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Immunotoxicity assessment of recombinant mouse IL-2, a cancer immunotherapeutic agent

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Interleukin-2 (IL-2) is a 15 Kd protein produced by helper T lymphocytes upon antigen stimulation of resting T cells. IL-2 has been shown to augment NK cell activity, mediate antitumor activity, and enhance the immune response in acquired immunodeficiency states. The immunological safety of recombinant mouse IL-2(rmIL-2) as a cancer immunotherapeutic agent was evaluated in tumor-bearing BALB/c mouse model. Tumor-bearing BALB/c mice were treated with rmIL-2. Under the anti-tumor immunotherapeutic dosage administered on the basis of surface area,there were not significant alternations of body weight, relative spleen weight, and splenic cellularity. Significant difference of histamine level in blood was not observed after rmIL-2 administration,but IgE concentration in blood was increased significantly for 7 days after rmIL-2 administration. On the one hand, to evaluate the autoimmune potential of rmIL-2 therapy, emergence of autoantibodies (ANA, anti-dsDNA, and anti-histone) in blood was measured after rmIL-2 treatment. The results showed that thelevels of ANA and anti-dsDNA did not changed, but the level of anti-histone was increased significantly owing to rmIL-2 therapy. Distribution ratios of T cell subsets in thymus were analysed using flow cytometry. Without regard to dosage of rmIL-2, the ratio of CD4-CD8- T cells was increased in accordance with survival of solid tumor but that of CD4+CD8+ T cells was decreased dramatically. These results indicate rmIL-2 immunotherapy is to induce the autoimmune potential and the anti-histone measurement as a biomarker of autoimmunity is useful in cancer immunotherapy

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