Inhibiting proteins may prevent cartilage breakdown in arthritis patients

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Current arthritis medications can ease the pain, but stopping the progression of the disease requires more aggressive treatments: use of very limited available drugs or surgical intervention. University of Missouri researchers hope to find new therapeutic targets for arthritis by studying the interaction between two proteins that, if interrupted, may prevent arthritis pain caused by joint damage. In a new study, researchers have found potential evidence that blocking the proteins responsible for inducing inflammation prevents cartilage breakdown.

"We are looking to intervene in specific molecular events to prevent the depletion of cartilage in arthritis," said Bimal K. Ray, professor of veterinary pathobiology in the MU College of Veterinary Medicine. "Certain proteins play a major role in the development of arthritis. When we understand how these proteins interact, we will have a better idea of how to slow or even reverse the progression of the disease."

When the human body develops arthritis, specific protein functions are altered and inflammation is triggered, leading to pain. In the MU study, Ray examined the interaction between the proteins AP-1 and SAF-1 and found that the interaction of these proteins plays a significant role in inducing inflammation. SAF-1 and AP-1 can partner to work together to induce activation of the MMP-1 gene causing breakdown of collagen (the proteins that constitute cartilage). Arthritis patients start to experience pain when cartilage starts to erode.

Because AP-1 and SAF-1 play a significant role in the activation of the

MMP-1 gene, researchers explored the site of the interaction as a possible contact point for competitive inhibition. In competitive inhibition, a molecule binds with an enzyme or a protein to decrease its activity and disable its function. Many pharmaceutical drugs that are successful for treating other diseases rely on enzyme inhibitors. In this study, researchers identified an active site in the SAF-1 protein molecule that is involved in the interaction with AP-1 to induce the expression of the MMP-1 gene.

"In this study, we looked at how and why MMP-1 is activated, particularly in the disease condition," Ray said. "Once we understand how this gene is activated, we can design drugs to control pathways to reduce the severity of MMP-1-mediated cartilage destruction. We found strong evidence that by blocking SAF-1, MMP-1 expression is inhibited. Now, we will continue to explore the interacting domain of SAF-1 as a possible contact point for competitive inhibition."

More information: The study, "Transcriptional synergy mediated by SAF-1 and AP-1: Critical Role of N-Terminal Polyalanine and Two Zinc Finger Domains of SAF-1," was recently published in the *Journal of Biological Chemistry*.

Source: University of Missouri-Columbia