学位の種類	博士（医学）
報告番号	甲第１４０６号
学位記番号	第１０１１号
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授与年月日	平成 26 年 3 月 25 日
学位論文の題名	Interleukin-6 released by colon cancer-associated fibroblasts is critical for tumour angiogenesis: anti-interleukin-6 receptor antibody suppressed angiogenesis and inhibited tumour-stroma interaction. （大腸癌関連線維芽細胞から放出されたインターロイキン 6 は、腫瘍血管新生に重要である：抗インターロイキン 6 レセプター抗体は血管新生と腫瘍間質相互作用を抑制する。） British Journal of Cancer. in press
論文審査担当者	主査：　城 卓志 副査：　高橋 智，竹山 廣光

Abstract

Background: Interleukin-6 (IL-6) is a multifunctional cytokine that plays a central role in the regulation of the inflammatory and immune responses. And it has an important role in cancer progression (Santer et al., 2010; Grivennikov et al., 2010 Liu et al., 2010), and high levels of plasma IL-6 are correlated with a poor prognosis in a variety of cancers (Okugawa et al., 2010; Yeh et al., 2010). It has also been reported that tumor stromal fibroblasts are necessary for steps in cancer progression, such as angiogenesis (Wu MH et al., 2011; Zhang et al., 2011). There have been few reports of a correlation between fibroblast actions and IL-6 levels. In this study, we examined the correlation between cancer stromal fibroblasts and IL-6, and the utility of IL6 as a therapeutic target in human colon cancer.

Results: We demonstrate that stromal fibroblasts isolated from colon cancer produced significant amounts of IL-6 and that colon cancer cells enhanced IL-6 production by stromal fibroblasts. Moreover, IL-6 enhanced VEGF production by fibroblasts, thereby inducing angiogenesis. *In vivo*, anti-IL6 receptor antibody targeting stromal tissue showed greater anti-tumor activity than did anti-IL6 receptor antibody targeting xenografted cancer cells.

Conclusions: Cancer stromal fibroblasts were an important source of IL-6 in colon cancer. IL-6 produced by activated fibroblasts induced tumor angiogenesis by

stimulating adjacent stromal fibroblasts. The relationship between IL-6 and stromal fibroblasts offers new approaches to cancer therapy.