Effect of Embryonic Signals on Activity of DNA Methyltransferases in Luminal and Stromal Cells of the Porcine Endometrium

Agnieszka Waclawik; Monika Zembrzuska; Ewelina Goryszewska-Szczurek; Monika Baryla; Piotr Kaczynski

Department of Hormonal Action Mechanisms, Institute of Animal Reproduction and Food Research, Polish Academy of Sciences, Olsztyn, Poland

The peri-implantation period in mammals, including pigs, is critical period of pregnancy due to occurrence of increased embryo mortality. Pregnancy establishment requires coordinated communication between developing embryos and the maternal organism. Uterine receptivity is defined as the state in which the endometrium is ready for embryo implantation. It is regulated by ovarian hormones. During the maternal recognition of pregnancy (days 11-12 of pregnancy), porcine conceptuses signalize their presence by secreting multiple factors, of which estradiol (E2) is considered as the major embryonic signal. Our previous study reported that DNA methylation patterns in some genes in the endometrial tissue changed that may be involved in regulation of expression of these genes during early pregnancy. DNA methylation is catalyzed by DNA methyltransferases (DNMTs). The aim of the research was to study whether estradiol and conceptus can regulate the activity of the DNMTs in luminal epithelial (LE) and stroma cells (ST) of the porcine endometrium in vitro.

LE and ST cells were isolated from porcine uterus collected from gilts (n=6) on day 11-12 of the estrous cycle. Epithelial and stroma cells (at confluency of 60%) were incubated with control medium, medium containing E2 (1,10 and 100 nM) or conceptus-exposed conditioned medium with or without estrogen receptor antagonist (ICI 182,780). The activity of DNMTs in endometrial LE and ST cells was determined in nuclear protein extracts of cells using commercially available colorimetric assays. Statistical analyses were performed using one-way ANOVA, followed by Tukey post-test.

Estradiol elevated DNMT activity in ST cells ($p<0.05$). In the contrast, estradiol and the conceptus-exposed conditioned medium decreased DNMT activity in LE cells ($p<0.05$). Co-treatment with ICI182780 reversed the effect of E2 on DNMT activity in LE cells. Results of the present study indicate that E2 and products secreted by conceptus differentially regulate DNMT activity in LE and ST cells in the porcine endometrium. The results suggest that putative changes in DNA methylation in LE and ST cells in response to conceptus could be important during pregnancy establishment and development.

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