



POSTER PRESENTATION

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Prostaglandin D2 enhances interleukin-1beta-induced cyclooxygenase-2 expression in osteoarthritic cartilage

N Zayed*, F E El Mansouri, N Chabane, J Martel-Pelletier, J P Pelletier, H Fahmi

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Objective

To investigate the effects of prostaglandin D2 (PGD2) on interleukin-1beta (IL-1beta)-induced cyclooxygenase (COX)-2 expression in human cartilage and the signalling pathways involved in these effects.

Methods

Chondrocytes were stimulated with IL-1 in the presence or absence of PGD2, and expression of COX-2 protein was evaluated by western-blotting. Messenger RNA (mRNA) expression was analyzed by real-time reverse transcription-polymerase chain reaction. The role of the PGD2 receptors D prostanoid receptor 1 (DP1) and chemoattractant receptor-like molecule expressed on Th2 cells (CRTH2) was evaluated using specific agonists.

Results

PGD2 increased in a dose-dependent manner IL-1-induced COX-2 protein and mRNA expression. DP1 and CRTH2 were expressed and functional in chondrocytes. The effect of PGD2 was mimicked by DK-PGD2 and Indomethacin, selective agonists of CRTH2, but not by BW245C, a selective agonist of DP1. Furthermore, treatment with an anti-CRTH2 antibody reversed the effect of PGD2, indicating that the stimulatory effect of PGD2 is mediated by CRTH2. Activation of CRTH2 is consistent with the activation of a receptor coupled to a phosphoinositide-specific phospholipase, suggesting that the effect of PGD2 is mediated by the CRTH2/PIP2/PKC.

Conclusion

PGD2 stimulates IL-1-induced production of COX-2 by chondrocytes through the CRTH2/PIP2/PKC signalling pathway.

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Osteoarthritis Research Unit, Research Centre of the University of Montreal
Hospital Center (CR-CHUM), Notre-Dame Hospital, Montreal, Quebec, Canada