News
Office of Medical Information
The University of Texas Southwestern Medical Center at Dallas
5323 Harry Hines Boulevard Dallas, Texas 75235-9060 214/688-3404

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CONTACT: Tommy Bosler
Home: 214/327-1773
Office: 214/688-3404

****NIH funds Specialized Center of Research
at UT Southwestern Medical Center

DALLAS -- A national Specialized Center of Research (SCOR) for rheumatoid arthritis will be located at The University of Texas Southwestern Medical Center at Dallas. The SCOR will be funded at $3 million over five years by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), one of the National Institutes of Health.

Dr. Peter Lipsky, chief of the Rheumatic Diseases Unit in the Department of Internal Medicine at Southwestern Medical School, will head the rheumatoid arthritis SCOR here. Lipsky is a professor of internal medicine and microbiology and co-director of the Immunology Graduate Program. He also directs the Simmons Arthritis Research Center at UT Southwestern, a major center for basic scientific research into inflammatory arthritis.

In 1983 the Harold C. Simmons Arthritis Research Center was established and named for the Dallas entrepreneur who pledged $8 million to fund it over a ten-year period. In 1987 he gave another $2 million to build new 10,000-square-foot laboratories for the center in the Green Biomedical Research Building.

The Simmons Center's research concentrates on a type of inflammatory arthritis called ankylosing spondylitis, which affects the spine. The new SCOR will concentrate on rheumatoid arthritis, which causes inflammation of the peripheral joints.

"The awarding of the SCOR in arthritis is another indication of the excellence of the research being done by Dr. Lipsky and his colleagues," said Dr. Kern Wildenthal, president of UT Southwestern.

"The combination of the Harold C. Simmons Arthritis Research Center and the SCOR for rheumatoid arthritis places UT Southwestern in the forefront of state-of-the-art research in a broad spectrum of arthritis problems. It also demonstrates the leverage that private funding can provide. The support of Harold Simmons was a catalyst for developing greater strength in arthritis research and this, in turn, made us even more competitive for these highly sought NIH funds," Wildenthal added.

"Although there are major differences in the two types of arthritis, there are certain similarities," explained Lipsky. "Both have a genetic component, and in both the immune system seems to be abnormal so that, rather than acting as the body's defense mechanism, it damages cell tissue. In ankylosing spondylitis there is an environmental trigger, a bacterium, that triggers the disease in genetically susceptible individuals. In rheumatoid arthritis, we really don't know what the environmental trigger is, but certain evidence suggests that it might be a virus."

Although the two research centers are separate, the scientists involved in the research will overlap. In addition, similar research tools will be used -- the latest technology in cellular immunology and molecular genetics.

Rheumatoid arthritis is a chronic inflammatory disease that affects more than two million Americans, almost twice as many women as men. The primary target of this disorder is the synovium or joint lining. This tissue, which normally is smooth and shiny, becomes inflamed, painful and swollen. The synovial fluid, which cushions the joints, also teems with auto-immune factors that promote inflammation. Eventually the inflammation damages cartilage and bone. It can produce general symptoms such as weakness, fatigue and loss of appetite, and it can affect other parts of the body such as blood vessels.

(More)

"What we think happens is that a virus, or perhaps a damaged cell protein, stimulates the entry of inflammatory cells into the synovial tissue," said Lipsky. "Those inflammatory cells release a variety of factors that lead to a cascade of events causing the various features of rheumatoid arthritis: an effusion of fluid in the synovial space, a proliferation of synovial cells, cartilage and bone damage and all the systemic symptoms of the disease.

"We probably understand more about the progression of rheumatoid arthritis than of most other diseases. We don't know what starts it and why it doesn't get better, why it doesn't resolve. We will examine the regulation of all these pathways and try to understand why they are persistently triggered and why they cause all this damage."

Some of the researchers who will be working on rheumatoid arthritis are:

*Dr. Peter Stastny was the first scientist to associate the genetic marker HLA-DR4 with rheumatoid arthritis. People who have that particular gene product seem to be at great risk of developing rheumatoid arthritis. After Stastny described the connection, it was confirmed everywhere, said Lipsky.

Stastny will now examine the nature of the genes that control rheumatoid factor, an auto-antibody produced in the course of the disease. An auto-antibody attacks the patient's own body as it would a foreign invader.

*Dr. J. Donald Capra is also analyzing the nature of the genes that control not only the production of rheumatoid factor but also the production of a variety of other auto-antibodies in patients with rheumatoid arthritis.

*Dr. Joel Taurog is involved in developing new animal models of rheumatoid arthritis. Although a number of animals are used, none of them is a very precise model because they can mimic only certain features of the disease. Taurog has been instrumental in developing an animal model that appears promising for ankylosing spondylitis. He will also try to analyze in detail the pathway or sequence of events that leads to the development of inflammatory arthritis.

*Dr. Alan Duby is determining whether the lymphocytes that congregate in the synovial tissue are specific for a given antibody, antigen or foreign material. Duby has isolated and cloned a number of the lymphocytes and will study the genes of the lymphocytes' receptors that recognize foreign substances. Since each receptor is unique and reacts to a specific substance, the presence of a number of lymphocytes with identical receptors may help identify the virus or other foreign trigger that initiates the whole process.

*Dr. Lipsky and others in his lab are involved in a detailed analysis of the immunologic processes that drive rheumatoid arthritis.

*Finally, a number of individuals in the Rheumatology Division are involved in analyzing the effects of drugs on the immune functions of patients with rheumatoid arthritis to determine which treatments are best at various stages in the disease. The drugs being tested include gold compounds, penicillamine, antimalarial drugs, monoclonal antibodies and a variety of other drugs in use today.

Lipsky explained, "For most of these drugs, the use is, unfortunately, empiric. We give it for a year, and if it works, great. And if it doesn't, we haven't learned anything. We want to understand who is likely to respond and how they will respond."

The SCOR for rheumatoid arthritis at UT Southwestern is one of three being created as part of a new program by NIAMS. The others are located at Duke University in Durham, N.C, and the University of Tennessee at Memphis. In addition to the research centers on rheumatoid arthritis, NIAMS has created three SCORs to deal with osteoarthritis (degenerative joint disease) and three to study osteoporosis. Each center will be funded for five years. NIAMS will spend $7.7 million the first year on the SCOR programs.

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