# Interleukin-1 ß disturbs the antioxidant enzyme system in bovine chondrocytes : a possible explanation for oxidative stress generation.

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## AIM OF THE STUDY.

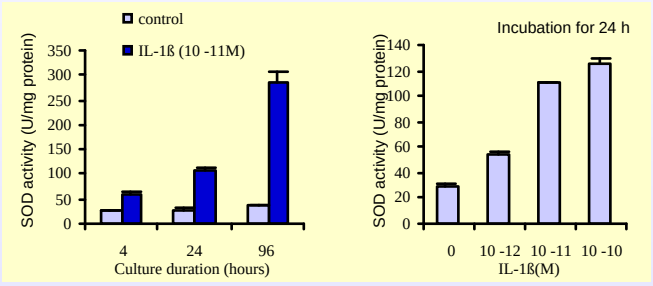
Reactive oxygen species (ROS) play a major role in the pathogenesis of degenerative joint diseases. To prevent ROS toxicity, chondrocytes possess a well-coordinated antioxidant enzyme system mainly formed by superoxide dismutases (SOD) and catalase (Cat). This work was designed to assess the effects of interleukin (IL)-1ß on the gene expression and enzymatic activity of SOD and Cat in bovine chondrocytes.

## METHODS.

Bovine chondrocytes were cultured in monolayer in the absence or in the presence of IL-1ß. Cells were co-incubated with IL-1ß and inhibitors of mitogen-activated protein kinases (MAPK) inhibitors (PD98059, SB203580, SP600125) or NF-κB inhibitors (BAY11-7082, MG-132). SOD and Cat enzymatic activities were evaluated in cellular extract by using respectively the SOD Assay Kit-WST (Dojindo Molecular Technologies) and the Amplex Red Catalase Assay (Molecular Probes). Cu SOD, Mn SOD and Cat gene expressions were quantified by real time RT PCR.

## RESULTS.

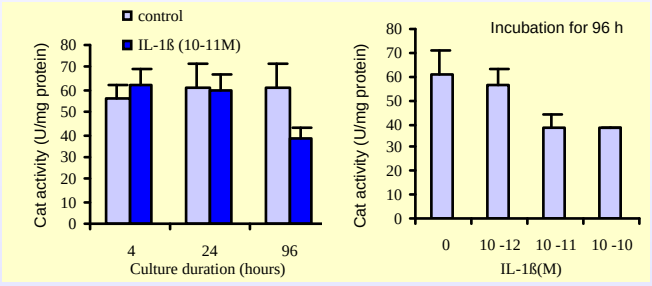
SOD activity was time and dose dependently increased by IL-1ß




IL-1ß time response effect on SOD activity

IL-1ß dose response effect on SOD activity

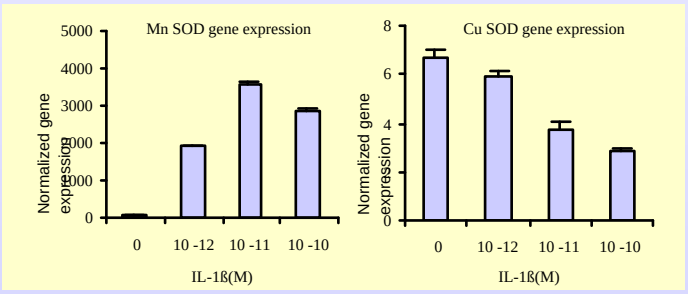
Cat activity was time and dose dependently




IL-1ß time response effect on Cat activity

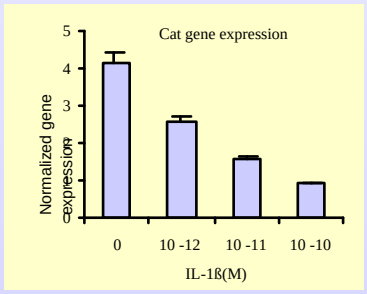
IL-1ß dose response effect on Cat activity

IL-1ß increased Mn SOD mRNA level, but decreased Cu SOD mRNA level



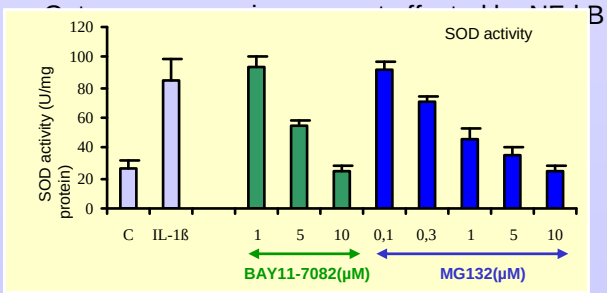

IL-1ß dose response effect on Mn and Cu SOD gene expression

IL-1ß decreased Cat mRNA level

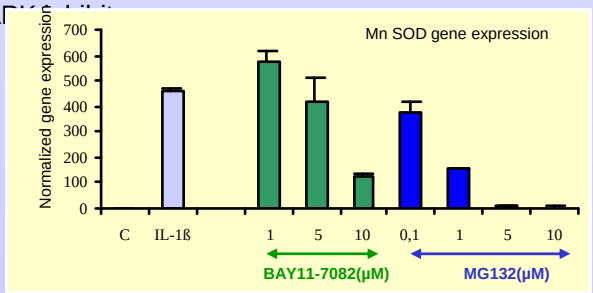



IL-1ß dose response effect on Cat gene expression

SOD activity and Mn SOD gene expression was prevented by NF-kB inhibitors but not by MAPK inhibitors.




BAY11-7082 and MG132 dose response effect on SOD activity




BAY11-7082 and MG132 dose response effect on Mn SOD gene expression

## CONCLUSIONS.

We have demonstrated that IL-1β disturbs the antioxidant enzyme system in chondrocytes. This cytokine induces a rapid increase of SOD activity and a delayed decrease of Cat activity. These regulatory effects occur at transcriptional level. MnSOD gene activation was mediated by NF-kB. The imbalance between SOD and Cat could result in $H_2O_2$ accumulation, and generate intracellularly an oxidative stress. To reinforce the antioxidant defences of chondrocytes should be considered in the management of osteoarthritis.