

Endometrial expression and in vitro modulation of the iron transporter divalent metal transporter-1: implications for endometriosis

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FERTILITY AND STERILITY

Volumen: 106

Número: 2

Páginas: 393-401

DOI: 10.1016/j.fertnstert.2016.04.002

Fecha de publicación: AUG 2016

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Resumen

Objective: To evaluate divalent metal transporter-1 (DMT1) expression in healthy women's and endometriosis patients' endometrium and to analyze DMT1 and ferritin light chain (Fn-L) expression modulation by iron overload and IL-1 beta in endometrial stromal cells (ESCs).

Design: Observational and experimental study. Setting: University hospital research laboratory.

Patient(s): Thirty-one healthy women and 24 endometriosis patients.

Intervention(s): Menstrual, proliferative, and secretory endometrial biopsies. Isolated ESCs from seven endometrial biopsies incubated with IL-1 beta or FeSO₄ overload for 24 hours.

Main Outcome Measure(s): Divalent metal transporter-1 endometrial protein expression assessed by immunohistochemistry and Western blot. Divalent metal transporter-1 and Fn-L proteins expression in stimulated ESCs evaluated by Western blot.

Result(s): Divalent metal transporter-1 is expressed throughout the menstrual cycle in human endometrium. Four endometrial DMT1 variants were identified accordingly to their molecular weight: DMT-80, -65, -55, and -50. Endometrial expression of DMT-80 and -55 is higher in endometriosis patients than in healthy women. In ESCs, iron overload induces an overexpression of DMT-80, DMT-50, and Fn-L, whereas IL-1b increases DMT-80 and -50 expressions and decreases Fn-L expression.

Conclusion(s): Divalent metal transporter-1 overexpression in endometriosis patients' endometrium can increase iron influx to endometrial cells, inducing oxidative stress-mediated proinflammatory

signaling. In turn, endometriosis-related conditions, as iron overload and inflammation (IL-1b), enhance endometriosis patients endometrial DMT1 expression, creating a vicious circle on DMT-1-modulated pathways. (Fertil Steril (R) 2016; 106: 393-401. (C) 2016 by American Society for Reproductive Medicine.)

Palabras clave

Palabras clave de autor: DMT1; endometriosis; interleukin-1 beta; iron

KeyWords Plus: FACTOR-KAPPA-B; HUMAN ENDOTHELIAL-CELLS; PERITONEAL ENDOMETRIOSIS; MENSTRUAL CHARACTERISTICS; INFLAMMATORY CYTOKINES; TRANSFERRIN RECEPTOR; OXIDATIVE STRESS; MESSENGER-RNA; STROMAL CELLS; 1 DMT1

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Financiación

Entidad financiadora	Número de concesión
Fondo Nacional de Desarrollo Científico y Tecnológico	FONDECYT 11080123
Fondo de Financiamiento de Centros de Excelencia de Investigación	FONDAP 15010006-8
Programa de Investigación Asociativa Comisión Nacional de Investigación Científica y Tecnológica	PIA-CONICYT ACT1114

[Ver texto de financiación](#)

Editorial

ELSEVIER SCIENCE INC, 360 PARK AVE SOUTH, NEW YORK, NY 10010-1710 USA

Categorías / Clasificación

Áreas de investigación: Obstetrics & Gynecology; Reproductive Biology

Categorías de Web of Science: Obstetrics & Gynecology; Reproductive Biology

Información del documento

Tipo de documento:Article

Idioma:English

Número de acceso: [WOS:000380763400030](#)

ID de PubMed: 27117373

ISSN: 0015-0282

eISSN: 1556-5653

Información de la revista

- **Impact Factor:** [Journal Citation Reports®](#)

Otra información

Número IDS: DS4PQ

Referencias citadas en la Colección principal de Web of Science: **78**

Veces citado en la Colección principal de Web of Science: **0**