The case of the missing monocyte: Scientists investigate gene that appears to protect against rheumatoid arthritis

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The hands of a person with arthritis. Image source: NIH.

(Medical Xpress) -- An estimated 1.3 million people in the United States suffer from rheumatoid arthritis. The causes behind this chronic disease - which can exhibit itself as pain, swelling, stiffness, deformation, and loss of function in the joints - have eluded scientists for centuries. A new study by UNC researchers offers tantalizing glimmers about the roles of a gene called CCR2, an immune system cell called Th17 cell, and a missing monocyte.

The study contributes to a better understanding of the disease mechanism and has implications to guide the clinical trial strategy, said lead researcher Peng Liu, MD, PhD, research assistant professor at the UNC Thurston Arthritis Research Center. Her team's findings were

reported online in *PLoS One* on Oct. 4.

The mystery began several years ago when arthritis researchers zeroed in on a gene called CCR2. CCR2 is highly expressed in the joints of patients with rheumatoid arthritis, which led researchers to believe it might contribute to the disease. "Scientists thought that if you inhibited CCR2 you would have a beneficial effect," said Liu. "But actually, the result was the opposite." Studies revealed that suppressing CCR2 in fact cannot ameliorate joint inflammation, in some cases, it leads to disease exacerbation.

Intrigued, Liu and her team used mice to investigate how CCR2 affects immune system cells. The immune system is critical because rheumatoid arthritis is an autoimmune disease, in which the immune system attacks the body's own tissues, causing inflammation.

They found the smoking gun when they looked at a type of immune cell known as Th17 cell. Arthritic mice without the CCR2 gene produced three times the amount of Th17 cells, increasing the inflammation in their joints.

"We found that an enhanced Th17 cell response is responsible, at least in part, for the increased disease severity," said Liu. Inhibiting the activities of Th17 cell, therefore, may be a promising new direction for drug treatments for rheumatoid arthritis.

The team also found that a particular type of monocyte (a type of white blood cell) disappeared from certain tissues in the mice without CCR2. They hypothesize that the CCR2-expressing monocyte plays an important regulatory role, so without the monocyte, Th17 cells proliferate. "The potential link between CCR2 and the Th17 cells is the monocyte subset," said Liu.

"This subset of monocytes may have a suppressive function in autoimmune disease," said Liu. The finding opens the door to new treatment possibilities, such as injecting this monocyte subset into patients with rheumatoid arthritis: "Finding this monocyte may be important for later development of cell-based therapy," said Liu.

More information: For a report of the research, see: www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0025833

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