Colloids Surf B Biointerfaces. 2019 Apr 8;179:309-316. doi: 10.1016/j.colsurfb.2019.04.013. [Epub ahead of print]

Enhanced osteogenic differentiation of bone mesenchymal stem cells on magnesium-incorporated titania nanotube arrays.

Yan Y[1], Wei Y[2], Yang R[1], Xia L[2], Zhao C[1], Gao B[2], Zhang X[2], Fu J[2], Wang Q[3], Xu N[4].
Author information

Abstract

Although titanium and its alloys have been widely used as implants in orthopaedics and dentals, it is still a challenge to realize excellent bioactivity of titanium surface. In this report, magnesium ion incorporated titania nanotube arrays (MgNT) was fabricated on Ti surface through electrochemical anodization and hydrothermal treatment. The magnesium loading capacity and release kinetics were controlled by modulating the conditions in the hydrothermal treatment process. The surface morphology and composition characterized by SEM, TEM, and XPS indicated that magnesium was incorporated into nanotube in the form of $MgTiO_3$. Bone mesenchymal stem cells (BMSCs) showed accelerated proliferation rate on MgNT surfaces and extended more microfilaments than that on Ti surface. The mRNA expressions of osteogenic related genes (ALP, Col-I, OCN, and RUNX2) and angiogenic related genes (HIF-2α and VEGF), and the OCN protein expression were all significantly up-regulated on MgNT surfaces. Moreover, the ERK1/2 signaling pathway was activated on MgNT surface. All the results demonstrated that MgNT surfaces enhanced the osteoinductive activity of Ti implants through ERK signaling pathway. This strategy is promising for improving the bioactivity of Ti implants and facilitating its clinic application.

Cytotherapy. 2019 Apr 9. pii: S1465-3249(19)30008-8. doi: 10.1016/j.jcyt.2018.12.006. [Epub ahead of print]

Manufacturing and characterization of extracellular vesicles from umbilical cord-derived mesenchymal stromal cells for clinical testing.

Rohde E[1], Pachler K[2], Gimona M[3].
Author information

Abstract

Extracellular vesicles (EVs) derived from mesenchymal stromal cells (MSCs) may deliver therapeutic effects that are comparable to their parental cells. MSC-EVs are promising agents for the treatment of a variety of diseases. To reach the intermediate goal of clinically testing safety and efficacy of EVs, strategies should strive for efficient translation of current EV research. On the basis of our in vitro an in vivo findings regarding the biological actions of EVs and our experience in manufacturing biological stem cell therapeutics for routine use and clinical testing, we discuss strategies of manufacturing and quality control of umbilical cord-derived MSC-EVs. We introduce guidelines of good manufacturing

practice and their practicability along the path from the laboratory to the patient. We present aspects of manufacturing and final product quality testing and highlight the principle of "The process is the product." The approach presented in this perspective article may facilitate translational research during the development of complex biological EV-based therapeutics in a very early stage of manufacturing as well as during early clinical safety and proof-of-concept testing.

Gastroenterol Rep (Oxf). 2019 Apr;7(2):127-138. doi: 10.1093/gastro/goy017. Epub 2018 Jun 8.

Bone marrow-derived CXCR4-overexpressing MSCs display increased homing to intestine and ameliorate colitis-associated tumorigenesis in mice.

Zheng XB[1,2], He XW[1,2], Zhang LJ[3], Qin HB[1,2], Lin XT[1,2,4], Liu XH[1,2], Zhou C[1,2], Liu HS[1,2], Hu T[1,2], Cheng HC[5], He XS[1,2], Wu XR[1,2], Chen YF[1,2], Ke J[1,2], Wu XJ[1,2], Lan P[1,2].
Author information

Abstract

BACKGROUND AND OBJECTIVE:

Increasing interest has developed in the therapeutic potential of bone marrow-derived mesenchymal stem cells (MSCs) for the treatment of inflammatory bowel disease (IBD) and IBD-induced cancer. However, whether MSCs have the ability to suppress or promote tumor development remains controversial. The stromal cell-derived factor 1 (SDF-1)/C-X-C chemokine receptor type 4 (CXCR4) axis is well known to play a critical role in the homing of MSCs. In this study, we aimed to evaluate the role of CXCR4-overexpressing MSCs on the tumorigenesis of IBD.

METHODS:

MSCs were transduced with lentiviral vector carrying either CXCR4 or green fluorescent protein (GFP). Chemotaxis and invasion assays were used to detect CXCR4 expression. A mouse model of colitis-associated tumorigenesis was established using azoxymethane and dextran sulfate sodium (DSS). The mice were divided into three groups and then injected with phosphate buffer saline (PBS), MSC-GFP or MSC-CXCR4.

RESULTS:

Compared with the mice injected with MSC-GFP, the mice injected with MSC-CXCR4 showed relieved weight loss, longer colons, lower tumor numbers and decreased tumor load; expression of pro-inflammatory cytokines decreased, and signal transducer and activator of transcription 3 (STAT3) phosphorylation level in colon tissue was down-regulated.

CONCLUSION:

CXCR4-overexpressing MSCs exhibited effective anti-tumor function, which may be associated with enhanced homing to inflamed intestinal tissues.

World Neurosurg. 2019 Apr 11. pii: S1878-8750(19)31047-2. doi: 10.1016/j.wneu.2019.04.055. [Epub ahead of print]

Intravenous Stem cell Therapy for High Grade Aneurysmal Subarachnoid Haemorrhage: Case Report and Literature Review.

Brunet MC[1], Chen SH[1], Khandelwal P[2], Hare J[1], Starke RM[3], Peterson EC[1], Yavagal DR[4].
Author information

Abstract

BACKGROUND:

and Importance: Aneurysmal subarachnoid haemorrhage is associated with high mortality (30-40%) and morbidity with long-term physical, neurologic and/or psychologic impairments; most of which are patients presenting with high initial Hunt & Hess grade. In view of the great need for efficacious therapies for high grade SAH, recent animal studies have demonstrated improved outcomes with administration of mesenchymal stem cells (MSCs) as a potential neuroregenerative strategy. We present the first case of human intravenous administration of MSCs after aneurysmal subarachnoid haemorrhage.

CLINICAL PRESENTATION:

An 80-year-old male presented with sudden severe headache with nausea and vomiting and CT-scan demonstrated subarachnoid haemorrhage with hydrocephalus from a ruptured basilar tip aneurysm. Initial exam of the patient was H&H and WFNS grade 5. The patient was treated with EVD placement and coiling of the aneurysm. The patient received an infusion of intravenous bone marrow derived allogeneic mesenchymal stem cells (MSCs) on day 3 post-bleeding. The patient made a better recovery then anticipated with an mRS of 3 at 6 months.

CONCLUSION:

Several studies using models of ischemic brain injury have found that mesenchymal stem cells administration may improve functional neurological recovery and decreases brain lesion volume. While there have been limited human studies in stroke patients, the role of stem cell therapy for aneurysmal SAH remains unclear. This is the first case of MSC use in human for the treatment of aSAH. In conjunction with the promising results in animal studies, this encouraging preliminary case report supports the need for additional clinical trials.