Abstract

The etiology and pathogenesis of endometriosis are complex with both genetic and environmental factors contributing to disease risk. Genome-wide association studies (GWAS) have identified multiple signals in the estrogen receptor 1 (ESR1) region associated with endometriosis and other reproductive traits and diseases. In addition, candidate gene association studies identified signals in the ESR1 region associated with endometriosis risk suggesting genetic regulation of genes in this region may be important for reproductive health. This study aimed to investigate hormonal and genetic regulation of genes in the ESR1 region in human endometrium. Changes in serum oestradiol and progesterone concentrations and expression of hormone receptors ESR1 and progesterone receptor (PGR) were assessed in endometrial samples from 135 women collected at various stages of the menstrual cycle. Correlation between hormone concentrations, receptor expression and expression of genes in the ESR1 locus was investigated. The effect of endometriosis risk variants on expression of genes in the region was analyzed to identify gene targets. Hormone concentrations and receptor expression varied significantly across the menstrual cycle. Expression of genes in the ESR1 region correlated with progesterone concentration; however, they were more strongly correlated with expression of ESR1 and PGR suggesting coregulation of genes. There was no evidence that endometriosis risk variants directly regulated expression of genes in the region. Limited sample size and cellular heterogeneity in endometrial tissue may impact the ability to detect significant genetic effects on gene expression. Effects of these variants should be validated in a larger dataset and in relevant individual cell types.