Analysis of differentially expressed genes and the promoters in bovine endometrium throughout estrus cycle and early pregnancy

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Title ：Analysis of differentially expressed genes and the promoters in bovine endometrium throughout estrus cycle and early pregnancy
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Thesis Summary

Endometrial gene expression is primarily regulated by the ovarian steroids and pregnancy recognition factors. A significant number of analyses of differential expression genes (DEGs) in bovine endometrium have been reported. These huge volume of data in comprehensive analysis provide a lot of valuable information on reproductive physiology as base line information. However, each gene expression is regulated by indirect control of various secreted factors and transcription factors. Therefore, in order to utilize the vast amount of information obtained from DEG as a reproductive technology, more detailed analysis of the gene expression mechanism is necessary. The aim of the present study was to comprehensively characterize DEGs in bovine endometrium together with the analysis of their promoter region.

Bovine uteri at follicular stage (FS), luteal stage (LS) and implantation stage (IS) at day18 of pregnancy were collected from the slaughterhouse. Uterus was opened longitudinally, and tissues were carefully cut from the lamina propria of the caruncular endometrium and conserved at -80°C. Total RNA extracted and prepared cDNA, were then subjected to high-throughput sequencing by using

HiSeq 2500 sequencer (Illumina). DEGs were considered significant based on the criteria of fold change and P-value (fold >2 and P <0.05). Data of DEGs were analyzed by Ingenuity Pathways Analysis software (IPA). For promoter analysis, 1kb upstream promoter region of each DEG was analyzed by dedicated analysis software (Softberry).

The comparison of the genes expressed at FS and LS showed that the number of DEGs were 496 and 597 for highly expressed at FS and LS, respectively. Moreover, when comparing LS and IS, there were 383 DEGs with higher expression and 346 with lower expression at IS compared to LS. The results of IPA showed that cell morphology, cell proliferation, cell to cell signaling and interaction are unique functions for FS. In addition, hepatic fibrosis in canonical pathway and ERBB2 in upstream regulator were the most significant at FS, respectively. While, small molecule biochemistry, lipid metabolism, energy production, carbohydrate metabolism and protein synthesis were found as specific functions for LS. Super pathway of cholesterol biosynthesis in canonical pathway and SREBF2 in upstream regulator were the most significant at LS, respectively. When DEGs of IS were compared with LS, cellular movement, protein synthesis, post translational modification and protein folding estimated as unique functions for IS. Complement system in canonical pathway and IFN in upstream regulator were the most significant at IS, respectively. It was also observed that 20-30 transcriptional factors (TFs) were included in each DEGs. Additionally, promoter analyses estimated 150-160 TFs for each stage. DLX4 and IRF4 at FS, and IRF5, IRF9, STAT1 and STAT2 at IS were in common to DEGs and estimated TFs, respectively.

The present study highlighted potential molecular mechanisms controlling endometrial function during estrus cycle and implantation stage, which will further guide to better understand the endometrial functions in future studies.