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P316. The importance of estrone-sulfate transporters in endometrial cancer

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Background: Intracrine synthesis of estrogens in postmenopausal women may have important roles in the pathogenesis of endometrial cancer (EC). Increased cellular uptake of circulating inactive steroid precursor estrone sulfate (E1-S) by the organic anion-transporting polypeptides (OATP) or organic anion transporters (OAT), and/or its decreased cellular efflux by ABC transporters can contribute to increased estradiol (E2) synthesis and cancer progression. To date, 20 transporters are known to be involved in E1-S transport and their roles in EC have not yet been examined. The present study has been undertaken to identify and quantify transporters in specimens from EC patients undergoing hysterectomies as well as in EC model cell lines and to evaluate the involvement of differentially expressed transporters in E1-S transport.

Methods: Gene expression analysis was performed on 43 pairs of cancer endometrium and adjacent control endometrium of patients as well as in model cell lines of EC Ishikawa and HEC-1-A, and in control endometrial cell line HIEEC. We examined the expression of 20 transporters by PCR array and qPCR. The cellular capacity for E1-S uptake and metabolism was determined by HPLC with on line scintillation detection after treatment of the cells with [3H]E1-S.

Results: We confirmed the expression of 13 SLCO, SLC and ABC genes encoding OATP, OAT and ABC transporters in specimens of EC and adjacent control tissue as well as in model cell lines. We found significant changes in expression of 4 transporters in postmenopausal patients. Genes ABCG2, SLC51B and SLC22A11 were down-regulated and ABCC1 was up-regulated in cancer versus adjacent control tissue. In patients without lymphovascular invasion gene SLCO1B3 was up-regulated. In both model cell lines of EC, Ishikawa and HEC-1-A, genes ABCC1, ABCC4 and SLC51A were up-regulated compared to control HIEEC cells. In addition, higher expression of SLCO1B3 and SLCO2B1 genes as well as increased E1-S metabolism was determined in HEC-1-A compared to Ishikawa cells. The result was in line with previous study which showed less E2 formation in Ishikawa compared to HEC-1-A cells (Hevir et al, 2015).

Conclusions: These results suggest an important role of OATP, OAT and ABC transporters for E1-S transport and local E2 formation in EC. To validate the involvement of differentially expressed transporters in E1-S transport, gene silencing studies on model cell lines are ongoing using siRNA silencing approach.

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