107. MOLECULAR PROFILE OF HUMAN ENDOMETRIUM DURING THE MENSTRUAL CYCLE

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Human endometrium undergoes a series of cyclic changes each month associated with cellular events such as proliferation, differentiation and apoptosis. The aim of this study is to investigate the gene expression profile of human endometrium during the menstrual cycle using cDNA microarray technology. Curettings of endometrium (n = 39) were snap frozen at the time of surgery. Menstrual cycle stage was determined by histological evaluation. Total RNA extracted from a mixture of endometrial samples was pooled to make a common reference RNA. Total RNA of the reference and individual samples were processed for reverse transcription with Cy3 and Cy5 fluorescent-labeled dCTPs respectively, and hybridized on a 10.5 K cDNA glass slide microarray. Expressed genes were identified using Scanarray 5000 UV laser scanner. Quantarray software was used to calculate the gene expression ratio between individual endometrial samples and the reference. Normalization and visualization of the gene expression changes were performed using GeneSpring software. Gene expression ratios between 9 different stages of the cycle were analysed by nonparametric ANOVA with Benjamini-Hochberg false discovery rate correction at the $P<0.05$ significance level. The analysis identified just over 1000 genes with significant changes across the cycle. Five of those genes are being validated by real-time RT-PCR. A CSIRO algorithm called GeneRave was used to determine whether histopathological evaluation correlated with molecular profile of the samples. The groups were treated as both ordered and disordered categorical data. Preliminary studies show that based on the expression profiles of 7 key genes, 23 samples correlated exactly with the stage of the cycle determined by the pathologist and 12 of the remaining 16 samples were only misclassified by 1 cycle stage. Thus 35 out of 39 endometrial biopsies show a high degree of correlation between histopathology and molecular profile. A bioinformatics algorithm that allows cycle stage prediction based on gene expression will allow identification of genes with expression changes associated with different endometrial physiology and pathology.

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