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Molecules involved in rheumatoid arthritis angiogenesis identified

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Two protein molecules that fit together as lock and key seem to promote the abnormal formation of blood vessels in joints affected by rheumatoid arthritis, according to researchers at the University of Illinois at Chicago College of Medicine, who found that the substances are present at higher levels in the joints of patients affected by the disease.

Their results are reported in the journal *Annals of the Rheumatic Diseases*.

"Our results show, for the first time, that these two proteins – a receptor and its corresponding binding protein - play a key role in the progression of rheumatoid arthritis pathology," said Shiva Shahrara, associate professor of rheumatology at UIC.

Rheumatoid arthritis is a chronic autoimmune inflammatory disease in which the body's own defenses attack the tissues lining the joints, causing painful swelling and bone erosion that can ultimately lead to joint deformities.

One of the hallmarks of rheumatoid arthritis is the development of new blood vessels, or angiogenesis, in the joints.

"The swelling of joints is caused by the abnormal migration of a variety of different cell types into the joint," Shahrara said. "And as these cells accumulate, they need to be supplied with oxygen and nutrients, and so angiogenesis accompanies the joint swelling."

Shahrara and her colleagues knew that a protein called CCL28 was found in the body under low oxygen conditions, or hypoxia. Joints affected by rheumatoid arthritis can become hypoxic, so the researchers wanted to see if the protein and its receptor could be found in patients' affected joints.

The researchers measured the levels of the proteins in the tissues and fluid of joints from patients with rheumatoid arthritis and with osteoarthritis, the more common joint inflammation caused by physical wear and tear. Patients of both types had protein levels in their joints that were significantly higher than individuals without joint disease.

The investigators found that CCL28, which is over-produced in joints affected by rheumatoid arthritis, attracts the surface-lining cells that carry its receptor.

When the researchers added CCL28 to cells carrying the receptor, the cells organized into blood vessels. But if they chemically blocked the receptor and added CCL28, formation of blood vessels was reduced.

The finding, Shahrara said, provides "strong evidence" that the binding of CCL28 to joint-lining cells carrying its corresponding receptor is a necessary step in angiogenesis.

Provided by University of Illinois at Chicago