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EGFR-mediated matrix metalloproteinase-7 up-regulation promotes epithelial-mesenchymal transition via ERK1-AP1 axis during ovarian endometriosis progression.

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Abstract

Endometriosis, characterized by extrauterine development of endometrial glands and stroma, is associated with increased risk of ovarian cancer development. In the present study, we investigated the role of matrix metalloproteinase-7 (MMP-7) on epithelial-mesenchymal transition (EMT) during ovarian endometriosis (N = 40) progression. We found that the expressions of EMT markers such as vimentin, slug, and N-cadherin were significantly elevated in late stages of ovarian endometriosis compared with those found in early stages. In addition, the activity and expression of ectopic MMP-7 were significantly higher in the late stages of endometriosis. In vitro studies revealed that increased expression of MMP-7 as well as epidermal growth factor (EGF), which was significantly elevated in severe stages of ovarian endometriosis, induced EMT in endocervical epithelial cells (End1/E6E7). Silencing the MMP-7 transcripts using small interfering RNA attenuated EMT responses, whereas treatment with recombinant active MMP-7 promoted EMT by cleaving E-cadherin. In addition, EGF receptor (EGFR) inhibitor treatments regressed endometriotic lesions and decreased MMP-7 activities in a mouse model of endometriosis. Chromatin immunoprecipitation assay identified EGFR-mediated ERK1 and activator protein 1 signaling for the transcriptional activation of MMP-7 in End1/E6E7 epithelial cells.-Chatterjee, K., Jana, S., DasMahapatra, P., Swarnakar, S. EGFR-mediated matrix metalloproteinase-7 up-regulation promotes epithelial-mesenchymal transition via ERK1-AP1 axis during ovarian endometriosis progression.