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of cancer by Sato and colleagues (42), who found that the frequency of MDSC in non-Hodgkin lymphoma patients was increased and inversely correlated with that of NK cells, not that of T cells (42). Other evidence that activated NK cells can lyse the MDSCs has been published by Gleason and colleagues (43). Even though NK cells and their expression of FcRγIII (CD16) are decreased in myelodysplastic syndromes (MDS) and inversely correlate with a substantial increase in MDSCs, the enhancement of CD16 signaling potently activates NK cells to lyse $CD33^+$ MDS and MDSC targets (43). Although we suggest a novel role for *ex vivo*–activated NK cells in overcoming the negative function of immune suppressor cells, identification of the underlying mechanism will require further study. To this end, additional analysis of interactions between NK and Treg or MDSC cells in a cancer model will not only provide valuable information, but may also improve efficacy in anticancer immunotherapy.

Several studies have examined the role of chemokines secreted from NK cells in experimental tumor models (24). In one report, significant induction of MIG, IP-10, RANTES, MCP-1, and IL8 from NK cells following IL12 administration suggested a role for NK cells in the initiation of the chemokine response (28). However, less is known about the chemokine response after the direct administration of NK cells. In our system, we found elevated MIG, MCP-1, MIP-1β, and RANTES concentrations, suggesting that activated NK cells secrete a broad array of T cell–attracting chemokines. These chemokines act together to recruit tumor-infiltrating T cells, resulting in a decreased incidence of recurrence and increased overall survival in cancer patients (28, 44–46). Moreover, our finding of secretion of T-cell–attracting chemokines following administration of activated NK cells suggests an additional mechanism through which T-cell infiltration to the tumor sites could be achieved.

In conclusion, the safety data for transplantation of MG4101 derived from unrelated random healthy donors will give increased opportunities to select donors that have either maximum KIR incompatibility against recipients or a potent KIR B haplotype. To enhance clinical benefit, we are currently considering a phase II study including immunosuppressive chemotherapy followed by MG4101 treatment, based on previous successful results involving lymphodepleting preparative regimens (9).

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

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Cancer Immunology Research

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