Suppression of lentivirus-mediated transgenic dendritic cells in graft-versus-host disease after allogeneic bone marrow transplantation in mice

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ABSTRACT. We determined whether genetically engineered immature dendritic cells (imDCs) mediated by lentiviral vectors alleviate acute graft-versus-host disease (GVHD) after allogeneic bone marrow transplantation (allo-BMT) in mice. We introduced the mouse chemokine receptor 7 (Ccr7) gene into the bone marrow-derived imDCs of C57BL/6 mice to construct genetically engineered imDCs. A 1:1 mixture of bone marrow and spleen cells from the donors was injected into the recipients, which were divided into four groups: radiation, transplantation, empty vector, and transgenic imDC groups. Symptoms, clinical scores, GVHD pathological changes, and survival times and rates of recipients were recorded; secretion of IFN-γ and IL-
4, and allogeneic chimerism rates were detected. The survival time of the transgenic imDC group (27.5 ± 7.55 days) was significantly longer than in the other three groups (P < 0.01). The GVHD score of the imDC group mice was significantly lower than in the transplantation and empty vector groups (P < 0.05), which meant that mice in the transgenic imDC group had the lightest pathology damage in the target organs. In the transplantation group, IFN-γ increased while IL-4 decreased. In contrast, IFN-γ decreased and IL-4 increased in both empty vector and trans-imDC groups, and the difference was significant in the latter (P < 0.01). Thirty days or more following transplantation, the allogeneic chimerism rate was still 95-100%, suggesting complete donor type implantation. Ccr7 transfection into imDCs suppressed occurrence and severity of acute GVHD after allo-BMT in mice; the mechanism might be associated with IFN-γ decrease and IL-4 increase.

Key words: Dendritic cells; Recombinant lentivirus; Transgenic; Chemokine; Immune tolerance; Graft-versus-host reaction