Combined inhibition of TNF-alpha, IL-17 effective in RA model

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(HealthDay)—Combined inhibition of tumor necrosis factor (TNF) α and interleukin (IL)-17 is more effective than single blockade in cultures of human fibroblast-like synoviocytes (FLS), according to an experimental study published in the January issue of *Arthritis & Rheumatology*.

Jens A.A. Fischer, Ph.D., from Roche Pharmaceutical Research and Early Development in Penzberg, Germany, and colleagues stimulated cultures of FLS with TNFα, IL-17, or both. They examined in vitro cytokine responses and in vivo development of arthritis and bone and cartilage destruction in TNFα-transgenic mice using single/combined neutralizing antibodies against TNFα and IL-17. The authors designed bispecific anti-TNFα/IL-17 antibodies and assessed their potential to block cytokine responses in FLS.

The researchers found that in FLS, TNFα and IL-17 had synergistic effects in promoting production of IL-6, IL-8, and granulocyte colony-stimulating factor, as well as matrix metalloproteinases. Superior efficacy was seen with bispecific anti-TNFα/IL-17 antibodies in blocking cytokine and chemokine responses in vitro. In arthritic mice, using neutralized antibodies, dual versus single inhibition of both cytokines was more effective in inhibiting the development of inflammation and bone and cartilage destruction.

"Bispecific anti-TNFα/IL-17 antibodies may have superior efficacy in the treatment of arthritis and may overcome the limited therapeutic responses obtained with single cytokine neutralization," the authors write.

Several authors disclosed financial ties to the pharmaceutical and biotechnology industries; several authors have a pending patent application for TNFα/IL-17 bispecific antibodies.

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