

Researchers discover specific inhibitor for rheumatoid arthritis treatment

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Collaborating with researchers from the Northwestern University Feinberg School of Medicine in Chicago, a research team at Wayne State University's School of Medicine led by Kezhong Zhang, Ph.D., has contributed to an important discovery in the inflammatory stress mechanism and specific inhibitor for the treatment of rheumatoid arthritis.

The team led by Zhang, associate professor of immunology and microbiology and Wayne State's Center for Molecular Medicine and Genetics, and the team led by Deyu Fang, Ph.D., associate professor of pathology at Northwestern University Feinberg School of Medicine, worked together to discover the key inflammatory stress response that drives the development of rheumatoid arthritis. Their studies revealed that inflammatory stimuli trigger cell surface toll-like receptors of macrophages, the white blood cells that subsequently activate the Unfolded Protein Response transducer IRE1a to promote arthritis syndrome in the tissues around the joints.

Their work identified a specific IRE1a inhibitor that can efficiently prevent arthritis in animal models.

The study, "Toll-like receptor-mediated IRE1a activation as a therapeutic target for [inflammatory arthritis](#)," was published in the prestigious scientific journal *EMBO*. Zhang served as a corresponding author.

"This is a notable work in the understanding of the stress mechanism for the development of [rheumatoid arthritis](#)," Zhang said. "For the first time, we revealed the molecular targets of Unfolded Protein Response and Toll-like Receptor signaling and their interaction mechanism in the progression of inflammatory arthritis. Our study not only identified previously unknown molecular targets, but also pointed out a specific inhibitor that can efficiently suppress arthritis."

Dr. Zhang said the next step toward the development of therapeutics may be testing the effects of specific inhibitors of Unfolded Protein Response in curing inflammatory arthritis with animal models and clinical trials.

Rheumatoid arthritis is an autoimmune disease that causes a chronic, systemic inflammatory disorder that can affect many tissues and organs, but principally flexible joints. Rheumatoid arthritis is one of the most common rheumatic diseases, affecting approximately 1.3 million people in the United States. The disease is three times more common in women than in men and afflicts people of all races. The disease can begin at any age, but it often occurs in adults between the ages of 40 and 60. The cause is unknown.

The disease is a costly one for the nation. According to the Arthritis Foundation, [arthritis](#) and rheumatic conditions cost the U.S. economy \$128 billion annually, including \$80.8 billion in medical expenditures and \$47 billion in lost earnings.

More information: www.nature.com/emboj/journal/v.../emboj2013183a.html

Provided by Wayne State University

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