Biomedicine

Rescuing red cells to boost blood supply

The human body normally takes about a week to replace a mature red blood cell, but after a major blood loss it can replenish the supply within only a few days. Physicians and researchers have long marveled at this ability, noting that much of the credit goes to a hormone called erythropoietin. When released by the kidneys after a blood loss, or when given as a drug, erythropoietin enhances red-cell production in the bone marrow. But just how it works has remained unclear.

Now, hematologists at Vanderbilt University Medical Center in Nashville provide evidence that erythropoietin works not by initiating new red-cell production but by preventing the "programmed death" of very young red cells in bone marrow.

Mark J. Koury and Maurice Bondurant used a unique system of cultured, immature red blood cells from mice, which mimics conditions in the bone marrow. Their research indicates that many of the billions of red-cell precursors produced in marrow every day are systematically destroyed before they develop into mature cells. At high enough levels, erythropoietin grants many of these precursor cells a stay of execution, enabling them to complete their marrow-based maturation and to take jobs as oxygen transporters in the circulatory system.

Their model suggests that red cells not granted an erythropoietin reprieve are especially susceptible to having their DNA digested by an enzymatic executioner or are impaired in their ability to repair damaged DNA. Since the erythropoietin protects cells already several days into their development, a surge of the hormone can boost the number of circulating cells more rapidly than would be possible if it exerted its influence at the very first stages of red-cell production.

An understanding of the mechanisms by which erythropoietin prevents DNA digestion or enhances DNA repair may lead to new therapies for anemias caused by vitamin deficiencies, toxic drugs or radiation therapies, Koury says. Details appear in the April 20 SCIENCE.

Cancer-fighting cell receptor cloned

Researchers have deciphered the genetic code for a receptor molecule that serves as the docking site for a naturally occurring cancer-fighting compound. The achievement may help explain why treatment with the compound, called tumor necrosis factor (TNF), has yielded inconsistent results in cancer patients, and may lead to improved cancer therapies, the researchers say.

Produced in small quantities by white blood cells, TNF can directly attack tumor cells and can activate other immune-system cells to attack cancerous tissues. But when physicians give high doses to cancer patients, TNF sometimes helps, sometimes has no effect, and sometimes induces severe side effects.

The key differences between TNF's good and bad sides may become clear with a better understanding of the compound's receptor, says Gale Granger of the University of California, Irvine, who led the effort to clone the TNF receptor.

While TNF receptors normally reside on the membranes of white blood cells, some cancer patients have circulating versions of the receptor in their blood. Grange suggests that these soluble receptors may "mop up" therapeutic doses of the drug before it gets to its tumorous target. Knowledge gained from cloning the receptor may someday enable physicians to "get rid of the circulating receptors first, give the TNF [to a cancer patient], then add more receptors" to sop up any excess that could cause side effects, he says. Moreover, further analysis of the receptor's structure may reveal details about how it functions, providing an opportunity to modify its activity, the researchers assert in the April 20 CELL.

Earth Sciences

Termites not to blame for methane

As concern builds over the threat of global warming, scientists are trying to understand why atmospheric levels of methane, a greenhouse gas, have more than doubled in the last two centuries. Researchers in the early 1980s suggested termites may deserve partial blame for the increase, but a comprehensive study downplays their role.

"Although the uncertainties are still very large, the weight of the scientific evidence is shifting toward the conclusion that termites are not an important global source of methane," report M. Aslam K. Khalil and R. A. Rasmussen at the Oregon Graduate Center in Beaverton along with Australian colleagues. They describe their work in the March 20 JOURNAL OF GEOPHYSICAL RESEARCH.

The researchers measured gases emitted by six termite species in Australia and reviewed the published data concerning how much food termites consume. They estimate termites worldwide emit about 12×10^{12} grams per year of methane, which amounts to about 2 percent of the methane released by all global sources each year. This number agrees with results from lab measurements and a field study in Africa.

In 1982, researchers from the National Center for Atmospheric Research in Boulder, Colo., sparked the debate over termites when they reported estimates based on laboratory work that termites emit 150×10^{12} grams each year, which would constitute about 30 percent of the world's annual methane emissions. They also suggested that human activities such as deforestation have boosted termite populations, which could explain part of the rise in methane concentrations.

Khalil says the earlier study overestimated the amount of food consumed by termites each year and did not take into account methane absorption by the ground near their mounds, a fact discovered only during field experiments. According to Khalil, the methane buildup in the atmosphere stems not from a population explosion in termites but from increasing numbers of rice fields, cattle and sheep.

Cuba proposed site for K/T impact

The asteroid or comet that purportedly snuffed out the last remaining dinosaurs some 65 million years ago may have slammed into the Earth just south of Cuba, according to speculations by two scientists. Since 1979, when researchers first raised the impact theory, a number of investigators have proposed locations in Iowa, the Indian Ocean and elsewhere as possible sites for the impact at the boundary between the Cretaceous and Tertiary (K/T) periods. Recent work, however, has pointed to the Caribbean region, report Bruce F. Bohor of the U.S. Geological Survey in Denver and Russell Seitz of Cambridge, Mass., in a letter published in the April 12 NATURE.

Bohor and others have long proposed that the impact occurred in the vicinity of North America, because the largest pieces of "shocked" mineral grains — apparently from the impact — appear on that continent. The Caribbean attracted attention as a possible site last year after Alan Hildebrand and William V. Boynton of the University of Arizona in Tucson discovered an unusually thick K/T sediment layer in Haiti containing pieces of glassy stone chips, often taken as evidence of an impact. This evidence led Hildebrand and Boynton to propose an impact off the coast of Colombia.

After studying geologic reports written in the 1930s and 1940s, however, Bohor and Seitz speculate the extraterrestrial body hit south of western Cuba. The K/T boundary layer on Cuba contains huge boulders that may have been ejected from a nearby crater. They suggest the Isle of Pines just south of Cuba might be uplifted rock, often seen in the center of impact craters. Diplomatic problems have so far stymied efforts to test the Cuba hypothesis, Bohor says.