



Molecular mechanisms of migration and homing of intravenously transplanted mesenchymal stem cells

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Abstract

Mesenchymal stem cells (MSCs) isolated from various tissues are currently regarded as one of the most convenient starting materials for preparation of cell therapy and tissue engineering products. Numerous research groups conducted detailed studies of their therapeutic effects and mechanisms of action in animal models. Some of those effects have been already confirmed in clinical trials. One of the most important properties of mesenchymal stem cells crucial for their medical use is the ability for targeted migration to the sites of ischemic, inflammatory or mechanical injury or site of tumor growth and homing within and around the damaged area. The aim of this review is to delineate the available data concerning the organ and tissue distribution of intravenously transplanted MSCs and the molecular mechanisms underlying their transfer within the bloodstream, penetration through the vascular wall and tissue invasion. The review reveals involvement of chemokines and their receptors, adhesion molecules and matrix metalloproteinases in those processes. Some of the data related to other roots of MSC transplantation, but critical for understanding the essential features of their migration and homing were also included.

Keywords: Mesenchymal stem cells, migration, homing, transplantation, distribution

Introduction

At present stem cell-based technologies comprise the main trend in the emerging field of regenerative medicine, while mesenchymal stem cells (MSCs) isolated from different tissues are regarded as one of the most handy and versatile raw materials for preparation of cell therapy and tissue engineering products. Bone marrow-derived mesenchymal stem cells (BM-MSCs) are definitely the best characterized type of mesenchymal cells, although attention is gradually switching to alternative sources of MSCs, such as adipose tissue, placenta, umbilical cord/Wharton's jelly, umbilical cord blood, and others.

Regardless of the source, cultured MSCs have common characteristics and behavioral traits. The ability to plastic adherence is widely used for their isolation from different tissues [1]. All MSCs have similar fibroblast-like morphology *in vitro* and are able to differentiate into cells of mesodermal lineage, namely, osteocytes, chondrocytes and adipocytes. MSCs from diverse sources may show certain differences in the expression of surface markers. However, in general, the phenotypes of these cells are very similar, and the typical mesenchymal stem cell surface markers are CD44 (receptor for hyaluronic acid), CD54 (ICAM-1; Intercellular Adhesion Molecule 1), CD90 (Thy-1), CD105 (endoglin), CD106 (VCAM-1; vascular cell adhesion molecule 1), HLA-I (MHC class I). Also MSCs do not express hematopoietic and endothelial cell markers, such as CD31, CD34, CD38,

CD45, CD133, MHC class II [2,3].

Furthermore, MSCs have unique immunomodulatory properties [4]. *In vitro* co-cultured MSCs modulate differentiation of certain immune precursor cells and/or maturation of differentiated immune cells [5]. The *in vitro* results are in accordance with immunomodulatory action seen both in animal experiments [6] and in clinical studies. Therefore, MSCs are being tested in clinical trials to reduce graft-versus-host disease, and for the treatment of autoimmune disorders such as multiple sclerosis [7,8].

An important property of MSCs is their capacity for migration and homing in or around the zones damaged by ischemia, inflammation, and trauma or tumor sites. Understandably, the efficacy and time course of cell invasion into the damaged tissues depends upon the route of transplantation. Many ways of MSCs administration have been tested in cell therapy experiments and clinical trials. Among those, local (e.g., directly into ischemic myocardium or brain), intra-arterial or epidural routes of cell administration usually demand at least minor surgery and are often associated with major risks. Iv infusion is probably the most convenient way of MSCs delivery both in experiments and clinical trials. This method is minimally invasive and allows repeated injections of multiple doses of cells at certain time intervals. Moreover, it possibly imitates the likely physiological mechanism of bone marrow-derived stem cell participation in regeneration

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Reactions of Aromatic Compounds R.G. Compton, C.H. Bamford, C.F.H. Tipper†, 1972-01-01 *Reactions of Aromatic Compounds* *Biomedical Index to PHS-supported Research: pt. A. Subject access A-H* ,1994 *Organic Geochemistry in Petroleum Exploration* L. Mattavelli, L. Novelli, 2013-10-22 This volume presents the most significant papers given during the 13th International Meeting in Organic Geochemistry The intention of the publication is to provide the scholars of this science with its state of the art and recent papers not only in academic research but above all in practical applications Several papers attest to an increased use of organic geochemistry not only in the oil industry during all phases of petroleum exploration but also in the other research areas of coal origin and structure metallogeny sedimentology molecular palaeontology

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McKillop's Problems builds upon Alexander Sandy McKillop's popular text Solutions to McKillop's Advanced Problems in Organic Reaction Mechanisms providing a unified methodological approach to dealing with problems of organic reaction mechanism. This unique book outlines the logic, experimental insight and problem solving strategy approaches available when dealing with problems of organic reaction mechanism. These valuable methods emphasize a structured and widely applicable approach relevant for both students and experts in the field. By using the methods described, advanced students and researchers alike will be able to tackle problems in organic reaction mechanism from the simple and straightforward to the advanced.

Mechanisms and Significance of Cell Volume Regulation Florian Lang, 2006. It is essential for the survival of cells to maintain their volume within certain limits. Profound alterations interfere with the integrity of the cell membrane and the cytoskeletal architecture. Cells use various methods to adjust osmotic pressure gradients which in turn govern water movement across cell membranes. The most rapid and efficient means is ion transport across the cell membrane. However, to avoid excessive alterations of intracellular ion concentration, cells additionally employ organic osmolytes for osmoregulation and modify their metabolism, thus generating or disposing osmotically active organic substances. But a given cell uses only part of the cell volume regulatory mechanisms at their disposal. The large repertoire available allows for a selection of those which have the least untoward impact on cell function. The present book is a collection of reviews on the various aspects of cell volume regulation written by internationally leading experts and constitutes a valuable addition to the library of those working in the field.

Environmental Health Perspectives, 1993 Learning Directory, 1970 **The Biology and Therapeutic Application of Mesenchymal Cells, 2 Volume Set** Kerry Atkinson, 2017-01-17. The Biology and Therapeutic Application of Mesenchymal Cells comprehensively describes the cellular and molecular biology of mesenchymal stem cells and mesenchymal stromal cells, describing their therapeutic potential in a wide variety of preclinical models of human diseases and their mechanism of action in these preclinical models. Chapters also discuss the current status of the use of mesenchymal stem and stromal cells in clinical trials in a wide range of human diseases and disorders for many of which there are limited or no other therapeutic avenues. Provides coverage on both the biology of mesenchymal stem cells and stromal cells and their therapeutic applications. Describes the therapeutic potential of mesenchymal stem and stromal cells in a wide variety of preclinical models of human diseases and their mechanism of action in these preclinical models. Discusses the current status of mesenchymal stem and stromal cells in clinical trials in a wide range of human diseases and disorders for many of which there are limited or no other therapeutic avenues. Written and edited by leaders in the field. The Biology and Therapeutic Application of Mesenchymal Cells is an invaluable resource for those studying stem cells, cell biology, genetics, gene or cell therapy or regenerative medicine.

Stem Cells and Cancer Stem Cells, Volume 11 M.A. Hayat, 2013-10-21. Volume 11 in this series discusses therapeutic applications of stem cells in disease and tissue injury. Coverage includes pluripotent stem cells which can give rise to the endodermal, ectodermal and mesodermal lineages.

multipotent stem cells which can generate all cells in a particular lineage and unipotent stem cells which can give rise to only one cell type This volume also examines cancer stem cells tumor initiating cells which possesses the capacity of self renewal and can give rise to the heterogeneous lineages of cancer cells that comprise the tumor Coverage extends to molecular mechanisms underlying the derivation and expansion of human embryonic stem cells the role of specific proteins in the maintenance and inhibition of extraembryonic differentiation of these cells and the role of signaling responsible for the self renewal of mouse embryonic stem cells Nine chapters discuss the clinical importance of cancer stem cells encompassing glioma leukemia ovarian cancer pediatric sarcomas and head and neck squamous cell carcinoma The role of cancer stem cells is also elucidated in epithelial to mesenchymal transition in spreading head and neck squamous cell carcinoma The book goes on to survey therapeutic application of stem cells of hematopoietic and non hematopoietic origin for regeneration of bones including in osteoporotic bone disease to illuminate the application of hematopoietic stem cells in bone regeneration and to discuss their use as a biomarker to facilitate determination of a treatment The contributors review cells as biomarkers for pediatric solid tumors and weigh the advantages and limitations of hematopoietic stem cell transplantation Also included are details of neural stem cell engraftment in the injured spinal cord the regenerative potential of neural stem progenitor cells of newborns and cancer gene therapy potential using neural stem cells Like the preceding volumes in the series this book is distinguished for its comprehensive approach its distinguished roster of 58 contributors representing 10 different countries and its thorough review of leading edge technology and methods

Medicinal Plants for Preventing and Treating Cardiovascular Diseases and the Discovery of Active Natural Products : Advanced Models, Novel Paradigms and New Mechanisms Ling Zhang, Yi Wang, Mirko Baruscotti, 2023-03-16

Encyclopedia of Neuroscience, Volume 1 Larry R. Squire, 2009-06-12 The Encyclopedia of the Neuroscience explores all areas of the discipline in its focused entries on a wide variety of topics in neurology neurosurgery psychiatry and other related areas of neuroscience Each article is written by an expert in that specific domain and peer reviewed by the advisory board before acceptance into the encyclopedia Each article contains a glossary introduction a reference section and cross references to other related encyclopedia articles Written at a level suitable for university undergraduates the breadth and depth of coverage will appeal beyond undergraduates to professionals and academics in related fields

Cytoskeletal Mechanics Mohammad R. K. Mofrad, Roger D. Kamm, 2006-09-04 This book presents a full spectrum of views on current approaches to modeling cell mechanics The authors come from the biophysics bioengineering and physical chemistry communities and each joins the discussion with a unique perspective on biological systems Consequently the approaches range from finite element methods commonly used in continuum mechanics to models of the cytoskeleton as a cross linked polymer network to models of glassy materials and gels Studies reflect both the static instantaneous nature of the structure as well as its dynamic nature due to polymerization and the full array of biological processes While it is unlikely that a single unifying approach will evolve from this diversity it is the

hope that a better appreciation of the various perspectives will lead to a highly coordinated approach to exploring the essential problems and better discussions among investigators with differing views *Continuum Mechanics and Theory of Materials* Peter Haupt, 2013-04-17 This exposition of the theory of materials has its origins in the lectures I gave at the universities of Darmstadt and Kassel from 1978 onwards Research projects carried out during the same period have been the source of extensive refinements to the subject matter The reason for adding yet another book to the existing wealth of volumes dealing with continuum mechanics was my desire to describe the phenomenological theory of material properties from my own point of view As a result it is without doubt a subjectively inspired and incomplete work This particularly applies to the selection of quotations from the literature The text has been influenced and enhanced by the numerous discussions I had the privilege of holding with students and experts alike I should like to thank them all sincerely for their contributions and encouragement 1 My special thanks go to my academic teachers Rudolf Trostel and Hubertus 1 Weinitschke 2 whose stimulating lectures convinced me at the time that continuum mechanics is a field of science worth pursuing I greatly appreciate the long and amicable collaboration with Babis Tsakmakis and Manfred Korzen during which a number of indispensable fundamental aspects emerged Valuable inspiration regarding the development of the thermomechanical theory of materials was given by Roman Bonn Markus Horz Marc Kamlah and Alexander Lion It was Lion's skill that provided the link between the theoretical modelling and experimental investigation of material behaviour

Advances in Heterocyclic Chemistry, 1990-10-25 *Advances in Heterocyclic Chemistry* **Comprehensive Chemical Kinetics** Clement Henry Bamford, Charles Frank Howlett Tipper, 1969 *Advances in Hematopoietic Stem Cell Research* Rosana Pelayo, 2012-01-27 This book provides a comprehensive overview in our understanding of the biology and therapeutic potential of hematopoietic stem cells and is aimed at those engaged in stem cell research undergraduate and postgraduate science students investigators and clinicians Starting from fundamental principles in hematopoiesis *Advances in Hematopoietic Stem Cell Research* assemble a wealth of information relevant to central mechanisms that may regulate differentiation and expansion of hematopoietic stem cells in normal conditions and during disease

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