MEDICAL UNIVERSITY OF VIENNA

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Endometriosezentrum

MLLT11 expression is reduced in eutopic and ectopic endometrium of women with advanced endometriosis

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Objective

MLLT11 (AF1q) is a protein coding gene with a dual role in cancer. As a tumor-promoter its overexpression was associated with poor clinical outcomes in breast and ovarian cancer, whereas tumor suppression function was indicated by its regulation of cancer cell apoptosis. Endometriosis ectopic lesions share some cancer-like features such as local adhesion, invasion and resistance to apoptosis. Thus, in this study we hypothesized that MLLT11 may contribute to endometriosis lesion development in women with the disease.

Study design

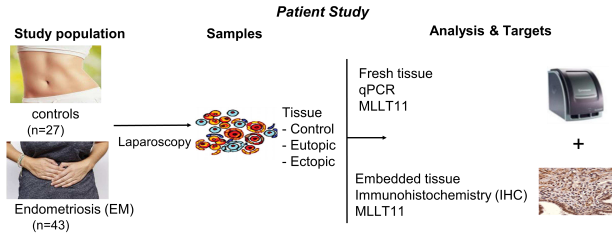


Figure 1. In total, 70 patients were analyzed and the results correlated with clinical parameters, such as menstrual cycle phase and rAFS score. 23 women without and 41 women with endometriosis were analyzed using qRT-PCR. Stromal and epithelial glandular MLLT11 protein expression levels were evaluated separately in eutopic and ectopic tissue samples of 24 women without and 30 women with endometriosis using immunohistochemistry.

Figure 3. A-F. The intensity score (0-3) and the percentage score (0-3) of the stained cells were multiplied to derive a final IHC score (0-9).
(Percentage score code: 0=0%, 1=0-33%, 2=33-66%, 3=66-100%).

Results

I. MLLT11 gene expression is reduced in ectopic lesions of women with advanced endometriosis

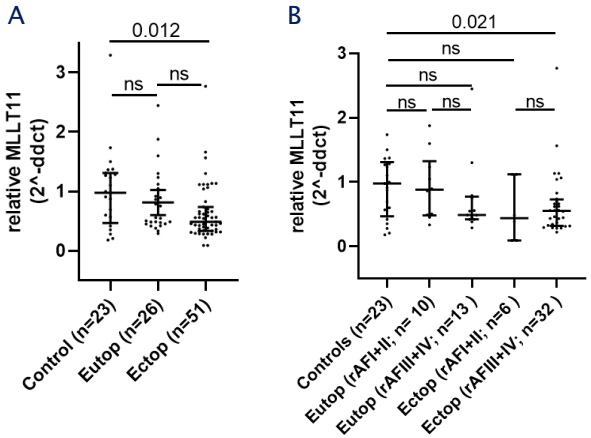
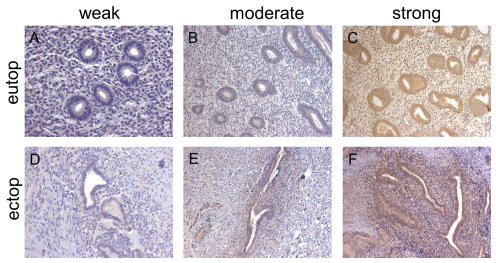


Figure 2. A. Gene expression levels of MLLT11 were found to be significantly reduced in ectopic lesions compared to eutopic tissue samples of women without endometriosis (2-fold change; p=0.012). B, This downregulation was only found in women with high rAFS scores.

II. MLLT11 protein expression is reduced in women with advanced endometriosis



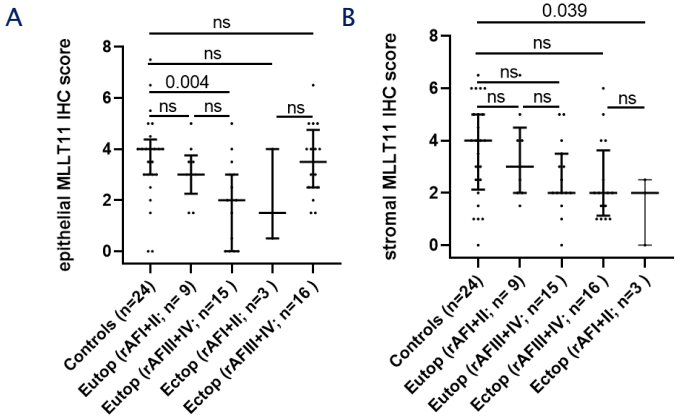


Figure 4. A. Women with a high rAFS score showed significantly reduced epithelial MLLT11 expression in eutopic samples compared to controls (2-fold change). B. In these women, stromal MLLT11 expression was significantly reduced in ectopic samples compared to controls (2-fold change; p=0.039) leading to conclusion that the reduced stromal MLLT11 protein expression in ectopic lesions is at least in part due to the downregulation of the MLLT11 gene expression.

III. Reduced eutopic epithelial MLLT11 protein expression can predict advanced endometriosis

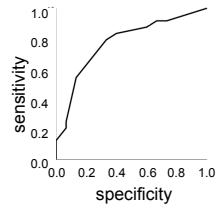


Figure 5. ROC curve analysis (n=39) showed that reduced MLLT11 protein expression in epithelial glands of eutopic samples could be used as a semi-invasive marker to predict advanced endometriosis with 79.2% specificity and 66.7% sensitivity (AUC=0.772; p=0.005).

Conclusion

Reduced MLLT11 protein expression in epithelial glands of eutopic samples of women with advanced endometriosis could be used as a semi-invasive marker to diagnose endometriosis.