

EXPRESSION AND REGULATION OF PROSTAGLANDIN RECEPTORS AND TRANSPORTER, AND CYCLOOXYGENASES 1 AND 2 IN BOVINE CORPUS LUTEUM DURING THE ESTROUS CYCLE AND MATERNAL RECOGNITION OF PREGNANCY

Arosh JA¹, Banu SK¹, Madore E¹, Parent M¹, Chapdelaine P¹, Kimmins S², MacLaren LA² and Fortier MA^{1,1} *Ontogénie et Reproduction, Centre de Recherche du CHUL, Université Laval, Canada.* ²*Department of Plant and Animal Sciences, Nova Scotia Agricultural College, Canada.*

Introduction: During the bovine estrous cycle, days 16-17 are considered as the “critical period” for either Maternal Recognition of Pregnancy (MRP), in the presence of viable embryo or luteolysis and return to a new estrous cycle. In ruminants, trophoblastic interferon tau (IFN τ) is known as the pregnancy recognition signal. Endometrial PGF_{2 α} is the luteolytic signal and PGE₂ is considered to be a temporary luteostatic signal at the time of establishment of pregnancy. Luteal PGF_{2 α} and PGE₂ may also play an important role in corpus luteum functions. Cyclooxygenases (COX) -1 and 2 are the rate limiting enzymes involved in the biosynthesis of PGs. PGF_{2 α} and PGE₂ exert their effects through G protein coupled receptors designated EP (EP1, EP2, EP3_{A-D} and EP4) and FP. Recently, we have found that the prostaglandin transporter (PGT), a facilitator of cellular transport of PGs is expressed and regulated in the bovine uterus. No information is available on the biosynthetic, signaling and cellular transport of PGF_{2 α} and PGE₂ in bovine corpus luteum during the estrous cycle and MRP. **Objectives:** Study the expression and regulation of (1) COX-1 and COX-2, (2) EP2, EP3, EP4 and FP receptors (3) PGT, in bovine corpus luteum during the estrous cycle and MRP. **Experimental Design:** In study-1, bovine ovaries were collected from the abattoir. Days of the estrous cycle were determined and tissues classified into 7 groups (n=4) covering the entire cycle length. In study-2, beef heifers were used. Estrus was synchronized using double PG regimen. Between days 14 and 16, control group (n=4) received 4 doses of 0.5% BSA (5 ml /dose) and IFN group (n=4) received 4 doses of IFN τ (0.25 mg /dose-5 ml) intra-uterine at 12 h intervals. On day 16 animals were slaughtered. In the two studies, corpora lutea were collected for extraction of total RNA and proteins. Expression of COX-1, COX-2, FP, EP2, EP3, EP4 and PGT were studied using RT-PCR, Northern and Western analyses. **Results:** COX-1 mRNA and protein is constitutively expressed throughout the estrous cycle. The level of expression COX-2 mRNA and protein is high, poor and moderate on days 1-9, 10-12 and 16-21 of the estrous cycle respectively. FP, EP2, EP3 and PGT are expressed and modulated during the estrous cycle. The level of expression of FP mRNA is maximal between days 10-12, EP2 and EP3 mRNAs is higher between days 13-18, PGT mRNA and protein is maximal between days 13-18 of the estrous cycle. During MRP, the level of expression of FP, EP2 and EP3 were decreased whereas no change was observed in the pattern of expression of COX-1, COX-2 and PGT in IFN τ treated animals. **Discussion:** The results suggest the existence of PG biosynthetic, signaling and transporting mechanisms in corpus luteum, and their differential regulation at the time of luteolysis and MRP. **Conclusions:** PGF_{2 α} (FP) and PGE₂ (EP2, EP3) receptors are differentially and selectively regulated at the time of luteolysis and MRP. **Clinical Applications:** Treatments targeting PGF_{2 α} and PGE₂ receptors might constitute the basis for new therapeutic strategies to treat reproductive disorders such as premature luteal regression, persistent CL, luteal insufficiency and early embryonic mortality, and to improve the conception rate in bovine. Supported by NSERC, Canada.

Key words: PG receptors, COX, PGT, Corpus luteum, Estrous cycle, MRP, Bovine.