

**Biological Role of Conceptus Derived Factors
During Early Pregnancy in Ruminants**

Kelsey Brooks

Dr. Thomas Spencer, Dissertation Supervisor

ABSTRACT

In domestic animals the majority of pregnancy loss occurs during early gestation and is characterized by endometrial dysfunction, or asynchrony between the conceptus (embryo and outer trophoctoderm) and uterus. This work tested that hypothesis that conceptus derived factors regulated gene expression changes in the trophoctoderm which are essential for trophoctoderm development and conceptus elongation in sheep. The hypothesis was addressed by determining the physiological roles of: (1) Interferon tau and interferon receptors 1 and 2 (IFNAR1 and IFNAR2) in conceptus development; (2) PG signaling through PPARD and PPARG in the elongating conceptus; (3) the cortisol converting enzymes HSD11B1 and HSD11B2 in conceptus development; (4) the role of the glucocorticoid receptor (GR) in cortisol signaling during conceptus elongation. Gene knockout studies utilizing osmotic pumps to deliver morpholino antisense oligonucleotides, lentiviral transduction of shRNAs, and CRISPR/Cas9 based genome editing were used to target the elongating conceptus during elongation. Results of the studies established that IFNT, PPARG and HSD11B1 are essential for conceptus elongation during early pregnancy in ruminants. Knowledge gained from these studies provides new insight into the physiological pathways governing conceptus development and elongation. Information from these studies provides a foundation for future translation research that is necessary to increase fertility of domestic ruminants.