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The Endocrinology and Physiology of Parturition: Understanding the Process through Mining Genome Databases

Parturition is initiated by the fetal-placental unit and involves a cascade of endocrinological and physiological events that ideally culminate in birth of healthy offspring. The article in this issue titled "Gene Expression Profiling of Rat Uterus at Different Stages of Parturition" by Drs. Milena Girotti and Hans Zingg (Laboratory of Molecular Endocrinology, McGill University Health Centre; Ref. 1) provides results from a study of uterine gene expression in periparturient rats using Affymetrix rat genome U34A DNA microarrays in conjunction with Northern blotting and real-time RT-PCR.

The authors note that aberrations in signaling events for parturition lead to preterm births that are associated with 70% of neonatal deaths and up to 75% of neonatal morbidity, and a lack of diagnostic indicators and treatment protocols to predict or prevent preterm birth. Thus, understanding events that trigger normal parturition is expected to provide insight into causative pathophysiological conditions and suggest treatment modalities to prevent preterm births.

The authors examined uterine gene expression on: 1) d 0 of the estrous cycle; 2) d 20 of pregnancy; 3) d 23 and not in labor; 4) d 23 and in labor; and 5) 36 h post partum. A total of 8740 genes were analyzed, and 562 genes that changed significantly were assigned to five cluster groups. Cluster 1 genes increased during labor and were associated with immune defense, inflammation, and immediate early response genes such as transcription factors nurr77 and egr-1. Cluster 2 genes were expressed throughout pregnancy and linked to metabolism and intracellular trafficking of molecules. Cluster 3 genes were suppressed during labor and included extracellular matrix and cell-to-cell interaction genes. Cluster 4 genes were expressed during the postpartum period and were related to cytoskeleton and cellular motility reflecting uterine involution. Cluster 5 genes varied as to time of expression but include ribosomal genes and genes for extracellular matrix proteins, proteases, lipases, *etc.* Interestingly, more genes were suppressed than activated during labor. Several identified genes were associated with uterine development and conceptus implantation, including Wnt/frizzled and Rank/Rank1, and signaling molecules erg-1, daf-1, and ebnerin.

Expression of 249 uterine genes increased and 112 decreased on d 20 of pregnancy compared with d 0 of the estrous cycle. Between d 20 and 23 of pregnancy before onset of labor, expression of 54 additional genes increased, and most were for extracellular matrix and cytoskeleton. With onset of labor on d 23, expression of many genes decreased, particularly those for regulation of growth and nutrient transport. For example, uroguanylin and osteopontin gene expression increased 73- and 60-fold, respectively, between d 0 of the estrous cycle and d 20 of pregnancy but decreased 20-fold and 2.2-fold, respectively, on d 23 with onset of labor.

The results of transcriptional profiling by microarray analysis were validated for selected genes using Northern blotting and/or real-time RT-PCR. These genes included decay-accelerating factor 1 from cluster 1, IGF binding protein 2 from cluster 2, osteopontin from cluster 3, frizzled-related protein from cluster 4, osteoprotegerin from cluster 4, estrogen responsive gene 1 from cluster 5, and ebnerin from cluster 5. The authors reported excellent agreement in expression trends detected using the three methodological approaches.

Drs. Girotti and Zingg used DNA microarrays to identify a complex set of genes that change in response to pregnancy and endocrine events during the peri-parturient period and discuss roles of some of these genes relative to uterine biology during pregnancy and parturition. Their results do not define new mechanisms, but they do provide an exceptional data set to inform the scientific community of changes in uterine gene expression to be explored through research aimed at alleviating or ameliorating mortality and morbidity resulting from preterm labor.

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Reference

1. **Girotti M, Zingg HH** 2003 Gene expression profiling of rat uterus at different stages of parturition. Endocrinology 144:2254–2265