Shyu WC, Lee YJ, Liu DD, Lin SZ, Li H.
Front Biosci. 2006 Jan 1;11:899-907. Review.
PMID: 16146779 [PubMed - indexed for MEDLINE]
Related citations

Curr Opin Neurol. 2005 Feb;18(1):59-64.

Adult stem cell therapy in stroke.

Haas S, Weidner N, Winkler J.
Department of Neurology, University of Regensburg, Regensburg, Germany.

Abstract
PURPOSE OF REVIEW: Acute cerebral infarction causes irreversible locally restricted loss of the neuronal circuitry and supporting glial cells with consecutive functional deficits and disabilities. The currently available and effective therapy targets fast vessel recanalization accompanied by symptomatic measures. Research activities focusing on stem cells, which represent a promising source for organotypic cell replacement and functional recovery after stroke, have gained momentum in recent years, making regenerative cell-based therapies a much more feasible realistic approach. This review provides an update about preclinical and clinical cell-based studies in stroke focusing on stem cells derived from the adult central nervous and hematopoetic systems. RECENT FINDINGS: Endogenous neural stem cells, which have been shown to reside throughout life in the central nervous system, have the capacity to replace lost neurons in models for numerous disorders, including cerebral ischemia. Considering adult neural stem cell transplantation as a regenerative strategy after stroke, progress has been made in isolating human adult neural stem cells and demonstrating the feasibility of autologous neural stem cell transplantation. An increasing number of studies provide evidence that hematopoietic stem cells, either after stimulation of endogenous stem cell pools or after exogenous hematopoietic stem cell application (transplantation), improve functional outcome after ischemic brain lesions. Various underlying mechanisms such as transdifferentiation into neural lineages, neuroprotection through trophic support, and cell fusion have been deciphered. SUMMARY: Many preclinical studies employing adult stem cell-based strategies hold great promise. For endogenous approaches the correlate of cell replacement underlying functional improvement needs to be demonstrated. Transplantation approaches on the experimental level need further development before clinical application can be considered.

PMID: 15655404 [PubMed - indexed for MEDLINE]

Front Biosci. 2006 Jan 1;11:899-907.

Homing genes, cell therapy and stroke.

Shyu WC, Lee YJ, Liu DD, Lin SZ, Li H.
Neuro-Medical Scientific Center, Tzu-Chi Buddhist General Hospital, Tzu-Chi University, Hualien, Taiwan.

Abstract
Stem cell therapies, such as bone marrow transplantation, are a promising strategy for the treatment of stroke. Bone marrow-derived stem cells (BMSCs) including both hematopoietic and mesenchymal stem cells (HSCs and MSCs) can exhibit tremendous cellular differentiation in numerous organs. BMSCs may also promote structural and functional repair in several organs such as the heart, liver, brain, and skeletal muscle via stem cell plasticity. Interestingly, ischemia is known to induce mobilization of BMSCs in both animal models and humans. The tissue injury is "sensed" by the stem cells and they migrate to the site of damage and undergo differentiation. The plasticity, differentiation, and migratory functions of BMSCs in a given tissue are dependent on the specific signals present in the local micro-environment of the damaged tissue. Therefore, the ischemic micro-environment has critical patho-biological functions that are essential for the seeding, expansion, survival, renewal, growth and differentiation of BMSCs in damaged brain remodeling. Recent studies have identified the specific molecular signals, such as SDF-1/CXCR4, required for the interaction of BMSCs and damaged host tissues. Understanding the exact molecular basis of stem cell plasticity in relation to local ischemic signals could offer new insights to permit better management of stroke and other ischemic disorders. The aim of this review is to summarize recent studies into how BMSCs reach, recognize, and function in cerebral ischemic tissues, with particular regard to phenotypical reprogramming of stem cells, or "stem cell plasticity".

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Pathophysiology. 2005 Jul;12(1):47-62.

Angiogenesis and stem cell transplantation as potential treatments of cerebral ischemic stroke.

Wei L, Keogh CL, Whitaker VR, Theus MH, Yu SP.

Department of Pathology and Laboratory Medicine, Medical University of South Carolina, Charleston, SC 29425, USA.

Abstract

Ischemic stroke is a leading cause of human death and disability. Although stroke survivors may gain spontaneous partial functional recovery, they often suffer from sensory-motor dysfunctions, behavioral/neurological alterations, and various degrees of paralysis. Currently, limited clinical intervention is available to prevent ischemic damage and restore lost function in stroke victims. In addition to the extensive research on protective maneuvers against ischemia-induced cell death, increasing attention has been focused on potential strategies of promoting tissue repair and functional recovery in the damaged post-ischemic brain. Angiogenesis, or the growth of new blood vessels, may contribute to cell survival and functional recovery of the area of insult. The study of angiogenesis will increase the understanding of the mechanism underlying post-ischemia neurovascular plasticity and regeneration. Additionally, stem cell transplantation has emerged in the last few years as a potential therapy for ischemic stroke, because of their capability to differentiate into multiple cell types and the possibility that they may provide trophic support for cell survival, tissue repair, and functional recovery.

PMID: 15927824 [PubMed - as supplied by publisher]

Restor Neurol Neurosci. 2009;27(1):41-54.

Systemic delivery of umbilical cord blood cells for stroke therapy: a review.

Yu G, Borlongan CV, Stahl CE, Hess DC, Ou Y, Kaneko Y, Yu SJ, Yang T, Fang L, Xie X.

Department of Cardiology, Xiangya Hospital, Southern Central University, Changsha, PR China. yuguolong123@yahoo.com.cn

Abstract

PURPOSE: This review paper summarizes relevant studies, discusses potential mechanisms of transplanted cell-mediated neuroprotection, and builds a case for the need to establish outcome parameters that are critical for transplantation success. In particular, we outline the advantages and disadvantages of systemic delivery of human umbilical cord blood (HUCB) cells in the field of cellular transplantation for treating ischemic stroke. METHODS: A MEDLINE/PubMed systematic search of published articles in peer-reviewed journals over the last 25 years was performed focusing on the theme of HUCB as donor graft source for transplantation therapy in neurological disorders with emphasis on stroke. RESULTS: Ischemic stroke remains a leading cause of human death and disability. Although stroke survivors may gain spontaneous partial functional recovery, they often suffer from sensory-motor dysfunction, behavioral/neurological alterations, and various degrees of paralysis. Currently, limited clinical intervention is available to prevent ischemic damage and restore lost function in stroke victims. Stem cells from fetal tissues, bone marrow, and HUCB has emerged in the last few years as a potential cell transplant cell source for ischemic stroke, because of their capability to differentiate into multiple cell types and the possibility that they may provide trophic support for cell survival, tissue repair, and functional recovery. CONCLUSION: A growing number of studies highlight the potential of systemic delivery of HUCB cells as a novel therapeutic approach for stroke. However, additional preclinical studies are warranted to reveal the optimal HUCB transplant regimen that is safe and efficacious prior to proceeding to large-scale clinical application of these cells for stroke therapy.

PMID: 19164852 [PubMed - indexed for MEDLINE]

Ann N Y Acad Sci. 2005 May;1049:67-83.

Umbilical cord blood-derived stem cells and brain repair.

Sanberg PR, Willing AE, Garbuzova-Davis S, Saporta S, Liu G, Sanberg CD, Bickford PC, Klasko SK, El-Badri NS.

Center of Excellence for Aging and Brain Repair, Department of Neurosurgery, College of Medicine, University of South Florida, 12901 Bruce B. Downs Blvd., MDC 78, Tampa, FL 33612, USA. psanberg@hsc.usf.edu

Abstract

Human umbilical cord blood (HUCB) is now considered a valuable source for stem cell-based therapies. HUCB cells are enriched for stem cells that have the potential to initiate and maintain tissue repair. This potential is especially attractive in neural diseases for which no current cure is available. Furthermore, HUCB cells are easily available and less immunogenic compared to other sources for stem cell therapy such as bone marrow. Accordingly, the number of cord blood transplants has doubled in the last year alone, especially in the pediatric population. The therapeutic potential of HUCB cells may be attributed to inherent ability of stem cell populations to replace damaged tissues. Alternatively, various cell types within the graft may promote neural repair by delivering neural protection and secretion of neurotrophic factors. In this review, we evaluate the preclinical studies in which HUCB was applied for treatment of neurodegenerative diseases and for traumatic and ischemic brain damage. We discuss how transplantation of HUCB cells affects these disorders and we present recent clinical studies with promising outcome.

PMID: 15965108 [PubMed - indexed for MEDLINE]

Prog Brain Res. 2006;157:207-22.

Novel cell therapy approaches for brain repair.

Garbuzova-Davis S, Willing AE, Saporta S, Bickford PC, Gemma C, Chen N, Sanberg CD, Klasko SK, Borlongan CV, Sanberg PR.

Center of Excellence for Aging and Brain Repair, Department of Neurosurgery, College of Medicine, University of South Florida, MDC 78, 12901 Bruce B. Downs Blvd., Tampa, FL 33612, USA. sgarbuzo@health.usf.edu

Abstract

Numerous reports elucidate that tissue-specific stem cells are phenotypically plastic and their differentiation pathways are not strictly delineated. Although the identity of all the epigenetic factors which may trigger stem cells to make a lineage selection are still unknown, the plasticity of adult stem cells opens new approaches for their application in the treatment of various disorders. There is increasing researcher interest in hematopoietic stem cells for treatment of not only blood-related diseases but also various unrelated disorders including neurodegenerative diseases. Human umbilical cord blood (hUCB) cells, due to their primitive nature and ability to develop into nonhematopoietic cells of various tissue lineages, including neural cells, may be useful as an alternative cell source for cell-based therapies requiring either the replacement of individual cell types and/or substitution of missing substances. Here we focus on recent findings showing the robustness of adult stem cells derived from hUCB and their potential as a source of transplant cells for the treatment of diseased or injured brains and spinal cords. Depending upon the pathological microenvironment in which the hUCB cells are introduced, neuroprotective and/or trophic effects of these cells, from release of various growth or anti-inflammatory factors to moderation of immune-inflammatory effectors, may be more likely than neural replacement. These protective effects may prove essential to maintaining restored tissue integrity over the course of various diseases or injuries.

PMID: 17046673 [PubMed - indexed for MEDLINE]

Acta Neurochir Suppl. 2006;99:137-9.

Stem cell therapy in stroke: strategies in basic study and clinical application.

Liu DD, Shyu WC, Lin SZ.

Department of Dentistry, Tzu-Chi Buddhist General Hospital, Tzu-Chi University, Hualien, Taiwan.

Abstract

Stem cell therapies are an important strategy for the treatment of stroke. Bone marrow-derived stem cells (BMSCs) may promote structural and functional repair in several organs via stem cell plasticity. The tissue damage could stimulate the stem cells migration, and they track into the site of damage and then undergo differentiation. The plasticity functions of BMSCs in an injuries tissue are dependent on the specific signals present in the local environment of the damaged tissue. Recent studies have also identified the specific molecular signals, such as SDF-1/CXCR4, required for the interaction of BMSCs and damaged host tissues. This review summarizes the current understanding of how BMSCs reach and function in cerebral ischemic tissues.

PMID: 17370780 [PubMed - indexed for MEDLINE]

Cell Prolif. 2008 Feb;41 Suppl 1:94-114.

Stem cells and neurological diseases.

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Abstract

Cells of the central nervous system were once thought to be incapable of regeneration. This dogma has been challenged in the last decade with studies showing new, migrating stem cells in the brain in many rodent injury models and findings of new neurones in the human hippocampus in adults. Moreover, there are reports of bone marrow-derived cells developing neuronal and vascular phenotypes and aiding in repair of injured brain. These findings have fuelled excitement and interest in regenerative medicine for neurological diseases, arguably the most difficult diseases to treat. There are numerous proposed regenerative approaches to neurological diseases. These include cell therapy approaches in which cells are delivered intracerebrally or are infused by an intravenous or intra-arterial route; stem cell mobilization approaches in which endogenous stem and progenitor cells are mobilized by cytokines such as granulocyte colony stimulatory factor (GCSF) or chemokines such as SDF-1; trophic and growth factor support, such as delivering brain-derived neurotrophic factor (BDNF) or glial-derived neurotrophic factor (GDNF) into the brain to support injured neurones; these approaches may be used together to maximize recovery. While initially, it was thought that cell therapy might work by a 'cell replacement' mechanism, a large body of evidence is emerging that cell therapy works by providing trophic or 'chaperone' support to the injured tissue and brain. Angiogenesis and neurogenesis are coupled in the brain. Increasing angiogenesis with adult stem cell approaches in rodent models of stroke leads to preservation of neurones and improved functional outcome. A number of stem and progenitor cell types has been proposed as therapy for neurological disease ranging from neural stem cells to bone marrow derived stem cells to embryonic stem cells. Any cell therapy approach to neurological disease will have to be scalable and easily commercialized if it will have the necessary impact on public health. Currently, bone marrow-derived cell populations such as the marrow stromal cell, multipotential progenitor cells, umbilical cord stem cells and neural stem cells meet these criteria the best. Of great clinical significance, initial evidence suggests these cell types may be delivered by an allogeneic approach, so strict tissue matching may not be necessary. The most immediate impact on patients will be achieved by making use of the trophic support capability of cell therapy and not by a cell replacement mechanism.

PMID: 18181951 [PubMed - indexed for MEDLINE]

Cell Transplant. 2007;16(2):171-81.

Regenerative therapy for stroke.

Chang YC, Shyu WC, Lin SZ, Li H.

Department of Pediatrics, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Chang Guang University College of Medicine, Taiwan.

Abstract

Stroke remains a leading cause of death and disability worldwide. An increasing number of animal studies and preclinical trials have, however, provided evidence that regenerative cell-based therapies can lead to functional recovery in stroke patients. Stem cells can differentiate into neural lineages to replace lost neurons. Moreover, they provide trophic support to tissue at risk in the penumbra surrounding the infarct area, enhance vasculogenesis, and help promote survival, migration, and differentiation of the endogenous precursor cells after stroke. Stem cells are highly migratory and seem to be attracted to areas of brain pathology such as ischemic regions. The pathotropism may follow the paradigm of stem cell homing to bone marrow and leukocytes migrating to inflammatory tissue. The molecular signaling therefore may involve various chemokines, cytokines, and integrins. Among these, stromal cell-derived factor-1 (SDF-1)/CXC chemokine receptor-4 (CXCR4) signaling is required for the interaction of stem cells and ischemia-damaged host tissues. SDF-1 is secreted primarily by bone marrow fibroblasts and is required for BMSC homing to bone marrow. Overexpression of SDF-1 in ischemic tissues has been found to enhance stem cell recruitment from peripheral blood and to induce neoangiogenesis. Furthermore, SDF-1 expression in the lesioned area peaked within 7 days postischemia, in concordance with the time window of G-CSF therapy for stroke. Recent data have shown that SDF-1 expression is directly proportional to reduced tissue oxygen tension. SDF-1 gene expression is regulated by hypoxic-inducible factor-1 (HIF-1), a hypoxia-dependent stabilization transcription factor. Thus, ischemic tissue may recruit circulating progenitors regulated by hypoxia through differential expression of HIF-lalpha and SDF-1. In addition to SDF-1, beta2-integrins also play a role in the homing of hematopoietic progenitor cells to sites of ischemia and are critical for their neovascularization capacity. In our recent report, increased expression of beta1-integrins apparently contributed to the local neovasculization of the ischemic brain as well as its functional recovery. Identification of the molecular pathways involved in stem cell homing into the ischemic areas could pave the way for the development of new treatment regimens, perhaps using small molecules, designed to enhance endogeneous mobilization of stem cells in various disease states, including chronic stroke and other neurodegenerative diseases. For maximal functional recovery, however, regenerative therapy may need to follow combinatorial approaches, which may include cell replacement, trophic support, protection from oxidative stress, and the neutralization of the growth-inhibitory components for endogenous neuronal stem cells.