HUMAN ORGANIC CATION TRANSPORTER (hOCT1) GENE POLYMORPHISM AND THERAPEUTIC EFFECTS OF METFORMIN

Eriko Shikata¹, Ichiro Ieiri¹, Hiroshi Takane¹, Tomoko Koide¹, Rei Yamamoto², Tadasu Ikeda¹, Yuichi Sugiyama⁴ and Kenji Otsubo¹
¹Dept. of Hospital Pharmacy; ²Dept. of Molecular Medicine and Therapeutics; ³Dept. of Adult and Elderly Nursing, Faculty of Medicine, Tottori University, Nishi-machi 36-1, Yonago, 683-8504 and, ⁴School of Pharmaceutical Sciences, Tokyo University, Hongo, Bunkyo-ku, Tokyo, 113-0033, Japan

The genetic variations in drug transporters underlie the inter-individual differences in drug response. Organic cation transporters (OCT1, 2 and 3) mediate the facilitated transport of a variety of structurally diverse organic cations. Recently, hepatocellular uptake of metformin, an antidiabetic drug, was reported to decrease in Oct1 knockout mice. In the present study, we analyzed mutations of 3 hOCT genes, and investigated whether any contribute to the large interpatient variability in the clinical efficacy of metformin. We identified numerous variants in hOCT genes. Of the 8 variants identified in the OCT1 gene, 6 were SNPs and 2 were deletions. Of the 6 SNPs, 3 were non-synonymous mutations; L160F, P341L and M408V, and their allelic frequencies were 0.891, 0.161 and 0.828, respectively (n = 96 in Japanese). Thirty three patients treated with metformin for at least 1 month at Tottori University Hospital were enrolled; while 24 patients were well response to metformin therapy, remaining were non-responders. Therapeutic effects were monitored during the therapy by HbA1c. We compared allelic frequencies of the mutations between the two patients groups. We will present phenotype-genotype relation with regard to hOCT gene polymorphisms.