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Changes of microenvironment in an in vitro co-culture system

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For the enhanced understanding of fundamental cancer biology and improving molecular diagnostics and therapeutics, the role of the microenvironment during the initiation and progression of carcinogenesis is thought to be of critical importance (1, 2). The aim of this study was to establish an in vitro model based on a co-culture of healthy human fibroblasts (HFs) and human osteosarcoma cells (MG-63s) to simulate the microenvironment including tumor and healthy cells.

The HFs and MG-63s were in vitro co-cultured for a period of time ranging from 24h to 7 days. Cell morphology and organization were studied by phase contrast microscopy while the expression of Human Cartilage Glycoprotein 39 (YKL-40), Vascular Endothelial Growth Factor (VEGF), Matrix Metalloprotease 1 (MMP1) and IL1 alpha was investigated by Real Time PCR and Western Blotting. To better correlate the role of YKL-40, VEGF, MMP1 and IL1 alpha, siRNA knockdown of YKL-40 in MG-63 cells was performed, and changes in protein expression in the co-cultures were analyzed.

Results showed a characteristic disposition of tumor and healthy co-cultured cells in columns which are not visible in tumor and healthy cells grown singularly. The expression of YKL-40, VEGF and MMP1 significantly changed in co-cultured cells compared to HFs and MG-63s separately cultured. siRNA knockdown of YKL-40 was responsible of a down-regulation of VEGF expression on HFs, and an increase of IL1 alpha expression in MG-63s.

These results suggest that the tumor microenvironment has an influence on the protein expression of the healthy surrounding tissues and the process of tumorigenicity.

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