

Title: Endometriosis Expresses a Gene Expression Pattern Suggesting Decreased Retinoid Uptake and Metabolism

Authors: ME Pavone, S Reierstad, E Pearson, Y H Cheng, S Bulun

Background

Retinoic acid (RA) regulates many biological processes including differentiation, apoptosis as well as cell survival. Our laboratory has previously shown that RA mediates the progesterone-dependent induction of 17 beta-hydroxysteroid dehydrogenase type 2, which catalyzes the conversion of estradiol to estrone, in endometrium but not in endometriosis because of a defect in endometriotic stromal cells. This defect may involve both the uptake and metabolism of RA.

Objective

To analyze the expression of genes involved in the retinoic acid signaling pathway, including those involved in retinol uptake, metabolism, transport and transcriptional activation in normal endometrium from disease-free women and endometriosis from ovarian endometriomas.

Methods

Tissues from ovarian endometriomas and eutopic endometrium from disease-free women were collected. Real-time reverse transcription-polymerase chain reaction was used to measure mRNA levels. Western blotting was used to evaluate protein expression.

Results

We found significantly decreased mRNA expression of the major genes involved in the retinoic acid pathway, including cellular retinol binding protein-1, aldehyde dehydrogenase 1A2, cellular retinoic acid binding protein 2 and cytochrome p450 (CYP 26A1), which is responsible for retinoic acid metabolism. In addition, the expression of the gene stimulated by retinoic acid 6 (STRA6), which has recently been found to be responsible for retinol uptake into cells, was also found to be significantly decreased in endometriosis compared to normal endometrium. Nuclear extracts from stromal cells showed that RAR α was underexpressed in endometriotic stromal cells compared to normal endometrial stromal cells. Differences in protein levels were confirmed by western blotting.

Conclusions

Endometriosis is characterized by a gene expression pattern which suggests a decrease in the uptake and metabolism of RA. Because RA is integral in regulating key biological processes involved in cell survival, this alteration could explain the resistance to apoptosis found in endometriosis.