

Curcumin delays endometriosis development by inhibiting MMP-2 activity.

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Abstract

Endometriosis is a common reproductive disorder believed to be associated with matrix metalloproteinases (MMPs) activities for invasion and remodeling of endometrial tissues. Ectopic endometrium has higher capacity to produce proMMP-2 than eutopic tissues; however, the role of MMP-2 during early phase of endometriosis development is still unclear. In the present study, we investigated the role of MMP-2 in establishment and development of endometriosis in mouse model. The effect of curcumin on regression of endometriosis through protease/antiprotease balance between MMP-2 and TIMP-2 was also examined. After endometrial inoculation into peritoneum, we observed a significant elevation of proMMP-2 activity from day 2 onwards. This increased MMP-2 activity was associated with decreased expression of tissue inhibitor of MMP (TIMP)-2, while a significant up-regulation of active MMP-2 activity was observed from day 3 onwards. The activation of proMMP-2 to active MMP-2 was associated with increased expression of membrane type 1 matrix metalloproteinase (MT1MMP). Curcumin at a dose of 48 mg/kg b.w. repressed the MMP-2 activity via up-regulation of bound TIMP-2 expression, thus delayed endometriosis development. In addition, curcumin inhibited production of active MMP-2 by down-regulating MT1MMP expression. Moreover, endometriotic progression was directly linked with increased MMP-2/TIMP-2 ratio which was delayed by curcumin pretreatment. In summary, our study documents the regulation of MMP-2 activity by TIMP-2 during the early phase of endometriosis development and inhibitory action of curcumin thereon.