

Increased MG-63s invasion potential mediated by HFs

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During a malignant transformation, the crosstalk between the stroma and the cancer cells is described as a growing network of physical and paracrine signals, and it seems to have a direct influence on the phenotypic, genetic and epigenetic changes that affect the cells (1). In order to invade and metastasize to distant tissues, cancer cells transform themselves via ECM, induce tumor angiogenesis as well as undergo proliferation, detachment, migration, and invasion through secretion of various tumor derived factors (2). In this study we decided to analyze morphological and molecular aspects due to the coexistence between tumor cells MG-63s and fibroblasts HFs, verifying in particular the ability of MG-63s of invasion and microenvironment modulation. Monolayers of co-cultured cells were morphologically analyzed in time-laps by HR-SEM microscopy and a trans-well migration assay was performed over 24 h, 48 h, 72 h, and 96 h. The expression of several proteins, focusing on those involved in cancer cell invasion, inflammatory responses, and angiogenesis (TNF alpha, IL-6, YKL-40, MMP-1, MMP-9, and VEGF) was validated by Western blotting analysis. The images in time-laps for HR - SEM showed that fibroblasts in contact with MG-63 lost their spatial orientation, while the MG-63 quickly reached the confluence advancing towards HF cells, invading their space and overlying them. The increased MG-63s invasion mediated by the coexistence with HFs was confirmed by invasion assays in transwell co-culture. The protein levels of TNF-alpha, IL-6, YKL-40 and VEGF confirmed that tumor cells can regulate the development of a "tumor-stroma" via the aberrant expression of growth factors in the stromal compartment. Our results showed how tumor-stroma interactions play a significant role in tumor development and progression.

References

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Keywords

Tumor microenvironment; cell invasion; co-culture.