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Bone Morphogenetic Protein-7 Inhibits Constitutive and Interleukin-1β -Induced Monocyte Chemoattractant Protein-1 Expression in Human Mesangial Cells: Role for JNK/AP-1 Pathway

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Bone morphogenetic protein-7 (BMP-7), which belongs to the TGF-β superfamily, has been shown to reduce macrophage infiltration and tissue injury in animal models of inflammatory renal disease. To explore the mechanism involved in the anti-inflammatory effect, we investigated the effect of BMP-7 on monocyte chemoattractant protein-1 (MCP-1) expression in cultured human mesangial cells. BMP-7 significantly inhibited constitutive and IL-1β-induced MCP-1 protein production and MCP-1 mRNA expression by mesangial cells in a time- and concentration-dependent manner. BMP-7 also inhibited IL-1β-induced monocyte chemotactic activity released from the mesangial cells. We examined the role of transcription factors NF-κB and AP-1 in BMP-7 inhibition of IL-1β-induced MCP-1 expression. IL-1β increased NF-κB and AP-1 activity and both transcription factors mediated IL-1β-induced MCP-1 expression in mesangial cells. BMP-7 inhibited IL-1β-induced AP-1 activity in a concentration-dependent manner. In contrast, IL-1β-induced NF-κB activity and IκBα degradation were not affected by BMP-7. Furthermore, IL-1β-induced phosphorylation of c-Jun N-terminal kinase was inhibited by BMP-7. These data suggest that BMP-7 inhibits constitutive and IL-1β-induced MCP-1 expression in human mesangial cells partly by inhibiting c-Jun N-terminal kinase activity and subsequent AP-1 activity, and provide new insight into the therapeutic potential of BMP-7 in the inflammatory renal diseases.