ML 21-08 (20/03/2021)

Methods Mol Biol
.
. 2021;2269:49-61.
doi: 10.1007/978-1-0716-1225-5_4.

Bioimaging of Mesenchymal Stem Cells Spatial Distribution and Interactions with 3D In Vitro Tumor Spheroids

Luís P Ferreira[1], Vítor M Gaspar[2], João F Mano[3]
Affiliations expand

- PMID: 33687671

- DOI: 10.1007/978-1-0716-1225-5_4

Abstract

In solid tumors, mesenchymal stem cells (MSCs) are recognized to establish complex intercommunication networks with cancer cells and to significantly influence their invasion and metastasis potential. Such bidirectional interplay occurs between both tissue resident/tumor-associated MSCs (TA-MSCs) and also tumor infiltrating MSCs (TM-MSCs) that migrate from distant sites such as the bone marrow. Interestingly, malignant cells interactions with MSCs in the tumor microenvironment extends beyond conventional exchanges of signaling factors and extracellular vesicles, including unconventional direct exchanges of intracellular components, or cancer cells cannibalism of MSCs. In the context of 3D in vitro tumor models, cell tracking assays making use of cell-labeling probes such as membrane penetrating dyes, can be leveraged to shed light on these events, and allow researchers to analyze overtime cell-to-cell spatial distribution, fusion, internal organization, and changes in co-cultured populations ratios. Herein, we describe a high-throughput compatible method through which MSCs positioning and permanence within in vitro 3D multicellular tumor spheroid models (3D-MCTS) can be tracked overtime. Although we have focused on the interactions of human bone marrow-derived MSCs (hBM-MSCs) within heterotypic lung cancer A549 3D-MCTS, these procedures can be

implemented for other 3D tumor spheroid models and types of cells, taking into consideration that optimization steps are undertaken.

Methods Mol Biol
. 2021;2269:3-23.
doi: 10.1007/978-1-0716-1225-5_1.

Consistent Inclusion of Mesenchymal Stem Cells into In Vitro Tumor Models

Luís P Ferreira[1], Vítor M Gaspar[2], João F Mano[3]
Affiliations expand

- PMID: 33687668

- DOI: 10.1007/978-1-0716-1225-5_1

Abstract

Over recent years, the role of distinct mesenchymal stem cell populations in cancer progression has become increasingly evident. In this regard, developing in vitro preclinical tumor models capable of portraying tumor-associated mesenchymal stem cells (TA-MSCs) interactions with the tumor microenvironment (TME), cellular and extracellular components, would allow to improve the predictive potential of these platforms and expedite preclinical drug screening. Although recent studies successfully developed in vitro tumor models in which the biomolecular and cellular behaviors of TA-MSCs were recapitulated in the context of their interactions with specific TME components, no consensus has yet been reached regarding distinct TA-MSCs influence in the evolution of solid tumors. The paradoxical observations regarding the roles of MSCs on in vitro tumor models can in part be associated to a lack of standardization in how MSCs integration is performed. Herein, we summarize some of the main parameters linked to phenotypic variations established upon MSCs inclusion and interaction within in vitro tumor models. A critical overview of recent studies and how standardization of key parameters could improve the reproducibility and predictability of current preclinical validation models containing MSCs is also provided.