MRNAs and miRNAs expression profiles in adenomyosis and their potential uses as diagnostic biomarkers

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Introduction: Adenomyosis is a gynaecological disease which is poorly molecularly characterized. In addition, to date, there are very few studies using large scale profiling methods (OMICS) to investigate molecular signatures of this enigmatic pathology. The aim of this study was to improve molecular characterization of adenomyosis and identify potential biomarkers. For this purpose, transcriptomes et miRNomes of endometrium patients with and without adenomyosis were investigated.
Materials & Methods: Endometrial biopsies were obtained from hysterectomy specimens of patients with (n=13) pure and without (n=11) adenomyosis used as control. No endometriosis was associated with adenomyosis group. Presence or absence of adenomyosis was validated by anatomo-pathological examination and all endometrial specimens were during the proliferative menstrual phase. Then, RNAs were extracted and gene and miRNA expression profiles were investigated using the Affymetrix HG-U133 plus 2.0 GeneChip oligonucleotide microarrays and Affymetrix miRNA 4.1 Array Strips. The differential gene and miRNA expression profiles between pathological and control groups were evaluated with bioinformatics system. The differential gene and miRNA expression profiles between endometrial samples were investigated in patients with adenomyosis (fold-change >2, p-value <5%) without adenomyosis. The lists of significant genes were cross-intersected to identify of list of genes exclusive to the pathological group. Potential endometrial biomarkers of adenomyosis were investigated by RT-qPCR.
Main Results: Using transcriptomic analysis, we identified a list of 542 genes exclusive to adenomyosis group with 280 and 262 genes up- and down-regulated in endometrium respectively. The top up- and down-regulated genes exclusive to the endometrium from the adenomyosis patients were ATP8A2 (x35), SH2D3A (x32), KLHL31 (x15), ADAMTS16 (x14), FOXP2 (x-31), F2RL2 (x-29), DGKB (-14), LEFTY2 (x-12) and play roles in several functions including membrane trafficking, migration and extracellular remodeling. In the other hand, miRNome analysis revealed that 3 miRNAs (miR-490-3p, miR-6738-5p, miR-4763) were differentially expressed in endometrium in patients with adenomyosis compared with control patients. Supervised clustering using these 3 miRNAs revealed a great segregation between adenomyosis and control groups, opening news perspectives in the diagnosis of adenomyosis. Interestingly, one miRNA targets 16 mRNAs identified in our transcriptomic analysis that were reached to several biological functions including the BMP signaling pathway and the estrogen receptor signaling playing crucial roles in the physiopathology of adenomyosis.
Conclusion: These results could contribute for improving our understanding of the physiopathology of adenomyosis and should open new perspectives in the diagnosis of this pathology.

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