The establishment of pregnancy requires the participation of a receptive endometrium and the development of the embryo to the implantation competent stage. In mammalian species, including pigs, embryo can attach to the uterus only when the uterus acquires a limited window of receptivity (implantation window). As part of achieving this receptivity, the endometrium undergoes a transformation in response to the physiological changes triggered by ovarian hormones to prepare for embryo attachment and implantation.

Under the influence of ovarian steroids, locally acting soluble factors synthesized by the endometrium can affect conceptus development and implantation. Developing embryos, in turn, synthesize and secrete molecules that can act to improve conceptus survival in the uterus. Among the factors involved in embryo-maternal interactions are prostaglandins, growth factors, cytokines and their receptors and hormone estradiol. Leukemia inhibitory factor (LIF), interleukin (IL)-6 and IL-1B are present within the uterine luminal microenvironment during early pregnancy. The conceptuses ability to modify the maternal uterine environment into an environment favorable for growth and survival occurs through the activation of inducible transcription factors within the conceptus and uterine endometrium. Many cytokines expressed by the conceptuses and endometrium stimulate a tightly controlled proinflammatory response within the uterus. However, induction of cytokines is not limited to the immune system but it can regulate cell differentiation, proliferation and survival.

Many studies have identified that the LIF, a cytokine produced by uterus, is an essential regulator of implantation in mice. It is well established that LIF and IL6 by binding to their cell surface receptors or to glycoprotein (gp)130 activate transcription factor Signal Transducers and Activators of Transcription (STAT)3 in the mouse and human uterine cells. LIF and IL-6 have also been shown to be upregulated in porcine endometrium during early pregnancy. Additionally, STAT3 has been revealed to be a major regulator of proteins differentially expressed between cyclic and pregnant animals and STAT1 was earlier shown to be induced by E2 and IFN in porcine endometrium. However, whether the aforementioned cytokines activate STAT genes/proteins in porcine endometrium and the precise mechanism via which activated STAT promotes changes responsible for uterine and conceptus development and implantation are not well understood in the uterine environment.

The goal of our research is to understand the signaling mechanisms involving cytokines and hormone E2 that might induce STAT activation in the developing porcine conceptus and maternal endometrium essential for establishment of pregnancy and implantation in the pig. We will study the expression and activation of STATs (STAT 1, STAT2 and STAT3) in endometrium and conceptuses. STAT proteins are transcription regulators known to be activated by various cytokines, growth factors and hormones. This activation is essential for processes such as cell differentiation, cell proliferation, extracellular remodeling and cell adhesion. All these processes are also involved in endometrial remodeling essential in developing receptivity for embryo and its implantation. Therefore, we would also like to investigate the mechanisms by which STAT mediates the effect of a variety of cytokines, growth factors and estradiol (E2) in endometrium and/or in conceptuses. We would further explore the functional role of STATs in embryo attachment.

For our research straightforward techniques such as quantitative real time polymerase chain reaction (qPCR), western blot, immunohistochemistry, gene silencing and chromatin immunoprecipitation assay will be used. Technique qPCR will help us to evaluate whether STAT family genes are expressed in porcine endometrium and if pregnancy status has any effect on its upregulation. qPCR will also be used to check the expression of many other genes that are responsible for endometrial remodeling, cell proliferation and also about molecules that control the adhesiveness of epithelium for embryo attachment. Western blot will be used to evaluate the activation of STAT, whereas immunohistochemistry will give us an idea in which compartment of endometrium STAT and its downstream targets are expressed. Finally, gene silencing will allow us to silence the expression of STAT in epithelial cells to evaluate whether STAT has any functional role in attachment of trophoblast to the endometrial epithelium.

The results of our study will yield data on expression of various genes/protein and mechanism responsible for endometrial remodeling and embryo adhesion. The endometrial remodeling being common across the mammalian species, the results of present study can also be extrapolated to other farm animals and also humans for which rodent models are not sufficient.