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Cryopreservation of Mesenchymal Stem Cells Using Medical Grade Ice Nucleation Inducer

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Free article

Abstract

Mesenchymal stem cells (MSCs) can differentiate into multiple different tissue lineages and have favourable immunogenic potential making them an attractive prospect for regenerative medicine. As an essential part of the manufacturing process, preservation of these cells whilst maintaining potential is of critical importance. An uncontrolled area of storage remains the rate of change of temperature during freezing and thawing. Controlled-rate freezers attempted to rectify this; however, the change of phase from liquid to solid introduces two extreme phenomena; a rapid rise and a rapid fall in temperature in addition to the intended cooling rate (normally -1 °C/min) as a part of the supercooling event in cryopreservation. Nucleation events are well known to initiate the freezing transition although their active use in the form of ice nucleation devices (IND) are in their infancy in cryopreservation. This study sought to better understand the effects of ice nucleation and its active instigation with the use of an IND in both a standard cryotube with MSCs in suspension and a high-throughput adhered MSC 96-well plate set-up. A potential threshold nucleation temperature for best recovery of dental pulp MSCs may occur around -10 °C and for larger volume cell storage, IND and fast thaw creates the most stable process. For adhered cells, an IND with a slow thaw enables greatest metabolic activity post-thaw. This demonstrates a necessity for a medical grade IND to be used in future regenerative medicine manufacturing with the parameters discussed in this study to create stable products for clinical cellular therapies.

Methods Mol Biol
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Bone Marrow Stromal Cell Assays: In Vitro and In Vivo

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Abstract

Populations of bone marrow stromal cells (BMSCs, also known as bone marrow-derived "mesenchymal stem cells") contain a subset of cells that are able to recapitulate the formation of a bone/marrow organ (skeletal stem cells, SSCs). It is now apparent that cells with similar but not identical properties can be isolated from other skeletal compartments (growth plate, periosteum). The biological properties of BMSCs, and these related stem/progenitor cells, are assessed by a variety of assays, both in vitro and in vivo. Application of these assays in an appropriate fashion provide a great deal of information on the role of BMSCs, and the subset of SSCs, in health and in disease.

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Human-derived osteoblast-like cells and pericyte-like cells induce distinct metastatic phenotypes in primary breast cancer cells

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Abstract

Approximately 70% of advanced breast cancer patients will develop bone metastases, which accounts for ~90% of cancer-related mortality. Breast cancer circulating tumor cells (CTCs) establish metastatic tumors in the bone after a close interaction with local bone marrow cells including pericytes and osteoblasts, both related to resident mesenchymal stem/stromal cells (BM-MSCs) progenitors. *In vitro* recapitulation of the critical cellular players of the bone microenvironment and infiltrating CTCs could provide new insights into their cross-talk during the metastatic cascade, helping in the development of novel therapeutic strategies. Human BM-MSCs were isolated and fractionated according to CD146 presence. CD146+ cells were utilized as pericyte-like cells (PLCs) given the high expression of the marker in perivascular cells, while CD146- cells were induced into an osteogenic phenotype generating osteoblast-like cells (OLCs). Transwell migration assays were performed to establish whether primary breast cancer cells (3384T) were attracted to OLC. Furthermore, proliferation of 3384T breast cancer cells was assessed in the presence of PLC- and OLC-derived conditioned media. Additionally, conditioned media cultures as well as transwell co-cultures of each OLCs and PLCs were performed with 3384T breast cancer cells for gene expression interrogation assessing their induced transcriptional changes with an emphasis on metastatic potential. PLC as well as their conditioned media increased motility and invasion potential of 3384T breast cancer cells, while OLC induced a dormant phenotype, downregulating invasiveness markers related with migration and proliferation. Altogether, these results indicate that PLC distinctively drive 3384T cancer cells to an invasive and migratory phenotype, while OLC induce a quiescence state, thus recapitulating the different phases of the *in vivo* bone metastatic process. These data show that phenotypic responses from metastasizing cancer cells are influenced by neighboring cells at the bone metastatic niche during the establishment of secondary metastatic tumors.

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3D hydrogel mimics of the tumor microenvironment: the interplay

among hyaluronic acid, stem cells and cancer cells

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Abstract

The present work reports on a 3D model of the tumor microenvironment that contains hyaluronic acid (HA) and alginate, and demonstrates the utility of this model to study the effect of HA size on the crosstalk between cancer cells and mesenchymal stem cells (MSCs). The system incorporates a core that contains HA of specific size (i.e. 6.4, 741 or 1500 kDa) with encapsulated epithelial MKN45 cancer cells and a shell with MSCs that mimic the presence of stem cells next to the tumor site. It was found that short HA (i.e. 6.4 kDa) promotes the invasion of cancer cells from the core to the shell, whereas longer HA (i.e. 741 and 1500 kDa) recruits the MSCs into the core, i.e. the tumor site, where a reduction of the formation of cancer cell aggregates was observed. In summary, the developed 3D model recapitulates some key tumor features related to the effect of HA size on both cancer cell invasiveness and MSC behavior at the tumor site.

Transl Oncol
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Mesenchymal stem/stromal cells: Developmental origin, tumorigenesis and translational cancer therapeutics

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Free article

Abstract

While a large and growing body of research has demonstrated that mesenchymal stem/stromal cells (MSCs) play a dual role in tumor growth and inhibition, studies exploring the capability of MSCs to contribute to tumorigenesis are rare. MSCs are key players during tumorigenesis and cancer development, evident in their faculty to increase cancer stem cells (CSCs) population, to generate the precursors of certain forms of cancer (e.g. sarcoma), and to induce epithelial-mesenchymal transition to create the CSC-like state. Indeed, the origin and localization of the native MSCs in their original tissues are not known. MSCs are identified in the primary tumor sites and the fetal and extraembryonic tissues. Acknowledging the developmental origin of MSCs and tissue-resident native MSCs is essential for better understanding of MSC contributions to the cellular origin of cancer. This review stresses that the plasticity of MSCs can therefore instigate further risk in select therapeutic strategies for some patients with certain forms of cancer. Towards this end, to explore the safe and effective MSC-based anti-cancer therapies requires a strong understanding of the cellular and molecular mechanisms of MSC action, ultimately guiding new strategies for delivering treatment. While clinical trial efforts using MSC products are currently underway, this review also provides new insights on the underlying mechanisms of MSCs to tumorigenesis and focuses on the approaches to develop MSC-based anti-cancer therapeutic applications.