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Molecular Characterization of Endometrium of Women with PCOS: Application of a Knowledge-based Approach for Interpreting Genome-wide Expression Profiles

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Background & Objectives: Polycystic Ovary Syndrome (PCOS) is a common endocrinepathy characterized by chronic oligo/anovulation, hyperandrogenemia, infertility, and metabolic alterations related to insulin resistance, such as hyperinsulinemia and obesity. These characteristics suggest that PCOS could revise physiology of endometrium in these patients. However, the molecular mechanisms by which PCOS affect endometrial homeostasis still remain unexplored. Thus to understand molecular characteristics of endometrium of women with PCOS, expression profiles of endometrium of PCOS patients during the proliferative phase of the menstrual cycle were analyzed.

Method: Endometrial tissues from PCOS patients and healthy women as control were obtained and divided into two pieces for histological analysis and RNA preparation, respectively. In all tissue samples, histological dating and classification were evaluated by appropriate criteria, such as 2003 ESHRE/ASRM PCOS criteria. Endometrial RNA prepared from 4 controls and 4 PCOS patients was utilized to perform oligo microarrays with Affymetrix HG-U133A 2.0 containing ~22,000 human genes. Gene set enrichment analysis (GSEA) was applied to interpret expression profiles from microarrays. Semi-quantitative and/or realtime RT-PCR was carried out with additional RNA samples to validate results analyzed by GSEA.

Results: GSEA with a priori established data sets defined by known biological pathways or certain experimental environments provides a list of biological pathways aberrantly operating in endometrium of PCOS patients. Analysis with GSEA demonstrated that biological pathways associated with cell cycle and apoptosis in endometrium of PCOS patients are less active compared to those in controls. In addition, metabolic enzymes involved in glycolysis are consistently downregulated in endometrium of PCOS patients, suggesting that glucose metabolism in endometrium affected by PCOS is significantly altered.

Conclusions: Biological pathways associated with cell cycle, apoptosis, glycolysis, and integrin signaling are negatively regulated in endometrium of PCOS patients during proliferative phase of menstrual cycle. GSEA is a powerful tool to provide an insight to understand pathophysiology of certain diseases, such as cancer and PCOS with gene expression profiles.