

MECHANISM OF INDUCTION OF VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF) IN OSTEOARTHRITIS

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ABSTRACT

Vascular endothelial growth factor (VEGF) is an endothelial cell mitogen and an angiogenic factor. Angiogenesis regulated by VEGF is a critical event in the pathogenesis of Osteoarthritis (OA). Over-expression of VEGF in arthritis plays an important role in the progression of the disease.

This study was directed at understanding the regulation of VEGF in OA. In the pathogenic condition of OA, a novel transcription factor called Serum Amyloid A-activating factor (SAF-1) is abundantly present and is involved in the regulation of several genes in the diseased joint tissue. To assess whether SAF-1 plays any role in the VEGF expression in arthritic joint, transient transfection, and CAT assay in articular chondrocyte cells were preformed which showed that SAF-1 increases VEGF promoter linked reporter gene expression in a dose dependent manner. Deletion of SAF binding sites in the promoter region of VEGF completely abolishes cytokine-induced VEGF promoter activity. Electrophoretic Mobility Shift Assay demonstrated that SAF-1 directly binds to VEGF promoter, and NF- κ B interrupts the binding of SAF-1 to VEGF promoter. These results suggest that SAF-1 play a crucial role in promoting VEGF expression in OA.