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Cancers (Basel)

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Role of MSC in the Tumor Microenvironment

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Free article

Abstract

The tumor microenvironment represents a dynamically composed matrix in which tissue-associated cancer cells are embedded together with a variety of further cell types to form a more or less separate organ-like structure. Constantly mutual interactions between cells of the tumor microenvironment promote continuous restructuring and growth in the tumor. A distinct organization of the tumor stroma also facilitates the formation of transient cancer stem cell niches, thereby contributing to progressive and dynamic tumor development. An important but heterogeneous mixture of cells that communicates among the cancer cells and the different tumor-associated cell types is represented by mesenchymal stroma-/stem-like cells (MSC). Following recruitment to tumor sites, MSC can change their functionalities, adapt to the tumor's metabolism, undergo differentiation and synergize with cancer cells. Vice versa, cancer cells can alter therapeutic sensitivities and change metastatic behavior depending on the type and intensity of this MSC crosstalk. Thus, close cellular interactions between MSC and cancer cells can eventually promote cell fusion by forming new cancer hybrid cells. Consequently, newly acquired cancer cell functions or new hybrid cancer populations enlarge the plasticity of the tumor and counteract successful interventional strategies. The present review article highlights some important features of MSC within the tumor stroma.

Arthroscopy

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Editorial Commentary: Please Don't Call It a Mesenchymal Stem Cell

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Abstract

One of the holy grails in orthopedics, and for medicine in general, is to have easy access to an immediately available and viable source of progenitor cells for use in tissue regeneration. The use of the term "mesenchymal stem cell" has been called into question, as it has historically represented a wide variety of tissue-specific cell types, only some of which can be categorized as true stem cells. More recent literature has better defined the characteristics of a stem cell, yet the landscape is still littered with unsubstantiated claims of cures for many human diseases, both within orthopaedic surgery as well as other fields of medicine. Although attention is needed to more carefully define the characteristics of the cells under investigation in any particular line of research, significantly more work will be involved to learn the biological mechanisms and signaling involved in coaxing these cells into in vivo tissue regeneration.

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Endometrial and Menstrual Blood Mesenchymal Stem/Stromal Cells: Biological Properties and Clinical Application

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Abstract

A highly proliferative mesenchymal stem/stromal cell (MSC) population was recently discovered in the dynamic, cyclically regenerating human endometrium as clonogenic stromal cells that fulfilled the International Society for Cellular Therapy (ISCT) criteria. Specific surface markers enriching for clonogenic endometrial MSC (eMSC), CD140b and CD146 co-expression, and the single marker SUSD2, showed their perivascular identity in the endometrium, including the layer which sheds during menstruation. Indeed, cells with MSC properties have been identified in menstrual fluid and commonly termed menstrual blood stem/stromal cells (MenSC). MenSC are generally retrieved from menstrual fluid as plastic adherent cells, similar to bone marrow MSC (bmMSC). While eMSC and MenSC share several biological features with bmMSC, they also show some differences in immunophenotype, proliferation and differentiation capacities. Here we review the phenotype and functions of eMSC and MenSC, with a focus on recent studies. Similar to other MSC, eMSC and MenSC exert immunomodulatory and anti-inflammatory impacts on key cells of the innate and adaptive immune system. These include macrophages, T cells and NK cells, both *in vitro* and in small and large animal models. These properties suggest eMSC and MenSC as additional sources of MSC for cell therapies in regenerative medicine as well as immune-mediated disorders and inflammatory diseases. Their easy acquisition via an office-based biopsy or collected from menstrual effluent makes eMSC and MenSC attractive sources of MSC for clinical applications. In preparation for clinical translation, a serum-free culture protocol was established for eMSC which includes a small molecule TGFβ receptor inhibitor that prevents spontaneous differentiation, apoptosis, senescence, maintains the clonogenic SUSD2^{+} population and enhances their potency, suggesting potential for cell-therapies and regenerative medicine. However, standardization of MenSC isolation protocols and culture conditions are major issues requiring further research to maximize their potential for clinical application. Future research will also address crucial safety aspects of eMSC and MenSC to ensure these protocols produce cell products free from tumorigenicity and toxicity. Although a wealth of data on the biological properties of

eMSC and MenSC has recently been published, it will be important to address their mechanism of action in preclinical models of human disease.