Uptake of an estrogen precursor in estrogen receptor-positive breast cancer cells: Focusing on organic anion transporting polypeptide 2b1

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Uptake of estrogen precursors is important for cell proliferation in estrogen receptor (ER)-positive breast cancer. Estrone sulfate (E1S) is known as the main precursor of estradiol (E2). Since E1S is a hydrophilic compound, it likely requires a solute carrier to cross plasma membrane. The transporter for E1S therefore seems to be a good candidate as a new therapeutic target against ER-positive breast cancer. The aim of this study is to clarify the relationship between the expression level of the transporter for E1S and cell proliferation in ER-positive breast cancer. The uptake of E1S resulted in an increase in cell proliferation and expression of Ki-67 in MCF-7 cells (a breast cancer-derived cell line). Organic anion transporting polypeptide (OATP, SLCO) is reported to be involved in uptake of various organic anions, including E1S. The expression of SLCO1A2, 2B1 and 3A1 mRNAs was detected in normal breast tissues, malignant breast tissues and MCF-7 cells. The expression level of SLCO2B1 mRNA in malignant breast tumors was significantly higher than that in normal breast tissues. Significant positive correlations were observed between the expression level of SLCO2B1 mRNA and histological grade, expression of Ki-67 protein and STS mRNA in breast malignant tumors. Overexpression of OATP2B1 caused enhancements of E1S uptake, E2 secretion, ER-signal transduction and cell proliferation in MCF-7 cells. The present study has suggested that the transporter for E1S, such as OATP2B1, affects progression of ER-positive breast cancer, and inhibition of E1S uptake may be enumerated as a new therapeutic target against ER-positive breast cancer.

Biography

Jun Matsumoto completed his PhD from Graduate School of Pharmaceutical Sciences, Chiba University in 2015. He is currently a research assistant at Department of Pharmaceutical Sciences, International University of Health and Welfare in Japan. His major research interests include PK/PD/PG studies associated with OATP and CYP, in particular OATP2B1 and CYP3A5. He is looking for collaborators who are interested in the research field of PK/PD/PG studies.

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