

p12^{DOC-1} Expression Regulation by Steroid Hormones in the Uterus of the Mouse

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Proliferation of endometrial cells is essential step in uterine preparation for embryonic implantation. Division of the epithelial cell and the stromal cell is regulated during pregnancy and its regulation is under the control of steroid hormones in the pregnant uterus through expression of cell cycle regulatory complexes such as cyclin G1 and G2. During early pregnancy, the stromal cells proliferate and then undergo differentiation for the implantation and placentation. However there is not much information about the proliferation related genes to explain the uterine modifications for implantation. To get profile for genes expressing at the time of implantation we employed a PCR-select cDNA subtraction method and identified a few genes including p12^{DOC-1}. p12^{DOC-1} mRNA expression was induced by progesterone and estrogen in the OVX uteri. Interestingly p12^{DOC-1} mRNA also is a late response gene to estrogen. RU 486 suppressed the p12^{DOC-1} mRNA expression. p12^{DOC-1} is a tumor suppressor gene and modulate CDK2 activity. During pregnancy p12^{DOC-1} mRNA expression increase after implantation and showed peak on day 5 of gestation and dramatically decreased after day 7 of gestation. p12^{DOC-1} mRNA transcript was localized in luminal epithelial cells but it was very faint during preimplantation. After starting the implantation, it localized in the stromal cells; heightened expression of p12^{DOC-1} mRNA correlates with intense stromal cell proliferation surrounding the implanting blastocyst on day 6 morning. However in the decidualized cells, the intensity of localized doc-1 mRNA was very weak. From those results, it is revealed that p12^{DOC-1} express regulated by progesterone and estrogen in the uterus. In addition, it expression is primary mediated by progesterone receptor and mainly localized at the differentiating areas. It is suggested that p12^{DOC-1} expression is critically modulated by progesterone and estrogen and result in the embryonic implantation.