New research sheds light on role of IL-17 in the pathogenesis of osteoarthritis

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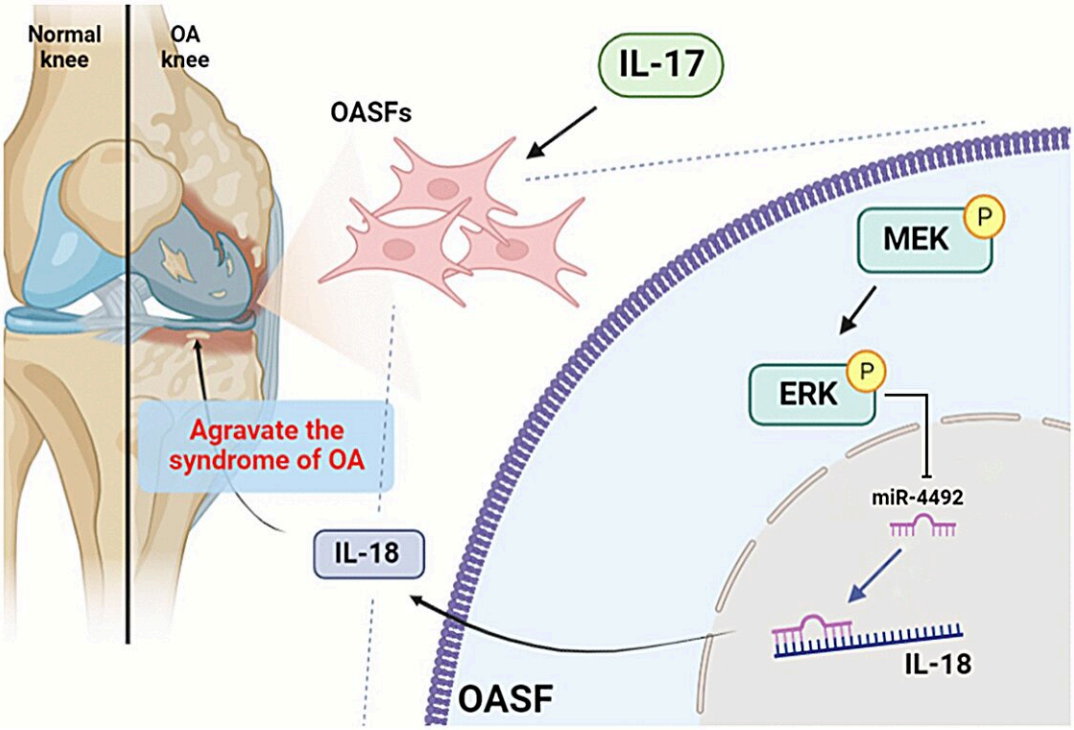

Schematic diagram illustrates the process whereby IL-17 treatment promotes IL-18 production in OASFs. Credit: *Aging* (2024). DOI: 10.18632/aging.205462

A new research paper titled "IL-17 promotes IL-18 production via the MEK/ERK/miR-4492 axis in osteoarthritis synovial fibroblasts" has been published in *Aging*.

The concept of osteoarthritis (OA) as a low-grade inflammatory joint disorder has been widely accepted. Many inflammatory mediators are implicated in the pathogenesis of OA. Interleukin (IL)-18 is a pleiotropic cytokine with versatile cellular functions that are pathogenetically important in immune responses, as well as autoimmune, inflammatory, and infectious diseases. IL-17, a proinflammatory cytokine mainly secreted by Th17 cells, is upregulated in OA patients. However, the role of IL-17 in OA progression is unclear.

In this new study, researchers used synovial tissues collected from healthy donors and OA patients to detect the expression level of IL-18 by immunohistochemistry stain.

"Elucidation of the molecular mechanisms and main factors involved in OA pathogenesis may help with the development of novel therapeutic targets that relieve OA pain or prevent the disease from progressing," the researchers write.

The OA synovial fibroblasts (OASFs) were incubated with recombinant IL-17 and subjected to Western blot, qPCR, and ELISA to examine IL-18 expression level. The chemical inhibitors and siRNAs that targeted signal pathways were used to investigate signal pathways involved in IL-17-induced IL-18 expression. The microRNAs participating in IL-18 expression were surveyed with online databases miRWalk and miRDB, followed by validation with qPCR.

This study revealed significantly higher levels of IL-18 expression in synovial tissue from OA patients compared with healthy controls, as well as increased IL-18 expression in OASFs from rats with severe OA. In vitro findings indicated that IL-17 dose-dependently promoted IL-18 production in OASFs. Molecular investigations revealed that the MEK/ERK/miR-4492 axis stimulated IL-18 production when OASFs were treated with IL-17.

The researchers conclude, "This study provides novel insights into the role of IL-17 in the pathogenesis of OA, which may help to inform OA treatment in the future."

More information: Kun-Tsan Lee et al, IL-17 promotes IL-18 production via the MEK/ERK/miR-4492 axis in osteoarthritis synovial fibroblasts, *Aging* (2024). DOI: 10.18632/aging.205462

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