WS18-3 *3

IMMUNOTHERAPY OF SOLID TUMOR BY INTRATUMORAL INFUSION OF LAK CELLS

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Effects of intratumoral infusion of LAK cells on tumor growth were studied. Rat gliosarcoma(T9) cells were used to establish a solid tumor. For induction of LAK cells, rat spleen cells were cultured in vitro in the presence of 2U/ml of IL-2 for 4 days. When the tumor reached 1cm in diameter, one to fifty millions of LAK cells suspended in 0.1ml of IL-2 containing medium were infused into the tumor for one hour with use of microinfusion pump. The rats received 20U of IL-2 per day intraperitoneally for the subsequent 10 days. After 3 weeks of continuous growing, the tumor began to regress until it finally disappeared. This phenomenon was not observed in control rats which received normal spleen cell infusion plus IL-2. Immunohistochemical analysis of the regressing tumor revealed massive infiltration of Tc/s cells probably of host origin. These data suggested that intratumoral infusion of LAK cells is highly effective for rejection of the tumor by inducing strong host's immunity against the tumor.

WS18-4 *4

EFFECTS OF DIMETHYL SULFOXIDE (DMSO) TREATMENT ON H-2 EXPRESSION AND SUSCEPTIBILITY TO NK AND CTL MEDIATED LYSIS OF YAC-1 LYMPHOMA AND ITS β2MICROGLOBULIN (β2M) DEFICIENT VARIANT

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The H-2 induction by DMSO and its correlation to NK and CTL sensitivity in the murine T-cell lymphoma YAC-1 were investigated and compared to effects of interferon-γ (IFN). A YAC-1 derived β2m-deficient variant line lacking cell surface H-2, A.H-2-, was included. FACS analysis showed an induction of H-2 Kk and β2m 3 days after culture of YAC-1 with DMSO, whereas more than one week was required for optimal H-2 Dd induction. The induction of H-2 Kk and Dd by DMSO was equal to that by pretreatment with 100 U/ml and 10 U/ml IFN, respectively. The DMSO treatment protected YAC-1 cells from NK lysis as efficiently as the IFN treatment at 10 U/ml, while the A.H-2- line could not be protected. In contrast, the susceptibility of YAC-1 cells to anti-H-2a, H-2 Kk, and H-2 Dd specific CTLs was augmented after treatment with DMSO. While IFN-treated targets were less efficient than control cells in cold target inhibition assays, the reduced NK sensitivity of DMSO-treated cells did not correlate with lower effector binding or cold target inhibition capacities. Thus, DMSO can induce H-2 expression and alter the sensitivity to different effector cells in murine T-cell lymphoma. The possibility that DMSO induced protection from NK lysis depends on postbinding events controlled in association with target H-2 expression will be discussed.

WS18-5 *5

IMMUNOPHARMACOLOGICAL EFFECTS OF ELEUTHEROCOCCUS SENTICOSUS EXTRACT AS DETERMINED BY QUANTITATIVE FLOW CYTOMETRY

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An extract from the root of the Siberian plant eleutherococcus senticosus was found to exert strong effects on the cellular immune system in healthy individuals. In particular, there was a drastic increase in the number of T helper, but also of cytotoxic and natural killer cells. Since such effects were the more pronounced the less the respective subsets were represented before treatment, there seems to be a strong immunomodulating (not simply stimulatory) activity. Preliminary results from studies with tumor patients (postoperatively and as an adjuvant to chemo- and radiotherapy) will be discussed with respect to such immunoregulatory actions. Likewise, beneficial effects on the prevention of metastases in an artificial mouse model will be presented. Special attention will be focussed on the activity of killer cells, as determined by a novel two-color flow-cytometric technique employing fluorogenic substrates and monoclonal antibodies.Possible explanations for the mechanism of action by pleiotropic effects on the neuroendocrine-immunological network will be offered.