

Prostaglandins in the bovine uterine lumen during the preimplantation period

Principal actors, temporal sequential role and direction of action

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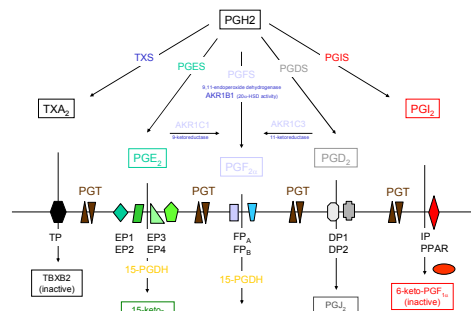
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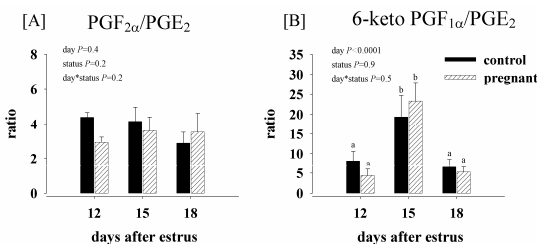
Introduction

The uterine histotroph comprises signalling molecules which critically account for an intact embryo-maternal communication. Most importantly during preimplantation development, a precise orchestration of all participants of this dialogue is essential. Prostaglandins (PG) are local paracrine mediators important for a vast variety of functions. During normal development, PG are not only involved in ovulation, cycle determination through induction of luteolysis in ruminants and fertilization, they also take part in early embryonic development and implantation thus contributing to the uterine milieu. We analyzed the most relevant PG in bovine uteri at different preimplantation pregnancy stages as compared to non-pregnant controls. Simmental heifers were artificially inseminated or received seminal plasma only. At days 12, 15 or 18 post estrus uteri were flushed for PG determination by LC-MS/MS. Endometrium and trophoblast tissue was sampled for RNA extraction and RT-qPCR analysis regarding specific enzymes and receptors involved in PG generation and function.

Synthesis Receptors Transport Metabolism

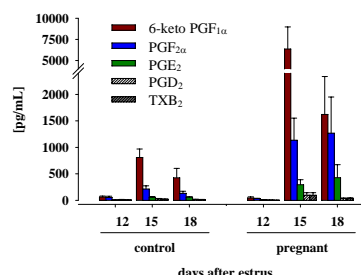


Prostaglandin ratios



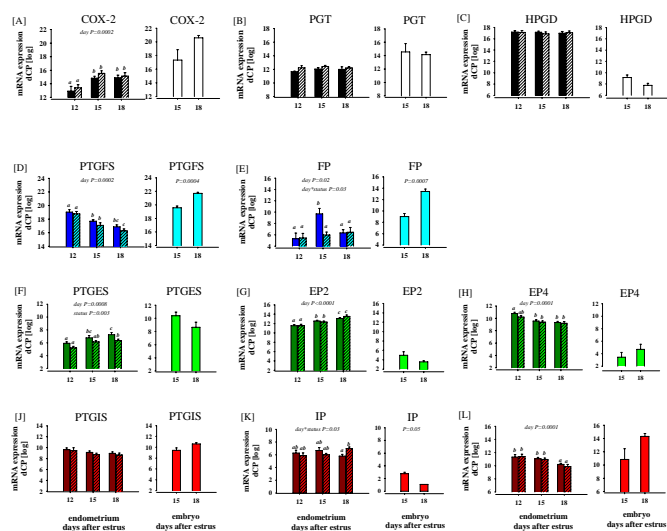
Ratios of PGF_{2α}/PGE₂ [A] and 6-keto PGF_{1α}/PGE₂ [B] during the preimplantation period. Data are expressed as means ± SEM of the quotients of absolute PG in uterine flushings.

Prostaglandins and metabolites

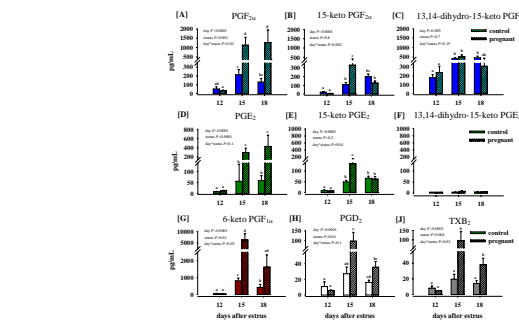


Predominant PG present in control and pregnant bovine uterine flushings. Data are presented as means ± SEM in 100 mL flushing/uterus quantified by LC-MS/MS.

Endometrial and trophoblast synthase and receptor expression



Transcript abundance of PG synthases, the prostaglandin transporter, specific receptors and the metabolic enzyme *HPGD* in endometrium and trophoblast tissue. For both endometrium and trophoblast tissue equal amounts of total RNA was used for reverse transcription and subsequent qPCR. Results are depicted as means of dCT [log₂] mRNA expression ± SEM. Different superscript letters indicate significant differences between groups ($P < 0.05$).



The concentrations of prostaglandins and metabolites vary with respect to day and status in uterine flushings. Different superscript letters indicate significant differences between groups ($P < 0.05$).

Discussion

At all days and points of time examined, 6-keto PGF_{1α} (the stable metabolite of PGI₂) was predominant in the uterine lumen followed by PGF_{2α} > PGE₂ > PGD₂ ≈ TXB₂. At days 15 and 18 PG increased from overall low levels at day 12, with a much more pronounced increase during pregnancy. The PGF_{2α}/PGE₂ ratio was not influenced by status. Minor changes of endometrial PG biosynthesis enzymes occurred due to pregnancy. Trophoblasts revealed high transcript abundance of general and specific PG synthases contributing to uterine PG. As PGI₂ and PGF_{2α} receptors were abundantly expressed by the trophoblast, the presence of PGI₂ and PGF_{2α} at the embryo-maternal interface points towards an essential role of PG for the developing embryo. There is no suppression of uterine PG during pregnancy, rather a suppression of PGF_{2α} pulses acting luteolytically. High amounts of PG other than PGE₂ in the preimplantation uterus may be essential rather than detrimental for successful reproduction.

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