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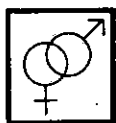
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# SOCIETY FOR THE STUDY OF REPRODUCTION

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OF REPRODUCTION  
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**EVIDENCE FOR THE PRESENCE OF INHIBITORY EP-PROSTANOID RECEPTORS IN THE BABOON BUT NOT IN THE SHEEP PREGNANT MYOMETRIUM NEAR TERM**

R.Garcia-Villar\*, L.R.Green\*, S.Jenkins\*, R.Wentworth\* & R.A.Coleman\*<sup>1</sup>  
L.P.N.R., Coll Vet. Med., Dept. Physiol., Cornell Univ., Ithaca, NY, 14853 USA.  
& <sup>1</sup>Dept. Cardiovasc-Resp. Pharm., GLAXO Res., Ware, Herts, SG12 0DP UK.

Prostaglandins (PG) E<sub>2</sub> and PGF<sub>2α</sub> are involved in the regulation of myometrial contractility under different physiological conditions including parturition in several animal species and in the human. Nevertheless, although PGF<sub>2α</sub> appears to be consistently stimulatory via interaction with stimulatory prostanoid receptors, PGE<sub>2</sub> has been shown to produce either activation or inhibition of myometrial contractions by interacting with either stimulatory or inhibitory prostanoid receptors.

The present study was aimed at determining the presence of functional inhibitory and/or stimulatory prostanoid receptors in the myometrium of pregnant sheep and baboons using an *in vitro* superfusion system. Strip preparations of uterine muscle from ten sheep at 107-145 days gestation age (dGA) and five baboons (159-184 dGA), were superfused with 37°C oxygenated Krebs buffer containing 3 μM indomethacin. Contractions of the myometrial strips were recorded with strain gauges, displayed on a printer and automatically quantified as integrated area of activity, using a microcomputer. Cumulative concentration-response curves (CRCs) were constructed to PGE<sub>2</sub> (0.1nM to 1 μM) and PGF<sub>2α</sub> (1 nM to 100 μM), added sequentially to the buffer, and EC<sub>50</sub> values calculated.

Under baseline conditions, all myometrial strips from both species displayed an almost regular pattern of activity, in the form of spontaneous episodes of contractions of about 1 min duration, separated from each other by resting periods of 2-3 min. As expected, PGF<sub>2α</sub> stimulated myometrial activity in concentration-related fashion in all preparations from both sheep and baboon. The EC<sub>50</sub> value for PGF<sub>2α</sub> in sheep myometrium (69 nM) was significantly (p<0.05) lower than that in baboon myometrium (177 nM). In contrast, effects of PGE<sub>2</sub> were species-related: PGE<sub>2</sub> caused a concentration-related stimulation of myometrial activity in sheep tissue (EC<sub>50</sub> = 2.5 nM), but induced a concentration-related inhibition of activity in baboon myometrium (IC<sub>50</sub> = 70 nM). These observations indicate that both sheep and baboon myometrium contain prostanoid receptors mediating stimulation, whereas baboon myometrium also contains prostanoid receptors mediating inhibition. The precise identity of these various receptors remains to be established. However the present work suggests that the baboon may represent a suitable animal model for the investigation of potential inhibitory prostanoids intended for clinical use as tocolytics in the relief of premature labor.

Name, address, telephone and FAX numbers of presenting author:

Rafael Garcia-Villar

Laboratory for Pregnancy and Newborn Research  
~~Dept. Physiology, College of Vet. Med.~~  
818 VRT, Cornell University

Ithaca, NY 14853-6401  
(607) 253-3082; FAX: (607) 253-3455

97 EXPRESSION OF PROLACTIN RECEPTOR AND LH RECEPTOR GENES IN FETAL RATS AND MICE. F.-P. Zhang\*, T. Hämäläinen\*, P. Pakarinen\*, I. Huhtaniemi, A. Bartke<sup>1</sup>. Dept. of Physiology, Univ. of Turku, 20520 Turku, Finland, and Dept. of Physiology<sup>1</sup>, Southern Illinois Univ. Sch. of Med., Carbondale, IL 62901-6512.

Ontogeny of prolactin receptor (PRL-R) gene expression in the testes, ovaries, brain and other fetal organs of rats and mice was studied using reverse transcription-polymerase chain reaction (RT-PCR) and Southern hybridization. The multiplied fragment of PRL-R mRNA corresponded to approximately 700 bp from the region coding for the extracellular domain of the PRL-R which is homologous in rats and mice but differs for the corresponding domain of the GH-R. LH-R mRNA was detected by RT-PCR, Southern and Northern hybridization. Both methods were validated by studies in immature and adult animals in which developmental patterns of PRL-R and LH-R are already known. In the rat, PRL-R mRNA was consistently detectable in the testes and ovaries starting on day 15.5 of fetal life i.e. coinciding with the appearance of full length LH-R mRNA in the testes but preceding the previously reported appearance of LH-R mRNA in the ovary. The truncated form of LH-R mRNA was detectable in the testis one day before the appearance of the full length LH-R mRNA (day 14.5) and the number of different size LH-R mRNA transcripts increased from 2 to 4 during fetal and postnatal development. In neonatal animals, the DNA signals generated were weaker and in the case of ovarian PRL-R, not consistently observed. PRL-R mRNA was present in the fetal rat brain (starting on day 14.5), kidney, lung (day 20.5) and placenta but was not detected in the fetal liver. In the mouse, PRL-R mRNA was present in the testes, ovaries and liver on day 15 of fetal life. In the fetal mouse brain, DNA signal generated was extremely weak on day 15 but clearly present on day 18. These results suggest that PRL-R and LH-R genes are expressed very early in development, preceding secretion of the corresponding ligands from the fetal pituitary. The possible role of placental hormones as inducers and ligands of these receptors in the fetus remains to be investigated. The presence of PRL-R mRNA in fetal brain suggests that lactogenic hormones may influence prenatal development and function of the central nervous system. (Supported by the Academy of Finland)

99 EVIDENCE FOR THE PRESENCE OF INHIBITORY EP-PROSTANOID RECEPTORS IN THE BABOON BUT NOT IN THE SHEEP PREGNANT MYOMETRIUM NEAR TERM

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98 MELATONIN-INDUCED DOWN-REGULATION OF UTERINE PROLACTIN RECEPTORS IN MINK.

Jack Rose\* and Fredrick Stormshak, Department of Biological Sciences, Idaho State University, Pocatello, ID 83209, and Department of Animal Sciences, Oregon State University, Corvallis, OR 97331.

Implantation and pregnancy in mink are associated with increasing serum prolactin (PRL) and progesterone concentrations and decreasing estrogen concentrations. Although PRL is luteotropic in mink, implantation cannot be induced with estrogen or progesterone, either alone or in combination. Because PRL receptors have been detected in the uterus of the mink and other carnivores, a direct action of the hormone on the uterus is possible. Secretion of PRL in mink is suppressed by the administration of melatonin. Continuous suppression of PRL secretion in mink with melatonin may provide insights into the regulation of uterine PRL receptors and associated changes in ovarian steroid hormone production. An experiment was conducted to investigate the effects of exogenous melatonin on serum estradiol-17β, progesterone and uterine PRL receptor concentrations in mated mink. Sixteen adult standard dark female mink were assigned randomly to two groups and mated to fertile males on March 8 or 9, 1990. On March 16, a Silastic capsule was inserted s.c. in the interscapular region of each mink. Mink in group 1 (N=8) each received an empty capsule and represented controls. Mink in Group 2 (N=8) each received a capsule containing 10 mg melatonin. On April 2, all animals were lightly anesthetized and blood samples collected via cardiac puncture were analyzed for serum levels of estradiol-17β and progesterone. The animals were then sacrificed and their uteri collected for assay of PRL receptors. Exogenous melatonin reduced serum progesterone concentrations to almost undetectable levels (Controls, 8.08 ± 0.73 vs. Treated, 0.82 ± 0.12 ng/ml; P < 0.001) and resulted in increased concentrations of estradiol (Controls, 13.3 ± 1.9 vs. Treated, 22.0 ± 1.9 pg/ml; P < 0.01). Uterine PRL receptor concentrations decreased (P < 0.05) from 32.74 ± 9.36 fmol/mg protein (Controls) to 23.74 ± 9.02 fmol/mg protein in response to melatonin treatment. These data illustrate the requirement for PRL secretion in order to maintain progesterone synthesis. Further, it appears that a high systemic ratio of progesterone to estrogen and/or increased levels of PRL are requisite for stimulating synthesis of uterine PRL receptors in mink.

100 Specific oxytocin binding sites in the porcine endometrium during the estrous cycle and early pregnancy

Akira OKANO<sup>1</sup>, Kiyoshi OKUDA<sup>2</sup> and Masashi TAKAHASHI<sup>1\*</sup> Dept. of Reproduction, National Institute of Animal Industry<sup>1</sup>, Ibaraki 305; Div. of Animal Science and Technology, Faculty of Agriculture, Okayama Univ<sup>2</sup>, Okayama 700, Japan

It has been demonstrated that exogenously administered oxytocin (OT) to sows in late stage of estrous cycle induces a prompt increase in uterine secretion of prostaglandin F<sub>2α</sub> (PGF) and that the porcine endometrium responds *in vitro* to OT with increased secretion of PGF. The presence of specific receptors for OT in endometrium is a prerequisite for PGF secretion. In the present study, we examined OT receptors in the porcine endometrium at different stages of the estrous cycle (days (D) 0, 5, and 15, n=3, respectively), and in early pregnancy (D 5 and 15 after fertilization, n=4, respectively) by a radio receptor assay using the [<sup>125</sup>I]-labeled OT antagonist [d(CH<sub>2</sub>)<sub>2</sub>, Tyr(Me)<sub>2</sub>, Thr<sup>4</sup>, Tyr-NH<sub>2</sub>]-vasotocin. Binding assay was conducted with 50 μg/tube membrane protein precipitated between 1,000 and 120,000g. Binding specificity was demonstrated in displacement studies with four related and two unrelated peptides. OT binding capacities and equilibrium dissociation constant (K<sub>d</sub>) were obtained by Scatchard analyses. The binding affinity of endometrial OT receptors on D0 and D5 were similar (D0: K<sub>d</sub>=1.95±0.26 and D5: 2.33 ± 0.57 nM, all values mean ± S.E). But B max on D0 (1.45 ± 0.11 pmol/mg protein) was significantly higher than D5 and D15 (D5: 0.09 ± 0.01 and D15: 0.34 ± 0.02 pmol/mg protein, P < 0.01). In the luteal phase, the binding affinity (D15: K<sub>d</sub>=0.57 ± 0.10 nM) was lower than the levels on D0 and D5. However, it was not possible to characterize the binding affinity in the endometrium of early pregnant sows by Scatchard analysis due to the low concentration of specific binding sites. Our results reveal the existence of specific binding sites for OT in the porcine endometrium, and further demonstrates that there is a direct action of OT on the porcine endometrium mediated by OT receptors. The changes in specific OT binding to the endometrium at different stages of estrous cycle suggest that OT plays an important role to regulate the estrous cycle of the pig as seen in other animals. The low concentration of OT receptors during early pregnancy may be due to the existence of conceptuses in the oviduct or uterus. Supported by Bio Media Program from Ministry of Agriculture, Forestry and Fishery of Japan.