

OSTEOPONTIN-MODULATED ENDOMETRIOTIC CELL MIGRATION AND INVASION

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Purpose: Endometriosis is a common gynecological disease with tumor-like characteristics such as cell migration and invasion. The etiology and pathogenesis of endometriosis disease is poorly understood. Recently, increased osteopontin (OPN) expression was found in the plasma of the endometriotic patients. We suggested that OPN might contribute to the endometriotic cell migration and invasion, and play a pivotal role in the development of endometriosis. In this study, we plan to identify the molecular pathway of OPN-modulated endometriotic cell outgrowth.

Materials and methods: The endometrium was obtained from the patient with endometriosis. To address the effects of OPN on endometriotic cell migration and invasion, we constructed the expression vector and siRNA vector specific for osteopontin. The wound healing assay, matrigel invasion assay, and gelatin-zymography were performed to evaluate cell migration, invasion, and MMP activity. Wortmannin (PI3K inhibitor) and $\alpha\text{v}\beta 3$ antibody was used to identify molecular pathway. Cellular NF- κ B protein was detected by Western blotting. The ATP content was detected by Luminescence ATP Detection Assay System. Actin remodeling was observed by Confocal microscope. Finally, the in vivo migration assay was performed by IVIS imaging system.

Results: A significant increase of OPN was found in the ectopic endometrium. OPN could facilitate endometriotic cell migration, invasion, and MMP2/9 activation. The OPN induced cell migration and invasion was attenuated or inhibited by anti- $\alpha\text{v}\beta 3$ antibody or Wortmannin. OPN-induced cell migration was mediated by the OPN- $\alpha\text{v}\beta 3$ interaction and activate the PI3K and NF- κ B signaling pathway. In addition, OPN was found to induce the mitochondria biogenesis and ATP production. We speculate that OPN could enhance mitochondrial function to generate energy and promote actin remodeling and cell migration. Finally, the real-time IVIS Imaging System showed that OPN-treated endometriotic cells can outgrowth in mouse.

Conclusion: The results will unravel the causal role of OPN in the regulation of endometriotic cell growth, which may promote the development of OPN-directed therapies for patients with endometriosis.