ML 21-19 (01/07/2019)

Biochem Biophys Rep. 2019 May 14;18:100645. doi: 10.1016/j.bbrep.2019.100645. eCollection 2019 Jul.

Novel dual-reporter transgenic rodents enable cell tracking in animal models of stem cell transplantation.

Morikawa K[1], Nakamura K[2,3], Suyama Y[4], Yamamoto K[5], Fukuoka K[4], Yagi S[4], Shirayoshi Y[5], Ohbayashi T[3], Hisatome I[1,5].
Author information

Abstract

In the present study, we have established a novel transgenic mouse and transgenic rats with dual reporters of EGFP and ELuc. In these transgenic (Tg) rodents, both GFP fluorescent and luciferase luminescent signals were ubiquitously detected in the heart, liver, kidney and testis, while only the GFP signal was detected in the brain. This expression system is based on a P2A linked EGFP/ELuc protein allowing both signals to be generated simultaneously. Microscopy experiments, FCM, and luciferase assays showed strong expression in freshly isolated ADSCs from Tg rodents upon transplantation of Tg rat-derived ADSCs into wild-type-mice. The ELuc transgene signal was observed and traced *in vivo*, and EGFP positive cells could be recovered from ELuc positive tissues in engraftment sites of wild-type mice for multiple analysis. These dual reporter Tg rodents are a useful reconstituted model system of regenerative medicine and are a valuable tool to study stem cells.

Stem Cells Int. 2019 May 2;2019:9178436. doi: 10.1155/2019/9178436. eCollection 2019.

Does the Harvesting Site Influence the Osteogenic Potential of Mesenchymal Stem Cells?

Nguyen VT[1], Tessaro I[1], Marmotti A[2,3], Sirtori C[4], Peretti GM[1,5], Mangiavini L[1,5].
Author information

Abstract

Total hip arthroplasty (THA) represents one of the commonest surgical procedures in the orthopedic field. Osteointegration of the implant with native bone is essential for an optimal result; thus, the quality of the patient's bone surrounding the implant (i.e., the bone stock) is crucial. However, in some cases, the bone stock is insufficient and needs to be improved with autologous grafts rich in multipotent cells (i.e., from the iliac crest, from the head of the femur, or from the subchondral bone harvested from the acetabulum) or allogenic frozen bone. It is not known if the harvesting site may influence the osteogenic potential of these cells. Thus, our aim was to characterize and compare multipotent cells collected from the bone marrow, acetabular subchondral bone, and trabecular bone on the femoral head with a focus on osteogenic differentiation. The cells from three sources had a fibroblast-like phenotype and expressed surface antigens CD73, CD90, and CD105 and are negative to CD11b, CD34, and CD45. Although all these cells could be induced to differentiate into osteoblasts, chondrocytes, and adipocytes, they displayed different differentiation potentials. In osteogenic differentiation condition, the cells from the acetabulum had the lowest accumulation of calcium deposit while the cells originated from the bone marrow and femur created a considerably increased amount of the deposit. These

findings were confirmed by quantitative polymerase chain reaction (qPCR). In chondrogenic and adipogenic conditions, bone marrow cells possessed a predominant differential capacity compared with the others, illustrated by high collagen type II expression together with a cartilage-like lacuna structure and the presence of fat-specific markers, respectively. To our knowledge, this is the first study comparing and demonstrating that the progenitor cells obtained from diverse surgical sites in hip replacement procedure share common characteristics of MSC but differ about plasticity and may provide rational for clinical application in cell therapy and bone grafting. The project number L1033 is registered with ClinicalTrials.gov NCT03369457.

Cytotherapy. 2019 Jun 7. pii: S1465-3249(19)30405-0. doi: 10.1016/j.jcyt.2019.04.003. [Epub ahead of print]

Manufacturing mesenchymal stromal cells for clinical applications: A survey of Good Manufacturing Practices at U.S. academic centers.

Phinney DG[1], Galipeau J[2]; MSC COMMITTEE OF THE INTERNATIONAL SOCIETY OF CELL AND GENE THERAPY.

Author information

Abstract

BACKGROUND AIMS:

Mesenchymal stromal cells (MSC) have gained prominence in the field of regenerative medicine due to their excellent safety profile in human patients and recently demonstrated efficacy in late-stage clinical studies. A prerequisite to achieving successful MSC-based therapies is the development of large-scale manufacturing processes that preserve the biological potency of the founder cell population. Because no standardized manufacturing process exists for MSCs, understanding differences in these processes among U.S. academic facilities would allow for better comparison of results obtained in the clinical setting.

METHODS:

We collected information through a questionnaire sent to U.S. academic centers that produce MSCs under Good Manufacturing Practice conditions.

RESULTS:

The survey provided information on the number and geographic location of academic facilities in the United States and major trends in their manufacturing practices. For example, most facilities employed MSCs enriched from bone marrow by plastic adherence and expanded in media supplemented with pooled human platelet lysate. Sterility testing and product identification via cell surface phenotype analysis were commonly reported practices, whereas initial and working cell plating densities, culture duration, product formulation and the intended use of the MSC product were highly variable among facilities. The survey also revealed that although most facilities assessed product potency, the methods used were limited in scope compared with the broad array of intended clinical applications of the product.

CONCLUSIONS:

Survey responses reported herein offer insight into the current best practices used to manufacture MSC-based products in the United States and how these practices may affect product quality and potency. The responses also provide a foundation to establish standardized manufacturing platforms.

Autophagy. 2019 Jun 12. doi: 10.1080/15548627.2019.1630223. [Epub ahead of print]

Autophagy: a potential key contributor to the therapeutic action of mesenchymal stem cells.

Ceccariglia S[1,2], Cargnoni A[3], Silini AR[3], Parolini O[1,3].
Author information

Abstract

Macroautophagy/autophagy occurs at basal levels in all eukaryotic cells and plays an important role in maintaining bio-energetic homeostasis through the control of molecule degradation and organelle turnover. It can be induced by environmental conditions such as starvation, and is deregulated in many diseases including autoimmune diseases, neurodegenerative disorders, and cancer. Interestingly, the modulation of autophagy in mesenchymal stem cells (MSCs) represents a possible mechanism which, affecting MSC properties, may have an impact on their regenerative, therapeutic potential. Furthermore, the ability of MSCs to modulate autophagy of cells in injured tissues/organs has been recently proposed to be involved in the regeneration of damaged tissues and organs. In particular, MSCs can affect autophagy in immune cells involved in injury-induced inflammation reducing their survival, proliferation, and function and favoring the resolution of inflammation. In addition, MSCs can affect autophagy in endogenous adult or progenitor cells, promoting their survival, proliferation and differentiation supporting the restoration of functional tissue. This review provides, for the first time, an overview of the studies which highlight a possible link between the therapeutic properties of MSCs and their ability to modulate autophagy, and it summarizes examples of disorders where these therapeutic properties have been correlated with such modulation. A better elucidation of the mechanism(s) through which MSCs can modulate the autophagy of target cells and how autophagy can affect MSCs therapeutic properties, can provide a wider perspective for the clinical application of MSCs in the treatment of many diseases.