Bidirectional crosstalk between uveal melanoma cells and hepatic myofibroblasts promotes inflammation-induced chemokines expression

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Background
Uveal melanoma (UM) is the most common primary ocular neoplasm in adults. The metastatic disease develops in up to 50% of patients, and usually involves the liver. Treatment rarely extend the survival, because metastases are highly resistant to most chemotherapeutic agents. Tumor cells may modulate the functions of surrounding cells to facilitate their own growth, survival, invasion, and metastasis. This study was conducted to investigate the role of the hepatic microenvironment on UM cells (UMCs) aggressiveness.

Experimental conditions

A/ Bidirectional crosstalk between UMCs and activated HSCs

B/ UMC-HSC crosstalk promotes inflammation-induced expression of chemokine transcripts

C/ UMC-HSC crosstalk promotes the secretion of chemokines

D/ UMC-HSC crosstalk has no effect on cell proliferation

E/ UMC-HSC crosstalk induces the expression of cell adhesion receptors

Conclusion
The hepatic microenvironment increased the expression of numerous genes. The number of genes overexpressed in metastatic co-cultures is three times higher than in non-metastatic co-cultures. Overexpressed genes in co-culture were linked to inflammation and included several interleukins. The hepatic microenvironment had no effect on cell proliferation. UMC-HSC crosstalk induced expression of transmembrane receptors such as integrins, and increased particularly the adhesion to fibronectin. Our results provide evidence for an important role of inflammation in the progression of metastatic UM. The inflammatory characteristics of the tumor microenvironment might offer new therapeutic opportunities.