Cranking Up Cancer Treatments

A bright future for growth factors

By RICK WEISS

Like the famous exhortation "Go west, young man," and like the single word "plastics" whispered to Ben in "The Graduate," there's some simple, sage advice going around these days in cancer treatment circles: "growth factors."

Researchers know these naturally occurring molecules by many acronyms, including G-CSF, GM-CSF and EPO. The general public, for the most part, knows little about them. But in the next few years, many cancer specialists say, these biologically active chemicals will spark the first real revolution in oncology since chemotherapy and radiation became commonplace in the 1960s. While the compounds themselves do not cure cancer, they significantly speed the recovery of healthy cells after treatment with traditional cancer therapies.

"Never before have we been presented with a group of compounds for which we can so readily see the application," says Howard Ozer of the University of North Carolina in Chapel Hill.

Growth factors are proteins that regulate the growth and maturation of various cells in the body. Most tantalizing to cancer researchers are the so-called colony stimulating factors (CSFs) and a hormone called erythropoeitin, each of which triggers proliferation of specific cells.

Put simply, colony stimulating factors shift the body's white-blood-cell-making machinery into high gear. They act on progenitors of immune-system cells in the bone marrow, stimulating increased cell production, speedy maturation and quick release into the blood. Various cells in the body make small amounts of CSFs. But with recombinant DNA techniques, scientists now can routinely mass-produce these compounds.

Granulocyte colony stimulating factor (G-CSF) boosts bacteria-gobbling granulocytes — the most common kind of white cells in blood. Monocyte colony stimulating factor (M-CSF) increases the numbers and activity of two types of aggressive immune cells — monocytes in the bloodstream and macrophages in body tissues. Granulocyte-macrophage colony stimulating factor (GM-CSF) works on all three cell lineages.

The Food and Drug Administration has yet to approve any CSF for general use. But approval for GM-CSF, the most thoroughly tested, appears "very close," says Jules E. Harris of the Rush Presbyterian St. Lukes Medical Center in Chicago. In San Francisco last month, at the annual meeting of the American Society of Clinical Oncology, researchers reported results of ongoing clinical trials involving CSFs and erythropoeitin, which stimulates production of red blood cells.

"Bone marrow injury is usually the limiting factor for [cancer] chemotherapeutics," says James O. Armitage of the University of Nebraska College of Medicine in Omaha. If doctors use chemotherapy doses low enough to preserve bone marrow function, cancer cells often survive. But higher doses decimate bone marrow along with the cancer cells, leaving patients susceptible to life-threatening infections. Colony stimulating factors show promise as "rescue" compounds to speed recovery of normal, healthy cells after radiation and chemotherapy treatments.

Ongoing studies in Australia, West Germany and the United States indicate that CSFs accelerate bone marrow recovery in patients receiving radiation or chemotherapy. In most cases, doctors give the compounds in conjunction with an autologous bone marrow transplantation, removing a sample of the patient's marrow before chemotherapy, then reinfusing it with CSFs to quickly "reseed" the marrow and blood supply with new white blood cells. Some clinicians subject the marrow to cancer-killing treatments before reinfusing it, although the need to do so remains debatable.

With CSFs, doctors can shorten marrow recovery time from the two to four weeks seen with normal bone marrow transplants to as little as five days. With white blood cell counts rising more rapidly after chemotherapy, periods of fever have decreased and in some cases the numbers and intensities of infections have dropped. This has led to shorter periods of postchemotherapy hospitalization and antibiotic therapy. Some oncologists envision high-dose chemotherapy becoming an outpatient procedure when coupled with CSFs.

Perhaps most important, CSFs already allow oncologists to use double doses of cancer-fighting drugs. While most high-dose studies have involved leukemias and solid tumors called lymphomas, a combination of high-dose chemotherapy and autologous bone marrow transplantation also looks promising in breast cancer patients and may ultimately prove useful for other tumors, says Karen Antman of the Dana-Farber Cancer Institute in Boston.

Researchers express similar enthusiasm for genetically engineered erythropoeitin (EPO), a kidney hormone that boosts production of oxygen-carrying red blood cells. The FDA approved the drug on June 1 for the treatment of anemia in patients with severe kidney disease. Researchers are also experimenting with EPO's ability to correct the anemia that often results from cancer or its treatment. Preliminary research by Carole B. Miller and her colleagues at the Johns Hopkins Oncology Center in Baltimore suggests EPO could lessen the need for blood transfusions in cancer patients.

Although side effects of CSFs so far include nothing more than mild bone pain and headaches that respond to over-the-counter analgesics, the compounds are not risk free. "The initial euphoria associated with these clinical successes needs to be tempered with concern for . . . potential long-term toxicity," notes Peter J. Quesenberry of the University of Virginia Medical School in Charlottesville in an editorial in the May 18 NEW ENGLAND JOURNAL OF MEDICINE.

He warns, for example, that the stress of forced cell differentiation could eventually lead to marrow failure. While fears of marrow failure appear unsubstantiated for now, a few studies do suggest that under certain circumstances CSFs may stimulate preleukemic cells to become full-blown cancer cells. But with proper planning, even this reaction might prove useful, researchers say, because some antileukemia drugs kill only cancer cells that are actively dividing.

Though colony stimulating factors are not a cancer cure-all — or even a cure — the mood among CSF researchers is clearly upbeat. Says Roland Mertelsmann of the University Hospital in Mainz, West Germany: "After 15 years in this [cancer] field, I finally have something to get excited about." □