Study on the Role of lncRNA H19 in Promoting the Development of Endometriosis Through Regulation of EMT

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Abstract

Background: Previous studies have shown that epithelial-mesenchymal transition (EMT) plays a critical role in cellular proliferation and migration. Long non-coding RNA H19 (lncRNA H19) is the first identified lncRNA with oncogenic properties and has demonstrated key functions in various cancers. *Objective*: This study aims to clarify the role of lncRNA H19 in promoting cell proliferation and migration in endometriosis (EMs) through the regulation of the EMT pathway and explore its feasibility as a diagnostic biomarker for EMs. *Methods*: Patients who underwent ovarian cystectomy for ovarian endometriotic cysts at Jinshan Hospital, Fudan University, between January 2022 and August 2024 were selected as the study group (EMs group). Serum samples were collected preoperatively, and peritoneal fluid and cyst tissue were collected intraoperatively. Patients undergoing surgery for other reasons, excluding EMs, served as the control group (non-EMs group), with serum, peritoneal fluid, and endometrial tissue collected in a similar manner. Quantitative real-time PCR (qRT-PCR) and Western blot (WB) were used to detect the expression levels of lncRNA H19 and EMT-related molecules, including E-cadherin, N-cadherin, SNAL1, MMP-9, and MMP-2, in ectopic endometrial tissues of the EMs group and endometrial tissues of the non-EMs group, as well as in primary ectopic endometrial epithelial cells (ec-EEC) and primary endometrial epithelial cells (EEC) from EMs and non-EMs patients, and in ectopic endometrial epithelial cell lines (12Z) and normal endometrial epithelial cell lines (hEEC). Enzyme-linked immunosorbent assay (ELISA) was employed to assess the expression of lncRNA H19 and the aforementioned EMT pathway molecules in the serum and peritoneal fluid of the EMs and non-EMs groups. The differences in proliferation and migration capabilities between hEEC and 12Z were evaluated using CCK-8, EDU, Transwell invasion, and wound healing assays. *Results*: Compared to the non-EMs group, the EMs group showed upregulated expression of lncRNA H19, N-cadherin, SNAL1, and MMP-9 ($P<0.05$) in ectopic endometrial tissues, while E-cadherin expression was downregulated ($P=0.1319$), with no significant differences in MMP-2. In serum and peritoneal fluid, lncRNA H19, N-cadherin, and MMP-9 levels were significantly increased ($P<0.05$), whereas E-cadherin, SNAL1, and MMP-2 levels showed no significant differences. In comparison to hEEC and EEC, 12Z and ec-EEC exhibited higher expression levels of lncRNA H19, N-cadherin, SNAL1, MMP-9, and MMP-2 ($P<0.05$) and lower expression of E-cadherin ($P<0.05$). Moreover, 12Z cells demonstrated enhanced proliferation and migration abilities compared to hEEC cells ($P<0.05$). *Conclusion*: lncRNA H19 promotes ectopic endometrial cell proliferation and migration by regulating EMT, contributing to the development of EMs.

Keywords

lncRNA H19, Epithelial-Mesenchymal Transition (EMT), Proliferation, Migration