

# Granulocyte Macrophage Colony-Stimulating Factor: Current Practice and Novel Approaches

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Endogenous colony-stimulating factors (CSFs) are a class of glycoproteins that act on hematopoietic cells by binding to specific cell surface receptors to stimulate proliferation, differentiation, commitment, and on-cell function activity (Dereskinski & Kempter, 1998). Until recently, CSFs have been found only in humans, but development of recombinant DNA techniques have allowed these agents to be mass produced and studied in a variety of applications. Two major endogenous myeloid CSFs exist: granulocyte macrophage CSF (GM-CSF) and granulocyte CSF (G-CSF). GM-CSF has broad activity in the proliferation and differentiation of myeloid lineage progenitor cells, whereas G-CSF acts selectively on cells of the granulocyte lineage.

Clinical applications of GM-CSF have expanded enormously since it was first introduced in the early 1990s for acceleration of myeloid engraftment in patients with neutropenia. Current studies suggest that GM-CSF decreases the course of mucositis, stimulates dendritic cells, prevents infection, acts as a vaccine adjuvant, and facilitates immunologic tumor control. The purpose of this article is to discuss current and future applications of yeast-derived GM-CSF and nursing practice issues in the administration of this agent.

Endogenous myeloid colony-stimulating factors (CSFs) have demonstrated the ability to enhance the clinical management of immunosuppressed patients with cancer. These agents are associated with significant decreases in chemotherapy-associated infections, antibiotic use, length of hospital stays, and mortality. Two major endogenous recombinant myeloid CSFs currently are being manufactured. Granulocyte macrophage CSF (GM-CSF) (sargramostim, Leukine®, Immunex Corporation, Seattle, WA) has broad activity in the proliferation and differentiation of myeloid lineage progenitor cells, whereas granulocyte CSF (filgrastim, Neupogen®, Amgen, Inc., Thousand Oaks, CA) acts selectively on cells of the granulocyte lineage. Clinical trials suggest that GM-CSF has clinical benefits beyond enhancing neutrophil recovery, including shortening the duration of mucositis and diarrhea, stimulating dendritic cells, preventing infection, acting as an adjuvant vaccine agent, and facilitating antitumor activity.

The modular sequence of endogenous human GM-CSF was identified in 1985. Three types of recombinant GM-CSF were manufactured: yeast-derived GM-CSF from *Saccharomyces cerevisiae* (sargramostim), bacteria-derived GM-CSF from *E. coli* (molgramostim), and mammalian-derived GM-CSF from Chinese hamster ovary cells (regramostim) (Armitage, 1998). Early clinical studies in GM-CSF were conducted using *E. coli*-derived agents; however, only yeast-derived GM-CSF is available in the United States. Present misconceptions that

yeast-derived GM-CSF has a similar side profile to those occurring from *E. coli*-derived GM-CSF are common because early clinical trials in the United States used bacteria-derived GM-CSF. The latter product is no longer available in the United States. Table 1 compares the clinical properties of yeast-derived GM-CSF to bacteria-derived GM-CSF.

GM-CSF is a recombinant CSF that “turns on” the immune system by stimulating production of the myeloid progenitor stem cells of neutrophils, monocytes, macrophages, eosinophils, and dendritic cells. It also has a role in functional cell activities, such as T cell activation. Increased monocyte activity generates macrophages and allows for increased phagocytosis that may prevent or diminish the

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