

CSIR-CDRI Discovers Peptide Effective in Fighting Rheumatoid Arthritis

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Group Photo : L-R: Chirag Kulkarni, Naibedya Chattopadhyay, Yasir Khan, Mahesh Tiwari and Geet K. Nagar

RHEUMATOID arthritis is an inflammatory disease that affects the joints in the human body. It is the most common type of autoimmune disease. Rheumatoid arthritis causes swelling and pain in and around the joints. Most commonly, it affects the hand and foot and then elbow, shoulders, neck, jaw, ankles, knee and hips.

Due to rheumatoid arthritis, the cartilaginous protective cover between the joint bones is severely degraded followed by the erosion of the joint bones. Several studies show that approximately one per cent of the human population is living with rheumatoid arthritis globally and it is one of the leading causes of disability.

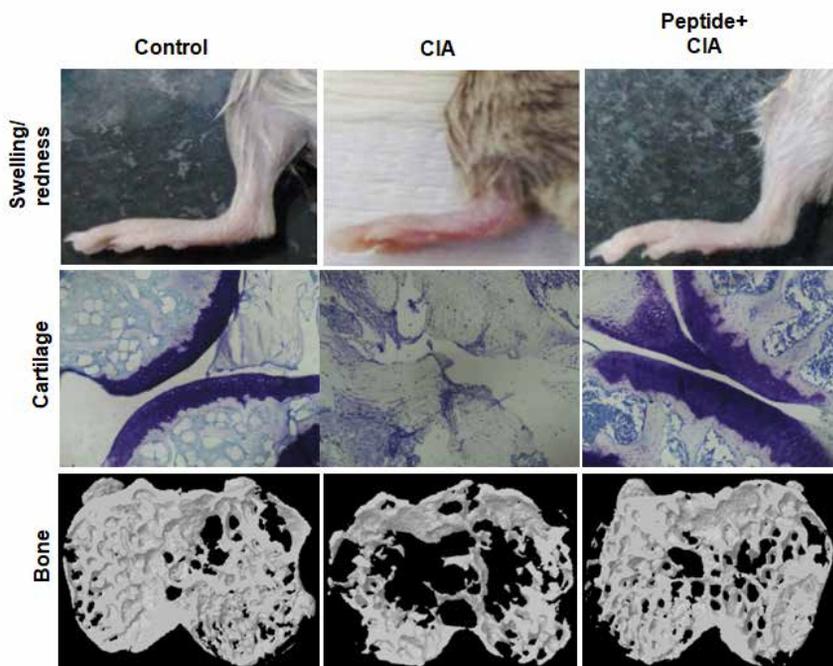
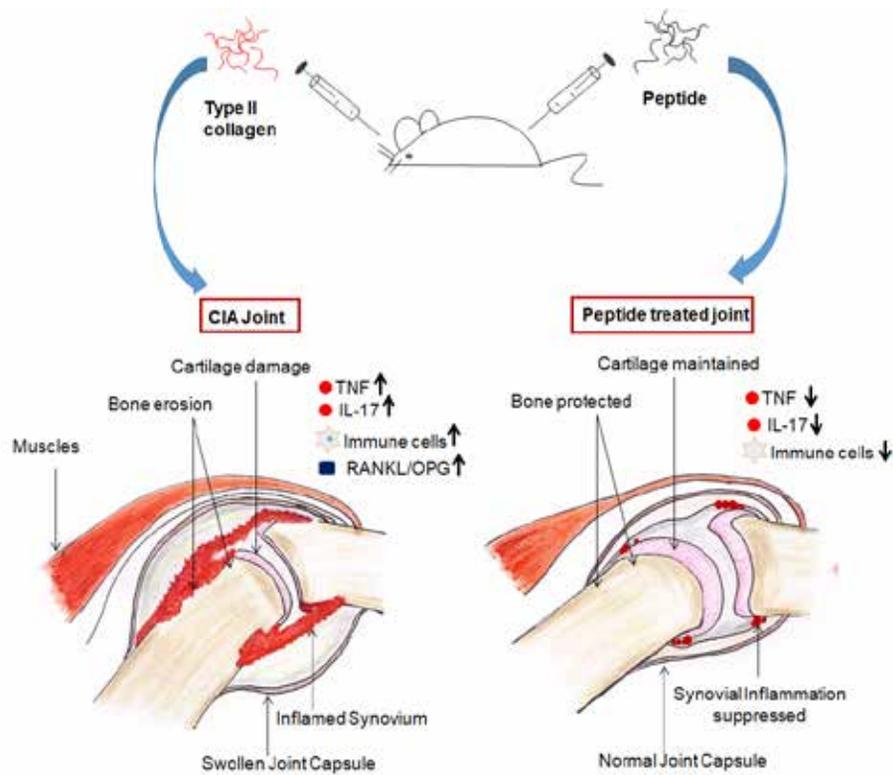
Rheumatoid arthritis occurs when the body's immune system becomes "confused" and aberrantly attacks the self, *i.e.* own cells/tissues to damage their functions. In this case, it attacks the lining of our joints which causes swelling and pain. When the disease progresses further, it results in bone erosion, joint deformity finally leading to physical disabilities.

Since this disease is related to the immune system, researchers have always been eager to discover a kind of treatment that attacks the disease selectively and doesn't affect the immune system in general.

Researchers at the CSIR-Central Drug Research Institute (CSIR-CDRI), Lucknow have recently reported that a specific fragment of a protein potentially helps in treating rheumatoid arthritis. Besides reducing the inflammation in joints, it also prevents the joint bones from being destroyed. This protein does not affect the overall immune system of the body and instead selectively protects the joints in case of rheumatoid arthritis.

This protein is secreted by a liver fluke or parasitic worm called *Fasciola* which helps these parasites in concealing their identity from the host immune system by diminishing the inflammatory attack that is set in motion by the host as a defensive strategy to kill the parasites. This protein is called *Fasciola Helminth Defense Molecule-1* (FhHDM-1) and is similar to a human protein that plays an important role in reducing inflammatory responses. The liver fluke protein also has a very high anti-inflammatory response. This similarity motivated the CDRI researchers to investigate the protein and to employ it in treating rheumatoid arthritis.

To test this protein, a mouse model was developed that mimicked the human conditions of rheumatoid arthritis. For developing the model, type-II collagen, the protein against which autoimmunity is developed in humans was introduced in large quantities into mice to initiate the process of cartilage



Lower panel showing key examples of disease mitigation parameters; CIA mice (having rheumatoid arthritis) had redness and thickening of paw at the end of the duration of the experiment. (Courtesy: The *FASEB Journal*, John Wiley and Sons)

destruction. After 20 days, when the researchers could observe the autoimmune response in the mice, FhHDM-1 was administered every second day to the mice. It was observed that FhHDM-1 prevented the destruction of cartilage in the joints of the mice although it could not repair the already damaged cartilage because the damage is reversible in the case of rheumatoid arthritis. Besides, it also prevented bone destruction. There was no paw swelling after 25 days in the medicated mice.

The cartilage of the mouse who did not receive the extracted peptide suffered damage in 46 days.

The best part of the experiment was that no other effect of the extracted peptide was observed on the overall immune system, which confirmed the selective nature of the peptide. The researchers are excited about the results and are curious to know the involved mechanism of this selective treatment quality of the peptide.

Currently, treatment of rheumatoid arthritis involves the usage of an anti-rheumatic drug (methotrexate) which also affects the overall immune system and alters the anti-bacterial ability of the immune system. Even the monoclonal antibodies which fight the individual inflammatory molecules target and suppress the tumour necrosis factor (TNF alpha), which is considered as the first line of defense against mycobacterium. This makes treating patients highly susceptible to different kinds of infections including tuberculosis.

Dr Naibedya Chattopadhyay says, “This is a major improvement over the existing therapies (disease-modifying anti-rheumatoid arthritis drugs or DMARDs) that act by suppressing the complete immune system of the body which makes patients vulnerable to bacterial infections such as tuberculosis. Although in economically advanced countries the prevalence of tuberculosis is negligible, in India it is very high. Thus, in the Indian scenario, an ideal DMARD should be the one that would specifically prevent joint inflammation and destruction without affecting the body’s overall immune function.”

The CDRI researchers are considering this study as an important breakthrough in terms of effectiveness and selectivity in treating rheumatoid arthritis. Future studies are necessary for developing this peptide for clinical use.

The studies have been published in the *FASEB Journal*.

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