4. H3K9 demethylation by LSD1 contributes to IL-1-induced mPGES-1 expression in OA chondrocytes.

Fatima Ezzahra El Mansouri, Johanne Martel-Pelletier, and Hassan Fahmi.
Unité de Recherche en Arthrose, Centre de Recherche- Centre Hospitalier de l'Université de Montréal, Montréal, QC, Canada.

Introduction: Microsomal prostaglandin E synthase-1 catalyzes the terminal step in the biosynthesis of PGE2, which plays a critical role in the pathophysiology of osteoarthritis

Objective: To investigate the role of histone H3 (H3K9) methylation in interleukin-1b (IL-1)-induced microsomal prostaglandin E synthase-1 (mPGES-1) expression in human osteoarthritic (OA) chondrocytes.

Methods: Chondrocytes were stimulated with IL-1 and the expression of mPGES-1mRNA was analyzed using real-time reverse transcriptase-polymerase chain reaction. H3K9 methylation and the recruitment of the histone demethylase LSD1 to the mPGES-1 promoter were evaluated using chromatin immunoprecipitation assays. The role of LSD1 was further evaluated using the the amino oxidase inhibitor tranylcypromine (a potent inhibitor of LSD1 activity).

Results: Treatment with IL-1 induced mPGES-1 expression in a time dependent manner. The induction of mPGES-1 expression by IL-1 was associated with H3K9 demethylation at the mPGES-1 promoter. These changes were concomitant with the recruitment of the histone demethylase LSD1. Treatment with tranylcypromine inhibited IL-1-induced H3K9 demethylation as well as IL-1-induced mPGES-1 expression.

Conclusion: These results indicate that H3K9 demethylation by LSD1 contributes to IL-1-induced mPGES-1 expression and suggest that this pathway could be a potential target for pharmacological intervention in the treatment of OA and possibly other arthritic diseases.