UTERINE AND PLACENTAL FACTORS REGULATING CONCEPTUS GROWTH: INSIGHTS FROM THE EWE

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Uterine adenogenesis is the process whereby endometrial glands differentiate and develop and is primarily a postnatal event in all mammals. In domestic animals and humans, adenogenesis involves initial differentiation and budding of glandular epithelium followed by invagination and extensive tubular coiling and branching morphogenesis through the endometrial stroma to the myometrium. Transient exposure of the neonatal ewe to a progestin from birth to postnatal Day 56 resulted in a uterine gland knock out (UGKO) phenotype in the adult. UGKO ewes exhibit a peri-implantation defect in conceptus (embryo/fetus and associated extraembryonic membranes) survival, indicating the functional importance of uterine glands and their secretions. Genomic and proteomic analysis of uterine endometrium from UGKO ewes has identified many candidate genes that regulate conceptus development and implantation, including endogenous Jaagsiekte sheep retroviruses (enJSRVs), glycosylated cell adhesion molecule one (GlyCAM-1), osteopontin and galectin-15. Galectin-15, also known as OVGAL11, and a previously uncharacterised member of the galectin family of secreted β-galactoside lectins, was discovered in the endometrium of sheep. In endometria of cyclic and pregnant sheep, galectin-15 mRNA was expressed specifically in the endometrial luminal epithelium but not in the conceptus. In pregnant sheep, galectin-15 mRNA expression appeared in the epithelia between Days 10 and 12 and increased between Days 12 and 16. Progesterone induced and interferon tau stimulated galectin-15 mRNA in the endometrial epithelium. Galectin-15 protein was concentrated near and on the apical surface of the endometrial luminal epithelia and localised within discrete cytoplasmic crystalline structures of conceptus trophectoderm. Galectin-15 is hypothesised to function extracellularly to regulate trophectoderm migration and adhesion to the endometrial epithelium and intracellularly to regulate cell survival, growth and differentiation. In sheep, the sequential actions of ovarian steroid hormones (oestrogen and progesterone), interferon tau, placental lactogen and placental growth hormone constitute a servomechanism that directly regulates endometrial gland morphogenesis and terminal differentiated function to provide increasing histotrophic nutrition for conceptus growth and development. Knowledge gained from this research will be used to prevent or treat infertility, fetal growth retardation and disease in domestic animals and humans.

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