Arthritis: Looking for Immunotherapy

Preliminary results released last week may offer a better alternative to current treatments for rheumatoid arthritis, many of which either treat specific symptoms or affect the entire immune system. Concentrating on specific elements of the abnormal immune response that characterizes the disease, scientists are reaching into biotechnology's bag of tricks to develop immunotherapy techniques.

Rheumatoid arthritis, which primarily strikes middle-aged women, is a crippling disease affecting 7 million people in the United States. This severe form of arthritis not only affects bone joints but can also spread to body organs. Although the exact cause of the disease remains unknown, individual cases of rheumatoid arthritis are apparently due to one or more factors thought to include genetic predisposition and viruses.

Whatever initiates the disease, it is the immune system's inappropriate response – by attacking the body's own cartilage and joint linings – that brings about the characteristic symptoms. This autoimmune response has caught the attention of scientists seeking replacements for the standard treatment, regimens of ingestible gold or anti-inflammatory drugs (SN: 10/19/85, p.244). Tinkering with the immune system was the focus of several preliminary research projects reported at last week's annual meeting in Washington, D.C., of the Federation of American Societies for Experimental Biology.

At Case Western Reserve University in Cleveland, Thomas F. Kresina and his coworkers are using a common animal model of arthritis to study the effect of so-called hybridomas on the disease. When collagen (the tough structural protein of cartilage) from another species is injected into certain strains of mice, the mice produce anticollagen antibodies, which eventually destroy the joints and cause collagen-induced arthritis. However, if mice are given collagen from their own species prior to immunization with foreign collagen, they become resistant to collagen-induced arthritis. Researchers can pass the resistance from animal to animal by cell transfer.

Taking advantage of this resistance, Kresina's group created hybridomas by fusing a strain of cancer cells with spleen cells from resistant animals, thereby making a cell line that multiplies indefinitely (thanks to the cancer cells) and suppresses collagen-induced arthritis. According to Kresina, injection of hybridoma cells into 13 mice with the disease resulted in reduced hind-paw redness and swelling in six of the mice. Nonhybridoma cells used as a control did not suppress arthritis in 10 of 11 mice tested.

One month after injection of nonhybridoma cells into the arthritic control mice, foot swelling remained at an average of 40 percent above that found in nonarthritic mice, and in some cases it even increased. Yet in the hybridoma-treated animals, swelling had decreased to an average of 8 percent above normal. Microscopic examination of joint tissue supported the findings that arthritic mice were helped by hybridoma treatment, says Kresina.

Because injection of cancer cells is ultimately an unacceptable treatment, the Case Western group is exploring ways to kill the cells prior to injection. Another probable drawback, explains Kresina, is that the human body, recognizing mouse cells as foreign, may reject them before any benefit occurs.

Using a variation of the same test system, scientists at the University of Tennessee in Memphis have treated nonarthritic mice with spleen and thymus cells from resistant mice in an attempt to prevent the onset of collagen-induced arthritis. Compared with mice that did not receive resistant cells, the cell-treated mice developed much less severe arthritis at a slower rate after both groups were later immunized with collagen, according to Linda K. Myers.

In a parallel study, Myers has separated a small subpopulation of spleen cells that may be responsible for the resistance. She told SCIENCE NEWS that these cells could be the same as those used by Kresina to make hybridomas. Myers and Kresina agree that much remains to be learned about the process leading to resistance, but that the significance of the resistance-inducing cell may be its production of a soluble factor that could be used in arthritis treatment. Both groups are searching for such a factor.

Taking a narrower approach to treatment of collagen-induced arthritis, scientists at the Mayo Clinic in Rochester, Minn., and the VA Medical Center in Memphis are targeting the T-cell lymphocyte in attempts to stop the production of anticollagen antibodies. Because a T cell, when activated by exposure to collagen, aids in the production of anticollagen antibody by B-cell lymphocytes, these researchers are using antibodies against receptors on the T-cell surface, according to Mayo's Subhashis Banerjee. He says the onset of arthritis took two weeks longer in the receptor-antibody-treated mice than in mice not given the blocking antibody.

When arthritis does appear, it is less severe than that seen in mice not treated with the antireceptor antibody. As in other studies of collagen-induced arthritis in mice, the progression of arthritis was measured on the basis of paw swelling, joint deformity and whether joints were immobile.

Treatment, however, did not prevent the disease. "All we did was delay the onset and reduce the severity," says Banerjee, who adds that the next step will be to increase the dose of blocking antibody.

Whether data from an animal model of rheumatoid arthritis can be extrapolated to the human patient remains controversial. Nonetheless, although the results are preliminary and the numbers of animals tested are small, the current studies mark a possible advance in arthritis immunotherapy over previous studies using immunosuppressant drugs and radiation (SN: 4/20/85, p.246). As Kresina points out, these approaches are aimed at halting a specific component of the immune response, rather than general suppression with its possible adverse side effects. *– D.D. Edwards*

Marvelous mystery cosmic radiation

Over the decades, accelerator laboratories and cosmic radiation have tended to alternate as arenas in which new high-energy particle physics phenomena have been discovered. Right now, after a long stretch of time in which particle physics news usually came from accelerators, the cosmic rays are coming up with unusual effects. One of the most spectacular and controversial of these are what Gaurang Yodh of the University of Maryland in College Park calls "Marvin's marvelous muons." Now Yodh is adding a few unusual muons of his own.

Marvin is Marvin Marshak of the University of Minnesota in Minneapolis, and the muons are particles that he and colleagues have been finding in a detector called Soudan buried deep in a mine in northern Minnesota (SN: 1/3/87, p.8). Presumably these muons are produced in the detector by some highly energetic, extremely penetrating radiation that comes from certain sources in the sky – Cygnus X-3 and Hercules X-1 are among those implicated – and can penetrate the earth's atmosphere and several thousand feet of rock to reach the detector.

The existence of these strange, unidentified rays – which have been called cygnets because they were first seen coming from the direction of Cygnus X-3 – has been variously supported, denied and maybe-ed by other underground