

MS05-2 Bidirectional roles of carnitine/organic cation transporters OCTNs

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Carnitine/organic cation transporters, OCTN1 (SLC22A4) and OCTN2 (SLC22A5) are ubiquitously expressed in various organs and accept various types of organic cations such as tetraethylammonium, verapamil and quinidine as substrates. Physiologically pivotal roles of OCTN2 in renal tubular reabsorption of carnitine, a vitamin-like substance essential for beta-oxidation of fatty acids has already been identified: a missense mutation in the *OCTN2* gene of humans leads to systemic carnitine deficiency. Using a naturally occurring *octn2* mutant mice, we have recently clarified that OCTN2 is also responsible for renal secretion of beta-lactam, cephaloridine. Thus, OCTN2 may play bidirectional roles in the kidney including both carnitine reabsorption and efflux of renal toxic compound from tubular epithelial cells. To understand the physiological roles of OCTN1, on the other hand, we have recently constructed *octn1* gene knockout mice. The metabolome analysis of blood and several organs indicated complete deficiency of a naturally occurring potent antioxidant ergothioneine in the knockout mice among 112 metabolites examined. Further pharmacokinetic analyses revealed pivotal role of OCTN1 in absorption, distribution and proximal reabsorption of ergothioneine, demonstrating functional expression of OCTN1 in the various organs.