Nature Reviews Rheumatology **11**, 683 (2015); published online 20 October 2015; doi:10.1038/nrrheum.2015.145

OSTEOARTHRITIS

Autophagy prevents age-related OA

Autophagy, a mechanism of organelle recycling that promotes cell survival, has been previously implicated in osteoarthritis (OA). One of the proteins fundamental to this process, autophagy protein 5 (Atg5), has now been shown to be protective against late-onset OA in a new study in mice.

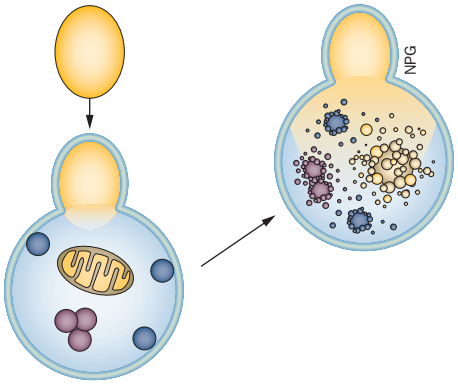
"Despite numerous suggestions of a connection between autophagy and OA, direct physiological evidence [was] missing," explains Andrei Chagin, corresponding author of the study. To evaluate the importance of autophagy in the development of OA, Chagin and colleagues studied the onset of age-related and trauma-induced OA in mice lacking *Atg5* specifically in chondrocytes (Atg5cKO mice).

Evidence of fibrillation and reduced proteoglycan deposition in articular cartilage was first observed in male Atg5cKO mice at the age of 6 months, a time when no abnormalities were detected in control or female Atg5cKO mice.

At 1 year of age, Atg5cKO male mice showed extensive fibrillation, further reduction in proteoglycan deposition and increased collagenase-3 expression in joints compared with controls. Cartilage degradation was also observed in age-matched female Atg5cKO mice, and OARSI histopathology scores were higher in male and female Atg5cKO mice than in gender-matched controls ($P = 0.002$ and $P = 0.006$, respectively).

The researchers also found evidence of increased chondrocyte apoptosis in Atg5cKO mice compared with controls, as well as a higher number of chondrocytes positive for cleaved caspase-3 and caspase-9, two apoptosis markers. Intriguingly, none of the differences reported between Atg5cKO mice and controls in the onset of age-related OA were observed in a model of trauma-induced OA in which mice were subjected to partial medial meniscectomy.

"These data are in line with the general view of autophagy as a protective mechanism which facilitates cell survival in unfavourable conditions," concludes Chagin. "New questions now require attention, including how autophagy protective mechanisms work and whether autophagy has a role in other cells of the joint."



João H. Duarte

Original article Bouderlique, T. *et al.* Targeted deletion of *Atg5* in chondrocytes promotes age-related osteoarthritis. *Ann. Rheum. Dis.* doi:10.1136/annrheumdis-2015-207742