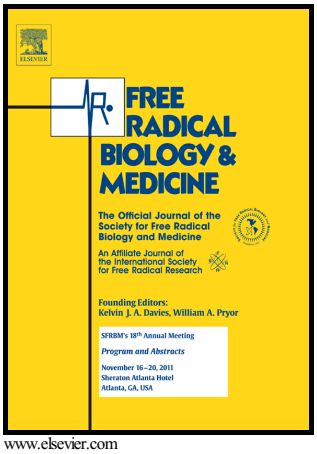
The autophagic response to oxidative stress in osteoarthritic chondrocytes is deregulated

Andreas Goutas, Christina Syrrou, Ioanna Papathanasiou, Aspasia Tsezou, Varvara Trachana



www.elsevier.com

PII: S0891-5849(18)30973-0
DOI: https://doi.org/10.1016/j.freeradbiomed.2018.08.003
Reference: FRB13867

To appear in: *Free Radical Biology and Medicine*

Received date: 31 May 2018
Revised date: 31 July 2018
Accepted date: 1 August 2018

Cite this article as: Andreas Goutas, Christina Syrrou, Ioanna Papathanasiou, Aspasia Tsezou and Varvara Trachana, The autophagic response to oxidative stress in osteoarthritic chondrocytes is deregulated, *Free Radical Biology and Medicine,* https://doi.org/10.1016/j.freeradbiomed.2018.08.003

The autophagic response to oxidative stress in osteoarthritic chondrocytes is deregulated

Andreas Goutas[1,2], Christina Syrrou[2], Ioanna Papathanasiou[2], Aspasia Tsezou[1,2], Varvara Trachana[1*]

[1]Laboratory of Biology, Faculty of Medicine, School of Health Sciences, University of Thessaly, Biopolis 41500, Larissa, Greece

[2]Laboratory of Cytogenetics and Molecular Genetics, Faculty of Medicine, School of Health Sciences, University of Thessaly, Biopolis 41500, Larissa, Greece

agoutas@uth.gr

csyrrou@bio.uth.gr

iopapat@med.uth.gr

atsezou@med.uth.gr

vtrachana@med.uth.gr

[*]Corresponding author.

Abstract

It has been reported that oxidative stress (OS) is involved in the pathogenesis of osteoarthritis (OA) and that defective autophagy is accompanying this age-related disease. Moreover, it has been proposed that induction of autophagy could serve as therapeutic mean, as it was shown to alleviate several symptoms in OA animal models. On the contrary, it is also known that autophagic death, which results from over-activation of autophagy, is also a contributor in the development of this disease. Given this discrepancy, in this study we aimed at analysing the autophagic response against acute exogenous oxidative insult of chondrocytes from healthy individuals (control) and OA patients (OA). Cells were treated with sublethal concentrations of hydrogen peroxide (H_2O_2) and then allowed to recover for different periods of time. Firstly, mRNA levels of autophagy-related genes (ATG5, Beclin-1 and LC3) were found significantly reduced in OA chondrocytes compared to control chondrocytes under physiological conditions. After the exposure to OS, in control cells mRNA and protein levels of these genes initially increased and decreased back to their basal levels 6 to 24h after treatment. On the contrary, in OA chondrocytes the levels of autophagy-related genes remained high even 24h post-treatment, indicating their inability to attenuate autophagy. Under the same conditions, the staining pattern of LC3, known marker of autophagosome formation, was analysed, and possible morphological differences between mitochondria of control and OA cells were microscopically assessed. These analyses revealed higher number of impaired mitochondria as well as increased autophagosome formation in OA cells as compared to control cells at all time points. Taken together, our results demonstrate a deregulation of the autophagic response against the