学位論文の要旨

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主論文の題名

Loss of tumoral expression of soluble IL-6 receptor is associated with disease progression in colorectal cancer

主論文の要旨

BACKGROUND: Interleukin-6 (IL-6) binds both the membrane and soluble forms of the IL-6 receptor (sIL-6R), which induces a complex with gp130, and proliferation of tumour cells. The aim of this study is to clarify the relationship between tumoral sIL-6R expression and disease progression in colorectal cancer patients.

METHODS: We measured tissue concentrations of sIL-6R in tumour and normal mucosa from 161 colorectal cancer patients undergoing surgery, and in supernatants from colon cancer cell lines. The expression of IL-6, IL-6R and gp130 was evaluated by immunohistochemical analysis.

RESULTS: Loss of tumour expression of sIL-6R as defined by sIL-6R Ca/N ratio <1.0 was significantly associated with factors reflecting disease progression, and was an independent prognostic factor not only in all the patients in this study, but also in the patients with curative intent. Colon cancer cell lines produced sIL-6R in vitro, and the production of sIL-6R in cancer cell lines was stimulated by cytokine stimulation. Immunohistochemistry revealed that loss of tumour expression of sIL-6R was significantly inversely correlated with intense IL-6 expression in the cytoplasm of cancer cells. In addition, tumoral IL-1beta expression was significantly correlated with sIL-6R expression.

CONCLUSION: Loss of sIL-6R expression is associated with colorectal cancer disease progression.