



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

Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1

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Mechanisms of Molecular Migration B. S. Thyagarajan, 1969 **Advanced Organic Chemistry** Francis Carey, 2012-12-06 Biomedical Index to PHS-supported Research, 1987 **Mechanisms of DNA Recombination and Genome Rearrangements: Methods to Study Homologous Recombination**, 2018-02-17 Mechanisms of DNA Recombination and Genome Rearrangements Methods to Study Homologous Recombination Volume 600 the latest release in the Methods in Enzymology series continues the legacy of this premier serial with quality chapters authored by leaders in the field Homologous genetic recombination remains the most enigmatic process in DNA metabolism The molecular machines of recombination preserve the integrity of the genetic material in all organisms and generate genetic diversity in evolution The same molecular machines that support genetic integrity by orchestrating accurate repair of the most deleterious DNA lesions however also promote survival of cancerous cells and emergence of radiation and chemotherapy resistance This two volume set offers a comprehensive set of cutting edge methods to study various aspects of homologous recombination and cellular processes that utilize the enzymatic machinery of recombination The chapters are written by the leading researches and cover a broad range of topics from the basic molecular mechanisms of recombinational proteins and enzymes to emerging cellular techniques and drug discovery efforts Contributions by the leading experts in the field of DNA repair recombination replication and genome stability Documents cutting edge methods **Reactions of Aromatic Compounds** R.G. Compton, C.H. Bamford, C.F.H. Tipper†, 1972-01-01 Reactions of Aromatic Compounds *Environmental Health Perspectives*, 2000 **Biomedical Index to PHS-supported Research: pt. A. Subject access A-H**, 1994 **Catalysis** C Kemball, D A Dowden, 2007-10-31 There is an increasing challenge for chemical industry and research institutions to find cost efficient and environmentally sound methods of converting natural resources into fuels chemicals and energy Catalysts are essential to these processes and the Catalysis Specialist Periodical Report series serves to highlight major developments in this area This series provides systematic and detailed reviews of topics of interest to scientists and engineers in the catalysis field The coverage includes all major areas of heterogeneous and homogeneous catalysis and also specific applications of catalysis such as NO_x control kinetics and experimental techniques such as microcalorimetry Each chapter is compiled by recognised experts within their specialist fields and provides a summary of the current literature This series will be of interest to all those in academia and industry who need an up to date critical analysis and summary of catalysis research and applications Catalysis will be of interest to anyone working in academia and industry that needs an up to date critical analysis and summary of catalysis research and applications Specialist Periodical Reports provide systematic and detailed review coverage in major areas of chemical research Compiled by teams of leading experts in their specialist fields this series is designed to help the chemistry community keep current with the latest developments in their field Each volume in the series is published either annually or biennially and is a superb reference point for researchers www.rsc.org/spr **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 biochemistry and pollution

General Biophysics M. V. Volkenstein, 2013-10-22 General Biophysics Volume II studies biological phenomena at the supramolecular and cellular levels of structure The book considers biological phenomena on the basis of general physical principles The text presents topics on bioenergetic processes structure and properties of mitochondria photo biological processes nonlinear dynamic processes and physical interpretation of the most general problems of biology Graduate and postgraduate students in the field of physical and life sciences will find this book very useful

Photophysical and Photochemical Properties of Aromatic Compounds Jacob Malkin, 1992-06-10 Photophysical and Photochemical Properties of Aromatic Compounds is the first book to collect and classify all available quantitative data on the photochemistry and luminescence of aromatic compounds Compounds are classified by both spectral luminescent e g extinction coefficients energies and lifetimes of lower excited states and photochemical properties In addition all of the quantum yields available have been collected The variety of photochemical reactions of aromatics is examined based on eight types of elementary monomolecular and bimolecular photochemical processes Aromatic compounds are grouped into eight categories and the book analyzes the possibilities of occurrence of all types of elementary photoprocesses

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

Strategies and Solutions to Advanced Organic Reaction Mechanisms Andrei Hent, John Andraos, 2019-06-26 Strategies and Solutions to Advanced Organic Reaction Mechanisms A New Perspective on 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 straight forward to the advanced

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

Comprehensive Organic Chemistry, Volume 6 Derek Barton, C. J. Drayton, W. David Ollis, 1979-04-09 Vol 6

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

Polymer and Ceramic Electrolytes for Energy Storage Devices, Two-Volume Set Prasanth Raghavan, Jabeen Fatima, 2021-04-08 Polymer and Ceramic Electrolytes for Energy Storage Devices features two volumes that focus on the most recent technological and scientific accomplishments in polymer ceramic and specialty electrolytes and their applications in lithium ion batteries These volumes cover the fundamentals in a logical and clear manner for students as well as researchers from different disciplines to follow The set includes the following volumes Polymer Electrolytes for Energy Storage Devices Volume I offers a detailed explanation of recent progress and challenges in polymer electrolyte research for energy storage devices Ceramic and Specialty Electrolytes for Energy Storage Devices Volume II investigates recent progress and challenges in a wide range of ceramic solid and quasi solid electrolytes and specialty electrolytes for energy storage devices These volumes will be invaluable to researchers and engineers working on the development of next generation energy storage devices including materials and chemical engineers as well as those involved in related disciplines

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

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Table of Contents Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1

1. Understanding the eBook Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1
 - The Rise of Digital Reading Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1
 - Advantages of eBooks Over Traditional Books
2. Identifying Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1
 - Exploring Different Genres
 - Considering Fiction vs. Non-Fiction
 - Determining Your Reading Goals
3. Choosing the Right eBook Platform
 - Popular eBook Platforms
 - Features to Look for in an Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1
 - User-Friendly Interface
4. Exploring eBook Recommendations from Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1
 - Personalized Recommendations
 - Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1 User Reviews and Ratings
 - Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1 and Bestseller Lists

5. Accessing Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1 Free and Paid eBooks
 - Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1 Public Domain eBooks
 - Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1 eBook Subscription Services
 - Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1 Budget-Friendly Options
6. Navigating Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1 eBook Formats
 - ePub, PDF, MOBI, and More
 - Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1 Compatibility with Devices
 - Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1 Enhanced eBook Features
7. Enhancing Your Reading Experience
 - Adjustable Fonts and Text Sizes of Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1
 - Highlighting and Note-Taking Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1
 - Interactive Elements Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1
8. Staying Engaged with Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1
 - Joining Online Reading Communities
 - Participating in Virtual Book Clubs
 - Following Authors and Publishers Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1
9. Balancing eBooks and Physical Books Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1
 - Benefits of a Digital Library
 - Creating a Diverse Reading Collection Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1
10. Overcoming Reading Challenges
 - Dealing with Digital Eye Strain
 - Minimizing Distractions
 - Managing Screen Time
11. Cultivating a Reading Routine Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1
 - Setting Reading Goals Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1
 - Carving Out Dedicated Reading Time
12. Sourcing Reliable Information of Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1
 - Fact-Checking eBook Content of Mechanisms Of Molecular Migration Mechanisms Of Molecular Migration Vol 1

- Distinguishing Credible Sources
- 13. Promoting Lifelong Learning
 - Utilizing eBooks for Skill Development
 - Exploring Educational eBooks
- 14. Embracing eBook Trends
 - Integration of Multimedia Elements
 - Interactive and Gamified eBooks

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