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# 사람유기음이온수송체 4의 유전적 다형질

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# Genetic Polymorphisms of Human Organic Anion Transporter 4

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Single nucleotide polymorphisms (SNPs) are the most common form of human genetic variation. The non-synonymous SNPs (nsSNPs) cause changes in certain amino acid sequence, and are likely to be failed to show functional diversity of encoded proteins. The organic anion transporters (OATs) play an important role for elimination or reabsorption of endogenous or exogenous organic anionic compounds. Among OATs, hOAT4 mediated the high affinity transport of estrone sulfate and dehydroepiandrosterone sulfate. The rapid bone loss that occurs in post- menopausal women is mainly due to the net decrease of estrogen. From 50 healthy subjects and 50 subjects with osteoporosis we screened for genetic polymorphism in coding region of SLC22A11 (hOAT4) by denaturing gradient gel electrophoresis (DGGE). Using GC- clamp PCR and DGGE assay, we were able to find three SNPs of hOAT4 in Korean osteoporosis and normal subjects. Two of these SNPs were found in osteoporosis group (C483A and G832A) and one of them in normal group (C847T). Among these SNPs, G832A was nsSNP that change 278th amino acid glutamic acid to lysine E278K). The uptake of [3H] estrone sulfate via hOAT4 mutant E278K was reduced when compared with wild- type hOAT4. The Km value for wild type and E278K was 0.7 mM and 1.2 mM, and the Vmax for wild- type and E278K was 1.8 and 0.47 pmol/oocyte/h, respectively. The present study demonstrates that the importance of hOAT4 variant will contribute to inter- individual variations leading to the differences in anionic drug disposition and perhaps used as a marker to certain disease including osteoporosis.

**Key Words :** 유기음이온수송체, 유전적다형질, 골다공증
Orgnaic anion transporter, Genetic polymorphism, Osteoporosis