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Irradiated haploidentical donor leukocyte infusions as an adoptive immunotherapy strategy to induce host-versus-tumor effects

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ABSTRACT

Aims and background. Previous research has shown that irradiated splenocytes preserve the antitumor effect and induce relatively weaker graft-versus-host disease in parent C57BL/6→CB6F1 transplantation. The present study was designed to investigate the antitumor effect of 5-Gy-irradiated haploidentical donor leukocyte infusions (DLI) without prior bone marrow transplantation and the possibly involved mechanism in (H-$2^{d/k}$)→(H-$2^{b/d}$) infusion model systems.

Methods. Hepa 1-6 tumor-bearing mice were used to evaluate the antitumor effect and the possible mechanism of irradiated haploidentical DLI treatment. Changes in tumor volume, lymphocyte proliferation and cytotoxicity, IFN-gamma and IL-2 secretion and donor cell survival *in vivo* were analyzed.

Results. After irradiated haploidentical DLI treatment of the poorly immunogeneic Hepa 1-6 tumor mouse model, the donor cells were rejected and disappeared within 4 days. Surprisingly, an antitumor response was still observed. The infusion treatment effectively inhibited tumor growth and prolonged the survival of recipients, and this effect could be enhanced by combined treatment with cyclophosphamide and impaired by deleting donor-derived T cells. Moreover, the infusion treatment increased the levels of type 1 cytokines including IFN-gamma and IL-2, and enhanced the proliferation of lymphocyte subsets, particularly $CD8^+$ T and NK cells. Specifically, multiple infusions proved to enhance the antitumor effect without inducing graft-versus-host disease.

Conclusions. As an adoptive therapy, irradiated haploidentical DLI without bone marrow transplantation might be a promising and safe treatment for cancer.

Key words: immunotherapy, cyclophosphamide, tumor, mouse.

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