

Effects of interleukin-1 beta and dexamethasone on the expression of antioxidant enzymes by chondrocytes

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AIM OF THE STUDY.

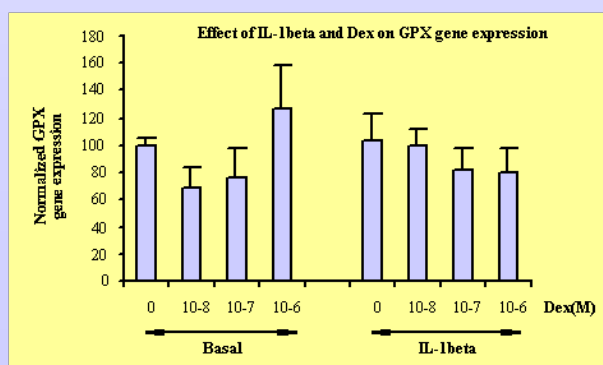
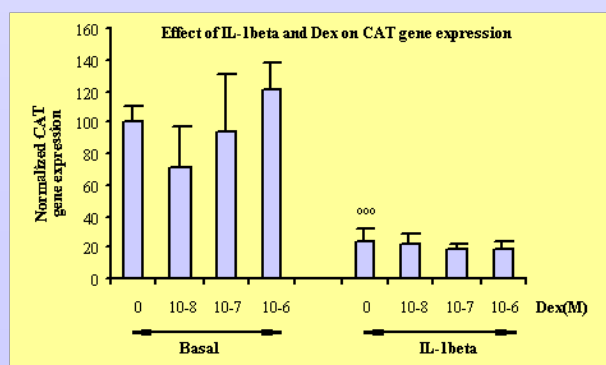
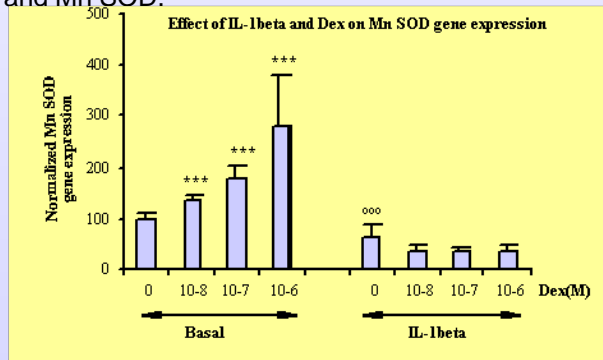
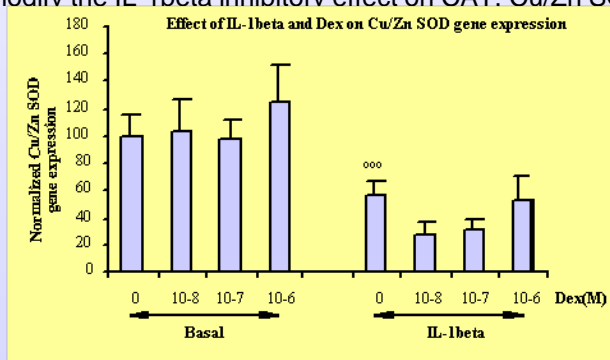
Reactive oxygen species (ROS) have been identified as potent mediators in cartilage tissue destruction and synovial membrane inflammation suggesting their roles in the pathophysiology of joint diseases. Chondrocytes exposed to soluble factors such as interleukin-1beta (IL-1beta) are capable to produce ROS. Cells are protected from ROS-induced damage by a variety of endogenous enzymes including copper-zinc (Cu/Zn) superoxide dismutase (SOD), manganese (Mn) SOD, glutathione peroxidase (GPX) and catalase (CAT). This research work was designed to assess the effects of IL-1beta and dexamethasone (Dex) on the gene expression by chondrocytes of the gene coding for Cu/Zn SOD, Mn SOD, GPX and CAT.

METHODS.

Primary bovine chondrocytes in monolayer were cultured for 24 h well-defined culture medium (DMEM supplemented with 2 mM glutamine, 0.17 mM proline, 50 µg/ml ascorbic acid, 10 mM HEPES, 100 U/ml penicillin, 0.1 mg/ml streptomycin and 1% of ITS⁺) in the absence or in the presence of Dex (10⁻⁸ to 10⁻⁶ M) and with or without IL-1beta (10⁻⁹ M). Cu/Zn SOD, Mn SOD, GPX and CAT gene expression was quantified by reverse transcription of mRNA followed by real time and quantitative polymerase chain reaction (RT PCR, LightCycler, Roche).

RESULTS.

At 10⁻⁹M, IL-1beta decreased Cu/Zn SOD, Mn SOD and CAT gene expression (p < 0.001). In contrast, IL-1beta did not modify GPX gene expression. Dex significantly and dose-dependently increased Mn SOD gene expression (***p < 0.001) but had no effect on Cu/Zn SOD, CAT and GPX mRNA levels. Further, Dex did not modify the IL-1beta inhibitory effect on CAT. Cu/Zn SOD and Mn SOD.



CONCLUSIONS.

This work shows that IL-1beta down-regulates the expression of genes coding for antioxidant enzymes indicating that IL-1beta contributes to decrease the cellular antioxidant defences. By this way, IL-1beta could promote the appearance of an oxidative stress into the cells and consequently metabolic dysfunction. In contrast, Dex increases SOD expression and then reinforces the cellular defences against the oxidative stress.