**66. Upregulated Fibulin-1 Increased Endometrial Stromal Cell Viability and Migration by Repressing EFEMP1-Dependent Ferroptosis in Endometriosis**

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Abstract

Endometriosis (EMS) is a prevalent disease in women characterized by the presence of endometrial stroma and glands outside the uterus. Recent studies have showed that EMS is correlated with the resistance of endometrial stromal cells (ESCs) to ferroptosis, an iron-dependent nonapoptotic cell death. Fibulin-1 (FBLN1) is a newly identified target regulated by progesterone in the process of ESC decidualization. However, the role of FBLN1 in regulating ESC ferroptosis and EMS remains unclear. In the present study, the gene expression profiles of GSE58178, GSE23339, and GSE25628 were downloaded from the Gene Expression Omnibus (GEO) database, and the commonly differential genes were identified using Venn diagram analysis. The role of FBLN1 in ESC viability and migration was evaluated using Cell Counting Kit-8, transwell, and western blot analysis. We found that the FBLN1 expression was increased significantly in eutopic and ectopic endometrial tissues of patients with EMS compared with normal endometrium. FBLN1 overexpression in normal ESCs (NESCs) promoted cell viability and migration, whereas FBLN1 inhibition in ectopic ESCs (EESCs) decreased cell viability and migration. Furthermore, FBLN1 inhibition facilitated EESC death by triggering ferroptosis, as evidenced by increased Fe2+, lipid ROS, and malondialdehyde (MDA) level and decreased glutathione peroxidase 4 (GPX4) expression and glutathione (GSH) level. Mechanistically, FBLN1 interacted with EGF-containing fibulin-like extracellular matrix protein 1 (EFEMP1) and increased the protein stability of EFEMP1. More importantly, EFEMP1 silencing repressed the effect of FBLN1 on regulating EESC ferroptosis, death, and migration. Taken together, these results verify the role of the FBLN1/EFEMP1/ferroptosis pathway in the pathogenesis of EMS, and silencing of FBLN1/EFEMP1 might be an effective approach to treat EMS.

