

Involvement of nuclear factor-kappaB in macrophage migration inhibitory factor gene transcription up-regulation induced by interleukin- 1 beta in ectopic endometrial cells.

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Abstract

OBJECTIVE:

To investigate the involvement of the nuclear factor (NF)-kappaB in the interleukin (IL)-1 beta-mediated macrophage migration inhibitory factor (MIF) gene activation.

DESIGN:

Prospective study.

SETTING:

Human reproduction research laboratory.

PATIENT(S):

Nine women with endometriotic lesions.

INTERVENTION(S):

Endometriotic lesions were obtained during laparoscopic surgery.

MAIN OUTCOME MEASURE(S):

The MIF protein secretion was analyzed by ELISA, MIF mRNA expression by quantitative real-time polymerase chain reaction (PCR), NF-kappaB translocation into the nucleus by electrophoresis mobility shift assay, I kappaB phosphorylation and degradation by Western blot, and human MIF promoter activity by transient cell transfection.

RESULT(S):

This study showed a significant dose-dependent increase of MIF protein secretion and mRNA expression, the NF-kappaB translocation into the nucleus, I kappaB phosphorylation, I kappaB degradation, and human MIF promoter activity in endometriotic stromal cells in response to IL-1 beta. Curcumin (NF-kappaB inhibitor) significantly inhibited all these IL-1 beta-mediated effects. Analysis of the activity of deletion constructs of the human MIF promoter and a computer search localized two putative regulatory elements corresponding to NF-kappaB binding sites at positions -2538/-2528 bp and -1389/-1380 bp.

CONCLUSION(S):

This study suggests the involvement of the nuclear transcription factor NF-kappaB in MIF gene activation in ectopic endometrial cells in response to IL-1 beta and identifies a possible pathway of endometriosis-associated inflammation and ectopic cell growth.