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Improving cell distribution on 3D additive manufactured scaffolds through engineered seeding media density and viscosity.

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Author information

Abstract

In order to ensure the long-term in vitro and in vivo functionality of cell-seeded 3D scaffolds, an effective and reliable method to control cell seeding efficiency and distribution is crucial. Static seeding on 3D additive manufactured scaffolds made of synthetic polymers still remains challenging, as it often results in poor cell attachment, high cell sedimentation and non-uniform cell distribution, due to gravity and to the intrinsic macroporosity and surface chemical properties of the scaffolds. In this study, the biocompatible macromolecules dextran and Ficoll (Ficoll Paque) were used for the first time as temporary supplements to alter the viscosity and density of the seeding media, respectively, and improve the static seeding output. The addition of these macromolecules drastically reduced the cell sedimentation velocities, allowing for homogeneous cell attachment to the scaffold filaments. Both dextran- and Ficoll-Paque -based seeding methods supported human mesenchymal stromal cells viability and osteogenic differentiation post-seeding. Interestingly, the improved cell distribution led to increased matrix production and mineralization compared to scaffolds seeded by conventional static method. These results suggest a simple and universal method for an efficient seeding of 3D additive manufactured scaffolds, independent of their material and geometrical properties, and applicable for bone and various other tissue regeneration.

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Time-lapse image analysis for whole colony growth curves and daily distribution of the cell number per colony during the expansion of mesenchymal stem cells.

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Abstract

Mesenchymal stem cells from the synovium (synovial MSCs) are attractive for cartilage and meniscus regeneration therapy. We developed a software program that can distinguish individual colonies and automatically count the cell number per colony using time-lapse images. In this study, we investigated the usefulness of the software and analyzed colony formation in cultured synovial MSCs. Time-lapse image data were obtained for 14-day-expanded human synovial MSCs. The cell number per colony (for 145 colonies) was automatically counted from phase-contrast and nuclear-stained images. Colony

growth curves from day 1 to day 14 (for 140 colonies) were classified using cluster analysis. Correlation analysis of the distribution of the cell number per colony at 14 days versus that number at 1-14 days revealed a correlation at 7 and 14 days. We obtained accurate cell number counts from phase-contrast images. Individual colony growth curves were classified into three main groups and subgroups. Our image analysis software has the potential to improve the evaluation of cell proliferation and to facilitate successful clinical applications using MSCs.

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Mesenchymal Stromal Cells: Role in the BM Niche and in the Support of Hematopoietic Stem Cell Transplantation.

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Abstract

Mesenchymal stromal cells (MSCs) are key elements in the bone marrow (BM) niche where they interact with hematopoietic stem progenitor cells (HSPCs) by offering physical support and secreting soluble factors, which control HSPC maintenance and fate. Although necessary for their maintenance, MSCs are a rare population in the BM, they are plastic adherent and can be ex vivo expanded to reach numbers adequate for clinical use. In light of HSPC supportive properties, MSCs have been employed in phase I/II clinical trials of hematopoietic stem cell transplantation (HSCT) to facilitate engraftment of hematopoietic stem cells (HSCs). Moreover, they have been utilized to expand ex vivo HSCs before clinical use. The available clinical evidence from these trials indicate that MSC administration is safe, as no acute and long-term adverse events have been registered in treated patients, and may be efficacious in promoting hematopoietic engraftment after HSCT. In this review, we critically discuss the role of MSCs as component of the BM niche, as recent advances in defining different mesenchymal populations in the BM have considerably increased our understanding of this complex environment. Moreover, we will revise published literature on the use of MSCs to support HSC engraftment and expansion, as well as consider potential new MSC application in the clinical context of ex vivo gene therapy with autologous HSC.

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Role of nanoparticles in osteogenic differentiation of bone marrow mesenchymal stem cells.

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Abstract

The present study aimed to investigate the osteoinductive potentiality of some selected nanostructures; Hydroxyapatite (HA-NPs), Gold (Au-NPs), Chitosan (C-NPs), Gold/hydroxyapatite (Au/HA-NPs) and Chitosan/hydroxyapatite (CH-NPs) on bone marrow- derived mesenchymal stem cells (BM-MSCs). These nanostructures were characterized using transmission electron microscope and Zetasizer. MSCs were isolated from bone marrow of rat femur bones and their identity was documented by morphology,

flow cytometry and multi-potency capacity. The influence of the selected nanostructures on the viability, osteogenic differentiation and subsequent matrix mineralization of BM-MSCs was determined by MTT assay, molecular genetic analysis and alizarin red S staining, respectively. MTT analysis revealed insignificant toxicity of the tested nanostructures on BM-MSCs at concentrations ranged from 2 to 25 µg/ml over 48 h and 72 h incubation period. Notably, the tested nanostructures potentiate the osteogenic differentiation of BM-MSCs as evidenced by a prominent over-expression of runt-related transcription factor 2 (Runx-2) and bone morphogenetic protein 2 (BMP-2) genes after 7 days incubation. Moreover, the tested nanostructures induced matrix mineralization of BM-MSCs after 21 days as manifested by the formation of calcium nodules stained with alizarin red S. Conclusively, these data provide a compelling evidence for the functionality of the studied nanostructures as osteoinductive materials motivating the differentiation of BM-MSCs into osteoblasts with the most prominent effect observed with Au-NPs and Au/HA-NPs, followed by CH-NPs