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

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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 5α-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 5α-reductase inhibitors dutasteride and finasteride repressed P4 metabolism. Furthermore, inhibition of 5α-reductase facilitated expression of differentiation markers, IGF-binding protein 1 and prolactin in P4/db-cAMP-stimulated ESCs. The expression of *SRD5A1*, which encodes 5α-reductases type 1, was reduced in differentiated ESCs and epithelial cells. These data suggests endometrial 5α-reductase metabolizes P4 and the enzyme-mediated metabolizing pathway maybe involved in the increase in P4 level for promoting ESC differentiation.