

## HUMAN ENDOMETRIAL CYCLE STAGES CAN BE DETERMINED BY GLOBAL GENE EXPRESSION PROFILING

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Endometrium is a dynamic tissue which undergoes cyclic changes each month, under the overall control of oestrogen and progesterone. The aims of this study were to investigate the changing global gene expression profile of human endometrium during the menstrual cycle using microarray technology and to determine the correlation between histopathological evaluation and molecular profile of the samples. Curettings of endometrium were collected from 43 cycling women and immediately snap frozen. The menstrual cycle was divided into seven stages by histological evaluation. Standard two-color cDNA microarrays were performed on the 43 samples against a common reference, using a 10.5 K cDNA glass slide microarray. Expressed genes were identified using a Scanarray 5000 UV laser scanner. Quantarray software was used to quantify the relative gene expression values. Normalisation and visualisation of the gene expression changes were performed using the GeneSpring software package. Hierarchical clustering of all 43 samples was performed, based on the expression profile of 571 genes, which were identified as differentially expressed by parametric ANOVA with Benjamini-Hochberg correction. The 43 samples were sorted into nine groups which all agreed with histopathology by either being in the same group or an adjacent group apart from four samples. For further analysis, the four outliers were removed, one group was excluded due to lack of replicates and two groups were merged to get the final molecular classification of the cycle. The statistical analysis was repeated and 1452 genes were identified as differentially expressed at  $P \leq 0.05$ . The data were also independently analysed by a CSIRO algorithm called GeneRave and the results from both methods were comparable. mRNA expression profiles of the genes TGF  $\alpha$  (Hs.170009), NCR3 (Hs.509513) and FUT4 (Hs.390420) were verified using real-time PCR. We have shown for the first time that endometrial cycle stage prediction is possible based on global gene expression profile.