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Cell to cell communications in human endometrial decidualization

박동욱[*,**] · 최동순[*] · 김미란[**] · 민철기[***] · 조미영[**] · 황경주[**]
[*]아주대학교 대학원 분자과학기술학과, [**]아주대학교 의과대학 산부인과학교실,
[***]아주대학교 자연대학 생명과학과

Introduction: There is considerable evidence supporting that decidualized cells in the uterine act as functional layers that are required for successful implantation and conception. Several lines of evidence implicate the differentiation of stromal cells in the decidualization. It is becoming evident that uterine stromal cells (USC) modify the function of uterine epithelial cells (UEC) under certain conditions *in vivo*; however, relatively little is known about the effect of epithelial cells on the stromal cell differentiation and function. The transforming growth factor (TGF)-betas are multifunctional cytokines, and they play an important role in the controlled growth of trophoblasts. Moreover, they are implicated in maternal-fetal interaction during early gestation. To investigate the role of TGF-ß involved in the paracrinic communication during decidualization between UEC and USC, we have employed a co-culture system composed of human endometrial epithelial and stromal cells in defined hormonal conditions.

Design: In the co-culture, endometrial epithelial cells cultured in the matrigel-coated cell culture insert are seeded on top of the endometrial stromal cells cultured within a collagen gel. The co-culture was maintained for 48 hours under the following hormonal conditions: progesterone dominant condition (100 nM P4 and 1 nM E2) or estrogen-dominant condition (100 nM E2 and 1 nM P4). 10 ng/mℓ HGF and/or 10 ng/mℓ TGF-ß1 are added when necessary.

Methods: Reverse transcriptase-polymerase chain reaction (RT-PCR) is utilized to detect mRNAs quantitatively. Enzyme-linked immunosorbent assay (ELISA) and immunohistochemical staining are utilized to detect proteins in the tissue.

Patients: Gynecological surgery patients

Results: Prolactin mRNA is expressed in the co-cultured stromal cells under the progesterone dominant condition. TGF-ß1 and its receptors are expressed in both the co-cultured epithelial and stromal cells irrespective of the steroid present, which is in contrast with no or negligible expression of TGF-ß1 or its receptor in cells separately cultured. Both estrogen and progesterone significantly elevate the concentration of hepatocyte growth factor (HGF) in the conditioned medium of the co-culture with the value of 4325 pg/mℓ in E2-dominant and 2000 pg/mℓ in P4-dominant condition compare to 150 pg/mℓ in no hormone. In separately cultured stromal cells, administration of HGF induces the expression of TGF receptor 1 in both hormonal conditions, but induction of TGF receptor 2 is manifest in the P4-dominant condition only. Administration of TGF-ß and HGF directly induce prolactin mRNA in separately cultured stromal cells.

Conclusion: It is likely that progesterone induces the decidualization indirectly by promoting the cell to cell communication between the stromal and the epithelial cells. TGF-ß and HGF are two possible paracrine mediators in the human endometrial decidualization.