

Hypoxia stimulates CXCR4, an EMT-related factor expression in endometrial epithelial cells

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Endometriosis is characterized by the ectopic inflammation, growth, and fibrotic changes in the lesion. Previous study indicates that peritoneal bleeding may accelerate inflammation partially through the activation of protease-activated receptor (PAR) and the prostaglandin (PG) EP2 receptor in endometriosis-like graft of the mouse model. To explore the involvement of hypoxia and/or the inflammatory mediators in epithelial-mesenchymal transition (EMT) of endometrial cells, we examined the effects of thrombin, a PAR agonist and PGE2 on EMT marker expression and cell migration in human endometrial stromal (EtsT499) and epithelial (EM-1) cells. The endometrial cells in 3D culture system incubated for 18 h under hypoxia were cultured in the presence or absence of the combined treatment of thrombin and PGE2 (Throm/PG) for 72 h. Hypoxic conditions increased expression of CXCR4, an EMT marker in EM-1, but not in EtsT499, whereas Throm/PG did not affect CXCR4 in both cells. Throm/PG treatment promoted the migration of EM-1 under hypoxia. Thus, Throm/PG stimulation under hypoxia enhanced CXCR4 expression and accelerated migration of the endometrial epithelial cells. Our data suggests that the inflammatory mediators in retrograde menstrual fluid may be associated with the pathophysiology of ectopic endometrial EMT and migration.