ABSTRACTS

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Endocrine and molecular control of luteal and placental function in dogs

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In the dog Corpus luteum (CL) is the only source of progesterone (P4) in pregnant and cyclic animals. Also the respective progesterone secretion profiles are almost identical in either case until the last third of dioestrus when the gradual progesterone decline turns into a steep one in pregnant bitches indicating the onset of parturition [1]. Consequently, the length of the CL-phase in non-pregnant dogs exceeds the luteal lifespan in pregnant ones. This is a peculiarity if compared with other domestic animal species.

Furthermore, also in contrast to other animals depending on the gonadotropic support throughout the luteal phase, canine CL are independent of gonadotropic support during the first third of dioestrus. During this time PGE2 appears to be one of the most important luteotropic factors acting in the auto- and/or paracrine manner [2]. Thereafter PRL is the main luteotropic factor and hypophyscetomy and, thereby, deprivation of gonadotropic support, leads unequivocally to cessation of luteal function [3]. Surprisingly, however, luteal regression/luteolysis occurs in spite of an increased gonadotropic support.

Recently the expression of PRL-receptor (PRLr) was shown in canine CL giving a new insight into possible PRL-mediated regulatory mechanisms and indicating that the provision of P4 in later stages of the CL-phase could be controlled upstream of the steroidogenic machinery, at the level of PRLr expression and/or function [4]. The cycle-related expression of PRLr, resembling luteal expression patterns of steroidogenic acute regulatory protein (STAR) and 3β-hydroxysteroid dehydrogenase (3BHSD), the two rate-limiting steps in the P4-synthesis and reflecting the course of peripheral P4 concentrations [4], further supports this hypothesis. As for the biological function of LH, in our on-going project, the luteal expression of LH-receptor in cyclic animals was biphasic with highest levels observed in the early and late stages of dioestrus. The functional implication of this finding remains to be elucidated.

The canine CL unveils an inherent lifespan that, at least in non-pregnant animals, is independent of an uterine luteolysin. In contrast, in pregnant animals the prepartal PGF2α increase in maternal peripheral blood indicates its involvement in processes of luteolysis and parturition. According to our recent data this appears to origin from the strongly upregulated expression of cyclooxygenase 2 (COX2) in the utero/placental compartment [5]. If COX2 is the limiting factor, the system is strongly activated at this time [5]. As concluded from experiments utilizing a selective progesterone receptor blocker, alterations in the placental feto-maternal communication appear to possess an important signalling function in this process [5]. Similar conclusions have been drawn from our recent observations concerning the expression of PRLr in canine uterus and placenta [4].

With our studies a new focus has been put on canine placenta as an important endocrine organ. It gave also a rise to the hypothesis that the prepartal luteolysis in the dog might be a result of a lower threshold of the luteal progesterone reached during the course of the gradual luteal regression, leading to the activation of the utero/placental prostaglandin biosynthetic pathways. This, in turn, would result in the prepartal output of the luteolytic PGF2α and final drop of progesterone levels. The decreased expression of 15PGDH, an enzyme catalyzing the conversion of PGF2α to its biologically inactive metabolite 15-ketodihydro-PGF2α, and the colocalization with the PGF2α-synthase expression in the uterus and placenta prior to parturition, further support this hypothesis and introduce 15PGDH as a new possible local regulator of prostaglandin provision in the dog.

Finally, even if there are no hints for an active luteolytic system of luteal or uterine origin in non-pregnant animals an interesting observation has been made concerning the luteal expression of PGF2α-receptor (PGFR); it is constitutionally expressed with significantly increasing levels in the later stages in the CL-phase, possibly explaining the receptivity of canine CL to exogenously applied PGF2α [6]. An endogenous source of a luteolytic agent is apparently lacking letting the luteal regression in cyclic bitches appear as a passive degenerative process. This is in contrast to pregnant dogs where prepartal luteolysis seems to be an active process of CL-destruction by PGF2α of utero/placental origin targeting the luteal PGFR.

