METHYLOME GENOMEWIDE ANALYSIS UNVEILS THE ROLE OF ESTROGEN-RELATED GENES IN OVARIAN ENDOMETRIOMA

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Introduction and Objectives: The establishment of endometriotic lesions appears to be driven by epigenetic alterations. Some data have been accumulated on key genes showing differential methylation status of their promoter in the lesion as compared to the eutopic endometrium. However the extent of the epigenetic alterations at the genome level is largely unknown. We proposed to compare the methylome of the endometriotic lesion and the matched eutopic endometrium.
Methods: We screened three endometriomas and matched endometrium using 450K Illumina Infinium array. We analyzed windows of 10 consecutive CpG on a chromosome-wide basis with p-values considered significant following a Monte-Carlo simulation. We validated ten genes harboring differential methylation profile by enzymatic digestion and qPCR in 8 independent samples.
Results: A total of 277 regions significantly hypomethylated or hypermethylated were identified near or inside 312 genes. There was an excellent correlation between the differences of the methylation levels in the microarray and the qPCR validation (R=0.875). We could report three major results: (i) Differential methylation concentrated near chromosome ends; (ii) Differential methylation in endometrioma was often associated with gene expression deregulation, but did not foretell the sense of the deregulation; (iii) Differential methylation in endometriomas affects a very high proportion of transcription factors with a significant clustering of genes involved uterine neoplasms and centered on Estrogen Receptor 1 (ESR1).
Discussion and Conclusion: This study demonstrates the existence of wide epigenetic alterations in endometriosis and unveils new genes potentially implicated in endometriosis pathogenesis.

Keywords : methylation, epigenetic, genomewide, endometriosis
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