



POSTER PRESENTATION

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Egr-1 mediates the suppressive effect of IL-1 on PPAR γ expression in human OA chondrocytes

Salwa Sarah Nebbaki^{1*}, Fatima Ezzahra El Mansouri¹, Nadia Zayed¹, Mohamed Benderdour², Johanne Martel-Pelletier¹, Jean-Pierre Pelletier¹, Hassan Fahmi¹

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Background

Peroxisome proliferator-activated receptor gamma (PPAR γ) is a ligand activated transcription factor and member the nuclear hormone receptor superfamily. Several lines of evidence indicate that PPAR γ have protective effects in osteoarthritis (OA). Indeed, PPAR γ has been shown to down-regulate several inflammatory and catabolic responses in articular cartilage and chondrocytes and to be protective in animal models of OA.

Aim

We have previously shown that IL-1 down-regulated PPAR γ expression in OA chondrocytes. In the present study we will investigate the mechanisms underlying this effect of IL-1.

Methods

Chondrocytes were stimulated with IL-1, and the level of PPAR γ and Egr-1 protein and mRNA were evaluated using Western blotting and real-time reverse-transcription polymerase chain reaction, respectively. The PPAR γ promoter activity was analyzed in transient transfection experiments. Egr-1 recruitment to the PPAR γ promoter was evaluated using chromatin immunoprecipitation (ChIP) assays. Small interfering RNA (siRNA) approaches were used to silence Egr-1 expression.

Results

We demonstrated that the suppressive effect of IL-1 on PPAR γ expression requires de novo protein synthesis and was concomitant with the induction of the transcription factor Egr-1. ChIP analyses revealed that IL-1 induced Egr-1 recruitment at the PPAR γ promoter. IL-1 inhibited

the activity of PPAR γ promoter and overexpression of Egr-1 potentiated the inhibitory effect of IL-1, suggesting that Egr-1 may mediate the suppressive effect of IL-1. Finally, Egr-1 silencing with small interfering RNA blocked IL-1-mediated down-regulation of PPAR γ expression.

Conclusion

These results indicate that Egr-1 contributes to IL-1-mediated down-regulation of PPAR γ expression in OA chondrocytes and suggest that this pathway could be a potential target for pharmacologic intervention in the treatment of OA and possibly other arthritic diseases.

Author details

¹Osteoarthritis Research Unit, University of Montreal Hospital Research Center (CRCHUM), Notre-Dame Hospital, Montreal, Quebec, Canada. ²Centre de recherche Hôpital Sacré-Coeur de Montréal, Montreal, Quebec, Canada.

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¹Osteoarthritis Research Unit, University of Montreal Hospital Research Center (CRCHUM), Notre-Dame Hospital, Montreal, Quebec, Canada
Full list of author information is available at the end of the article