

Scientists discover an epigenetic cause of osteoarthritis

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In what could be a breakthrough in the practical application of epigenetic science, U.K. scientists used human tissue samples to discover that those with osteoarthritis have a signature epigenetic change (DNA methylation) responsible for switching on and off a gene that produces a destructive enzyme called MMP13. This enzyme is known to play a role in the destruction of joint cartilage, making MMP13 and the epigenetic changes that lead to its increased levels, prime targets for osteoarthritis drug development. In addition to offering a new epigenetic path toward a cure for osteoarthritis, this research also helps show how epigenetic changes play a role in diseases outside of cancer. This finding was recently published online in the *FASEB Journal*.

"As the population gets older, osteoarthritis presents increasing social and economic problems," said David A. Young, Ph.D., a researcher involved in the work from the Musculoskeletal Research Group at the Institute of Cellular Medicine at Newcastle University in Newcastle upon Tyne in the United Kingdom. "Our work provides a better understanding of the events that cause [cartilage damage](#) during osteoarthritis and provides hope that tailored drug development to prevent the progress of disease will improve the quality of life and mobility of many [arthritis sufferers](#)."

To make the discovery, Young and colleagues compared the extent to which DNA methylation was different in cartilage from patients suffering from osteoarthritis and healthy people of similar age. They found that at one small position, the gene for MMP13 had less DNA

methylation in diseased patients. Then they confirmed that reduced methylation of this gene increases levels of the destructive enzyme MMP13.

"We've already seen how epigenetics has advanced our approach to cancer. Now we're seeing it with other diseases and even exercise." said Gerald Weissmann, M.D., Editor-in-Chief of the [FASEB Journal](#). "This study not only lays the groundwork for a new understanding of osteoarthritis, but also shows that the old 'either/or' nature v. nurture argument is outdated: epigenetics teaches us that nature (the daily wear and tear of joints) regulates nurture (the genes in our cartilage) to cause arthritis."

More information: Catherine Bui, Matt J. Barter, Jenny L. Scott, Yaobo Xu, Martin Galler, Louise N. Reynard, Andrew D. Rowan, and David A. Young. cAMP response element-binding (CREB) recruitment following a specific CpG demethylation leads to the elevated expression of the matrix metalloproteinase 13 in human articular chondrocytes and osteoarthritis. *FASEB J.* July 2012 26:3000-3011; doi:10.1096/fj.12-206367

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