2P-03
Chemokine BRAK stimulates apoptosis elicited by gefitinib in oral squamous cell carcinoma

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Objectives: The chemokine BRAK/CXCL14, a non ELR-motif chemokine, is expressed in many normal tissues, but absent or down regulated in transformed cells and cancerous tissues including oral carcinoma. We reported previously that BRAK had suppressive activity toward tumor progression of oral carcinoma in vivo when over-expressed in tumor cells. In this study, we investigated whether BRAK expression is associated with the tumor suppression by gefitinib, an inhibitor of the epidermal growth factor receptor (EGFR).

Methods: To examine the mechanism of the tumor suppression in vivo, we xenografted nude mice with HSC-3 cells that had been transfected with control Sh-scrambled vector or ShRNA of BRAK to down-regulate BRAK mRNA expression. In order to investigate the cell proliferation and/or apoptosis with regard to the suppression of tumorigenicity, we prepared paraffin sections and used them for immunohistochemical detection of Ki-67, a marker of cell proliferation and for the TUNEL method to detect apoptosis.

Results: As to the cell proliferation, the number of Ki-67-positive cells in both Sh-Scrambled-treated control tissue sections and Sh-BRAK-treated one was decreased, when the animals were treated with gefitinib. There was no difference between Sh-Scrambled vector-treated tumor cells and Sh-BRAK vector-treated ones with respect to the responsiveness to gefitinib. On the other hand, with respect to apoptosis, we found a significant increase (P<0.05) in the number of apoptotic cells in the Sh-Scrambled vector-treated control tumor cells concomitant with the suppression of tumor mass after the mice had been treated with gefitinib. In contrast, gefitinib affected neither the number of apoptotic cells nor tumor volume suppression in the case of Sh-BRAK vector-treated tumor cells.

Conclusions: These results suggest that a BRAK dependent signal(s) was essential for the stimulation of apoptosis by gefitinib and reduction in tumor volume in vivo.

2P-04
Basic study on prescription of effective conservative combined therapy for malignant tumor using quantitative imaging analysis for vascular structure

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Objective: The aim of this study was the development of a detailed and quantitative X-ray imaging evaluation method for analyzing the vascular structures of malignant tumor in experimental small animals like mouse, and to develop effective conservative combined therapy for malignant tumor by using our analysis method.

Methods: The digital X-ray imaging was used to quantitatively analyze the vascular structures in mice. The vascular structures were quantitatively analyzed as various parameters, after the vascular structure patterns were extracted from the digital X-ray image data. The therapeutic effects of various conservative combined therapies were evaluated by in vitro and in vivo experiments.

Results: The vascular structures in the mice were indicated as various parameters by our analyzing method [1]. The combined therapy of radiotherapy plus chemotherapy or radiotherapy plus hyperthermia sensitized therapeutic effect of each therapy. Furthermore, the combined therapy of radiotherapy plus chemotherapy plus hyperthermia remarkably sensitized therapeutic effect. KB tumors in the mice showed complete response with the dose of less than half of conventional treatment.

Conclusions: The results of investigation suggest that our quantitative X-ray imaging evaluation method is useful for the analysis of the vascular structure of tumors in experimental small animals. It is also indicated that our conservative combined therapy is very effective for the treatment of malignant tumor, and our evaluation method proved it.

Reference