Normal endometrial stromal cells regulate 17β-estradiol-induced epithelial-mesenchymal transition in endometriotic eutopic epithelial cells via Notch signaling pathway.

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Introduction
Epithelial mesenchymal transition (EMT) is involved in the pathogenesis of adenomyosis, and Notch signaling is crucial to EMT. We had previously demonstrated normal stromal cells (NSCs) inhibited the growth of endometrial carcinoma cells. However, whether NSCs regulate 17β-estradiol-induced epithelial-mesenchymal transition in endometriotic eutopic epithelial cells (EuECs) via Notch signaling pathway remain under-studied. Here, we studied the mechanistic role of NSCs in driving relegated EMT in adenomyosis.
Methods
Full-thickness-biopsy specimens from endometrium were collected after hysterectomy from women with adenomyosis for cell culthure. E-cadherin (epithelial cell marker) and N-cadherin (mesenchymal cell markers), Numb, Notch, Snail,Slug were examined at the protein levels by Western Blot using EuECs which co-culturing with conditioned culture medium (CM) by NSCs. Transwell assay was performed to detect the migration and invasion of EuECs. CCK8 assay was also applied to determine the growth of EuECs.
Results
CCK8 analysis identified CM by NSCs reduced cell growth in EuECs. CM by NSCs inhibited 17β-estradiol-induced cell growth in EuECs in adenomyosis. Moreover, CM by NSCs inhibited the migration and invasion, and 17β-estradiol-induced migration and invasion in EuECs. Meanwhile, CM by NSCs decreased Slug/Snail/Notch/N-cadherin expression and 17β-estradiol-induced Slug/Snail/Notch/N-cadherin expression, increased E-cadherin/Numb expression and abolished 17β-estradiol-induced E-cadherin/Numb reduction in EuECs.
Conclusion
In conclusion, normal stromal factors can inhibit 17β-estradiol-induced cell proliferation, and abolished 17β-estradiol-induced EMT in EuECs in adenomyosis via regulating Notch signaling pathway.

Keywords : 17?-estradiol, adenomyosis, epithelial-mesenchymal transition, Normal endometrial stromal cells, Notch signaling pathway
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