Engineered rats reveal arthritic surprise

Texas researchers report developing the first animal model for a group of debilitating arthritic diseases that afflict an estimated 200,000 people in the United States. Their work with the genetically engineered rats adds to the growing evidence that a specific human gene may trigger an autoimmune response that causes these painful and poorly understood disorders, collectively known as the spondyloarthropathies.

"This is a remarkable scientific advance," says Lawrence E. Shulman, director of the National Institute of Arthritis and Musculoskeletal and Skin Diseases in Bethesda, Md.

Biologist Peter Parham at Stanford University calls the report a "landmark" that may help scientists uncover the mechanism causing these inflammatory diseases – which include, among others, ankylosing spondylitis (fusion of spinal bones), an arthritis associated with the skin disorder psoriasis, and an arthritis accompanied by bowel inflammation. An understanding of how such conditions develop in humans might someday lead to more effective therapies, and perhaps even to preventive treatment.

In 1973, U.S. and British scientists separately reported that 90 percent of people with ankylosing spondylitis carry a gene called HLA-B27, which affects immune system regulation. Soon after, other researchers found that people with other spondyloarthropathies are more likely than the general population to carry HLA-B27. However, many scientists viewed the gene as a red flag marking people at risk, rather than an active player in the development of disease.

Now, Robert E. Hammer and Joel D. Taurog at the University of Texas Southwestern Medical Center in Dallas say their findings suggest that HLA-B27 contributes directly to these disorders.

Hammer and Taurog created several lines of "transgenic" rats by injecting a batch of fertilized rat eggs with HLA-B27 and a second gene that joins forces with B27 to code for a specific protein product. After two to six months, they noted that some of the rats developed the same symptoms seen in the human spondyloarthropathies, including persistent diarrhea, joint inflammation and changes in the skin and nails. Control rats without the human genes remained healthy, the team reports in the Nov. 30 CELL.

The results surprised the investigators, who had spent years trying to develop such an animal model.

"It's as if the things that one sees in a spectrum of patients are compressed and are more dramatic in the rats," Taurog told SCIENCE NEWS. Shulman calls the thickening and scaling of rat skin and nails a particularly striking symptom that closely resembles problems afflicting people with psoriatic arthritis.

The spontaneous development of the disorder as the rats matured hinted that the HLA-B27 gene or its protein product contributes directly to the disease process, perhaps by triggering an abnormal immune response, Parham says. He and others believe the spondyloarthropathies arise when infection-fighting white cells mistakenly attack joints and other tissues.

Taurog speculates that people who inherit HLA-B27 may run an increased risk of developing these diseases after exposure to an environmental trigger, such as a common bacterium. For example, normal intestinal bacteria may have sparked the symptoms seen in the HLA-B27 rats, he says.

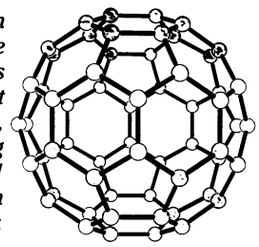
He adds, however, that the team has yet to prove HLA-B27's guilt. Jack Strominger of Harvard University agrees. "There's no evidence in the paper that HLA-B27 specifically caused the rat symptoms, which could erupt with the insertion of another HLA gene," he says.

Taurog says further research must erase such doubts before scientists can proceed with the urgent work of preventing these potentially crippling disorders.

– K.A. Fackelmann

Buckeyballs get their first major physical

For eight hours last week, a hotel ballroom in Boston percolated with excitement as materials researchers from around the world shared their hot-off-the-bench discoveries about fullerenes – beautifully symmetric molecules they've been finding in soot.



Sixty carbon atoms arrange into the world's smallest soccerball, measuring about 7.1 angstroms in diameter.

UCLA

This new class of materials joins diamond, with its tetrahedral arrangement of atoms, and graphite, whose structure resembles layers of chicken wire, to become the third known form of carbon. At last week's meeting of the Materials Research Society, the fullerene-of-honor was a 60-carbon (C_{60}) molecule known as a buckeyball or Buckminsterfullerene (SN: 1/28/89, p.56). Its extremely stable, soccerball-shaped configuration, echoing Buckminster Fuller's geodesic domes, has 12 pentagonal and 20 hexagonal sides.

Like zoologists studying a newly discovered animal, materials scientists are probing how these new carbon species behave as individual molecules, as crystalline films and in the presence of other chemical species. By poking and prodding their specimens with lasers and electrodes, researchers are learning about the bonds linking a fullerene's atoms and the amount of energy needed to pull electrons away from them. With scanning tunneling microscopes, some investigators have even sneaked tantalizing peeks at what appear to be individual spheres of different sizes – presumably C_{60} and C_{70} fullerenes. Others have tried studding the C_{60} buckeyballs with hydrogen atoms or trapping metal ions inside them.

Most of the work described last week was inspired by a report in the Sept. 27 NATURE (SN: 10/13/90, p.238). In that paper, a team led by Donald R. Huffman of the University of Arizona in Tucson and Wolfgang Krätschmer of the Max Planck Institute in Heidelberg, Germany, showed that making molecular soccerballs takes little more than a vacuum chamber, one or two heated graphite rods, and a brush to help collect the fullerene-ridden soot that deposits on chamber surfaces.

Although much of the new research has focused on buckeyballs, scientists at the Boston meeting also shared observations of more oddly shaped C_{70} and C_{84} fullerenes. And gargantuan fullerenes with 240, 540 or more carbon atoms may be in the offing, notes Harold W. Kroto of the University of Sussex in Brighton, England.

In 1988, Kroto and his colleagues suggested that scientists might create huge all-carbon structures, including some that spiral around a core to ultimately resemble a nautilus shell. "I don't have any doubt that people will make these objects," Kroto reiterated last week. "It's early days yet."

Conference participants agree that it's too early to predict the eventual uses of fullerenes. Like graphite, the new materials might serve as lubricants; like diamond, they might provide superhard coatings. Although Defense Department researchers say their early tests indicate C_{60} may not measure up as a rocket fuel, other scientists report signs that C_{60} has the electrical properties of a semiconductor.

"I'm staggered by the wealth of talent that so quickly has been brought to bear on this topic," Huffman told SCIENCE NEWS. Already, he says, fullerene research has demonstrated that new phenomena await discovery, that important science doesn't have to cost much, and that science is fun.

– I. Amato