DEEP ENDOMETRIOSIS: ANALYSIS OF MMPS REGULATORS (TIMPS, CANONICAL AND NON-CANONICAL SPLICING RECK ISOFORMS AND SPARC).

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Introduction: Endometriosis is a benign gynecological disorder characterized by ectopic growth of endometrial cells. The etiologic theory of endometriosis proposes that viable endometrial tissue is refluxed through the Fallopian tubes during menstruation implanting on the peritoneal surface or pelvic organs. The ectopic endometrium degrades the extracellular matrix (ECM), through the activity of metalloproteinases (MMPs) and other molecules, and invades the surrounding tissue with corresponding cell proliferation and neoangiogenesis. These degradation by MMPs is closely regulated by Tissue Inhibitors of Proteases (TIMPs) under normal physiological conditions. Additional MMPs regulators are: RECK, which negatively regulates MMPs in tumors, SPARC, which upregulates MMPs, both of which have never been analyzed in deep infiltrating endometriosis. We have recently described three new RECK gene isoforms (RECKB, RECKD, RECKI), which are modulated in glioblastoma.

Objectives: To date, no studies are available on expression of canonical and non-canonical splicing RECK isoforms, SPARC or their correlation with other regulators in deep infiltrating endometriosis. The objective is to analyze the expression profiles of MMPs and their regulators, to describe their involvement in endometriosis.

Material and Methods: Using qRT-PCR, the expression profiles of MMPs-2,-3,-7,-9,-10,-14, TIMP-1,-2,-3, SPARC, RECK and their isoforms in eutopic and ectopic endometrium (N=40) were analyzed. The gene expression of ectopic endometrium was compared with a pool of endometrium from healthy fertile women (control N=25) and bowel.

Results: MMP7, MMP14, SPARC, and MMP2 and their regulator TIMP1 were upregulated in ectopic endometrium when compared to bowel. These results indicate the possible involvement of these genes in the progression of the disease. RECK, RECKD, RECKI did not show any modulation. RECKB expression was modulated in controls endometrium. Immunohistochemistry was performed for MMPs 2, 9, RECK and SPARC, and the results are being analyzed to correlate gene and protein expression.

Conclusion: Our results indicate that new genes, SPARC and RECK and its isoforms, are involved in endometriosis.

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