

experimental tumour systems elicited extensive expectations. These expectations, however, were unfortunately not correspondingly reflected in controlled clinical trials. Both, adverse effects of various cytokines and the low percentage of clinical responses obtained in clinical trials were extensively discussed. To improve the results of the cytokine therapy and cytokine gene therapy, utilization of cytokine combinations that could potentiate the effects of the cytokines and allow for utilization of lower and less toxic cytokine doses have been proposed. It can be presumed that the sensitivity of various tumour types to cytokine combinations will be different and, therefore, should be pretested in relevant experimental tumour systems.

In experimental tumour systems, interleukin 12 is one of the most powerful antitumour cytokines identified to date. Similarly as IL-2, IL-12 was found to be efficient in a wide variety of experimental tumours (for a review, see Shurin et al., 1997). Synergistic effects of IL-2 and IL-12 (Pappo et al., 1995) have been described in murine colon adenocarcinoma (Vagliani et al., 1996), and murine renal carcinoma (Wiggington et al., 1996). In this paper, we were interested whether the IL-2 plus IL-12 combination of cytokines will be efficient and synergistic also in a conventional murine chemically induced sarcomas.

Interleukin 18, originally described as an IFN γ -inducing factor in mice, has been reported to display an antitumour effect (Lebel-Binay et al., 2000), to induce IFN γ secretion in T lymphocytes and NK cells, even stronger than IL-12 (Golab, 2000), and to enhance the cytolytic activity of T cells when purified CD8⁺ cells were cultured in the presence of IL-18 and IL-2 (Kohyama et al., 1998). Therefore, we have used also this cytokine to study a possible synergistic antitumour effect with IL-2.

It has been found that IL-12, but not IL-18, monotherapy has an antitumour effect in the murine chemically induced sarcoma system utilized, and that in this system a synergistic effect of IL-2 can be demonstrated with IL-12 but not with IL-18. Intratumoral IL-2 gene transfer improved the therapeutic efficacy of IL-12; administration of the recombinant IL-12 can therefore be considered as an adjuvant treatment for IL-2 gene therapy of selected sarcomas with IL-2 gene-modified irradiated tumour vaccines.

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