Effect of Mammary Adenocarcinoma Supernatant on Hepatic Fibroblast Differentiation

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Abstract: Mammary adenocarcinoma is the most common malignant tumor in women, and the liver is one of the sites with a high incidence of metastasis. Previous studies have shown that the microenvironment of metastasis has deteriorated before tumor cell metastasis. However, angiogenesis and metabolism in the breast cancer premetastatic microenvironment have not been studied. This study established a mammary adenocarcinoma-associated fibroblast cell line (ME-iLX-2) that features premetasis niche based on coculture with the supernatant of hepatic stellate cells (LX-2) and mammary adenocarcinoma cells (TS/A). Multiple experiments, including 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT), Flow Cytometry (FCM), wound-healing, lactic acid, real-time quantitative polymerase chain reaction (qPCR) and WB assays, were carried out to investigate the connection between mammary adenocarcinoma cells and hepatic stellate cells and the source of cancer-associated fibroblasts in the premetastatic microenvironment and to confirm the importance of vascular endothelial growth factor (VEGF) in mammary adenocarcinoma supernatant-induced hepatic fibroblast differentiation. This study determined the following: 1. After long-term coculture with supernatant, LX-2 significantly promoted the proliferation and migration of tumor cells, and massive apoptosis of LX-2 cells occurred; 2. VEGF expression in LX-2 cells was positively correlated with the duration of coculture with supernatant. In addition, with an established linear regression model, high expression of VEGF is suggested to be one of the molecular properties of cancer-associated fibroblasts, which may provide a clear direction for the study of tumor treatment and prognosis.