Process found to play role in rheumatoid arthritis could lead to new treatment

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Although the origin of rheumatoid arthritis (RA) remains unclear, bioactive proteins known as cytokines, particularly TNFα and IL-6, which are involved in inflammation, play a major role in the disease by contributing to joint and tissue destruction. Placenta growth factor (PIGF), another cytokine, has been thought to be critical for a new blood vessel formation in the placenta to sufficiently deliver oxygen and nutrients to fetus. A new study examined the effects of PIGF on the inflammatory process of RA. The results suggest that PIGF may play an important role in inflammation in RA joints.

The study was published in the February issue of *Arthritis & Rheumatism* (http://www3.interscience.wiley.com/journal/76509746/home).

Led by Wan-Uk Kim of Catholic University of Korea inSeoul, Korea, researchers analyzed blood and synovial fluid cells from RA patients and healthy controls and found that synovial cells were the major source of PIGF production in RA patients and that PIGF stimulates TNFα and IL-6 production. They also found that the PlGF-induced increases in TNFα and IL-6 production may be caused by high levels of flt-1, a PlGF receptor, which are linked to the inflammatory response of RA patients. In addition, the researchers identified a novel peptide to inhibit PlGF action. When injected into arthritic mice, this peptide reduced the severity of arthritis and prevented its progression. They also found that elimination of PIGF gene in mice prevented the development of antibody-induced arthritis.

The peptide they identified inhibits binding of PIGF to its receptor flt-1and could be valuable from a clinical standpoint, since it is easily synthesized and does not elicit unwanted immune response.

"These findings provide new insight into the pathogenic mechanism of RA and emphasize the importance of PIGF and flt-1 as potential candidates for therapy, in addition to their being a common cue of angiogenesis and the inflammatory process," the authors conclude. They are currently conducting research to improve the activity of the anti-flt-1 peptide by modifying its structure and length.

Article: " Role of Placental Growth Factor and Its Receptor flt-1 in Rheumatoid Inflammation," Seung-Ah Yoo, Hyung-Ju Yoon, Hyun-Sook Kim, Chi-Bom Chae, Sandro De Falco, Chul-Soo Cho, Wan-Uk Kim, Arthritis & Rheumatism, February 2009.

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