Role of steroidogenic factor 1 (SF-1) and its target genes in ovarian endometriosis

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Introduction and Objectives: steroidogenic factor 1 (SF-1) is highly expressed in ovarian endometriotic cysts (so called endometriomas) in response to local inflammation. SF-1 has a key role in the development of the lesions by targeting steroidogenesis and local production of estradiol. This study aims to understand the mechanism of action of SF-1 on its target genes, according to their methylation status.

Methods: we selected six known target genes of SF-1: GATA4, CYP11A1, CD22, TCF21, ARX-MAGEB1 and CLDN11. Plasmid construction was performed with methylated and unmethylated sequences of each gene. Plasmid vectors were then transfected into steroidogenic human granulosa-like tumor cell lines (KGN cells), that constitutionally express SF-1, and siRNAs were used to silent SF-1 expression. Luciferase reporter assay was used to study gene expression according to the methylation status and SF-1 expression.

Results: SF-1 has an activating effect when the target gene is not methylated, with an overexpression ranging from 2 to 4, depending on the studied target gene. Conversely, no effect is found when the gene is methylated. These results were observed for all the studied genes.

Discussion / Conclusion: SF-1 has a methylation-dependent action on its target genes. This may explain the specific action of SF-1 on ovarian endometriosis, which is not observed in eutopic endometrium or in deep infiltrating endometriosis.

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Mots clés : steroidogenic factor 1 (SF1); ovarian endometriosis; methylation; target genes
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