Zayed et al. Journal of Translational Medicine 2010, 8(Suppl 1):P61
http://www.translational-medicine.com/content/8/S1/P61

JOURNAL OF TRANSLATIONAL MEDICINE

POSTER PRESENTATION Open Access

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

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From 5th European Workshop on Immune-Mediated Inflammatory Diseases
Sitges-Barcelona, Spain. 1-3 December 2010

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.

Published: 25 November 2010

doi:10.1186/1479-5876-8-S1-P61
Cite this article as: Zayed *et al.*: Prostaglandin D2 enhances interleukin-1beta- induced cyclooxygenase-2 expression in osteoarthritic cartilage. *Journal of Translational Medicine* 2010 **8**(Suppl 1):P61.

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