High cholesterol triggers mitochondrial oxidative stress leading to osteoarthritis

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High cholesterol might harm more than our cardiovascular systems. New research using animal models, published online in *The FASEB Journal*, suggests that high cholesterol levels trigger mitochondrial oxidative stress on cartilage cells, causing them to die, and ultimately leading to the development of osteoarthritis. This research tested the potential therapeutic role of mitochondria targeting antioxidants in high-cholesterol-induced osteoarthritis and provided proof-of-concept for the use of mitochondrial targeting antioxidants to treat osteoarthritis.

"Our team has already begun working alongside dietitians to try to educate the public about healthy eating and how to keep cholesterol levels at a manageable level that won't damage joints, in collaboration with orthopedic surgeons based at Prince Charles Hospital, Brisbane Australia," said Indira Prasadam, Ph.D., a researcher involved in the work from the Institute of Health and Biomedical Innovation, School of Chemistry, Physics and Mechanical Engineering at Queensland University of Technology in Brisbane, Australia.

To make this discovery, Prasadam and colleagues used two different animal models to mimic human hypercholesterolemia. The first was a mouse model that had an altered gene called ApoE-/- that made the animals hypercholesteremic. The other was a rat model, and the animals were fed a high-cholesterol diet, causing diet-induced hypercholesterolemia. Both models were fed a high-cholesterol diet or control normal diet, after which they underwent a surgery that mimics knee injuries in people and was designed to bring on osteoarthritis. Both

the mice and the rats that were subjected to surgery and fed with high-cholesterol diets showed more severe osteoarthritis development than seen in the normal diet group. However, when both the mice and the rats are were exposed to the cholesterol-lowering drug atorvastatin and mitochondrion-targeted antioxidants, the development of osteoarthritis was markedly decreased in relation to the untreated groups.

"Just when we thought all the angles on osteoarthritis had been uncovered, a new lead like this comes along," said Thoru Pederson, Ph.D., Editor-in-Chief of The FASEB Journal. "The focus of hypercholesterolemia, whether familial or sporadic, has, of course, always been on arterial disease, but here we have a fascinating new discovery."

More information: S. Farnaghi et al, Protective effects of mitochondria-targeted antioxidants and statins on cholesterol-induced osteoarthritis, *The FASEB Journal* (2016). DOI: 10.1096/fj.201600600R

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