67. Down-regulating HK2 inhibits proliferation of endometrial stromal cells through

a noncanonical pathway involving phosphorylation of STAT1 in endometriosis

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Abstract

Background: Endometriosis is a benign gynecologic disease that causes chronic pelvic pain,

dysmenorrhea and infertility and shares several characteristics with malignant tumors,

afflicting women of reproductive age. Hexokinase 2 (HK2) plays an essential role as the first

rate-limiting enzyme in the metabolic glycolysis pathway, and its abnormal elevation in

tumors is associated with tumor genesis and metastasis. However, the expression and role of

HK2 in endometriosis remain unclear.

Methods: We sequenced the primary endometrial stromal cells from patients with

endometrioma and utilized immunohistochemistry, quantitative real-time PCR and western

blot to determine the expression of HK2. Then wound healing assays, cell invasion assays,

cell proliferation assays were performed to explore the functions of HK2 in endometrial

stromal cells. Furthermore, mice models of endometriosis were used to observe the effects of

HK2 inhibitors in vivo. Lastly, glycolysis metabolism detection and transcriptome

sequencing were carried out in HK2-knockdown endometrial stromal cells to analyze the

mechanism of HK2 affecting cell function.

Results: Endometrial stromal cells of endometrioma displayed active glycolysis metabolism

and elevated expression of HK2. Downregulating HK2 reduced the migration, invasion and

proliferation capacity of endometrial stromal cells. Knockdown of HK2 induced upregulation

of signal transducer and activator of transcription 1 (STAT1) and their phosphorylation to

attenuate the proliferation of endometrial stromal cells.

Conclusions: HK2 is associated with the migration, invasion and proliferation of endometrial

stromal cells, which might provide new insights into the pathogenesis and treatment of

endometriosis.

Keywords: Endometriosis; HK2; STAT1; endometrial stromal cells; glycolysis.