

## **Stimulation of macrophage migration inhibitory factor expression in endometrial stromal cells by interleukin 1, beta involving the nuclear transcription factor NFkappaB.**

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### **Abstract**

Endometriosis, the ectopic development of endometrial tissue, is, particularly in peritoneal endometriosis, believed to result from tubal reflux of menstrual tissue. The release of cytokines and growth factors by refluxed endometrial cells in response to peritoneal inflammatory stimuli may enhance the capability of endometrial cells to implant and grow into the peritoneal host tissue. Herein we report that interleukin 1 (IL1), a major proinflammatory cytokine that is overproduced by endometriosis women-derived peritoneal macrophages and found in elevated concentrations in the peritoneal fluid of patients with endometriosis, stimulates the synthesis and the secretion of macrophage migration inhibitory factor (MIF) by human endometrial stromal cells. IL1B (0.1-100 ng/ml) exerted dose- and time-dependent effects of MIF protein secretion and mRNA synthesis, as shown by ELISA and reverse transcription-polymerase chain reaction, respectively. IL1B appeared to induce MIF gene transcription via the kappaB nuclear transcription factor (NFkappaB), as shown by electrophoretic mobility shift assay and Western blot analysis of IkappaB phosphorylation. Curcumin (10<sup>-8</sup> M), which is known for inhibiting NFkappaB activation, inhibited IL1B-induced MIF secretion as well as NFkappaB nuclear translocation and DNA binding. Taken together, these findings clearly show that IL1B up-regulates the expression of MIF in endometrial stromal cells in vitro and acts via NFkappaB. This may play an important role in the physiology of the human endometrium and the pathophysiology of endometriosis considering the immunomodulatory properties of MIF as well as its role in cell growth, angiogenesis and tissue remodeling.