MS researchers find missing immune link

New research shows that people with multiple sclerosis (MS) have immune cells that react with myelin basic protein, a key component of the protective sheaths surrounding nerve fibers in the brain and spinal cord. The finding raises the possibility that researchers may one day devise better treatment strategies for patients with this neurologic disease.

Other researchers had previously implicated myelin basic protein in the development of a neurologic disease in mice. They discovered that injecting healthy mice with the protein caused the mice to develop a central nervous system disorder similar to MS. Although the connection between myelin basic protein and the MS-like disease in mice was clear, researchers were unable to implicate the protein and the immune system in the development of human MS.

Now, Mark Allegretta, Subramaniam Sriram and their colleagues at the University of Vermont in Burlington report in the Feb. 9 SCIENCE that their clones of certain immune cells called T-lymphocytes (T-cells) obtained from the blood of MS patients indeed react to myelin basic protein. Scientists believe these T-cells proliferate in response to the protein and release substances that damage myelin. This, in turn, short-circuits electrical messages sent from the central nervous system to the rest of the body.

Other research teams had sought such activated T-cells in the blood of MS patients but failed because their methods weren't sensitive enough to find the few T-cells that respond to myelin basic protein, Allegretta says. Rather than examine all T-cells in the blood, the Vermont team studied those that had undergone a genetic mutation – often a sign of recent cell division. Focusing on this subset narrowed the search, because T-cells are believed to divide in response to myelin basic protein.

When they exposed the mutant cells to myelin basic protein in the laboratory, the researchers observed that cell division began in 11 of 258 cells derived from the blood of five of the six MS patients in their study. This suggests that these T-cells react to the protein in the body as well, they say. In contrast, none of the T-cells taken from healthy controls responded to the protein.

The new findings may help point the way to a therapy specifically designed to block the body's immune response to myelin basic protein, comments David A. Hafler at Harvard Medical School in Boston. Such a treatment, if given early in the course of the disease, might halt the progressive myelin destruction and prevent the disabling symptoms of MS, he says. – *K.A. Fackelmann*

Additional human gene transfers sought

Presenting evidence that the first U.S.-approved infusions of gene-altered cells into humans have triggered no ill effects in the six cancer patients treated so far, federal researchers this week asked an advisory panel to speed permission for expanded use of the experimental procedure. But the specter of biotech gadfly Jeremy Rifkin stalled approval of the request, forcing the researchers to delay expanded testing until at least April.

Several members of the Recombinant DNA Advisory Committee, which advises the National Institutes of Health on experiments involving genetic engineering, expressed support for the request. But committee members balked at an immediate okay, noting that Rifkin (president of the Washington, D.C.-based Foundation on Economic Trends) had sued NIH the last time they tried to expedite the approval process. Instead, they agreed to meet on March 30 – three months ahead of schedule – in a joint session with the NIH subcommittee that shares responsibility for such decisions, in hopes of resolving the issue then.

The experiments, led by NIH researchers W. French Anderson, Steven A. Rosenberg and R. Michael Blaese, are designed to track the movements and activities of genetically labeled cancer-fighting lymphocytes used in an experimental treatment in melanoma patients (SN: 5/27/89, p.324). The researchers say they will soon infuse four more patients, in keeping with a 1989 protocol granting them permission to administer the labeled cells to 10 terminally ill patients. But they express frustration that NIH guidelines might require them to wait six months or more to gain approval for additional trials, halting the experiments just when data have begun to accumulate.

Rosenberg reports that the engineered cells survive three weeks to two months in circulating blood and more than seven weeks in some tumors. In one patient, the researchers removed some of the gene-altered cells that had homed in on a tumor, then expanded this population in the laboratory and reinjected the cells into the patient. That patient, like several others in the study, has shown "dramatic" improvement, Rosenberg says. However, he adds, the researchers cannot perform the biological and statistical analyses required to understand and enhance those effects unless more patients receive the treatment. – *R. Weiss*

Artificial life: Stepping closer to reality

Creating synthetic life may not require miracles. This week, at the second Artificial Life Conference in Santa Fe, N.M., hundreds of investigators reported on computer, chemical, mathematical and robotic systems that behave somewhat like slime molds, ants, growing plants, sea animals and networks of biochemicals. They say their efforts could spawn insights into natural life, how life began on Earth and even life as we haven't yet known it.

Two unproved assumptions underlie this embryonic field, says physicist and conference organizer Christopher Langton of Los Alamos (N.M.) National Laboratory. One is that "life" refers more to the *organization* of matter than to any particular *kind* of matter. The other is that it's possible to create artificial systems that display living behavior by abstracting the operational principles and functional relationships of the parts of living organisms and recapturing these within other media – even nonbiological systems such as computers or novel sets of chemicals.

Just as computer simulation has opened a new brand of research especially suited for probing complex phenomena such as atmospheric chemistry and human intelligence, artificial life could open up powerful new ways of investigating what makes real living things tick, Langton says.

In a written statement, he and other organizers envision still other far-reaching discoveries: "By extending the empirical foundations upon which biology is based beyond the carbon-chain life that has evolved on Earth, Artificial Life can contribute to theoretical biology by locating life-as-we-know-it within the larger context of life-as-it-could-be."

Many of the studies described at the meeting involve a class of computer programs known as cellular automata. For a sense of how these work, imagine a computer monitor displaying a grid of cells that resembles an unworked crossword puzzle. Then fill in or empty the cells according to rules derived from the states of nearby cells. After repeating this exercise a number of times, sometimes according to rules that change with the evolving patterns of light and dark cells, you begin to see lifelike shapes, movements and interactions unfolding on the monitor. Researchers admit that even the most sophisticated cellular automata don't qualify as life, but they say these simulations of synthetic life may hold clues to real living things – and perhaps to some artificial ones that await creation. – *I. Amato*