In the Spotlight

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What the Endometrium Says About Adenomyosis

Adenomyosis is a relatively common clinical disorder affecting women, mostly on their late reproductive years, which is characterized by an abnormal invasion and proliferation of the endometrium into the myometrial layer of the uterus, leading to significant pelvic pain, dysmenorrhea, bleeding, and subfertility.[1] The etiology of the disease is poorly understood, and currently, the only effective treatment for women experiencing severe discomfort is hysterectomy. In order to unravel new therapeutic approaches to manage effectively the disease's symptoms, a more in-depth understanding of the molecular mechanisms regulating this pathology is certainly in need.

Several studies have addressed this need to better understand adenomyosis, many of which have recently been published in *Reproductive Sciences*.[2-7] In the current issue of the journal, Herndon et al[8] revisit the topic, this time importantly focusing on characterizing the global transcriptome of eutopic endometrium from women having clinically significant adenomyosis. Their aim was to determine whether abnormal dysregulation of genes and pathways in eutopic endometrium may predispose to ectopic implantation.

In order to address their goal, Herndon and colleagues collected endometrial samples from hysterectomy specimens on the proliferative phase from women with pathologically confirmed diffused adenomyosis and from normo-ovulatory participants without adenomyosis, who served as controls for the study. All participants included in the study were free from hormonal exposures, leiomyoma, and endometriosis, thus avoiding potential confounding factors. The authors then isolated purified total RNA from the specimens and performed microarray analysis, further validating the results by reverse transcription polymerase chain reaction for the genes of interest.

Results from the transcriptome analysis showed that 140 genes are upregulated and 884 are downregulated in samples of proliferative endometrium from women with adenomyosis as compared to the controls. The authors observed that the highly differentially expressed genes included those involved in regulation of apoptosis, steroid hormone responsiveness, extracellular matrix remodeling, and microRNAs of unknown significance. Herndon and colleagues also observed that the eukaryotic initiation factor signaling pathway, as well as the oxidative phosphorylation, mitochondrial dysfunction, estrogen signaling, and mTOR signaling pathways were particularly affected.

The findings presented by Herndon et al suggest that the eutopic endometrium of patients with significant adenomyosis has fundamental molecular abnormalities that may in fact predispose to penetration and survival beyond the myometrial interface. The implications and biological significance of the differentially expressed genes and consequentially dysregulated pathways that emerged from this pioneer study allow a platform to further elucidate the signaling pathway and molecular players underlying this complex disorder.

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