Analysis of the immune response of tumor-bearing host at the immunochemotherapy -from the viewpoint of optimum combination of chemotherapy and immunotherapy -

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## 2001 Fiscal Year Final Research Report Summary

Analysis of the immune response of tumor-bearing host at the immunochemotherapy -from the viewpoint of optimum combination of chemotherapy and immunotherapy -

chemotherapy and immunotherapy -Research Project Project/Area Number 12671212 **Research Category** Grant-in-Aid for Scientific Research (C) **Allocation Type** Single-year Grants Section 一般 Research Field Digestive surgery **Research Institution** Kanazawa University **Principal Investigator FUJIMOTO Toshihiro** Kanazawa University, Medical School, Assistant Professor, 医学部・附属病院, 講師 (00242561) Co-Investigator(Kenkyū-buntansha) MAI Masayoshi Kanazawa University, Cancer Research Institute, Professor, がん研究所, 教授 (80092807) TAKAHASHI Yutaka Kanazawa University, Cancer Research Institute, Associate Professor, がん研究所, 助教授 (10179541) Project Period (FY) 2000 - 2001 **Keywords** 

## **Research Abstract**

Irinotecan(CPT-11) / OK-432 / Th1 / IL-12 / immunochemotherapy / tumor bearing state

Chemotherapy with lower dose of irinotecan (CPT-II) exerts larger antitumor effect. In this study, SN-38, the active metabolite of CPT-II, exerted dose-dependent inhibition of interferon (IFN)- $\gamma$  and interleukin (IL)-10 production induced by streptococcal preparation OK-432 in mouse splenocytes. In contrast, the optimum concentration of SN-38 (0.4-0.8( $\mu$ g/mI) increased IL-6 and IL-12 production by OK-432 activated macrophages. In tumor-bearing mice (C57BL/6 mice bearing with B16 melanoma), CPT-11

inhibited tumor growth and OK-432 had an additive antitumor effect with CPT-11. Investigation of cytokine production showed that CPT-11 treatment principally inhibited IL-12 and IFN-y production, which was improved by the combined administration with OK-432. These results indicate that CPT-11 inhibits type-1 T helper (Th1) cells despite its potential to stimulate macrophages and that OK-432 enhances the antitumor activity of CPT-11 by increasing Th1-cytokine production (Anticancer Research 21 : 2505-2510, 2001).

In the treatment for the peritoneal metastasis of gastric carcinoma, we may control disseminated cancer cells by intraperitoneal immunochemotherapy using MMC and OK432 in patients with curative resection (Oncology, 2002, in press).

Briefly, these results have demonstrated the efficacy of the combination of chemotherapy and immunotherapy.

URL: https://kaken.nii.ac.jp/report/KAKENHI-PROJECT-12671212/126712122001kenkyu\_seika\_hokoku\_

## Research Products (10 results)

All Other All Publications [Publications] 藤本敏博: "胃癌の腹膜播種に対するMMC+OK-432腹腔内投与の臨床効果"Therapeutic Research. 21. 1940-1945 (2000) [Publications] T.Fujimoto, et al.: "The effect of OK-432 on the cytokine production of the tumor bearing mouse splenocytes" Biotherapy. 14. 528-528 (2000) [Publications] X.Wang, T.Fujimoto, et al.: "Streptococcal preparation OK-432 enhances the antitumor activity of CPT-11 by increasing Th1 cytokine production in tumorbearing mice"Anticancer Research. 21. 2505-2510 (2001) [Publications] T.Fujimoto, et al.: "Evaluation of intraoperative intraperitoneal cytology for advanced gastric carcinoma"Oncology. (in press). (2002) [Publications] 藤本敏博, 他: "肝転移、メカニズムと臨床「免疫療法」"医学書院. 228 (2000) [Publications] Fujimoto T: "The efficacy of intrapertioneal administration of MMC and OK-432 against peritoneal metastasis of gastric cancer"Therapeutic Research. 21. 1940-1945 (2000) [Publications] Wang X, Fujimoto T, Zhang B, Shimizu A, and Mai M: "The effect of OK-432 on the cytokine production of the tumor bearing mouse splenocytesy" Biotherapy. 14. 528 (2000) [Publications] Wang X, Fujimoto T, Zhang B, and Mai M: "Streptococcal preparation OK-432 enhances the antitumor activity of CPT-11 by increasing Th1 cytokine production in tumor-bearing mice"Vrticancer Research. 21. 2505-2510 (2001) [Publications] Fujrmoto T, Zhang B, Minami S, Wang X, Takahashi Y, and Mai M: "Evaluation of intraoperative intraperitoneal cytology for advanced gastric carcinoma"Oncology. (in press). (2002) [Publications] Fujimoto T: "Imraunotherapy for liver metastasis. Liver metastasis- its mechanism and clinical experience. (Mai M, Seiki M and Takahashi Y ed.)"Igaku-shoin, Tokyo. 212-219 (2000)

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