Hormone links malnutrition and immunity

When scientists first described leptin in 1995, they told a simple story: The hormone, secreted by fat cells into the blood, travels to the brain, where it signals how much energy the body has stored, and so leptin regulates appetite.

Leptin does more than just talk to the brain, however. In the Aug. 27 NATURE, researchers report that certain immune cells respond to the hormone. Its effects on the immune system may help explain why malnourished people are so vulnerable to infectious diseases.

Robert I. Lechler of Imperial College School of Medicine in London and his colleagues recently began to wonder whether leptin influences the activity of immune cells. "The logic behind the question was the long-established link between malnutrition and immunodeficiency," explains Lechler. At the other extreme, he adds, mice that are obese because of an inability to make leptin or to respond to it also possess an impaired immune system.

In initial test-tube experiments, the researchers found that leptin increases the ability of helper T cells, one class of immune cells, to proliferate after being stimulated into activity. The scientists then established that such cells indeed have leptin receptors, surface proteins that allow a cell to respond to the hormone.

Further experiments by Lechler's group suggested that leptin modifies the type of response the helper T cells make. Leptin encouraged helper T cells to make a so-called Th1 response, marked by secretion of chemicals such as interleukin-2 and interferon-gamma, rather than a Th2 response, which releases other interleukins.

Through the chemicals they secrete, helper T cells guide the actions of the immune system. For example, they may rally immune cells that fight off viruses or instead summon cells that defend against fungi and various bacteria.

To confirm that the test-tube experiments reflect a true immunological role for leptin, the scientists also studied the hormone's influence on the immune system in live mice. When mice are starved for 48 hours, which significantly reduces the amount of leptin in their blood, their T cells normally become much less responsive. Yet when the researchers administered leptin to mice while depriving them of food, the animals showed no T-cell impairment, even though they still lost weight.

Why would a hormone secreted primarily by fat cells regulate the immune system? "The best model of how leptin works is that it is a signal of starvation or malnutrition so that [the body knows when to] shut down energy-expensive functions," notes Lechler. For example, women with little body fat, such as marathon runners and ballet dancers, often cease their menstrual cycles, apparently because the body has interpreted the lack of leptin as a signal to avoid reproduction. Similarly, Lechler speculates, falling leptin concentrations in the blood may instruct the body to suspend temporarily the actions of the immune system.

The researchers are now testing whether administration of leptin can prevent malnourished mice from suffering an increased rate of infections. The results might indicate whether leptin could serve as an immune system booster for low-birthweight babies or people with AIDS or cancer, who often experience a wasting syndrome.

Ranjit K. Chandra of the Memorial University of Newfoundland in St. John's, who studies the impact of nutrition on the immune system, notes that nutritional disorders such as malnutrition bring about extensive metabolic and hormonal changes. "It's unlikely that a single one would be the key to all the immunological problems," he cautions.

"I wouldn't go so far as to say that [leptin] is likely to explain the entire immune collapse that occurs in patients who are severely malnourished, but it may be the biggest element," comments immunologist Terry B. Strom of Beth Israel Deaconess Medical Center in Boston. —*J. Travis*

Any Mars life would be hard to find

Some researchers propose that life on Earth first evolved in warm environments such as hot springs and deep thermal vents. According to this theory, where there's heat and water there may be life.

Now, a study indicates that Mars' geophysical heat could have supported the development of a modest population of microorganisms over its 4-billion-year history. Those microbes may be so scarce, however, that a mission to sample Martian soil could easily miss them or their remains, report geochemists Bruce M. Jakosky of the University of Colorado at Boulder and Everett L. Shock of Washington University in St. Louis.

Mars could have produced, at most, a planetwide average of 20 grams of microorganisms per square centimeter during its entire history, Jakosky and Shock calculate. Jakosky says, however, that most of that biomass would have decayed away.

Their study, described in the Aug. 25 JOURNAL OF GEOPHYSICAL RESEARCH, offers the first quantitative estimate of Martian biomass, says Kenneth H. Nealson of NASA's Jet Propulsion Laboratory (JPL) in Pasadena, Calif. "This puts in quantitative terms what biologists felt intuitively," Nealson says. "This is a very clever paper."

The study also bolsters previous arguments by biologists that expeditions should target thermally active areas of Mars to seek evidence of life, he says (SN: 11/1/97, p. 284). About half of the biomass would have derived its energy from hydrothermal vents, the report estimates. The authors suggest that oxidation of iron at the planet surface and underground could have provided sufficient energy to produce the remaining biomass.

Although scientists have not yet found conclusive proof of hydrothermal activity on Mars, Jakosky and Shock argue that it would have accompanied volcanism, which has occurred on the planet. Because there has been less volcanic activity on Mars than on Earth, they conclude that Mars must have generated proportionately less hydrothermal energy.

Considering only biomass produced by geophysical processes, Jakosky and Shock suggest that Mars could have produced only one-fortieth the quantity of life estimated on Earth. Since Earth also supports life through photosynthesis, which may not occur on Mars, Earth's total biomass througthout its history could easily be more than 4 million times that of Mars, they say.

Jakosky concedes that the study relies on the conjecture that Mars' little-understood geology has similarities to Earth's.That represents "a big assumption," says Jonathan I. Lunine, a planetary scientist at the University of Arizona in Tucson. Mars may lack adequate amounts of many trace elements, such as phosphorus, necessary to sustain life on Earth, he suggests.

"It's not clear whether life can exist without phosphorus, but it's not clear that it's impossible, either," Jakosky responds. However, without geophysical energy, "you're stuck," he says.

The new study also speculates that any microbial life on Europa, a moon of Jupiter, would be even more rare than on Mars. Scientists suspect that an ocean that may contain life exists beneath that moon's frozen surface and have discussed sending a robotic probe to find out (SN: 7/6/96, p. 8).

The amount of life possible on Europa may be especially small because that moon may lack volcanic activity, the report says. If microbes must be sustained by oxidizing reactions alone, too few would be released into the ocean to be detectable by a probe, Jakosky speculates. —*J. Brainard*