Stem Cells – Umbilical Cord Source

Umbilical cord mesenchymal stem cells: the new gold standard for mesenchymal stem cell-based therapies?

Tissue Eng Part B Rev. 2014 Oct;20(5):523-44. doi: 10.1089/ten.TEB.2013.0664. Epub 2014 Apr 22.

El Omar R[1], Beroud J, Stoltz JF, Menu P, Velot E, Decot V.

Author information

1 - 1 CNRS UMR UL 7365 , Bâtiment Biopôle, Faculté de médecine, Vandœuvre-lès-Nancy, France .

Abstract

Due to their self-renewal capacity, multilineage differentiation potential, paracrine effects, and immunosuppressive properties, mesenchymal stromal cells (MSCs) are an attractive and promising tool for regenerative medicine. MSCs can be isolated from various tissues but despite their common immunophenotypic characteristics and functional properties, source-dependent differences in MSCs properties have recently emerged and lead to different clinical applications. Considered for a long time as a medical waste, umbilical cord appears these days as a promising source of MSCs. Several reports have shown that umbilical cord-derived MSCs are more primitive, proliferative, and immunosuppressive than their adult counterparts. In this review, we aim at synthesizing the differences between umbilical cord MSCs and MSCs from other sources (bone marrow, adipose tissue, periodontal ligament, dental pulp,…) with regard to their proliferation capacity, proteic and transcriptomic profiles, and their secretome involved in their regenerative, homing, and immunomodulatory capacities. Although umbilical cord MSCs are until now not particularly used as an MSC source in clinical practice, accumulating evidence shows that they may have a therapeutic advantage to treat several diseases, especially autoimmune and neurodegenerative diseases.

PMID: 24552279

Promising new potential for mesenchymal stem cells derived from human umbilical cord Wharton's jelly: sweat gland cell-like differentiative capacity.

J Tissue Eng Regen Med. 2012 Aug;6(8):645-54. doi: 10.1002/term.468. Epub 2011 Sep 13.

Xu Y[1], Huang S, Ma K, Fu X, Han W, Sheng Z.

Author information

1 - Wound Healing and Cell Biology Laboratory, Burns Institute, First Affiliated Hospital/General Hospital of PLA, Trauma Centre of Postgraduate Medical College, Beijing, People's Republic of China.

Abstract

Mesenchymal stem cells derived from Wharton's jelly of the human umbilical cord (hUC-MSCs) possess various advantageous properties, similar to bone marrow-derived mesenchymal stem cells (BM-MSCs), including self-renewal, extended proliferation potential and multilineage differentiation potential. In this study, we hoped to determine whether hUC-MSCs could be induced to differentiate into sweat gland cell-like cells, that would be potential in sweat glands restoration after injury. In this study, the results of flow cytometry analysis revealed that hUC-MSCs showed the typical antigen profile of MSCs and were positive for CD29, CD44, CD90, CD105 and Oct-4; they were negative for the antigens of CD34, CEA and CK14. Remarkably, hUC-MSCs maintained proper proliferation and differentiation ability. After culture in sweat gland cell-conditioned medium (induction group 1) for 3 weeks, hUC-MSCs possessed sweat gland cell-like morphology and expressed markers of sweat gland cells (CEA, CK14 and CK19) more efficiently than those of induction group 2. In reverse-transcription PCR and western blotting analysis, it was further confirmed that induced hUC-MSCs (group 1) also expressed a higher level of sweat gland developmental genes (EDA and EDAR) than group 2. These results together provided evidence that hUC-MSCs could possess a new emerging potential to differentiate into sweat gland cell-like cells with a higher efficacy under our new induction system. Thus, hUC-

MSCs could be considered a new strategy for sweat glands restoration after skin injury as well as improvement of cutaneous regeneration.

PMID: 21916019

Human umbilical cord-derived mesenchymal stem cells direct macrophage polarization to alleviate pancreatic islets dysfunction in type 2 diabetic mice.

Cell Death Dis. 2018 Jul 9;9(7):760. doi: 10.1038/s41419-018-0801-9.

Yin Y[1], Hao H[2], Cheng Y[1], Zang L[1], Liu J[2], Gao J[1], Xue J[1], Xie Z[3], Zhang Q[4], Han W[5], Mu Y[6].

Author information

1 - Department of Endocrinology, Chinese PLA General Hospital, Beijing, China.

2 - Department of Molecular Biology, Institute of Basic Medicine, School of Life Science, Chinese PLA General Hospital, Beijing, China.

3 - Department of Geriatrics, China-Japan Friendship Hospital, Beijing, China.

4 - Department of Endocrinology, Beijing Tiantan Hospital, Capital Medical University, Beijing, China.

5 - Department of Molecular Biology, Institute of Basic Medicine, School of Life Science, Chinese PLA General Hospital, Beijing, China. hanwdrsw69@yahoo.com.

6 - Department of Endocrinology, Chinese PLA General Hospital, Beijing, China. muyiming@301hospital.com.cn.

Abstract

Progressive pancreatic β-cell dysfunction is recognized as a fundamental pathology of type 2 diabetes (T2D). Recently, mesenchymal stem cells (MSCs) have been identified in protection of islets function in T2D individuals. However, the underlying mechanisms remain elusive. It is widely accepted that β-cell dysfunction is closely related to improper accumulation of macrophages in the islets, and a series of reports suggest that MSCs possess great immunomodulatory properties by which they could elicit macrophages into an anti-inflammatory M2 state. In this study, we induced a T2D mouse model with a combination of high-fat diet (HFD) and low-dose streptozotocin (STZ), and then performed human umbilical cord-derived MSCs (hUC-MSCs) infusion to investigate whether the effect of MSCs on islets protection was related to regulation on macrophages in pancreatic islets. hUC-MSCs infusion exerted anti-diabetic effects and significantly promoted islets recovery in T2D mice. Interestingly, pancreatic inflammation was remarkably suppressed, and local M1 macrophages were directed toward an anti-inflammatory M2-like state after hUC-MSC infusion. In vitro study also proved that hUC-MSCs inhibited the activation of the M1 phenotype and induced the generation of the M2 phenotype in isolated mouse bone marrow-derived macrophages (BMDMs), peritoneal macrophages (PMs) and in THP-1 cells. Further analysis showed that M1-stimulated hUC-MSCs increased the secretion of interleukin (IL)-6, blocking which by small interfering RNA (siRNA) largely abrogated the hUC-MSCs effects on macrophages both in vitro and in vivo, resulting in dampened restoration of β-cell function and glucose homeostasis in T2D mice. In addition, MCP-1 was found to work in accordance with IL-6 in directing macrophage polarization from M1 to M2 state. These data may provide new clues for searching for the target of β-cell protection. Furthermore, hUC-MSCs may be a superior alternative in treating T2D for their macrophage polarization effects.

PMID: 29988034

Mesenchymal stem cells derived from Wharton's Jelly of the umbilical cord: biological properties and emerging clinical applications.

Curr Stem Cell Res Ther. 2013 Mar;8(2):144-55.

Batsali AK[1], Kastrinaki MC, Papadaki HA, Pontikoglou C.

Author information

Department of Hematology, University of Crete School of Medicine, Heraklion, Greece.

Abstract

In recent years there seems to be an unbounded interest concerning mesenchymal stem cells (MSCs). This is mainly attributed to their exciting characteristics including long-term ex vivo proliferation, multilineage potential and immunomodulatory properties. In this regard MSCs emerge as attractive candidates for various therapeutic applications. MSCs were originally isolated from the bone marrow (BM) and this population is still considered as the gold standard for MSC applications. Nevertheless the BM has several limitations as source of MSCs, including MSC low frequency in this compartment, the painful isolation procedure and the decline in MSC characteristics with donor's age. Thus, there is accumulating interest in identifying alternative sources for MSCs. To this end MSCs obtained from the Wharton's Jelly (WJ) of umbilical cords (UC) have gained much attention over the last years since they can be easily isolated, without any ethical concerns, from a tissue which is discarded after birth. Furthermore WJ-derived MSCs represent a more primitive population than their adult counterparts, opening new perspectives for cell-based therapies. In this review we will at first give an overview of the biology of WJ-derived UC-MSCs. Then their potential application for the treatment of cancer and immune mediated disorders, such graft versus host disease (GVHD) and systemic lupus erythematosus (SLE) will be discussed, and finally their putative role as feeder layer for ex vivo hematopoietic stem cell (HSC) expansion will be pointed out.

PMID: 23279098

Mesenchymal Stromal Cells for Transplant Tolerance.

Front Immunol. 2019 Jun 4;10:1287. doi: 10.3389/fimmu.2019.01287. eCollection 2019.

Podestà MA[1,2], Remuzzi G[1], Casiraghi F[1].

Author information

1 - Department of Molecular Medicine, Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Bergamo, Italy.

2 - Department of Health Sciences, Università degli Studi di Milano, Milan, Italy.

Abstract

In solid organ transplantation lifelong immunosuppression exposes transplant recipients to life-threatening complications, such as infections and malignancies, and to severe side effects. Cellular therapy with mesenchymal stromal cells (MSC) has recently emerged as a promising strategy to regulate anti-donor immune responses, allowing immunosuppressive drug minimization and tolerance induction. In this review we summarize preclinical data on MSC in solid organ transplant models, focusing on potential mechanisms of action of MSC, including down-regulation of effector T-cell response and activation of regulatory pathways. We will also provide an overview of available data on safety and feasibility of MSC therapy in solid organ transplant patients, highlighting the issues that still need to be addressed before establishing MSC as a safe and effective tolerogenic cell therapy in transplantation.

PMID: 31231393

Therapeutic effects of a single injection of human umbilical mesenchymal stem cells on acute and chronic colitis in mice.

Sci Rep. 2019 Apr 9;9(1):5832. doi: 10.1038/s41598-019-41910-x.

Chang YL[1,2,3,4], Lo HY[5,4,6], Cheng SP[5,4], Chang KT[4], Lin XF[2], Lee SP[1], Hsieh MF[7], Chan CK[8,9,10].

Author information

1 - Department of Urology, Taoyuan General Hospital, Ministry of Health and Welfare, Taoyuan, Taiwan.

2 - Department of Biomedical Engineering, College of Engineering, Chung Yuan Christian University, Chung Li, Taiwan.

3 - Department of Urology, School of Medicine, National Yang-Ming University, Taipei, Taiwan.

4 - Translational Medicine Center, Taoyuan General Hospital, Ministry of Health and Welfare, Taoyuan, Taiwan.

5 - Department of Rehabilitation, Taoyuan General Hospital, Ministry of Health and Welfare, Taoyuan, Taiwan.

6 - Department of Chemistry, Chung Yuan Christian University, Chung Li, Taiwan.

7 - Department of Biomedical Engineering, College of Engineering, Chung Yuan Christian University, Chung Li, Taiwan. mfhsieh@cycu.edu.tw.

8 - Department of Pediatrics, Taoyuan General Hospital, Ministry of Health and Welfare, Taoyuan, Taiwan. genejean620104@gmail.com.

9 - Department of Biotechnology, School of Health Technology, Ming Chuan University, Taoyuan, Taiwan. genejean620104@gmail.com.

10 - Translational Medicine Center, Taoyuan General Hospital, Ministry of Health and Welfare, Taoyuan, Taiwan. genejean620104@gmail.com.

Abstract

Multiple injections of bone marrow mesenchymal stem cells (BMMSCs) have been used for treatment of chronic colitis in mice. We aimed to report the therapeutic effects of a single injection of human umbilical cord mesenchymal stem cells (hUCMSCs) on acute and chronic colitis. Male C57BL/6JNarl mice were divided into control, phosphate-buffered saline (PBS), and hUCMSCs treated groups, respectively. Acute and chronic colitis were induced in the mice (except controls) using 3% dextran sulfate sodium (DSS). The mice in the hUCMSCs group underwent a single injection of hUCMSCs. The disease activity index (DAI), colon length, histology, colon inflammation score, in vivo stem cells images, and blood cytokine levels were recorded. The DAI was significantly higher in the hUCMSCs group than in the control group and lower than in the PBS group on all days. The colon length was significantly longer and the colon inflammation score was significantly lower in the hUCMSCs group than in the PBS group on days 8 and 25. IL17A, Gro-α, MIP-1α, MIP-2, and eotaxin were significantly lower in the hUCMSCs group than in the PBS group on days 8 and 25. Single-injection hUCMSCs improved DSS-induced acute colitis and decreased progression of acute colitis to chronic colitis.

PMID: 30967579

Therapeutic Effect of Human Umbilical Cord Mesenchymal Stem Cells at Various Passages on Acute Liver Failure in Rats.

Stem Cells Int. 2018 Nov 14;2018:7159465. doi: 10.1155/2018/7159465. eCollection 2018.

Zhang Y[1,2], Li Y[3], Li W[4], Cai J[1], Yue M[1], Jiang L[1], Xu R[1], Zhang L[1], Li J[1], Zhu C[1].

Author information

1 - Department of Infectious Disease, The First Affiliated Hospital of Nanjing Medical University, Nanjing 210029, China.

2 - Department of Pediatrics, The Affiliated Hospital of Yangzhou University, Yangzhou 225000, China.

3 - Department of Pediatrics, The First Affiliated Hospital of Nanjing Medical University, Nanjing 210029, China.

4 - Third Liver Unit, Department of Infectious Disease, The First Affiliated Hospital of Science and Technology of China, Hefei 230001, China.

Abstract

Recent studies have described beneficial effects of an infusion of mesenchymal stem cells (MSCs) derived from Wharton's jelly tissue, for the treatment of acute liver failure (ALF). However, data on the therapeutic potential of culture-expanded MSCs are lacking. We examined the therapeutic potential of passage five (P5) and ten (P10) human umbilical cord- (hUC-) MSCs via their transplantation into Sprague-Dawley (SD) rats with D-galactosamine (D-GalN) and LPS-induced acute liver failure (ALF). SD rats were randomly divided into three groups: control group, P5 hUC-MSCs group, and P10 hUC-MSCs group. After transplantation, P5 hUC-MSCs provided a significant survival benefit. The analysis of aspartate aminotransferase (AST), alanine aminotransferase (ALT), and total bilirubin (TBIL) levels showed that transplantation with P5 hUC-MSCs was more effective than treatment with P10 hUC-MSCs. P5 hUC-MSCs also successfully downregulated the hepatic activity index (HAI) scores. Compared to P10 hUC-MSCs *in vivo*, P5 hUC-MSCs significantly enhanced the regeneration and inhibited the apoptosis of hepatocytes. CM-Dil-labeled hUC-MSCs were found to engraft within the recipient liver, whereas the homing of cells to the recipient liver in the P10 hUC-MSCs group was less effective compared to the P5 hUC-MSCs group. Previous studies have shown that the concentration of hepatocyte growth factor (HGF) in the injured liver was significantly increased. HGF is commonly known as the ligand of c-Met. The level of c-Met in hUC-MSCs as detected by Western blotting indicated that at a higher passage number, there is a decrease in c-Met. These data suggest that direct transplantation of P5 hUC-MSCs can more efficiently home to an injured liver. Subsequently, the P5 hUC-MSCs can rescue ALF and repopulate the livers of rats through the stimulation of endogenous liver regeneration and inhibition of hepatocellular apoptosis for compensated liver function, which is dependent on the higher level of c-Met than P10 hUC-MSCs.

PMID: 30538751

Mesenchymal stromal cells as a potential therapeutic for neurological disorders.

Regen Ther. 2018 Aug 24;9:32-37. doi: 10.1016/j.reth.2018.08.001. eCollection 2018 Dec.

Mukai T[1,2], Tojo A[1,2], Nagamura-Inoue T[2].

Author information

1 - Division of Molecular of Therapy, Center for Advanced Medical Research, The Institute of Medical Science, The University of Tokyo, 4-6-1 Shirokanedai, Minato-ku, Tokyo 108-8639, Japan.

2 - Department of Cell Processing and Transfusion, The Institute of Medical Science, The University of Tokyo, 4-6-1 Shirokanedai, Minato-ku, Tokyo, 108-8639, Japan.

Abstract

Several studies have reported that mesenchymal stromal/stem cells (MSCs) restore neurological damage through their secretion of paracrine factors or their differentiation to neuronal cells. Based on these studies, many clinical trials have been conducted using MSCs for neurological disorders, and their safety and efficacy have been reported. In this review, we provide a brief introduction to MSCs, especially umbilical cord derived-MSCs (UC-MSCs), in terms of characteristics, isolation, and cryopreservation, and discuss the recent progress in regenerative therapies using MSCs for various neurological disorders.

PMID: 30525073

Human Umbilical Cord Mesenchymal Stem Cell-Derived Extracellular Vesicles Inhibit Endometrial Cancer Cell Proliferation and Migration through Delivery of Exogenous miR-302a.

Stem Cells Int. 2019 Mar 14;2019:8108576. doi: 10.1155/2019/8108576. eCollection 2019.

Li X[1], Liu LL[2], Yao JL[3], Wang K[3], Ai H[4].

Author information

1 - Department of Obstetrics and Gynecology, Third Affiliated Hospital of Jinzhou Medical University, Jinzhou, Liaoning 121001, China.

2 - Department of Obstetrics and Gynecology, Dalian Maternity Hospital, Dalian Obstetrics and Gynecology Hospital Affiliated to Dalian Medical University, Dalian, Liaoning 116000, China.

3 - Clinical and Translational Research Center, Shanghai First Maternity and Infant Hospital, Tongji University School of Medicine, Shanghai 200040, China.

4 - Department of Obstetrics and Gynecology, The First Affiliated Hospital, Key laboratory of Follicular Development and Reproductive Health of Liaoning Province, Jinzhou Medical University, Jinzhou, Liaoning 121001, China.

Abstract

MicroRNAs (miRNAs) are potential therapeutic targets in endometrial cancer, but the difficulties associated with their delivery to tumor target cells have hampered their applications. Human umbilical cord mesenchymal stem cells (hUCMSCs) have a well-recognized tumor-homing ability, emphasizing the capacity of tumor-targeted delivery of extracellular vesicles. hUCMSCs release extracellular vesicles rich in miRNAs, which play a vital role in intercellular communication. The purpose of this study was to verify a potential tumor suppressor microRNA, miR-302a, and engineered hUCMSC extracellular vesicles enriched with miR-302a for therapy of endometrial cancer. Here, we observed that miR-302a was significantly downregulated in endometrial cancer tissues when compared with adjacent tissues. Overexpression of miR-302a in endometrial cancer cells robustly suppressed cell proliferation and migration. Meanwhile, the proliferation and migration were significantly inhibited in endometrial cancer cells when cultured with miR-302a-loaded extracellular vesicles derived from hUCMSCs. Importantly, our data showed that engineered extracellular vesicles rich in miR-302 significantly inhibited the expression of cyclin D1 and suppressed AKT signaling pathway in endometrial cancer cells. These results suggested that exogenous miR-302a delivered by hUCMSC-derived extracellular vesicles has exciting potential as an effective anticancer therapy.

PMID: 31001342