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Interleukin-1β upregulates cyclooxygenase-2 and enhances invasion of human endometrial mesenchymal stem cells

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Endometriosis is a common gynecological disease. It is unique to have benign histology but with malignant characteristics. Easy recurrence, multiple organ involvement and malignant transformation potential make endometriosis a complex disease. Multi-factors contribute to the pathophysiology. Recently, endometriosis has been regarded as a stem cell disease. We successfully isolated eutopic and ectopic EN-MSCs derived from the same donor to examine the genetic difference analysis that provides a powerful tool for investigating the disease origin. this is the first study to identify ectopic and eutopic MSC from the same individual. Our results are consistent with the previous concept that endometriosis is a stem cell disease, and some studies have provided evidence of the possible existence of stem cells in endometrial tissue. We identified and characterized the MSCs from ectopic and eutopic endometrium by *in vitro* cell characteristics, including serpiginous morphology, surface biomarkers, a lack of gap junctional intercellular communication and the ability of differentiation and transdifferentiation into adipocytes, osteocytes, chondrocytes, neural cell and cardiomyocytes. In an *in vivo* animal study, we found the ability of invasion in eutopic and ectopic MSC. To further investigate the intrinsic factors of endometriosis, these early-passage eutopic and ectopic EN-MSCs (passage 2 to 4) were isolated from the same patient explored by the genome-wide mRNA expression analysis. This provides an opportunity for comparative study of these two types of EN-MSCs with homogeneous genetic background. In gene expression, ectopic EN-MSCs were significantly higher than eutopic EN-MSCs in *IL-1β* and *COX-2*, and expression of COX-2 in eutopic and ectopic EN-MSCs is distinctly regulated by IL-1β; IL-1β has more effect on ectopic EN-MSCs. Moreover, in the migration and invasion assays, ectopic EN-MSCs were more sensitive to IL-1β. Furthermore, in an *ex vivo* invasion model, the IL-1β-treated ectopic EN-MSCs were observed to stretch out many tentacle-like arms from a cell mass to invade surrounding area. These results will support endometriosis to be a stem cell disease and clarify the endometriosis pathogenesis. This study may open up avenues for the therapeutic targeting of this multifaceted disease.