How GPR40, a known receptor for dietary fatty acids, may protect from osteoarthritis?

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Osteoarthritis (OA) is one of the most common age-related degenerative joint concerns. Although articular cartilage degradation is its main feature, this disease induces whole-joint damage characterized by synovitis, bone remodelling and osteophyte formation. Regarding bone, Yohann Wittrant, a researcher at the Human Nutrition Unit (INRA -France), has recently reported that stimulation of the orphan receptor GPR40, a fatty acid-activated receptor, preserved bone mass. Dietary fatty acids were described to improve joint function and reduce pain in OA patients and to decrease both inflammatory markers and cartilage catabolism factors in preclinical studies.

To test the hypothesis that GPR40 may prevent or protect from OA, a whole body GPR40 deficient mouse strain was used. Primary chondrocytes, isolated from these rodents, exhibited a higher pattern of inflammatory mediators' secretion and an enhanced cartilage catabolic activity after their stimulation. An in vivo study using a model of surgical joint destabilization, revealed that GPR40 deficiency led to an aggravated OA phenotype characterized by a higher cartilage breakdown associated with subchondral bone sclerosis and osteophyte formation.

"Our results clearly demonstrate that GPR40 invalidation heightens inflammation, cartilage catabolism, and bone remodelling resulting in an aggravated OA phenotype;" stated Laurent-Emmanuel Monfoulet, researcher at the Human Nutrition Unit. These data, reported in the July 2015 issue of *Experimental Biology and Medicine*, demonstrates for the first time that the activation of GPR40 protects joints from OA. These

findings provide new insights into the design of innovative strategies for OA management especially by nutritional approaches.

Dr. Steven R. Goodman, Editor-in-Chief of *Experimental Biology and Medicine*, said "This intriguing study by Monfoulet et al provides both in vitro and in vivo evidence that GPR40 deficiency results in a more severe OA phenotype. This raises the promise that GPR40 can be an important therapeutic target for OA"

More information: *Experimental Biology and Medicine*, ebm.sagepub.com/content/240/7/854.full

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