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The effect of mesenchymal stromal cells ın the microenvironment on cancer development

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Abstract

Inflammatory signals secreted from the tumor microenvironment are thought to promote tumor growth and survival. It has been reported that stromal cells in the tumor microenvironment have similar characteristics to tumor-associated cells. In addition miRNAs play critical roles in various diseases, including cancer. In this study, we aimed to investigate the effects of co-culture of cancer cells and stromal cells isolated from normal and malignant breast tissue on each other and the possible effects of miRNAs on these interactions. The characterized stromal cells were co-cultured with an MDA-MB-231 cancer cell line. The proliferation capacity of the experimental groups was evaluated using the WST-1 assay. The expression of breast cancer-specific miRNAs and related genes were assessed by real-time PCR. ELISA assay was performed to determine the concentration of some cytokines and chemokines. We found that the microenvironment plays an important role in the development of cancer, confirming the changes in the expression of oncogenic and tumor suppressor miRNA and their target genes after co-culture with malignant stromal cells. As a result of the studies, specific gene expressions of related signaling pathways were detected in correlation with miRNA changes and the effects of tumor microenvironment on tumorigenesis were revealed in detail. miRNAs have been shown to play an important role in cancer development in recent studies. The idea that these small molecules can be used in diagnosis and treatment is becoming stronger day by day. We

believe that new treatment approaches involving the tumor microenvironment and using miRNAs as markers are promising.

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Human amniotic fluid mesenchymal stem cells attenuate pancreatic cancer cell proliferation and tumor growth in an orthotopic xenograft mouse model

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Abstract

Background: Pancreatic ductal adenocarcinoma (PDAC) is a malignant cancer and chemotherapy ineffectively treats PDAC, leading to the requirement for alternative tumor-targeted treatment. Human amniotic fluid mesenchymal stem cells (hAFMSCs) have been revealed to suppress tumor growth in various cancers and they are a strong candidate for treating PDAC.

Methods: To evaluate the effects of hAFMSCs on human pancreatic carcinoma cells (PANC1, AsPC1 and BxPC3 cell lines) and the possible mechanism involved, an in vitro cell coculture system was used. A PANC1 orthotopic xenograft mouse model was established and hAFMSCs were injected intravenously at 4 weeks post-xenograft.

Results: An in vitro coculture assay showed that hAFMSCs inhibited PANC1 cell proliferation by inducing S phase cell cycle arrest and increased cell apoptosis in a time-dependent manner. In PANC1 cells, hAFMSCs caused the downregulation of Cyclin A and Cyclin B1 as well as the upregulation of p21 (CDKN1A) at 24 h post coculture. The upregulation of pro-apoptotic factors Caspase-3/-8 and Bax at 24 h post coculture reduced the migration and invasion ability of PANC1 cells through inhibiting the epithelial-mesenchymal transition (EMT) process. In a PANC1 orthotopic xenograft mouse model, a single injection of hAFMSCs showed significant tumor growth inhibition with evidence of the modulation of cell cycle and pro-apoptotic regulatory genes and various genes involved in matrix metallopeptidase 7 (MMP7) signaling-triggered EMT process. Histopathological staining showed lower Ki67 levels in tumors from hAFMSCs-treated mice.

Conclusions: Our data demonstrated that hAFMSCs strongly inhibit PDAC cell proliferation, tumor growth and invasion, possibly by altering cell cycle arrest and MMP7 signaling-triggered EMT.