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Effects of Cell Density and Microenvironment on Stem Cell Mitochondria Transfer among Human Adipose-Derived Stem Cells and HEK293 Tumorigenic Cells

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Abstract

Stem cells (SC) are largely known for their potential to restore damaged tissue through various known mechanisms. Among these mechanisms is their ability to transfer healthy mitochondria to injured cells to rescue them. This mitochondrial transfer plays a critical role in the healing process. To determine the optimal parameters for inducing mitochondrial transfer between cells, we assessed mitochondrial transfer as a function of seeding density and in two-dimensional (2D) and semi three-dimensional (2.5D) culture models. Since mitochondrial transfer can occur through direct contact or secretion, the 2.5D culture model utilizes collagen to provide cells with a more physiologically relevant extracellular matrix and offers a more realistic representation of cell attachment and movement. Results demonstrate the dependence of mitochondrial transfer on cell density and the distance between donor and recipient cell. Furthermore, the differences found

between the transfer of mitochondria in 2D and 2.5D microenvironments suggest an optimal mode of mitochondria transport. Using these parameters, we explored the effects on mitochondrial transfer between SCs and tumorigenic cells. HEK293 (HEK) is an immortalized cell line derived from human embryonic kidney cells which grow rapidly and form tumors in culture. Consequently, HEKs have been deemed tumorigenic and are widely used in cancer research. We observed mitochondrial transfer from SCs to HEK cells at significantly higher transfer rates when compared to a SC-SC co-culture system. Interestingly, our results also revealed an increase in the migratory ability of HEK cells when cultured with SCs. As more researchers find co-localization of stem cells and tumors in the human body, these results could be used to better understand their biological relationship and lead to enhanced therapeutic applications.

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The Role of Mesenchymal Stem Cells in the Induction of Cancer-Stem Cell Phenotype

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Abstract

Cancer stem cells (CSCs) modify and form their microenvironment by recruiting and activating specific cell types such as mesenchymal stem cells (MSCs). Tumor-infiltrating MSCs help to establish a suitable tumor microenvironment for the restoration of CSCs and tumor progression. In addition, crosstalk between cancer cells and MSCs in the microenvironment induces a CSC phenotype in cancer cells. Many mechanisms are involved in crosstalk between CSCs/cancer cells and MSCs including cell-cell interaction, secretion of exosomes, and paracrine secretion of several molecules including

inflammatory mediators, cytokines, and growth factors. Since this crosstalk may contribute to drug resistance, metastasis, and tumor growth, it is suggested that blockade of the crosstalk between MSCs and CSCs/cancer cells can provide a new avenue to improving the cancer therapeutic tools. In this review, we will discuss the role of MSCs in the induction of cancer stem cell phenotype and the restoration of CSCs. We also discuss targeting the crosstalk between MSCs and CSCs/cancer cells as a therapeutic strategy.