学 位 論 文 の 要 旨

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主論文の題名

Improved Antitumor Effect of NK Cells Activated by Neutrophils in a Bone Marrow Transplant Model

主論文の主旨

The licensing process mediated by inhibitory receptors of the Ly49 C-type lectin superfamily that recognizes self-major histocompatibility complex class I in mice is essential for the proper antitumor function of natural killer (NK) cells. However, the appropriate adoptive transfer setting to induce efficient graft versus tumor/leukemia effects remains elusive, especially after hematopoietic stem cell transplantation (HSCT).

In this experiment, we demonstrate enhanced antitumor effects of licensed NK cells induced by weekly intraperitoneal injections of irradiated neutrophil-enriched peripheral blood mononuclear cells (PBMNCs) in recipient mice bearing lymphoma.

Bone marrow transplantation was performed using BALB/c mice (H-2d) as the recipient and B10 mice (H-2b) as the donor. The tumor was A20, a BALB/c-derived lymphoma cell line, which was injected subcutaneously into the recipient at the same time as the HSCT. The intraperitoneal injection of PBMNCs activated a transient licensing of NK subsets expressed Ly49G2, its corresponding NK receptor ligand to H-2d, and reduced A20 tumor growth in the recipient after HSCT. Pathological examination revealed that increased donor-oriented NK1.1+NK cells migrated into the recipient tumors, depending on neutrophil counts in the administered PBMNCs.

Collectively, our data reveal a pivotal role of neutrophils in promoting NK cell effector functions and adoptive immunotherapy for cancer.