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The aim of this issue is to describe and explain the importance of the chemokine system in hematology. As described in the “Introduction,” the chemokine system is probably important for many aspects of normal and malignant hematopoiesis. A major focus is the development and treatment of hematologic malignancies, including the immunobiology of stem cell transplantation.

The first main section includes three chapters, where the first review by Bonecchi et al. describes the chemokine decoy receptors, a group of receptors that recognize chemokines but are unable to activate transduction events. However, they seem to have important biological functions both in inflammation and possibly in carcinogenesis through removing, transporting, or concentrating their chemokine ligands. The next two chapters describe the function of the chemokine system in chemotaxis of natural killer cells and for regulation of angiogenesis. As described by Magazachi, natural killer (NK) cells are important in allogeneic stem cell transplantation; these cells are important as antileukemic effector cells that influence the risk of posttransplant leukemia relapse, and they are in addition involved in the development of graft-versus-host disease (GVHD). Allogeneic stem cell transplantation is used in the treatment of most hematologic malignancies and also certain nonmalignant hematologic disorders. The three major causes of death after allotransplantation are leukemia relapse, severe GVHD, and serious infections. NK cells seem to be involved in all these complications. Furthermore, increased angiogenesis is common in the pathogenesis of many hematologic malignancies. Leukemic cells often show constitutive release of proangiogenic chemokines, and antiangiogenic therapy is now considered in the treatment of these diseases. The importance of chemokines in this angioregulation is described in detail in Dimberg’s review.

The next three chapters focus on the immunobiology of allogeneic stem cell transplantation, an important therapeutic strategy first of all for hematologic malignancies. The treatment is increasingly used and the use of reduced intensity conditioning has made this treatment available for elderly patients. The grafts include both stem cells and immunocompetent cells, and allotransplantation should therefore be regarded as a combination of intensive chemotherapy with stem cell rescue.
and antileukemic immunotherapy. As reviewed by Löffler et al., single nucleotide polymorphisms in immunoregulatory genes influence the risk of severe and possibly lethal posttransplant complications. Furthermore, as described by Kittan and Hildebrandt, the transplanted immunocompetent cells are then important for the risk of developing GVHD and for the induction of specific antileukemic reactivity. Studies in animal models and in humans suggest that chemotaxis of immunoregulatory T-cell subsets is important in the development of GVHD. The last review describes the importance of immunosuppressive Treg and proinflammatory Th17 cells in the pathogenesis of GVHD.

The three last contributions describe the importance of the chemokine system in clinical hematology. First, Kittang et al. describe the chemokine system in acute myeloid leukemia (AML). This disease is characterized by accumulation of immature malignant cells that show constitutive release of several chemokines that may contribute to leukemia-associated angiogenesis, chemosensitivity, and regulation of antileukemic immune reactivity. The biological background for the possible use of CXCR4 inhibitors in the treatment of AML is outlined. Second, as described by Calandra et al., pharmacological CXCR4 inhibition can be used for mobilization and harvesting of peripheral blood stem cells that are used for autologous and allogeneic transplantations. These inhibitors are also considered for the treatment of AML. Finally, venous thromboembolic disease is one of the most common hematologic disorders. Cancer patients have an increased risk of this disease and are then treated with heparin. Heparin-induced thrombocytopenia (HIT) is an important complication during this treatment and is caused by antibodies directed against the chemokine CXCL4 (platelet factor 4)–heparin complex on the platelet surface. Previous reviews have focused on the clinical handling of this complication; the present review by Sandset includes a more detailed description of the immunobiology of this complication.

The present reviews illustrate that chemokines can be involved in leukemogenesis. The chemokine system is also important both for the crosstalk between malignant cells and their neighboring nonmalignant stromal cells (including endothelial cells) and for the immunoregulation in patients treated with allogeneic stem cell transplantation. Thus, chemokines are important both for the pathogenesis and treatment of hematological diseases.

Bergen, Summer 2010

Øystein Bruserud
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