Attenuation of 5 α -reductase-mediated progesterone metabolism promotes differentiation of human endometrial stromal cells for the establishment of pregnancy

Kazumi Kawamura¹, Mikihiro Yoshie¹, Sayaha Nakajima¹, Tsubasa Chiba¹, Junya Kojima², Hirotaka Nishi², Keiichi Isaka², Kazuhiro Tamura¹

¹Dept. Endocrine Pharmacol., Tokyo Univ. Pharm. Life Sci., ²Dept. OB/GYN., Tokyo Med. Univ.

Human endometrial stromal cells (ESCs) differentiate into decidual cells during the mid-secretory phase of the menstrual cycle following the postovulatory rise in progesterone (P4). Progesterone (P4) is a predominant inducer of the differentiation which is essential for the establishment of pregnancy. In this study, we explored the roles of 5 α -reductases-mediated P4 metabolism in the differentiation of ESCs induced by P4 and dibutyryl cAMP (P4/db-cAMP) treatment. The ability of P4 metabolism in differentiated ESCs was compared with that in undifferentiated cells. The residual P4 level in media was much higher in the differentiated ESCs than in control cells, whereas the amount of the P4 metabolite allopregnanolone was less in the differentiated cells. Treatment of ESCs and endometrial epithelial cells with the 5 α -reductase inhibitors dutasteride and finasteride repressed P4 metabolism. Furthermore, inhibition of 5 α -reductase facilitated expression of differentiation markers, IGF-binding protein 1 and prolactin in P4/db-cAMP-stimulated ESCs. The expression of *SRD5A1*, which encodes 5 α -reductases type 1, was reduced in differentiated ESCs and epithelial cells. These data suggests endometrial 5 α -reductase metabolizes P4 and the enzyme-mediated metabolizing pathway maybe involved in the increase in P4 level for promoting ESC differentiation.