進行肺癌に対する術前・術後養子免疫療法に関する基礎的並びに臨床的研究

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Study on Adoptive Immuno-therapy for Advanced Lung Cancer.

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Research Institution

Kanazawa University

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Research Abstract

It appears that lymph node metastases are more frequent in lung cancer than in other cancers due to impaired defensive mechanisms in the regional lymph nodes. However, little is known about the immunological function of Regional Lymph Node Lymphocytes (RLNL) in lung cancer patients. We have studied the immunological properties of RLNL in comparison with Peripheral Blood Lymphocytes (PBL). We measured the Natural Killer (NK) cell activity of RLNL and PBL in lung cancer patients and found that the NK activity was significantly more depressed in the RLNL than in the PBL. In contrast, Inter-Leukin-2 (IL-2) production was markedly higher in the RLNL than in the PBL. The cytotoxic effect of RLNL in non-metastatic lymph nodes on target cells, such as K562 cells, or PC-3 and PC-10 cells (NK-resistant, human lung cancer of adenocarcinoma and epidermoid carcinoma, respectively) was significantly enhanced by in vitro

incubation with recombinant IL-2 (rIL-2). Furthermore, we clarified that both rI L-2 and OK-432, which is a biological response modifier and IL-2 inducer as well, augmented the cytotoxicity of RLNL and that these effector cells were lymphokine activated killer (LAK) celis. The depletion of lymphocyte subsets by pretreatment with specific monoclonal antibody showed that the LAK activity in RLNL was mediated by CD3^+ and CD8^+ cells, while the lymphocyte subsets contributing the LAK activity in PBL were CD3^+ and CD16^+ cells. It was concluded that a majority of the effector cells in RLNL were LAK cells of the cytotoxic T-cell population. Thus, therapeutic effects can be expected by LAK cells endogenously induced by regional infusion of OK-432 abd addition of exogenous LAK cells which can be produced in vitro by incubating the patient's lymphocytes with rIL-2. Local AIT through bronchial artery was performed on 7 patients with advanced lung cancer. Some therapeutic effects were noted in 5 (71%) out of 7 patients : partial response in 2, minor response in 3 and no change in 2.
As the next step, possibility of adpotive immunotherapy using TIL (Tumor Infiltrating Lymphocyte) was studied Substantial augmentation of the cytotoxic activity against K562, Daudi and autologous tumor cell lines were induced by incubating the TILs with OK-432 or rIL-2, although these enhancement of the cytotoxicity was significantly low in comparison with that of the RLNLs and PBLs. By analysis of lymphocyte subsets, it was clarified that the majority of the TILs were T cells (most of them were CD8^+ cells), whereas B cells, macrophages and NK cells were minority. These tesults strongly indicates that, if not all, some part of cultured TIL contains cytotoxic T lymphocytes which have a specificity against autologous tumor cells. Accordingly, it was thought to be probable that some of the cytotoxic T cells (CTLs) in the TILs might have cytotoxicty against AT cells. Adoptive Immuno-Therapy (AIT) was tried on lung cancer patients with carcinomatous pleurosy. TILs were extracted from pleural effusion, and enhanced by rIL-2. The enhanced TILs with rIL-2 were infused into the thoracic cavity, and subsequently in two out of three cases the pleural effusion disappeared.▲ Less

Research Products (14 results)

All Other

All Publications (14 results)

[Publications] Y.Watanabe et al.: "Functional character and augmentation of lymphocytes in regional lymph nodes of patients with lung cancer." American Review of Respiratory Disease. 142. 769-774 (1990)

[Publications] 渡辺 進一郎 ほか: "肺癌患者における腫瘍浸潤リンパ球(TIL)のNK活性およびLAK活性について" Biotherapy. 5. 4 (1991)

[Publications] Y.Watanabe et al.: "Immune reactivity in bronchogenic carcinoma and its relation to 5ー year survival rate." Jouranal of Surgical Oncology. 45. 103-109 (1990)

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[Publications] J. Shimizu: "Studies on immunotherapy for lung cancer ; with special reference to induction of regional tumoricidal activity and its application to lung cancer patients." Journal of the Juzen Medical Society. 98. 161-174 (1989)

[Publications] M. Yoshida: "Studies on the induction of tumoricidal activity of peripheral blood lymphocytes in patients with lung cancer ; with special reference to tumoricidal activity against autologous tumor cells." Journal of the Juzen Medical Society. 99. 815-826 (1990)

[Publications] S. Watanabe: "Studies on tumoricidal activity of tumor-infiltrating lymphocytes and its application to lung cancer patients." Journal of the Juzen Medical Society. 99. 947-962 (1990)

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